Indian Journal of Anesthesia and Analgesia

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Readership: Anesthesiologists, Critical Care Physicians and Surgeons.

Office of Publication: Red Flower Publication Pvt. Ltd., 48/41-42, DSIDC, Pocket-II
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E-mail: info@rfppl.co.in, Website: www.rfppl.co.in

Journal Website

http://rfppl.co.in/about_journal.php?jid=24

Subscription Information

The Indian Journal of Anesthesia and Analgesia is published three times a year.

Volume 4 (4 issues) will be published in 2017.

pISSN: 2349-8471, eISSN: 2455-6238

For information on subscription rates please contact

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INDIAN JOURNAL OF ANAESTHESIA AND ANALGESIA

January - March 2017
Volume 4 Number 1

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Original Articles

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.1

Comparison of Buprenorphine Versus Fentanyl as an Adjuvant to Bupivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Introduction: Adjuncts to local anesthetics for brachial plexus blockmay enhance the quality and duration of analgesia. Buprenorphine and Fentanyl both are opioids, known to produce antinociception and enhance the effect of local anesthetics. The purpose of this study was to compare the effect of Buprenorphine and Fentanyl added to brachial plexus block by supraclavicular approach.

Methods: This was a prospective study carried out for a period of 2 years. The study group consisted of 60 patients between 15 to 55 years undergoing upper limb surgeries under supraclavicular block. Patients were randomly divided into two groups: Group BF (n = 30) were administered 38mL of 0.25% Bupivacaine with Fentanyl (2 ml, 50µg) and Group BB (n = 30) were given 38mL of 0.25% Bupivacaine with Buprenorphine (2 ml, 0.3mg). The onset time and duration of sensory and motor blockade were recorded. Hemodynamic variables, sedation scores were recorded for 24 hr postoperatively.

Results: The duration of sensory block and analgesia was significantly longer in Group BBcompared to Group BF ($p < 0.05$). Hemodynamics and sedation scores did not differ betweengroups in the post-operative period.

Conclusion: Buprenorphine (0.3mg) in combination with 38ml of Bupivacaine(0.25%) increases the duration of sensory block, and improved postoperative analgesia when used in brachial plexus block, without producing any adverse events.

Keywords: Bupivacaine; Fentanyl; Buprenorphine; Supraclavicular Brachial Plexusblock.

Introduction

Brachial plexus block provides a useful alternative to general anesthesia for upper limb surgeries. They achieve near-ideal operating conditions by producing complete muscular relaxation, maintaining stable intra-operative hemodynamics and the associated sympathetic block. The sympathetic block decreases postoperative pain, vasospasm and edema,of various local anesthetics, Bupivacaine is used most frequently, as it has a long duration of action varying from 3 to 8 hours. However there are many limiting factors like delayed onset, patchy or incomplete analgesia, and sometimes short duration of action.

Various drugs like Neostigmine, Opioids, Hyaluronidase, and Clonidine etc [1-4]. have been added to local anesthetics in order to modify the block in terms of quick onset, good quality, prolonged duration and post-operative analgesia. But these are not without adverse systemic effects or of doubtful efficacy.

Buprenorphine and fentanyl both are opioids. These are known to produce antinociception and to enhance the effect of local anesthetics when given epidurally or intrathecally. Both produce this effect by its action on opioid receptors.

So the present study is being undertaken in a randomized manner to evaluate the onset time and analgesic efficacy of Buprenorphine- Bupivacaine (0.25%) combination compared to Fentanyl - Bupivacaine (0.25%) for brachial plexus block by supraclavicular approach.

Materials and Methods

This was a prospective study carried out in the department of

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Received on 14.11.2016
Accepted on 26.11.2016

Anesthesiology, in Osmania General Hospital, attached to Osmania Medical College, Hyderabad, from November 2013 to October 2015. The study group consisted of 60 patients between 15 to 55 years undergoing upper limb surgeries under supraclavicular block. Informed written consent was taken from all the patients, and parents wherever applicable.

Inclusion Criteria

- ASA CLASS I & II
- Aged between 15 to 55 years
- SBP: 100 – 139mm of Hg
- DBP: 60 – 89mm of Hg

Exclusion Criteria

- Patient refusal
- Known case of hypersensitive reaction to any of the drugs in this study
- Patients with medical complications like severe anemia, severe hypovolemia, shock, septicemia, etc.
- Patients with abnormal coagulation profile.
- Local infection at the proposed site of puncture for supraclavicular block.

All the patients underwent following tests: Haemoglobin, Total and differential leucocyte count(DLC), Bleeding and Clotting Time, Random Blood Sugar(RBS), Blood urea and Serum Creatinine, ECG, HIV, HBSAg. Written informed consent was obtained. Intravenous access with a 20 guage intravenous cannula on the contralateral upper limb under aseptic techniques.

Procedure

A total of 60 patients posted for upper limb surgeries under supraclavicular block were assigned to 2 groups, each containing 30 patients.

Group BF: received 38 ml of 0.25% Bupivacaine with Fentanyl (2 ml, 50µg)

Group BB: received 38 ml of 0.25%Bupivacaine with Buprenorphine (2 ml, 0.3mg)

- Patients lay supine, arms by the side and head turned slightly to the other side.
- The interscalene groove and mid-point of clavicle were identified.
- After aseptic preparation of the area, at a point 1.5 to 2.0 cm posterior and cephalad to mid-point of clavicle, subclavian artery pulsations were felt. A skin wheal was raised with local anesthetic just cephalo-posterior to the pulsations.
- Next, a 22 gauge, 5 cm needle, mounted on a 20 ml syringe, was passed through the same point, parallel to the head and neck, in a caudad, slightly medial and posterior direction, until either paresthesia was elicited or first rib was encountered.
- If the first rib was encountered, the needle was moved over the first rib until a paresthesia was elicited either in the hand or arm.
- After eliciting paresthesia the study medication was injected.
- All patients were monitored for anesthesia and analgesia upto 24 hours post-operatively.
- Sensory block was evaluated by temperature testing using spirit soaked cotton on skin dermatomes C_4 to T_2 whereas, motor block was assessed by asking the patientto adduct the shoulder and flex the fore-arm against gravity.
- Onset of sensory block was defined as the time elapsed between injection of drug and complete loss of cold perception of the hand, while onset of motor blockade was defined as the time elapsed from injection of drug to inability to adduct arm and flex fore arm against gravity (inability to touch one's nose).

Sedation score described by Culebras et al [4] was used to assess sedation.

1. Awake and alert
2. Ssedated, responding to verbal stimulus
3. Sedated, responding to mild physical stimulus
4. Sedated, responding to moderate or severe physical stimulus
5. Not arousable

Heart rate, non-invasive blood pressure and O_2 saturation were also monitored. Duration of sensory block (the time elapsed between onset of sensory block to perception of temperature using spirit soaked cotton), duration of motor block (the time elapsed between onset of motor block and complete return of muscle power) duration of analgesia (the time elapsed between onset of sensory block to the time when patient first complaints of pain at the site of surgery) were recorded.

Quantitative data was analysed by student's 't' test. Qualitative data was analysed by Chi-square test. A p value of < 0.05 was considered statistically significant.

Results

This was a prospective, randomized study and the study group comprised of 60 patients, the age ranging from 15 to 55 years.

The mean age of the patients in group BF was 35 ± 11 and in group BB was 33 ± 11 years. The p value was 0.48 which is not significant. Age incidences between the two groups were comparable.

Time for Onset of Sensory Block (min)

The mean time for onset of sensory block in group BF was 5.6 ± 1.8 minand in group BB was 6.2 ± 1.8 min. This was slightly faster in BF group when compared to BB group. The statistical analysis by student's unpaired 't' test showed that, the time for onset of sensory block in group BF was not significantly faster when compared to group BB (p>0.05).

Time for Onset of Motor Block in Minutes

The mean time for onset of motor block in group BF was 3.9 ± 1.3 min and in group BB was 4 ± 1.4 min. This was slightly faster in BF group when compared with BB group. The statistical analysis by student's unpaired 't' test showed that, the time for onset of motor block in group BF was not significantly faster when compared to group BB(p>0.05).

Duration of Sensory Block in Minutes

Patients of both groups were observed for 24 hours. The mean duration of sensory block in group BF was 526 ± 107 minutes and in group BB was 600 ± 127 minutes. The duration of sensory block in group BB was significantly longer when compared to group BF (p< 0.05).

Duration of Motor Block in Minutes

Patients of both groups were observed for 24 hours. The mean duration of motor block in group BF was 290 ± 59 minutes and in group BB was 301 ± 72 minutes. This was slightly longer in BB group when compared with BF group. The duration of motor block in group BB was not significantly longer when compared to group BF (p> 0.05).

Duration of Analgesia in Minutes

Patients of both groups were observed for 24 hours. The mean duration of analgesia in group BF was 661 ± 91.5 minutes and in group BB was 891 ± 105 mins. The duration of analgesia in group BB was significantly longer when compared to group BF(p<0.05).

Table 1: Sedation score

Time of Assessment	Scores*	Bupivacaine -Fentanyl (BF)	Bupivacaine -Buprenorphine (BB)	X^2 Value, Significance
0 min	1	50 (100)	50 (100)	-
	2	0	0	No Difference
5 min	1	50 (100)	50 (100)	-
	2	0	0	No Difference
15 min	1	50 (100)	40 (80)	$X^2 = 9.0$
	2	0	10 (20)	P<0.05 Sig
30 min	1	50 (100)	34 (68)	$X^2 = 16.74$
	2	0	16 (32)	P<0.05 Sig
60 min	1	50 (100)	37 (74)	$X^2 = 12.73$
	2	0	13 (26)	P<0.05 Sig
2 hr	1	50 (100)	50 (100)	-
	2	0	0	No Difference
6 hr	1	50 (100)	50 (100)	-
	2	0	0	No Difference
12 hr	1	50 (100)	50 (100)	-
	2	0	0	No Difference
24 hr	1	50 (100)	50 (100)	-
	2	0	0	No Difference

1. Aware and alert
2. Sedated responding to verbal stimulus
3. Sedated, responding to mild physical stimulus
4. Sedated, respond to moderate to severe physical stimulus
5. Not arousable

In group BF, all patients were awake and alert and had sedation score of 1. In group BB, sedation corresponding to score 2 was observed in some patients between 15 min from time of injection and 60 min. 20% of patients at 15 min, 32% of patientsat 30 min and 26% of patients at 60 min had sedation score of 2. None of the patients had sedation score of 3 and above during the study period. Statistical analysis of sedation score by chi-square test showed that the difference in sedation score was significant ($p< 0.05$).

Hemodynamic Variables

Pulse rate, systolic BP, diastolic BP, O_2 saturation were recorded at 0 min, 5 min, 15 min, 30 min, 60 min, 2 hours, 6 hours, 12 hours, 24 hours.

Table 2: Pulse Rate (beats/min)

Time of Assessment	Mean+/- SD			p Value	Significance
	Bupivacaine-Fentanyl	Bupivacaine -Buprenorphine			
0 min	82±7	83	± 8.7	> 0.05	NS
5 min	81 ± 6	83	± 9	> 0.05	NS
15 min	82 ± 6	82	± 10	> 0.05	NS
30 min	82 ± 6	83	± 9	> 0.05	NS
60 min	81 ± 6	83	± 9	> 0.05	NS
2 hr	81 ± 5	83±	6.6	> 0.05	NS
6 hr	82 ± 6	85±	9	> 0.05	NS
12 hr	82 ± 6	84	± 9	> 0.05	NS
24 hr	80 ± 6	83	± 11	> 0.05	NS

NS: Not significant

In group BF, the mean pulse rate ranged from 80 ± 6 to 82 ± 7 beats / min.

In group BB, the mean pulse rate ranged from 82 ± 10 to 85 ± 9 beats / min. There was no significant difference in pulse rate between the two groups ($p> 0.05$).

Table 2: Systolic blood pressure in mm Hg

Time of Assessment	Bupivacaine and Fentanyl	Bupivacaine and Buprenorphine	P value	Significance
0 min	119 ± 10.03	118 ± 9.6	>0.05	NS
5 min	119 ± 9.26	118 ± 10	>0.05	NS
15min	119 ± 11.3	118 ± 10	>0.05	NS
30 min	119 ± 9.75	118 ± 9.5	>0.05	NS
60 min	118 ± 10.2	118 ± 10	>0.05	NS
2 hr	119 ± 9.24	118 ± 9.1	>0.05	NS
6 hr	117 ± 9.56	117 ± 9.7	>0.05	NS
12 hr	117 ± 9.87	117 ± 9.9	>0.05	NS
24 hr	118 ± 9.19	117 ± 9	>0.05	NS

NS: Not significant

Table 3: Diastolic blood pressure in mm Hg

Time of assessment	Bupivacaine and Fentanyl	Bupivacaine and Buprenorphine	P value	Significance
0 min	77 ± 7.72	75 ± 6.7	>0.05	NS
5 min	76 ±7.77	76± 7.9	>0.05	NS
15min	77 ± 7.19	76± 7.4	>0.05	NS
30 min	76 ± 6.15	76 ± 6.9	>0.05	NS
60 min	77 ± 6.57	76 ± 6.9	>0.05	NS
2 hr	77 ± 7.4	76 ± 7.6	>0.05	NS
6 hr	77 ± 7.51	76 ± 7.5	>0.05	NS
12 hr	77 ± 7.31	76 ± 7.5	>0.05	NS
24 hr	77 ± 6.62	76 ± 6.8	>0.05	NS

NS: Not significant

In group BF, the mean systolic blood pressure ranged from 117 ± 9.56 to 119 ± 10.03 mm of Hg. In group BB, SBP ranged from 117 ± 9 to 118 ± 10 mm of Hg. There was no significant difference in systolic blood pressure between two groups (p > 0.05)

In group BF, the mean diastolic blood pressure ranged from 76 ± 6.15 to 77 ± 7.77 mm of Hg. In group BB, DBP ranged from 75 ± 6.7 to 76 ± 7.9 mm of Hg. There was no significant difference in diastolic blood pressure between two groups (p > 0.05).

Table 4: Oxygen saturation (%)

Time of Assessment	Mean+/- SD		P Value	Significance
	Bupivacaine-Fentanyl	Bupivacaine-Buprenorphine		
0 min	100 ± 0.61	100 ± 0.6	> 0.05	NS
5 min	100 ± 0.61	100 ± 0.5	> 0.05	NS
15 min	100 ± 0.67	100 ± 0.7	> 0.05	NS
30 min	100 ± 0.77	100 ± 0.6	> 0.05	NS
60 min	100 ± 0.9	100 ± 0.5	> 0.05	NS
2 hr	100 ± 0.67	100 ± 0.6	> 0.05	NS
6 hr	100 ± 0.6	100 ± 0.5	> 0.05	NS
12 hr	100 ± 0.82	100 ± 0.6	> 0.05	NS
24 hr	100 ± 0.61	100 ± 0.6	> 0.05	NS

NS: Not significant

In group BF, the mean O_2 saturation ranged from 100 ± 0.6% to 100 ± 0.9%.In group BB, the mean O_2 saturation ranged from 100 ± 0.5% to 100 ± 0.7. There was no significant difference in O_2 saturation between the two groups (p> 0.05).

Discussion

Brachial plexus blockprovides postoperative analgesia of short duration, even when a long-acting local anesthetic like Bupivacaine is used alone. Various adjuvant drugs like opioids, clonidine, neostigmine and hyaluronidase have been evaluated in conjunction with local anesthetics to prolong the period of analgesia. Fentanyl and buprenorphine are known to produce antinociception and to enhance the effect of local anesthetics when administered intrathecally and epidurally. Both these produce this effect by their action on opioid receptors. Opioid receptors are also found in peripheral nerves.

Hence, an attempt has been made to assess the efficacy of fentanyl and buprenorphine as an adjuvant to bupivacaine (0.25%) in brachial plexus block (supraclavicular approach) in terms of time of onset, duration of analgesia and sedation. Hemodynamic variables in first 24 hours were studied.

In our study, we found that the onset of sensory and motor blockwas slightly faster with BF group when compared to BB group. Onset of sensory block (group BF, 5.6 ± 1.8min; group BB, 6.2 ±1.8 min). Onset of motor block (group BF, 3.9 ± 1.3 min; group BB, 4 ± 1.4 min). The statistical analysis by student's unpaired 't' test showed that, the time for onset of sensory and motor block in group BF was not significantly faster when compared to group BB (p>0.05). This does not correlate with the study done by Kardash et al [5] who achieved the onset of the sensory and the motor blocks at 2.9 ± 1.9 min and 4.0 ± 3.1 min, respectively with fentanyl.As compared to the study done by Nishikawa et al [6] 100µg of fentanyl may have reduced the rate of nerve penetration of lidocaine, thus resulting in a slower onset of analgesia. With 100µg of fentanyl in 40 ml of 1.5% lidocaine with 1:2,00,000 epinephrine in the brachial plexus block by the axillary approach, they found a similar delay in the time which was required for the complete sensory block. They concluded that the decrease in pH of lignocaine from 6.2 to 5.2 by the addition of 100µg of fentanyl.

Jadon et al [7] examined the benefit of adding buprenorphine to 30 ml of 0.3% bupivacaine in the supraclavicular block. In their study, the onset time of the motor block (4.05 ± 0.94 min) was significantly faster than the onset of the sensory block (6.65 ± 1.18 min), which correlates with our study. This can be explained by the "core and mantle concept" of Winnie et al [8].

Klein et al [9] in their study, observed that the mean onset time for both the motor and sensory blockade was < 6 min when 30 ml of 0.5% bupivacaine, 0.5% ropivacaine and 0.75% ropivacaine was used in 3 different groups in the interscalene block. They premedicated their patients with intravenous midazolam (1-5 mg) and fentanyl (50-250 ìg), which probably enhanced the onset of the block, which does not correlate with our study [9].

Duration of motor block slightly longer in BB group

when compared with BF group (group BF, 290 ± 59 min; group BB, 301 ± 72 min) but this was not significant.

In our study, we found that the duration of sensory block and analgesia was significantly longer in patients who received a combination of Buprenorphine and Bupivacaine compared with Fentanyl and Bupivacaine. Duration of sensory block (group BF, 526 ± 107 min; group BB,600 ± 127 min). Duration of analgesia (group BF,661 ± 91.5min; group BB, 891 ± 105 min). Jadonet al [7] noted that the total duration of motor block with buprenorphine was 329.2 ± 28.4 min, whereas in our study, it was 301 ± 72 min, which is comparable. This can be explained by the fact that bupivacaine, a long acting local anesthetic, was used and buprenorphine as such, does not have effect on the motor block. From the above findings, we can suggest that opioids can be safely and effectively used in the brachial plexus block for post- operative analgesia even in day care surgery.

The more lipophilic the opioid (buprenorphine> fentanyl) the longer the effect seems to last.

In our study, a volume of 40 ml of local anesthetic agent was taken as this volume was associated with a more complete spread forbrachial plexus block as found by Winnie and colleagues [10]. The particular dose of Buprenorphine (0.3 mg) was selected fromprevious studies [11,12]. The duration of sensory blockade in our studygroup was significantly longer in Buprenorphine and Bupivacaine group, this resultis comparable with other studies which found no difference in onset of sensory block but found longer duration of blockade [13,14]. Post-operative analgesia was prolonged in buprenorphine group, in which our study and other studies [12, 15] came to similar conclusions. With addition of buprenorphine to local anesthetic agents, the onset and duration of motor blockade was comparable, this finding corroborated with other such studies [11,13]. Many studies suggest that Buprenorphine and other opioids have action on peripheral nerves [16,17] along with portable local anesthetics [18]. This suggests the usefulness ofBuprenorphine in peripheral perineuronal route administration [19].

Conclusions

The onset time of sensory and motor block and the duration of motor block with buprenorphine compared to fentanyl were almost the same. However, the duration of sensory block was longer with buprenorphine and also provided longer duration of analgesia compared to fentanyl. The intraoperative sedation was comfortable without any need for airway assistance with buprenorphine. There were no significant differences in hemodynamic variables of pulse rate, systolic BP, diastolic BP and oxygen saturation.The easy availability and lack of significant side effects like respiratory depression and sedation makes Buprenorphine an attractive choice as an adjuvant for brachial plexus block.

References

1. Bone HG, van Aken H, Brooke M, Burkle H, Brooke M, Burkle H. Enhancement of axillary brachial plexus block anaesthesia by coadministration of neostigmine. RegAnesth Pain Med 1999; 24:405-10.
2. Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffler P. The addition of local anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia. 1997; 52:858-62.
3. Keeler JF, Simpson KH, Ellis FR, Kay SP. Effect of addition of hyaluronidase to bupivacaine during axillary brachial plexus block. Br J Anaesth. 1992; 68: 68-71.
4. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong post-operative analgesia after brachial plexus block but does induce haemodynamic changes. AnesthAnalg. 2001; 92: 199-204.
5. Kardash K, Schools A, Concepcion M. Effects of brachial plexus fentanyl on supraclavicular block: A randomized double-blind study. Regional Anesthesia. 1995; 20(4):311–5.
6. Nishikawa K, Kanaya N, Nakayama M, Igarashi M, Trunoda K, Namiki A. Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism.AnesthAnalg 2000; 91(2):384-7.
7. Jadon A, Panigrahi MR, Parida SS, Chakraborty S, Agrawal PS, Panda A. Buprenorphine improves the efficacy of bupivacaine in nerve plexus block: A double blind randomized evaluation in subclavian perivascular brachial block. J AnaesthClin Pharmacol. 2009; 25(2): 207-10.
8. Winnie AP, Tay CH, Patel KP, Ramamurthy S, Durrani Z. Pharmacokinetics of local anesthetics during plexus block. Anesth Analg.1977; 6(6):852-61.
9. Klein SM, Greengrass RA, Steele SM, D'Ercole FJ, Speer KP, Gleason DH et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block.Anesth Analg. 1998; 87(6):1316-9.

10. Winnie AP, Radonjic R, Akkineni SR, et al. Factors influencing distribution of local anaesthetic injected into the brachial plexus sheath. AnesthAnalg1979; 58:225–234.

11. Franco CD**,** Candido KD, Khan MA, Winnie AP, Raja DS**.** Buprenorphine added to thelocal anesthetics for brachial plexus block to provide postoperative analgesiainoutpatients. RegAnesth Pain Med. 2001; 26(4):352-6.

12. Candido KD, Winnie AP, Ghaleb AH, Fattouh MW, Franco CD. Buprenorphine Added to theLocal Anesthetic for Axillary Brachial Plexus Block Prolongs Postoperative Analgesia. RegAnesth Pain Med 2002; 27:162 167.

13. Jadon A, Panigrahi MR, Parida SS, Chakraborty S, Agrawal PS, Panda A.Buprenorphine Improves the Efficacy of Bupivacaine in Nerve Plexus Block: ADouble Blind Randomized Evaluation in Subclavian Perivascular Brachial Block. TheInternet Journal of Anesthesiology 2008; 16: 2.

14. Boogaerts J, Lafont N. Mechanism of action and clinical use of opioids administered bythe peripheral perineural route. CahAnesthesiol. 1991; 39(2):91-5.

15. Bazin JE, Massoni C, Bruelle P,Fenies V, Groslier D, Schoeffler P. The addition of opioids to local anaesthetics in brachial plexus block: the comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia1997; 52(9):858 –862.

16. Vitenbek IA, Zhakupov RK, Girshan AI, The perineural administration of opiates during regional conduction block of nerve trunks and plexuses. AnesteziolReanimatol.1991; (4):56-9.

17. Mays KS, Lipman JJ, Schnapp M .Local analgesia without anaesthesia using peripheral perineural morphine injections. AnesthAnalg. 1987; 66(5): 417-20.

18. Aaron GJ, Laverne GD, Datta S, John M, Benjamin CG. Effects of Fentanyl and Sufentanil on Peripheral Mammalian Nerves.AnesthAnalg1987; 66:1272-1276.

19. Stein Christoph, Priv Doz. Peripheral Mechanisms of Opioid Analgesia, AnesthAnalg1993; 76:182-191.


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Indian Journal of Anesthesia and Analgesia [IJAA]
ISSN:
2349-8471, 2455-6238
ICV 2015: 68.67
Previous evaluation ICV
Area: Technical science
Print version: yes
Electronic version: yes
The journal is indexed in:

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.2

Reduction of Cardiovascular Responses to Laryngoscopy and Intubation by Employing $MgSO_4$ Vs Normal Saline - A Comparative Study

C.K. Ramdas*, Deepak Falgunan**

Abstract

Background: Endotracheal intubation is often associated with a hypertension and tachycardia. Intravenous $MgSO_4$ is a popular method of blunting this response, because of its ability to depress sympathoadrenal response & catacholamine release.

Objective: it was undertaken to compare the effects of 50mg/kg $MgSO_4$ IV given 3 minutes before laryngoscopy and intubation**.**

Methods: A sample size of 60 patients aged 18 to 60 yrs were included in the study and they were allocated into 2 groups of n=30 each. Group I served as control. Group II received 50 mg/kg of IV magnesium sulphate 3 min before induction. HR, SBP were recorded pre-operatively, 30 sec, 1 min, 3min & 5min after intubation .

Results: Patient receiving iv MgSO4 had a better intubating conditions ($p<0.04$) statistically significant than in Group I. There was an increase in the HR at 1 minute after intubation compared to basal value ($p < 0.01$). Also, a decrease in SBP observed at 1 minute and 3 min after intubation when compared with basal value ($p<0.001$) and ($p<0.001$) respectively. The decrease in RPP at 1 minute & 3 minutte after intubation when compared with the basal value ($p <0.001$)& ($p<0.01$) respectively.

Conclusion: Magnesium sulphate 50 mg/kg IV infusion 3 minutes before induction, is a simple, effective and practical method of blunting cardiovascular responses to tracheal intubation, not associated with any adverse effect.

Keywords: Laryngoscopy; Tachycardia; Hypertension; Catacholamine.

Introduction

Direct laryngoscopy and endotracheal intubation following induction of anesthesia is almost always associated with hemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation [1]. This increased sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias [2-4]. This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. Hypertensive patients are more prone to have significant increases in blood pressure whether they have been treated before hand or not. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. These hemodyamic changes in such individuals may predispose to development of pulmonary oedema [5], myocardial insufficiency [6] and cerebrovascular accident [7]. At least in such individuals there is a necessity to blunt these harmful hemodyamic effects .

Many pharmacological methods have been devised to reduce the extent of hemodynamic events including high dose of opioids local anesthetics like lignocaine, alpha and beta adrenergic blockers and calcium channel blockers [1] vasodilatation drugs like nitro glycerine [8]. Topical anesthesia with lignocaine applied to the larynx and trachea in a variety of ways remains a popular method used alone or in combination with other techniques.

Intravenous $MgSO_4$ is a popular method of blunting this response, because of its ability to

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Received on 12.12.2016
Accepted on 13.12.2016

depress sympathoadrenal response & catacholamine release.

Hence the present study was undertaken to compare the effect of Intravenous $MgSO_4$ and intravenous normal saline as a placebo on blunting the haemodynamic responses to endotracheal intubation.

Material and Methods

This study was a comparative clinical study of attenuation of cardiovascular responses to laryngoscopy and intubation, employing $MgSO_4$ vs Normal Saline was undertaken in MNR Medical College and Hospital, Sangareddy, during the June 2014 to July 2016. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all the patients.

The study population were divided into two (2) sub groups with 30 patients in each group.

1. Control Group – Received normal saline as a placebo and served as control (n<30).
2. Study Group – Received 50 mg/kg of $MgSO_4$ i.v. 3 MIN before induction of anesthesia (n < 30).

Inclusion Criteria include patients belonging to ASA grades I and II and aged between 18 to 60 years undergoing various surgical procedure under general anaesthesia. Pre-anaesthetic evaluation and investigations was done on the evening before surgery. All patients were tested for any hypersensitivity reaction to local anaesthetics and an informed consent was obtained from all the patients. All the patients included in the study were premedicated with Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg orally at bed time the previous day.

Patients in control group received normal saline and served as control. Patients in study Group received Inj. $MgSO_4$ 50 mg/kg i.v. 3 minutes before induction of anesthesia. The intubating anesthetist was blinded to the study and dilutant procedure.

Anaesthesia was induced with inj. Thiopentone 5 mg/kg as 2.5% solution and endotracheal intubation was facilitated with succinylcholine 1.5 mg/kg administered one minute prior to laryngoscopy and intubation. The intubating conditions was evaluated and scoring was done according to the four step scale proposed by Goldberg and colleagues [9] by the intubating anaesthetist. It was graded as follow, Grade I- Excellent, Grade II- Good, Grade III- Poor, Grade IV- Impossible intubating condition. The patients were intubated using appropriate sized cuffed endotracheal tubes. After confirming bilateral equal air entry, the endotracheal tube was secured.

Anaesthesia was maintained using 66% nitrous oxide and 33% of oxygen. After the patients recovered from succinylcholine further neuromuscular blockade was maintained with non-depolarizing muscle relaxants. At the end of the procedure patients were reversed with neostigmine 0.05 mg/kg IV and glycopyrrolate 0.008 mg/kg IV

The cardiovascular parameters were recorded in all the patients and cardiovascular parameters were noted as below

1. Pre-operative assessment before giving any study drugs and premedication
2. 30 seconds after intubation
3. 1 minute after intubation
4. 3 minute after intubation
5. 5 minute after intubation

The results were statistically evaluated using student 't' test & ANOVA test comparing between the groups and within the group respectively. P<0.05 was considered statistically significant.

Results

It is a prospective, controlled, randomized, double blind study to evaluate the efficacy of intravenous $MgSO_4$ 50 mg/kg and intravenous normal saline as a placebo on hemodynamic responses to laryngoscopy and endotracheal intubation.

Statistically there was no significant difference in two groups regarding the age (p>0.39), sex (p>1.00) and weight (p>0.33) (Table 1 and 2).

Regarding Changes in Heart Rate in Study Group:

The basal HR was 89.16±10.65 bpm, 1 minute after intubation, it was 97.20±18.82.. Subsequently, the elevated heart rate started settling down. By 3 minutes it was 96.60±18.11bpm and by 5 minutes it was 91.40±14.67 bpm. The increase in the HR at 1 minute after intubation compared to basal value was statistically highly significant (p < 0.01) (Table 3).

Changes in Systolic Blood Pressure in Study Group

The basal value of SBP was 127.86±10.27 mm Hg, 1 minute following intubation the SBP was

122.40±15.32 mm Hg,. Afterwards the elevated blood pressure started coming down towards the baseline value.

By 3 minutes it was 119.50±10.90 mm Hg and by 5 minutes it was 117.53±9.34 mm Hg. The decrease in SBP observed at 1 minute and 3 min after intubation when compared with basal value was statistically significant ($p < 0.001$) and ($p<0.001$) respectively (Table 3).

Changes in Rate Pressure Product in Study Group

The basal RPP was 113.93±164.44. One minute after intubation, the RPP increased to 119.33±328.51. Subsequently the elevated RPP started settling down. By 3 minutes, it was 116.96±27.78 and by 5 minutes it was 107.20±185.24. The decrease in RPP 1minute & 3 minute after intubation when compared with the basal value was statistically significant ($p <0.001$) & ($p<0.01$) respectively (Table 3).

Table 1: Frequency distribution of cases according to age and weight

Parameter	Group	N	Mean ± SD	P value
AGE(years)	Group 1	30	35.0667±12.1199	0.39001
	Group 2	30	37.7333±11.7266	
Weight (kg)	Group 1	30	60.8667±7.9989	0.33939
	Group 2	30	63.1667±10.3460	

Table 2: Distribution of case according to gender

Group 1		Group 2	
Male	Female	Male	Female
18 (60%)	12 (40%)	18 (60%)	12(40%)

Table 3: Showing changes in mean heart rate, mean systolic bp and mean rate pressure product

Time	Group 1	Group 2
Mean Heart Rate		
Pre-operative	81.86±11.5	89.16±10.65
Intubation-30 sec	89.66±9.33	95.66±17.71
1 min	107.53±12.20	97.20±18.82
3 min	99.93±11.95	96.60±18.11
5 min	93.66±11.82	91.40±14.67
Mean Systolic Blood Pressure		
Pre-operative	122.66±11.72	127.86±10.27
Intubation- 30 sec	121.06±11.43	118.46±11.10
1 min	155.80±19.36	122.40±15.32
3 min	133.66±13.76	119.50±10.90
5 min	122.66±13.15	117.53±9.34
The Mean Rate Pressure Product (Rpp)		
Pre-operative	100.00±192.8	113.93±164.4
Intubation- 30 sec	108.26±161.30	113.30±271.6
1 min	168.26±326.52	119.33±321.5
3 min	134.33±254.43	11646.96±127.78
5 min	115.00±197.82	107.20±185.24

Discussion

Laryngoscopy and endotracheal intubation are associated with significant hypertension, tachycardia and arrhythmias. These hemodynamic responses were first recognised as early as in 1940 by Reid and Bruce et al [1]. They postulated that the disturbances in cardiovascular system were reflex in nature and mediated by the vagus nerve. In 1950 Burstein et al [2] studied the effects of laryngoscopy and tracheal intubation on ECG changes and suggested the pressor response as consequences of an increase in sympathetic and sympathoadrenal activity.

These responses are transitory, variable and unpredictable and are much more pronounced in hypertensive patients than in normotensive individuals [4]. This hemodynamic stimulus is associated with increase in plasma nor-adrenaline concentrations parallel with the increase in blood pressure [3,9].

Michael F. M. et al [14] did a study to evaluate the effects of pre-treatment with 60 mg/kg body weight magnesium sulfate intravenous on cardiovascular

responses and catecholamine release associated with tracheal intubation were measured in 15 normal patients and in 15 saline solution pre-treated controls.

Magnesium pre-treatment increased heart rate by 13 ± 3.9 beats/minute. After intubation, heart rate was unchanged in the magnesium group at 107.3 ± 3.6 beats/minute but increased in the control group to 120.9 ± 4.6 beats/minute ($P<0.05$). Systolic blood pressure increased after intubation from 106.8 ± 3.1 to 121.0 ± 4.4 mm Hg in patients given magnesium and from 106.4 ± 3.12 to 145.1 ± 5.6 mm Hg in the control group ($P<0.05$).

It was concluded that magnesium sulfate attenuates the catecholamine mediated responses after tracheal intubation.

In our study, we found that SBP falls significantly after 1 minute($p<0.001$) & 3 minutes ($p<0.001$) of intubation with decreased RPP after 1 minute ($p<0.001$) & 3 minutes ($p<0.01$) respectively in the study group. But at the same time, it is associated with considerable rise in the HR($p< 0.01$) compared to the control group, thus showing similar results with the study.

Another study done by Yap LC [11] et al (1994) to evaluate the effect of magnesium sulfate on heart rate, blood pressure and hyperkalemic response following succinylcholine injection during tracheal intubation, using 60 mg/kg of magnesium sulfate intravenously 1min before succinylcholine injection. The control group received an equal volume of normal saline in the same way. Heart rate, blood pressure, venous and arterial potassium levels were measured at 1, 3, 5 and 10 minutes after intubation.

The results showed that magnesium sulfate could attenuate the hypertensive response at 1 minute and the hyperkalemic response at 1 and 3 minutes following succinylcholine-facilitated intubation; the tachycardia response at 1 minute after intubation could not be reduced by this agent.

The efficacy of intravenous magnesium to block the effects of sympathetic stimulation after nasotracheal intubation was studied by Jain PN et al (1995) [12].They observed that IV magnesium sulphate in a dose of 60 mg/kg body wt. significantly ($p<0.05$) attenuated the haemodynamic response to nasotracheal intubation without producing a significant rise in serum magnesium levels.

This study also got the same results of hemodynamic attenuation with iv magnesium sulfate, but associated with some amount of tachycardia after 1 min of intubation.

In our study , magnesim sulfate causes increase in HR significantly after 1 min of intubation with significant reduction in SBP & RPP. After 3 min of intubation, further fall in SBP & RP occurred, thus showing consistency with the study [13]. However, we did not find any prolongation of neuromuscular blockade.

The hemodynamic variables were recorded in a study by G. D Puri et al [14] before induction, after the trial drug, after induction, and after endotracheal intubation. Magnesium sulfate administration was associated with increased cardiac index, a minimal increase in heart rate, and a significant decrease in mean arterial pressure (MAP) and systemic vascular resistance (SVR) .

The magnesium group patients had a significantly lesser increase in MAP and SVR compared with control patients who received lidocaine before endotracheal intubation. Thus, magnesium is a useful adjuvant to attenuate endotracheal intubation response in patients with CAD.

However, in our study, we found that SBP falls significantly after 1 minute & 3 minutes of intubation with decreased RPP after 1 minute & 3 minutes respectively in the study group. But at the same time, it is associated with considerable rise in the HR compared to controls. Due to rise in HR, magnesium sulfate should be used with caution used for patients having coronary insufficiency or CAD.

In a randomized trail done by KH Naghibi et al [15] (2000) comparing the effects of magnesium sulphate with lidocaine for attenuating of presser response to tracheal intubations in 120 patients undergoing general anesthesia for cataract surgery. They have studied the effect of pretreatment with magnesium sulphate 50 mg/kg or 1.5 mg/kg lidocaine on this presser response found that there were no significant differences between two groups with respect preinduction of heart rate, mean arterial pressure, sex and age. A combined analysis showed that the magnesium sulphate were significantly better than 1.5mg/kg lidocaine in attenuating presser response to tracheal intubation, preventing postoperative tachycardia and hypertension and it is better than lidocaine.

Magnesium sulfate infusion in this study is effective in preventing increase in SBP & RPP after intubation but not effective in decreasing the heart rate . It was associated with tachycardia which come down to pre-operative level after 5 min of intubation.

Pipelzadeh MR et al [16] (2001) concluded that magnesium sulfate had a very limited usefulness in the attenuation of blood pressure and heart rate in

young healthy patients if given during induction of anesthesia. However, in this study, they had used magnesium sulfate in dose of 50 mg/ kg body wt just before laryngoscopy & found marked decrease in SBP & RPP after 1 & 3 minutes of intubation respectively.

Lim SH [17] et al (2007) studied the effects of magnesium sulfate and remifentanil at attenuating the sympathetic responses were compared during laryngoscopy and endotracheal intubation.

Whether i.v. magnesium sulphate attenuates the haemodynamic stress responses to pneumoperitoneum by changing neurohumoral responses during laparoscopic cholecystectomy was studied by D. Jee et al [18] (2009) ,found that systolic and diastolic arterial pressures were greater in the control group ($P<0.05$) than in the magnesium group post-pneumoperitoneum, concluded that I.V. magnesium sulphate before pneumoperitoneum attenuates arterial pressure increases during laparoscopic cholecystectomy. This attenuation is apparently related to reductions in the release of catecholamine, vasopressin, or both.

In our study, we have found attenuation of SBP & RPP after intubation in magnesium sulfate group with slight increase in heart rate. This can be explained due to inherent property of drug in causing decreased catacholamine release [9] with vasodilatation thereby causing reduction in SBP & increase in heart rate.

Conclusion

We conclude that Magnesium sulphate 50 mg/kg IV infusion 3 minutes before induction, is a simple, effective and practical method of blunting cardiovascular responses to tracheal intubation , not associated with any adverse effect.

References

1. Reid LC and Bruce DE. Initiation of respiratory tract reflexes and its effects on heart. Surgy. Gynae. Obstretrics. 1940; 70:157.
2. Burstein CL, Lo Pinto FJ and Newman W. Electrocardiographic studies during endotracheal intubation 1, effects during usual routine techniques. Anaesthesiology. 1950; 11:224.
3. King BD, Harris IC Jr., Freifenstein FE, Elder JD and Dripps RD. Reflex circulating responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. Anaesthesiology. 1951; 12:556-566.
4. Prys-Roberts, Greene LT, Meloche R and Foex P. Studies of anaesthesia in relation to hypertension-II. Haemodynamic consequences of induction and endotracheal intubation. British Journal of Anaesthesia. 1971; 43:541-547.
5. Dalton B and Guiney T et al. Myocardial ischaemia from tachycardia and hypertension in coronary heart disease – Patient's undergoing anaesthesia. Ann. Mtg. American Society of Anaesthesiologists, Boston. 1972; 201-202.
6. Elisabeth J Fox, Garry S Sklar, Constance H Hill, Raymond Villanueva, Benton D King. Complication related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47:524-25.
7. Siedlecki J. Disturbances in the function of cardiovascular system in patients following endotracheal intubation and attempts of their prevention by pharmacological blockade of sympathetic system. Anaesth Resusc Intensive Ther 1975; 3:107–123.
8. van den Berg A A, Honjol D N M. Attenuation of the haemodynamic responses to noxious stimuli in patients undergoing cataract surgery. A comparison of magnesium sulphate, esmolol, lignocaine, nitroglycerine and placebo given i.v. with induction of anaesthesia. European Journal of Anaesthesi-ology 1997; 14:134-147.
9. Goldberg ME, Larijani GE, Azad SS, sosis M, Seltzer JL, Ascher J et. Al comparison of tracheal intubating conditions and neuro muscular blocking profiles after intubating doses of mivvacurium chlorider or succinly-choline in surgical outpatients. Anesth Analg 1989; 69:93-99.
10. Michael F. M., R. Eryk Beer, Jan D. Esser et al Anesthesia & Analgesia, 1989; 68(6):772-776.
11. Yap LC, Ho RT, Jawan B, Lee JH et al. Effects of magnesium sulfate pretreatment on succinylcholine-facilitated tracheal intubation Acta Analgesiol Sin 1994; 32(1):45-50.
12. Jain PN; Divatia JV, Manjure SS, Chattopadhayay G, Shah SC et al. Intravenous magnesium inhibits pressor response to nasotracheal intubation Journal of Anaesthesiology Clinical Pharmacology. 1995; 11(1):59-62.
13. Misuzu Nishiyama and Yuzuru Yanbe et al Journal of anesthesia, 1997; 11:18-21.
14. G D Puri, K S Marudhachalam, P Chari and R K Suri et al The effect of magnesium sulphate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. Anesthesia & Analgesia, 1998; 87:808-811.
15. KH Naghibi, M Akhtari et attenuation of the pressor response to tracheal intubations by magnesium sulphate, Journal of research in medical science,

2000; 5(1).

16. Pipelzadeh MR, Poormehdi Z, Mobasher M et al. Does Magnesium Sulfate attenuate hypertensive response to laryngoscopy and intubation? Acta Medica Iranica 2001; 39(3):150-152.
17. Lim SH, An DG, Choi SW, Lee SE, Kim YH, Lee JH, Lee KM, Cheong SH, Choi YK, Kim YJ, Shin CM The Comparison of Magnesium Sulfate and Remifentanil in Attenuating Hemodynamic Response to Endotracheal Intubation et al. Korean Journal of Anesthesiology 2007; 53(5):577-582.
18. D. Jee,D.Lee, S. Yun and C. Lee et Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy al Br. J. Anaesth. 2009; 103(4):484-489.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.3

Supraclavicular Brachial Plexus Block: A Comparative Clinical Study between Bupivacaine and Levobupivacaine

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Abstract

Background: The racemic bupivacaine is commonly used local anaesthetic drug brachial plexus block in as it provides longer duration of action but has risk of cardiotoxicity .The use of levobupivacaine in brachial plexus block seems promising considering its lower toxicity and the need of large volumes in this block. However there is possibility of unsatisfactory motor blockade.

Aim: To compare the efficacy and side effects of bupivacaine and levobupivacaine in brachial plexus block by supraclavicular approach. brachial plexus block

Methods: This study included 60 patients belonging to ASA grade I and II, either sex, between age group of 18 to 65 years and above, undergoing hand, forearm and arm surgery under supraclavicular block. These patients were randomly divided into two groups. The patients received 30 ml 0.5% bupivacaine (Group B) or 30 ml 0.5% levobupivacaine (Group L). Motor and sensory blocks were evaluated. Sensory and motor block onset times, durations of sensory and motor block and duration of postoperative analgesia were recorded.

Results: The two study groups were homogeneous with respect to age, sex, body weight and diagnosis type (type of fractures) and duration of surgery. The sensory and motor block onset times in Group B were significantly shorter than Group L ($p < 0.05$). The onset of sensory block was 9.33 $\pm$ 3.27 min. in group B whereas, it was 16.13 $\pm$ 2.83 min. in group L. The onset of motor block was 12.17 $\pm$ 2.18 in group B, whereas it was 20.00 $\pm$ 2.79 in group L. Sensory and motor block durations of Group B and L patients did not vary statistically significantly. In the present study, the mean duration of post operative analgesia was statistically insignificant between the two group (p= 0.766). It was 193.56 $\pm$ 23.51 in group B and 192.83 $\pm$ 23.54 in group L.

Conclusion:

30 ml 0.5% bupivacaine and levobupivacaine was enough to achieve adequate supraclavicular block. Bupivacaine leads to faster sensory and motor block onset compared to levobupivacaine; however it has similar duration of postoperative analgesia.

Keywords: Supraclavicular Block; Bupivacaine; Levobupivacaine; Cardiotoxicity.

Introduction

The techniques of peripheral neural blockade were developed early in the history of anaesthesia. The brachial plexus block is well-accepted component of comprehensive anesthetic care of upper limb surgeries. It is particularly useful in out-patient anaesthesia, for patients with full stomach, polytrauma and also patients with medical diseases like diabetes and those associated with cardiac, pulmonary, hepatic and renal impairments.

The supraclavicular approach to brachial plexus block provides the most reliable, uniform and predictable anesthesia for surgeries around elbow, forearm and hand [1]. The racemic bupivacaine is most commonly used local anaesthetic as it provides longer duration of action & favorable ratio of sensory to motor neural block [2].

The use of levobupivacaine in brachial plexus block seems promising considering its lower toxicity and the need of large volumes in this block. However there is possibility of unsatisfactory motor blockade, both in neuroaxis and brachial plexus block and there is lack of

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Received on 23.12.2016
Accepted on 29.12.2016

consensus regarding the use of levobupivacaine.

In this study, we investigated whether levobupivacaine with its inherent advantages-anesthetic potency, long duration of action; favorable toxicity profile is superior to bupivacaine in brachial plexus block.

Methods

After the institutional Ethics committee approval, written informed consent was obtained from all the patients. Sixty patients belonging to ASA physical status I&II of either sex and age more than 18 years under going elective orthopedic surgeries of upper limb were selected. The patients were randomly divided into two groups. The exclusion criteria was-uncooperative, obese patients, allergy and sensitivity to local anesthetic drugs, patients with cardiac, neurological, psychiatric disorders, altered coagulation profile and patients with contralateral phrenic nerve palsy and lung pathology. The patients and the observer were blinded to the study drugs.

After a detailed history taking, complete physical examination and routine investigations were undertaken for all patients. All the patients were pre-medicated with Tab. Ranitidine 150mg orally two hours prior to surgery and anxiolysis and sedation was given with Inj. Midazolam 0.02mg/Kg. Monitoring was done using electrocardiography, pulse-oxymeter and non-invasive blood pressure. Intravenous line was secured with 18G canula in large peripheral vein.

The brachial plexus block was performed under all aseptic precautions in supine position using supraclavicular approach by a trained anesthesiologist after eliciting paraesthesia. After negative aspiration, one of the following drug was administered –

Group B received 30 ml. of plain Inj. Bupivacaine 0.5% and *Group L* received 30ml. of plain Inj. Levobupivacaine 0.5%.

Assessment of Block

The sensory block was tested by sensation of pin prick and compared with same area on contralateral arm by using Hollmen scale [3].

The motor block was evaluated by movement at the fingers, wrist, elbow and shoulder joints by using Modified Bromage scale [4].

Onset of Sensory Block

This was defined as minimum of grade II of Hollmen scale in the distribution of any one of the four major nerves.

Onset of Motor Block

This was defined as minimum of grade I of modified Bromage scale.

Recovery from Sensory Block

This was the time at which the patient could perceive the normal sensation of pin prick in all the four major nerve distributions after the block placement (Grade I in Hollmen scale).

Recovery from Motor Block

This was the time at which the patient recovered completely from motor block and was able to do all movements of the limb (Grade 0 in modified Bromage scale).

Duration of Analgesia

It was taken from the time of onset of block to the first complaint of pain. Rescue analgesic was administered in the form of Inj. Diclofenac Sodium IM. In a dose of 1.5mg/kg.

Patients parameters like pulse rate, blood pressure, (systolic, diastolic and mean), $SpO_2$and pain score (VAS) monitored after administration of block and every 5 minutes intraoperatively and post operatively.

The characteristics of block like time for onset, as well as duration of motor and sensory block were noted using Hollmen's scale and Modified Bromage scale. Side effects such as nausea, vomiting, hypotension, bradycardia and sedation were also noted and recorded.

The collected data was compiled in Excel Sheet and master sheet was prepared. For analysis of the data SPSS software version 20th was used. Data was analyzed using chi-square test to check association between two techniques, chi-square test for trend and Fisher Exact test depending on type of data for comparison. $p<0.05$ statistically significant $p>0.05$ statistically not significant.

Results

The two study groups were homogeneous with respect to age, sex, body weight and diagnosis type (type of fractures) and duration of surgery (Table 1). ECG and SpO_2 were maintained throughout surgery in both groups.

The sensory block was assessed by Hollmen scale. In group B mean onset of sensory block was 9.33 ± 3.27min. While in group L, it was 16.13 ± 2.83.

this difference was statistically significant with earlier onset in group B.

The mean onset of motor block in group B was 12.17±2.18 min., while it was 20.00 ± 2.79 min. in group L. This difference was statistically significant with earlier onset in group B.

Table 1: Demography and baseline parameters

Parameter	Group B (n=30)	Group L (n=30)	p -value
Age (years)			
Mean + SD	31.17 ± 8.00	37.30 ± 7.88	0.948 NS*
21-30	6(20.0%)	6 (20.0%)	
31-40	15(50.0%)	14(46.7%)	
41-50	7(23.3%)	8(26.7%)	0.836**
>50	2(6.7%)	2(6.7%)	
Sex			
Male	20(66.7)	13(43.3)	0.076
Female	10(33.3)	17(56.7)	NS***
Weight (kgs) Mean + SD	57.60 ± 4.93	57.20 ± 4.79	0.751 NS*
Diagnosis			
#BBFA	16(53.3)	13(43.3)	
#Galleazzi	6(20.0)	7(23.3)	0.879
#Monteggia	3(10.0)	4(13.3)	NS****
#Radius & #ulna	5(16.7)	6(30.0)	

Value: Number (%) (Otherwise Mentioned)
Fracture
* Unpaired t test, two tailed p value>0.05 Not significant (@95%CL)
** Chi-Square test for trend, two tailed p value>0.05 Not significant (@95%CL)
***Fisher's exact test, p value>0.05 Not significant (@95%CL)
**** Chi-Square test, two tailed p value>0.05 Not significant (@95%CL)

Table 2: Onset, duration of sensory and motor block and duration of analgesia

	Time minutes	Group B (n=30)	Group L (n=30)	p-value
Onset time of sensory block (min)	< 120	0	0	p=1.00 NS**
Onset time of motor block (min)	121-150	6(20.0)	6(20.0)	
Duration of sensory block (min)	151-180	20(66.7)	20(66.7)	
Duration of motor block (min)	181-210	4(13.3)	4(13.3)	
Duration of analgesia (min)	211-240	0	0	
	Mean +SD	165.16 + 15.93	164.00 + 16.16	0.779 NS*

Value: Number (%) (Otherwise mentioned)
* Unpaired t test, two tailed p value>0.05 Not significant (@95%CL)
** Chi-Square test for trend, two tailed p value>0.05 Not significant (@95%CL)

Recovery

Recovery from motor block was, the time at which the patient had achieved grade 0 in modified Bromage scale of motor block. The mean time of recovery from motor block in group B was 165.16 ± 15.93 min. while it was 164.0 ± 16.16 in group L. This difference was statistically not significant. In both the groups, in majority of cases i.e. 20(66.7%) recovery from motor block was between 151-180 min.

Recovery from sensory block was the time at which the patient had achieved grade1 in Hollmen scale of sensory block. The mean time for the recovery of sensory block in group B was 174.90 ± 12.79 min., while it was 175.0 ± 12.41min. In group L this difference was statistically not significant .

Duration of Post-Operative Analgesia

Mean duration of post-operative analgesia in group B was 193.56 ±23 min while it was 192.83 ± 23.54 min. in group L. No significant statistical difference was observed.

Discussion

Brachial plexus block is close to the ideal anaesthesia technique for upper limb surgeries, as it

provides good intra-operative anaesthesia and also post- operative analgesia. Various local anesthetic agents were used in brachial plexus block like Lignocaine, Bupivacaine, Levobupivacaine and Ropivacaine. Lignocaine is very potent having earlier onset but has shorter duration of action, and high incidence of neurotoxicity. Bupivacaine is a popular local anaesthetic for brachial plexus block but is cardiotoxic. We compared bupivacaine with its levorotary isomer i.e. levobupivacaine in supraclavicular brachial plexus block. Levobupivacaine has potency similar to bupivacaine but levobupivacaine has less cardiovascular and central nervous system toxicity as compared to bupivacaine and thus levobupivacaine has a greater safety margin than bupivacaine [5].

This was a prospective, randomized, controlled clinical trial which included 60 patients belonging to ASA grade I and II, either sex, between age group of 18 years and above, undergoing elective upper extremity orthopaedic surgery under supraclavicular brachial plexus block.

In our study, onset of sensory block was 9.33 $\pm$ 3.27 min. in group B whereas, it was 16.13 $\pm$ 2.83 min. in group L. This difference was statistically significant ($p<0.0001$). These findings correlate with the findings of Cenk Ilham et al [6]. The sensory block onset time was 19.64 $\pm$ 10.70 min. in group B, whereas, it was 25.66 $\pm$10.72 min. in group L which was statistically significant ($p<0.036$).In another study, Dr. Charu J Pandya and colleagues [7]compared levobupivacaine 0.5% 0.8ml/kg and bupivacaine 0.5% 0.8ml/kg in supraclavicular brachial plexus block. They observed that the average sensory block onset time was less for levobupivacaine as compared with bupivacaine (10.5 min. Vs 18.7min.).

In the present study, onset of motor block was 12.17 $\pm$ 2.18 in group B, whereas it was 20.00 $\pm$ 2.79 in group L. this difference was statistically significant (0.0001). This means that the latency of motor blockade was more in the levobupivacaine group with earlier onset of motor blockade in the bupivacaine group. In both the groups there was no motor blockade as well as sensory blockade failure rates. Our findings were consistent with Cenk Ilham et al [6] who found that the motor block onset was statistically faster in group B (5.07 $\pm$ 4.07min.) than group L (9.2 $\pm$ 7.9 min). Their findings were statistically significant.

In this study, the duration of sensory block was 174.90 $\pm$ 12.79 min in group B and that in group L was 175.50 $\pm$ 12.41 min. As this difference proved to be statistically not significant ($p>0.05$), both bupivacaine and levobupivacaine had similar duration of sensory block. In the studies done by C.R. Cox et al [9], Baskan et al [10], H. Evten et al [11], Cenk et al [6] they observed no statistically significant difference in the sensory block duration between bupivacaine and levobupivacaine.

The duration of motor block was similar in both the groups which was statistically not significant ($p=0.779$); 165.1 $\pm$ 15.93 min in the bupivacaine group and 164.00 $\pm$ 16.16 min in the levobupivacaine group. Our results matched with the results in the studies done by C.R. Cox et al [9], Baskan et al [10], H. Evten et al [11], Cenk et al [6] and Dr. Charu J Pandya and Colleagues [7]. They all found no statistically significant difference between the motor block duration of the two drugs.

Moreover, our result showed that sensory block tended to last longer as compared to motor block. It is shown that Ropivacaine has a more selective action on pain transmitting A delta and C fibers rather than A beta fibers being large fibers. The minimal effective concentration of local anaesthetic for large (motor) fibers is greater than for small (sensory) fibers. Thus, motor function returns before pain perception and hence duration of motor block was shorter than the sensory block.

In the present study, the mean duration of post operative analgesia was statistically insignificant between the two group ($p=0.766$). It was 193.56 $\pm$ 23.51 in group B and 192.83 $\pm$ 23.54 in group L. Our results were consistent with the findings of Cenk et al [6] who had similar observations.

The immediate side effect like drowsiness, pruritus, respiratory depression, arrhythmias, hypotension, bradycardia, perioral numbness, convulsions, cardiac arrest were not seen in our study. Later complications associated with supraclavicular brachial plexus block techniques like haematoma, pneumothorax, recurrent laryngeal nerve palsy, phrenic nerve palsy, Horner's syndrome etc were also not observed in our study.

Local anaesthetic toxicity is an uncommon but well documented complication of regional anaesthesia. To reduce its occurrence, frequent aspiration and slow fractionalized injection with strict adherence drug dose schedule are recommended. Despite following these recommendations, cardiovascular toxicity may be unavoidable.

Several studies have been demonstrated and explained the mechanism of toxicity of bupivacaine [12,13]. Bupivacaine has been shown to have indirect depression of cardiac conduction (AV conduction, QRS complex) and contractility by blocking mainly inactivated state of sodium channels [13-15]. Studies

demonstrate dextro (R+) enantiomer has 2.4 times higher affinity for cardiac sodium channels and dissociates from it slowly as compared to levo (S+) enantiomer [13-15]. Levobupivacaine cause less rapid blockade of the cell firing in nucleus tractus solitarius (NTS) [13] which explains its lower CNS toxicity compared to racemic one. Also one more factor for difference in toxicity between two enantiomers can be explained on the basis of their pharmacokinetics. The protein binding of levobupivacaine is >97% as 95 against % in case of bupivacaine. That means <3% of levobupivacaine is free in plasma to have action on other tissues causing undesired toxic effect [16].

Thus levobupivacaine exhibits a wide margin of safety, less cardiodepressant activity which offers advantages over the currently used long acting agents like bupivacaine. Enough precautions were taken to use recommended dose and inject the anaesthetic in slow fractionalized doses. In our study, no side effect was observed related to local anaesthetic toxicity.

The major limitation of our study was that we did not use ultrasound guided blocks because of unavailability at the time of our study, this could have helped us to lower dosage and volume of local anaesthetic. Another limitation of the present study was the small number of cases. Though our results tend to suggest that levobupivacaine is a longer acting local anaesthetic with similar block quality and prolonged effect as that of bupivacaine, to obtain a definite result, study with enrolment of larger number of patients is required. Moreover, we included only patients with ASA I and II physical status only, a study of high risk patients to justify the safety of levobupivacaine has to be carried out.

Thus, we conclude that, 30ml of 0.5% bupivacaine and levobupivacaine was enough to achieve adequate motor and sensory supraclavicular block. Levobupivacaine has theoretical advantage of having less toxicity potential and being less cardiotoxic than bupivacaine. So, it may be safer drug in supraclavicular brachial plexus block; where accidental intravascular injection of large volume of local anaesthetic can occur and may be more detrimental especially in patients with cardiac disease.

References

1. De Tran QH Clemente A, Doan J, Finlayson RJ. Brachial plexus blocks: A review of approaches and techniques. Can J Anaesth 2007; 54(8):662-674.
2. De Jong R. Local anaesthetics pharmacology: Brown D L, ed. Regional anesthesia and Analgesia Philadelphia, Pa: Saunders; 1996:124-142.
3. Hollmen scale to assess motor and sensory blockage by peripheral nerve block. C Caponga, D cell no chal, Alkalization of local anaesthetic which block which anaesthetics ? Reg. Anaesth. 1995 Sept; 20(5) 369-77.
4. Sarkar DJ, Khurana G, A Chaudhary, J P Sharma. A comparative study on the effects of adding fentanyl and buprenorphine to local anaesthetics in brachial plexus block. Journal of Clinical and Diagnostic Research 2010; 4;6;3337-43.
5. Leone S, Di Cianni S, Casati A, Fanelli G: Pharmacology, toxicology and clinical use of new long acting local anaesthetics, Ropivacaine and levobupivacaine. Acta Biomed. 2008 Aug; 79(2): 92-105.
6. Cenk Ilham, Elif Bombaci, Serhan Yurtlu, Serhan Colacoglu: Efficiency of levobupivacaine and Bupivacaine for supraclavicular Block: a randomized double-blind comparative study; Rev Bras Anestesiol. 2014; 64(3):177-182.
7. Dr. Charu J. Pandya, Dr, Gauri M. Panjabi, Dr. Chirag Baranda, Saraspur, Ahmedabad: Analgesic and Anaesthetic property of Levobupivacaine comared with bupivacaine in patients undergoing a supraclavicular brachial plexus block: Indian Journal of Applied Basic Medical Sciences July 2014.
9. Cox CR, Checketts MR, Mackenzie N et al. Comparison of S(-)- bupivacaine with racemic (RS)-bupivacaine in supraclavicular brachial plexus block Br J Anesth, 1998; 80:594-598.
10. Baskan S, Taspinar V, Ozdogan L, Gulsoy KY, Erk G, Dikmen B, Gogus N, Anakara, Turkey: Comparison of 0.25% levobupivacaine and 0.25% Bupivacaine for posterior approach interscalene brachial plexus block; J Anesth. 2010 Feb; 24(1) 38-42.
11. H Evren Eker, Ayda Turkoz, Aysu Inan Kocum, Oya Yalcin Cok, Sercan Akpinar, Gulnaz Arslan, Baskent University Department of Anaesthesiology and Reanimation: The clinical properties of 0.25% Bupivacaine and levobupivacaine during interscalene brachial plexus block: Turk J Aaesth Reanim, 2012; 40(1):20-26.
12. Clarkson C W, Hondeghem L M. Mechanism for bupivacaine depression of cardiac conduction: fast block of sodium channels during the action potential with slow recovery from the block during diastole. Anesthesiology, 1985; 62:396-405.
13. Denson DD Behbehani MM Gregg RV Enantiomer-Specific Effects on an Intravenously Administered Arrhythmogenic Dose of Bupivacaine on Neurons of the Nuleus Tractus Soluatroius and the Cardiovascular System in the Anesthetized Rat Regional Anesthesia 17:311-316.
14 . Valenzuela C, Snyders DJ, Bennett PB. Stereoselective block of cardiac sodium channels by bupivacaine in

guinea pig ventricular myocytes. Circulation 1995; 92:3014–24.

15. Valenzuela C, Delpon E, Tamkun MM. Stereoselective block of a human cardiac potassium channel (K v 1.5) by bupivacaine enantiomers. Biophys J. 1995b; 69:418–27.
16. Ohmura S1, Kawada M, Ohta T, Yamamoto K, Kobayashi T. Systemic toxicity and resuscitation in bupivacaine-, levobupivacaine-, or ropivacaine-infused rats. Anesth Analg. 2001 Sep; 93(3):743-8.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.4

A Comparative Study of Inflation of Endotracheal Tube Cuff with Buffered Lidocaine, Saline and Air for Smooth Periextubation Period in Patient with Hyperactive Airway

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Abstract

Background: Increased cough and restlessness during emergence from general anaesthesia in patients with hyperactive airway undergoing surgical procedures might result in adverse effects like hypertension, tachycardia or tachy arrhythmias, myocardial ischaemia, bronchospasm, and increased bleeding at the surgical site. Hence, in such patients, we sought to determine the benefits of filling the endotracheal tube cuff with either buffered lidocaine, saline or air, so as to prevent endotracheal tube-induced coughing during emergence from general anaesthesia.

Aim and Objectives: To compare effects of ETT cuff inflation with buffered lidocaine 2%, saline and air for peri extubation period in patients with hyperactive airway for Initial & final ETT cuff pressure difference, Occurrence of cough in periextubation period & Incidence of sore throat post operatively.

Method: 240 patients of ASA grade 1 & 2, of 15 to 60 years old, either with a history of chronic smoking or recently treated upper respiratory tract infections were randomly assigned into three groups (n = 80), based on the type of endotracheal tube cuff inflation, as follows: Group A (air), Group B (normal saline) and Group C (Buffered lidocaine). Cough in periextubation period was graded at extubation as: Grade 0 (no cough), Grade 1 (cough < 15s) and Grade 2 (cough > 15s).

Result: Extubation was smooth in Group C compared with Groups B and A ($p < 0.0001$). Further, the incidence of sore throat was found to be lower in both liquid groups, B and C, compared with Group A at 1 h ($p < 0.0001$) and 24 h ($p < 0.01$) postoperatively.

Keywords: Buffered Lignocaine; Hyperactive Airway; Periextubation Period; Endotracheal Tube Cuff.

Introduction

Cuffed endotracheal tube provide secured airway for controlled or spontaneous ventilation and protection against aspiration. Amongst the sequelae inherent to the usage of cuffed endotracheal tube are local irritation and inflammation of the airway caused by prolonged inflation of the cuff which results in post intubation morbidities like sore throat, hoarseness of voice and cough [1].

Airway becomes hyperactive in chronic smokers and in patients those recently treated for upper respiratory tract infections (URTIs). In these patients the receptors meant for cough reflex, the rapidly adapting stretch receptors (RARs), are in a hypersensitised stage [2-8]. Hence, these patients tend to cough more frequently and violently during extubation and in postextubation period. Restlessness and coughing during emergence from General Anaesthesia can result in hypertension, tachycardia or tacharrhythmias, myocardial ischaemia, increased intraocular and intracranial pressures, myocardial ischemia, broncho spasm and increased bleeding at the surgical site [9,10].

So careful periextubation period is of utmost need for the patients of hyperactive airway to reduce postoperative morbidities. Lignocaine instilled in an endotracheal tube cuff diffuses slowly across the cuff membrane. The cuff would act as a potential reservoir for the local anaesthetic, allowing diffusion and subsequent anaesthesia of the underlying tracheal mucosa [17].

This comparative study was conducted to study the effect of low dose of alkanized Lignocaine, saline and air in the endotracheal tube cuff on cuff pressure changes, occurrence of cough and post-operative sore throat.

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Received on 10.12.2016
Accepted on 28.12.2016

Method

The study was conducted in the Department of Anesthesiology, S.M.S. hospital and attached group of hospitals, Jaipur with due permission from the institutional ethical committee and a written informed consent.

Hospital based, Prospective, Comparative, Randomized, Clinical trial.

This Study was conducted between May 2015 to May 2016.

The study recruited patients between the age of 15 to 60 years, of ASA grade I and II, with hyperactive airway (history of smoking for at least 2 yrs or recently treated URTI) presenting for elective or emergency surgery lasting more than 90 minutes duration.

Sample Size

The sample size was calculated 76 subjects in each 3 groups at α error 0.05 and power 80% assuming proportion of patients developing sore throat at 24 hrs in group-A, B or C to be 0.63, 0.40 & 0.28 respectively. Hence for study purpose, 80 patients were taken in each of three groups.

Patients listed for surgery were enrolled and assessed for eligibility. Those not meeting the inclusion criteria or those refusing to participate were excluded. Patients were then randomly allocated to one of the three groups (80 patients in each group)

Group A (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml of air.

Group B (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml normal saline.

Group C (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml buffered

Lignocaine (6 ml 2% lignocaine + 0.5 ml of 7.5% sodium bi carbonate).

Selection of study participants-

Inclusion Criteria

- Written Informed consent.
- Age between 15-60 years.
- Patient with ASA class I or II.
- Patient with a history of smoking for 2 years or more.
- Those that recently treated for URTI .

Exclusion Criteria

- Patients in whom general anaesthesia is contraindicated
- Patient in whom intubation failed in first attempt
- Patient with difficult airway who need Comparatively smaller size of endotracheal tube
- Patient who on ACE inhibitors
- Atrio-ventricular block
- Patient allergic to lignocaine
- Patients fitting in the criteria of difficult intubation (mallampati grade 3 & 4)
- Patients in whom total duration of laryngoscopy and intubation was more than 90 seconds.
- Patients unwilling to give consent for proposed study.

Pre-Anesthetic Check up

All patients were visited on the day prior to surgery and explained about the anesthetic technique and perioperative course. Each patient had pre-anesthetic checkups which include:

- Any significant present/past medical/surgical history
- Physical examination
- Vital parameters like B.P./Pulse/Temperature/ Respiratory rate
- Routine investigation – Hb, TLC, DLC, Bleeding time, Clotting time, Prothrombin time, Fasting blood sugar, Serum Urea and Creatinine, SGOT, SGPT, Alkaline Phosphatase, serum electrolytes, ECG, Chest X-ray, Echocardiography(if available).

Written and informed consent obtained for performance of anesthesia after complete explanation about the study protocol and the procedure.

Anesthetic Procedure

Patients was premedicated with inj ranitidine -1mg/kg +metoclopramide-0.2 mg/kg, then inj midazolam-0.02mg/kg +inj tramadol-2mg/kg +inj glycopyrolate-4mcg /kg.

Induction done with IV propofol- 1.5 to 2 mg/kg & the drug was administered in small doses over a period of 60-90 seconds, until there was loss of eyelash reflex and lack of response to vigorous voice commands and tactile stimuli. Muscle relaxation for intubation was facilitated with inj-vecuronium-0.1 mg/kg body wt. Positive pressure ventilation was

done with 100% oxygen for a period of three minutes. Patient was intubated with aid of macintosh laryngoscope with appropropiate size endotracheal tube with prechecked cuff for any leak.

Intubated patients was subsequently randomly divided into three groups based on the endotracheal tube cuff filling as:

Group A (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml of air.

Group B (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml normal saline.

Group C (n=80): Patients in whom endotracheal tube cuff were inflated with 6-8 ml buffered.

Lignocaine (6 ml 2% lignocaine + 0.5 ml of 7.5% sodium bi carbonate).

In all the patients the endotracheal tube cuff was filled depending upon the minimal occlusion volume (volume at which no palpable leak was felt over the trachea) of each patient & initial endotracheal tube cuff pressure was noted. Care was taken to ensure that the starting cuff pressure should be approximately 20 to 25 cm H_2O, measured using a high volume, low-pressure endotracheal tube cuff manometer. Anaesthesia was maintained with N_2O/ O_2 (60/40%) and 0.6% isoflurane. Further neuromuscular block was maintained with loading dose intermittent boluses of vecuronium (one-quarter of the intubating dose at 15 min interval). After surgery, residual neuromuscular block was reversed with inj neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Mechanical ventilation was maintained until swallowing or spontaneous ventilation resumed, and then assisted manual ventilation was done. Final endotracheal tube cuff pressure was recorded before extubation. The patient was extubated when the following criteria was met: (1) regular spontaneous ventilation; (2) ability to follow verbal commands (eye opening or hand grip) and (3) ability to demonstrate purposeful movements.

Following Recordings were done

- The endotracheal tube cuff pressure at intubation and at extubation were recorded with help of aneroid endotracheal tube cuff manometer.
- Cough reflex were checked just before extubation and after extubation. Grading of cough were done as following-

  Grade 0 – No cough; Grade 1 – Cough lasting for < 15 sec and Grade 2 – Cough lasting for > 15 sec.
- Sore throat was assessed in the recovery room with a visual analog scale (VAS : 0 –10 cm) after extubation at 1hr and 24 hr. Grading of sore throat were done as following-

  Score 0 – No pain; Score 1 –Tolerable (mild – moderate) and Score 2 – Intolerable pain (severe).

Data Processing and Analysis

Statistical analyses were done using computer software (SPSS trial version 20 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations. The difference in proportion was analysed by using chi square test and the difference in means were analyzed by using student T Test and one way ANOVA and post Hoc Test. Tukey Test applying to find out the most significant groups among all the groups. Significance level for tests were determined as 95% ($P< 0.05$).

Results

Data was recorded in terms of initial and final endotracheal tube cuff pressure, occurrence of cough in periextubation period and sore throat at 1hr & 24 hr. The final conclusions carried out are as follows –

The demographic profile of the patients in terms of age, sex ratio, ASA grade, smoking status, treated URTI and total surgical duration was comparable in both the groups.(Table-A)

The mean variables (initial and final endotracheal tube cuff pressure, occurrence of cough at periextubation period and sore throat at 1hr & 24 hr) were comparable in both the groups so desired study and control population was achieved with appropriate randomization.

No Significant difference was observed in mean initial cuff pressure among the groups. In group A mean was 22.71±11.16 cmH20; (with range 19 to 25), in group B mean was 22.55 ±11.135; (with range 20 to 24 cmH2O) and in group C mean was 22.44±1.22; (with range 20 to 25 cmH20) (P=0.33NS) (Table B).

Significant difference was observed in final cuff pressure among the groups. On applying post HOC test TUKEY test, group A was significantly have higher mean (55.49 ±5.59) as compared to group B(23.91±1.058) and group C(23.33 ±1.29). (<0.001S) There was no statistical significant increase in final endotracheal tube cuff pressure compared with initial cuff pressure in both the liquid groups, B and C (Table B).

Proportion of the cases with cough more than 15 second was maximum in group A (56.25%) as compared to group B (30%) and least was in group C (10%). Proportion of cases who did not have cough in periextubation period were maximum in group C (70%) as compared to group B (20%) followed by group A. (13.75). Proportion of the cases with cough less than 15 second were maximum in group B(50%), followed by group A (30%) and least in group C (20%). (P<0.001S) (Table C).

Proportion of the cases with Sore throat at 1 hr with Severe type were maximum in group A (20%) as compared to group B and group C (0%) while mild to moderate type of sore throat were maximum in group A(56.25%), followed by group B (25%) and least in group C (15%). There were no Sore throat at 1 hr maximum in group C (85%) as compared to group B (75%) followed by group A.(23.75%). (P<0.001S). (TableD). Proportion of the cases with Sore throat at 24 hr with Mild-to-Mod type were maximum in group A (43.75%) as compared to group B (15%) and least were in group C (12.5%) while no Sore throat at 24 hr were maximum in group C(87.5%) as compared to group B (85%) followed by group A.(56.25%) (P<0.001S) (Table E).

Table 1: Demographic data

	Groups		
	A	**B**	**C**
Age(years)	38.34 ±11.807	37.00±11.46	37.00±11.46
Sex(M/F)	19/16	23/57	24/56
Number of smoker	58	58	56
Treated URTI	19	21	24
Duration of surgery	140.66±25.078	136.25±16.114	136.25±16.114
ASA grade(I/II)	22/58	22/58	24/56

Table 2: ETT cuff pressures measured at the start and at the end of the surgery

Parameter	A	B	C
Initial cuff pressure(cm.H_2O)	22.71 ±1.160	22.55 ±1.135	22.44 ±1.221
Initial cuff pressure(cm.H_2O)	55.49 ±5.594	23.91 ±1.058	23.33 ±1.290

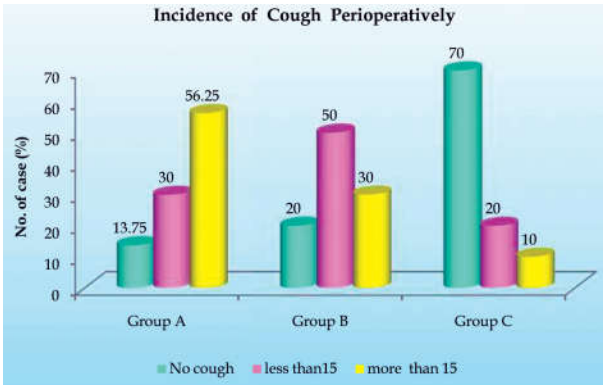

Fig. 1: Incidence of cough perioperatively

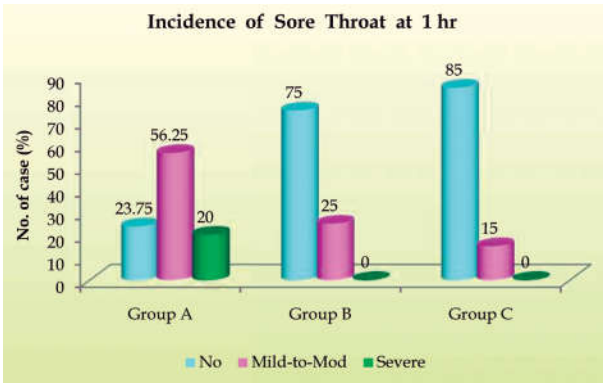

Fig. 2: Incidence of sore throat at 1 hour

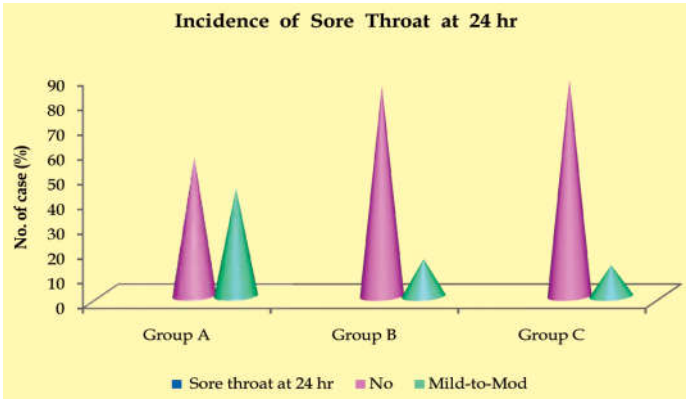

Fig. 3: Incidence of sore throat at 24 hours

Table 3: Incidence of cough perioperatively

	Group A		Group B		Group C	
Cough (seconds)	**No**	**%**	**No**	**%**	**No**	**%**
No cough	11	13.75	16	20	56	70
less than15	24	30	40	50	16	20
more than 15	45	56.25	24	30	8	10
Total	69	86.25	64	80	24	30

Table 4: Incidence of sore throat at 1 hour

	Group A		Group B		Group C	
Sore throat at 1 hr	**No**	**%**	**No**	**%**	**No**	**%**
No	19	23.75	60	75	68	85
Mild-to-Mod	45	56.25	20	25	12	15
Severe	16	20	0	0	0	0
Total	61	76.25	20	25	12	15

Table 5: Incidence of sore throat at 24 hours

	Group A		Group B		Group C	
Sore throat at 24 hr	**No**	**%**	**No**	**%**	**No**	**%**
No	45	56.25	68	85	70	87.5
Mild-to-Mod	35	43.75	12	15	10	12.5
Total	80	100	80	100	80	100

Discussion

Rapidly adapting stretch receptors in the tracheal mucosa are believed to be the irritant receptors meant for cough [3-5]. These receptors are highly sensitive to mechanical stimuli like touch, displacement and stretch. Tracheal intubation with endotracheal tube, cuff inflation and the resulting hyperinflation in turn stimulate these receptors, thus producing cough in normal patients during extubation (endotracheal tube-induced cough). In chronic smokers and those with recently treated URTI, the threshold stimulation for cough receptors is reduced [2-6].

Long-term smoking causes neutrophilic infiltrates in vulnerable smokers that sensitise the cough-sensitive nerves by the release of sensory neuropeptides and direct stimulation of the nerves/ receptors [7,8].

Empey et al report cough threshold values to be significantly low for up to two weeks following URTIs. Stimulation of these receptors also results in the release of substance P (which causes mucosal vasodilatation, plasma exudation and airway mucus secretion), calcitonin gene-related peptide (causes mucosal vasodilatation) and neurokinin A (causes bronchoconstriction) [5]. Hence smokers tend to cough more frequently and violently during emergence from general anaesthesia.

Cough and sore throat during emergence in a lighter plane of anaesthesia can result in hypertension, tachycardia, and myocardial ischemia, raised intraocular and intracranial pressures. These features are particularly undesirable in patients undergoing neurosurgical or ophthalmic procedures or those who are at an increased risk of adverse cardiovascular events [9-10].

Numerous methods of attenuating cough reflex during tracheal extubation have been advocated such as use of narcotics, extubation in a deeper plane of anaesthesia, use of topical lignocaine gelly, use of topical lignocaine spray and use of IV alkalinized lignocaine.

Intravenous and prior topical administration of lignocaine has been used to help in reducing cough during emergence from general anaesthesia. Intravenous lignocaine (IVL) is known to suppress cough through its central nervous system depressant effect (cough centre in the medulla) and hence it requires a minimal serum concentration (> 3 μg/ml) to be effective. In addition, IVL produces delayed emergence from anaesthesia. Moreover, the efficacy of IVL in suppressing cough is of short duration (5–20 min) [18].

Topical administration of lignocaine is known to produce its irritant effect long before its cough suppressant effect appears [9]. Other disadvantages encountered with this technique are that it requires a specially designed instrument for its application and the tracheal mucosa in direct contact with the endotracheal tube cuff wall is effectively shielded from exposure to lignocaine applied by this technique.

Klemola UM [19] studied the effect of laryngeal spray with alkalinized lignocaine and alkalinized

lignocaine jelly application on 95 patients. The incidence of sore throat when both the techniques used was 95%, when alkalinized lignocaine jelly alone used was 85% and in the control group it was 62%. Thus, stating that the use of alkalinized lignocaine jelly was associated with a high incidence of post extubation sore throat and hoarseness.

Injecting lignocaine alone into the endotracheal tube cuff causes a low diffusion rate across the cuff (1% released during a 6 h period) [19,32]. Higher doses of lignocaine (200–500 mg) are required to produce a clinical effect. Hence this had no advantages over saline, and could be dangerous if the cuff ruptures [16].

By filling the endotracheal tube cuff with buffered lignocaine, diffusion of the uncharged base form of the drug occurred across the hydrophobic PVC walls of the endotracheal tube cuff [1,10]. Lignocaine, as a weak basic and lipophilic drug, binds avidly to the respiratory mucosa. The absorption characteristics of the mucosa, epithelial thickness, number of membrane pores and tissue pH also serve to delay absorption. Thus the tracheal mucosa in direct contact with the endotracheal tube cuff wall can be anaesthetized locally with a longer than expected effect of lignocaine and with intact supraglottic reflexes, preventing aspiration in these patients [1,18].

Buffering not only helped in increasing the diffusion of the drug in our study but also allowed us to use lower doses of lignocaine (without exceeding the toxic limits). The toxicity of local anesthetics must be considered regardless of the route of the administration. In this regard, our concerns were twofold, the risks of systemic absorption and the consequences of cuff damage with subsequent leakage of 2% lignocaine or saline into the bronchial tree. Although 20 mg/mL lignocaine (2%) was used, the mean volume used per endotracheal tube was 6 to 8 mL . This is considerably less than the amount of lignocaine used in a study by Sutherland and colleagues [20], in which a fixed dose of 370 mg of lignocaine was used in 21 adult patients to topically anaesthetize the airway for fiberoptic bronchoscopy and no incidence of toxic plasma concentrations of lignocaine was recorded.

Another study by Efthimiou [21] with 41 patients undergoing fiberoptic bronchoscopy, using average doses of 9.3 mg/kg of lignocaine, recorded only two patients in which plasma levels exceeded the toxic levels (5.0μg/ml) and no complications were observed.

In this study, all patients were extubated without any complications, and no evidence of cuff damage was observed.

Previously done studies by Carl Fagan and colleague [1] have compared the incidence of sore throat and hemodynamic changes between intracuff alkalinized lignocaine, intracuff saline and intracuff air and concluded that incidence of sore throat is significantly lower in intracuff alkalinized lignocaine group .

In one study done by Soltani and colleagues [22] compared the incidence of sore throat after general anaesthesia in six different groups which included spraying of the distal end of endotracheal tube cuff with 10% alkalinized lignocaine, spraying of 10% to laryngopharyngeal structures, application of 2% alkalinized lignocaine jelly to cuff of the tube, intravenous alkalinized lignocaine at the end of surgery, Intracuff alkalinized lignocaine and application of normal saline to the cuff end of the tube. They concluded that IV lignocaine, intracuff alkalinized lignocaine considerably decreases the incidence of sore throat post extubation. The results of these studies favour our study results.

From the previous in vitro study by Jaichandran VV et al (2008) using high performance liquid chromatography, they found that by filling the endotracheal tube cuff with a mixture of 6 ml 2% lignocaine HCl + 0.5 ml NaHCO3 the minimum concentration of lignocaine (Cm = 155 μg/ml) that is required for blocking the cough receptors [12] was obtained at the end of 90 min across the cuff walls. Hence in our study, we used the above lignocaine buffered mixture for filling the endotracheal tube cuff in patients undergoing surgery with a minimum duration of 90 min [17]. The mean duration of anaesthesia in the group A was 140.66±25.078, in group B was 136.25±16.114 and in group C was 136.25±16.114 which were comparable and an insignificant 'p' value (0.26) in our study.

During anaesthesia with N_2O the cuff pressure increases with time as N_2O diffuses into it more rapidly than it diffuses out, because of the partial pressure gradient across the PVC membrane [10,11]. These findings are similar with our study. When the cuff pressure exceeds the capillary perfusion pressure (30–40 mmHg) tracheal mucosal erosion occurs, resulting in sore throat postoperatively, as evidenced in our study. Our data confirmed the increased cuff pressure and cuff volume after air inflation with N_2O and oxygen anaesthesia.

By replacing air with liquid (saline / buffered lignocaine), cuff hyperinflation problems can be avoided [10]. The lack of hyper pressure is probably

one advantage of liquid filling of endotracheal tube cuffs. In our study we monitored the endotracheal cuff pressure keeping the endotracheal cuff pressure at around 20-25 cm H_20 in all the groups after intubation. In our study, no significant difference was observed in mean initial cuff pressure among the groups. In group A mean was 22.71±11.16 cm H_20; (with range 19 to 25), in group B mean was 22.55 ±11.135; (with range 20 to 24 cm H_2O) and in group C mean was 22.44±1.22 ; (with range 20 to 25 cm H_20) (P=0.33=NS). But a Significant difference was observed in final cuff pressure among the groups . On applying post HOC test TUKEY test, group A was significantly have higher mean (55.49 ±5.59) as compared to group B(23.91±1.058) and group C(23.33 ±1.29). (P<0.001=S). There was no statistical significant increase in final endotracheal tube cuff pressure compaired with initial cuff pressure in both the liquid groups, B and C . The groups were incomparable and had a significant 'p' value (<0.001). Thus, confirming the data with previous studies.

In the study done by Estebe JP and others [16] on 60 patient intracuff alkalinized lignocaine was compared with intracuff saline and intracuff air. The results stated that there was a trend of reduced incidence of post operative sore throat in alkalinized lignocaine group. Jean Pierre Estebe et al., demonstrated that alkalinisation of intracuff lignocaine improves endotracheal tube induced emergence phenomenon. There was a decreased incidence of cough and other parameters like restlessness, Postoperative nausea and vomiting (PONV), dysphonia, hoarseness in the post extubation period.

Huang CJ et al., demonstrated that emergence coughing and the incidence of sore throat was significantly less than the control group when lignocaine 4% and alkalinized lignocaine were used. They suggested using alkalinized and warmed lignocaine prestored in the endotracheal tube cuff for smoother emergence from general anaesthesia [9].

In our study we found that the incidence of coughing at extubation was higher in the air and saline groups as compared to lignocaine. Proportion of the cases with cough more than 15 second were maximum in group A (56.25%) as compared to group B (30%) and least were in group C(10%). Proportion of cases who did not have cough in periextubation period were maximum in group C (70%) as compared to group B (20%) followed by group A.(13.75). Proportion of the cases with cough less than 15 second were maximum in group B(50%), followed by group A (30%) and least in group C (20%). (P<0.001S). These data was comparable with the results of previous studies.

In our study the incidence of sore throat was recorded at two different intervals. It was recorded as the severity or grade of sore throat. Proportion of the cases with Sore throat at 1 hr with Severe type were maximum in group A (20%) as compared to group B and group C (0%) while mild to moderate type of sore throat were maximum in group A (56.25%), followed by group B (25%) and least in group C (15%). There were no Sore throat at 1 hr maximum in group C (85%) as compared to group B (75%) followed by group A (23.75%). (P<0.001S). Proportion of the cases with Sore throat at 24 hr with Mild-to-Mod type were maximum in group A (43.75%) as compared to group B (15%) and least were in group C (12.5%) while no Sore throat at 24 hr were maximum in group C(87.5%) as compared to group B (85%) followed by group A.(56.25%)(P<0.001S). These data for incidence of sore throat was comparable with the results of previous studies.

Conclusions

Injecting buffered lidocaine into the Endotracheal tube cuff not only reduces the incidence of sore throat but also enables improved Endotracheal tube tolerance and helps in producing smooth Periextubation period in patients with hyperactive airways.

References

1. Fagan C, Frizelle HP, Laffey J, Hannon V and Carey M: The effects of intracuff lignocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. Anesth Analg 2000; 91:201-5. | Article | PubMed.
2. Dicpinigaitis PV, Gayle YE. Effect of Guaifenesin on cough reflex sensitivity. Chest 2003; 124:2178-81.
3. O'Connell F, Thomas YE, Studham JM, et al. Capsaicin cough sensitivity increases during upper respiratory infection. Respir Med 1996; 90:279-86.
4. Empey DW, Laitinen LA, Jacobs L, Gold WM, Nadel JA. Mechanisms of bronchial hyperactivity in normal subjects after upper respiratory tract infections. Am Rev Respir Dis 1976; 113(2):131-9.
5. Empey DW. Effect of airway infections on bronchial reactivity. Eur J Respir Dis (Suppl.) 1983; 128(1):

366-8.

6. Wong CH, Morie AH. Cough threshold in patients with chronic obstructive pulmonary disease. Thorax 1999; 54(1):62-4.
7. Lee LY, Burki NK, Gerhardstein DC, Gu O, Kou YR, Xu J. Airway irritation and cough evoked by inhaled cigarendotracheal tubee smoke: Role of neuronal nicotinic acetylcholine receptors. Pulm Pharmacol Ther 2006; 18.
8. Lee LY, Gerhardstein DC, Wang AL, Burki NK. Nicotine is responsible for airway irritation evoked by cigarendotracheal tubee smoke inhalation in men. J Appl Physiol 1993; 75(5):1955-61.
9. Huang CJ, Tsai MC, Chen CT, et al.In vitrodiffusion of lignocaine across endotracheal tube cuffs. Can J Anesth 1999; 46:82-6.
10. Dollo G, Estebe JP, Le Corre P, et al. Endotracheal tube cuffs filled with lignocaine as adrug delivery system: in vitroand in vivo investigations. Eur J Pharm Sci 2001; 13:319-23.
11. Jensen PJ, Hommelgaard P, Sondergaard P and Eriksen S: Sore throat after operation: influence of tracheal intubation, intracuff pressure and type of cuff. Br J Anaesth1982; 54:453-7. | Article| PubMed.
12. Sconzo JM, Moscicki JC and DiFazio CA: In vitrodiffusion of lignocaine across endotracheal tube cuffs. Reg Anesth 1990, 15:37-40. | PubMed.
13. Hers, IF. Disturbances of the ciliated epithelium due to influenza virus. Am Rev Respir Dis 1966; 93:162.
14. Gwaltney J Jr. The common cold. In: Mandell G, Bennendotracheal tube J, DolinR, eds. Principles and practice of infectious diseases. New York:Churchill Livingstone, 1995; 561– 6.
15. Karaman M, Tek A. Deleterious effect of smoking and nasal septal deviation on mucociliary clearance and improvement after septoplasty. Am J Rhinol Allergy. 2009; 23(1):2-7.
16. Estebe JP, Dollo G, Le Corre P, Le Naoures A, Chevanne F, Le Verge R and Ecoffey C: Alkalinization of intracuff lignocaine improves endotracheal tube-induced emergence phenomena. Anesth Analg 2002; 94:227-30.
17. VV Jaichandran, N Angayarkanni, Coral Karunakaran, IM Bhanulakshmi, V Jagadeesh: Diffusion of Lignocaine buffered to an optimal pH across the Endotracheal tube cuff- An in- Vitro study. Indian J Anaesth 2008, 52:536-40.
18. Minogue SC, Ralph J, Lampa MJ. Laryngotracheal topicalization with lignocaine before intubation decreases the incidence of coughing on emergence from general anesthesia. Anesth Analg 2004; 99: 1253-7.
19. Klemola UM, Saarnivaara L, Yrjola H. Post – operative sore throat: Effect of lignocaine jelly and spray with endotracheal intubation. Eur J Anaesthesiol, 1988; 5(6):391.
20. Sutherland AD, Santamaria JD, Nana A. Patient comfort and plasma lignocaine concentrations during fibreoptic bronchoscopy. Anaesth Intensive Care, 1985; 13:370–4.
21. Efthimiou J, Higenbottam T, Holt D, Cochrane GM. Plasma concentrations of lignocaine during fibreoptic bronchoscopy. Thorax, 1982; 37:68–71.
22. Hasan Ali Soltani, Omid Aghadavoudi. The effect of different lignocaine application methods on postoperative cough and sore throat. J Clin Anesth, 2004; 14(1):15-8.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.5

Estimation of an Efficient Antiemetic Agent for Prevention of Postoperative Nausea and Vomiting in Children Undergoing Tonsillectomy

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Abstract

Background: Postoperative nausea and vomiting (PONV) remains one of the commonest causes of significant morbidity after tonsillectomy in children. A variety of prophylactic anti-emetic interventions have been reported, but there has only been a limited systematic review in this patient group.

Aim: To find an efficient antiemetic agent for prevention of PONV in children undergoing tonsillectomy performed under G.A.

Methods: We included 75 patients in the age group of 5-15 years undergoing Tonsillectomy. Patients were randomly divided into 3 groups of 25 patients each. The patients of Group I received Metoclopramide 0.25mg/kg, Group II Ondansetron 100 mcg/kg and group III received Granisetron 40 mcg/kg intravenously just prior to induction of anesthesia. The following parameters were monitored during the study: Duration and quality of antiemesis, Pulse rate, Blood pressure, Modified Aldrete's Score and Side effects if any.

Results: Based on scoring system, it was found that the recovery score was 9. The patients were observed from 0–3 hrs and 3-24 hrs following Tonsillectomy for episodes of Nausea and / or Vomiting. Incidence of nausea and/or vomiting during 3-24 hrs after surgery is 44%, 20% and 8% in Groups I, II, and III respectively , with a statistically significant difference between Metoclopramide (Gr. I) and Granisetron (Gr. II).

Conclusion: Granisetron in a dose of 40 mcg/kg is more effective with very less side effects than Metoclopramide and Ondansetron in the long term prevention of PONV in the children undergoing tonsillectomy under GA.

Keywords: PONV; Tonsillectomy; GA; Antiemetic Agents.

Introduction

Postoperative Nausea and Vomiting (PONV) is one of the most common and significant complications associated with pediatric surgical procedures. Without prophylaxis, more than 70% of children undergoing tonsillectomy will experience at least one episode of vomiting in the postoperative period. PONV has been reported to be the commonest cause of delayed discharge or overnight admission in day- case tonsillectomy. It has also been reported to be associated with an increased risk of bleeding, aspiration of gastric contents, dehydration and electrolyte disturbances [1,2].

A variety of prophylactic antiemetic interventions have been reported, but there has only been a limited systematic review in this patient group. In a systematic search using Cochrane Controlled Trials Register, MEDLINE and EMBASE, they found that dexamethasone and the antiserotonergic agents appear to be the most effective agents for the prophylaxis of POV in children undergoing tonsillectomy. Metoclopramide was also found to be efficacious [2].

Incidence of PONV are 20-30% after G A with volatile anesthetics, up to 70% in High Risk patients and moreover pediatric patients have a higher incidence of POV than adults, with a peak incidence of 34- 50% in school children [3]. The lowest incidence occurs in infants (5%) and preschool children have an incidence of 20%

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Received on 12.12.2016
Accepted on 13.12.2016

[4,5]. This is associated with Morbidity like Decreased patient satisfaction, Delayed hospital discharge, Unexpected hospital admission, Wound dehiscence, bleeding, pulmonary aspiration, esophageal rupture and Fluid and electrolyte disturbances. So, the present study was aimed to compare the effectiveness of anti emetic agents (Metoclopramide, Ondansetron and Granisetron) in the prevention of PONV in patients (of age group 5- 15yrs) undergoing tonsillectomy performed under GA.

Materials and Methods

This study was carried out at MNR Medical College and Hospital, Sangareddy, during the June 2014 to December 2015. 75 patients belonging to both sexes in the age group of 5- 15 years, ASA physical status I and II, undergoing tonsillectomy were enrolled. The study was approved by the Hospital Ethical Committee and informed consent from parents was obtained.

Patients were randomly divided into three groups (Group I, II and III) consisting of 25 patients each. Patients were assessed at the preoperative visit for past and present history. Routine laboratory investigations were done. Patients were weighed prior to the operation., preoperative vital parameters namely, pulse and blood pressure were noted. Written informed consent of the parents or guardians of the children were obtained. The patients were not given any solid or liquid feeds for 6 – 8 hrs prior to surgery. All patients were premedicated with IV Glycopyrrolate 0.004 mg /kg and Fentanyl 2mcg/kg

Group 1- They were Given IV Metocloproamide in the dose of 0.25 mg/kg diluted, intravenously slowly over 2- 5 minutes just prior to induction of anaesthesia.

Group 2-They were given IV ondansetron 100 mcg/ kg prior to inductrion of anaesthesia

Group 3-They were given IV Granisetron in the dose of 40 mcg/ kg diluted to 10ml with normal saline, IV slowly over 2- 5 minutes immediately prior to induction of anaesthesia

The pulse and arterial pressure (both systolic and diastolic) were recorded at 1, 5 and 10 min intervals in all the patients. The mean arterial pressure of each patient was derived using the equation.

Induction was carried out with an I V Propofol 2 mg/kg. Intubation was facilitated by using IV suxamethonium (2mg /kg). Patients were intubated orally with portex endotradheal tube of appropriate size. The throat was packed. Anaesthesia was maintained with nitrous oxide in oxygen (60:40) by controlled ventilation using either a Bain's circuit or a Jackson Rees' circuit according to the weight of the patient. Atracurium (0.5 mg/kg) was the non-depolarizing muscle relaxant used in all the patients.

Intravenous fluid used was Isolyte P or Ringer's Lactate with 50 ml of 25% dextrose added to it. Half of the preoperative fluid deficit was corrected within the first hour and the remaining half subsequently , the neuromuscular blockade was reversed with a combination of anticholinesterase, Neostigmine (0.04-0.06) diluted to 10ml with distilled water administered IV slowly.

Patients were extubated when widely awake after thorough suctioning of the oropharynx and confirming the absence of any active bleeding from the tonsillar fossae. The Patients were shifted to the recovery room.

Each episode of nausea and/ or vomiting was recorded. Scoring was done. Repeat vomiting occurring within 1- 2 min of the previous episode was recorded as a single episode of vomiting. Any side effects were also noted. Postoperatively, the recovery time was noted , as the time from the end of surgery till the recovery score was 9. Postanaesthesia Aldrete Recovery Score was calculated based on G. E Morgan et al (2006). The patient should be discharged when the total score is 10, but minimum of 9 is required.

Statistical Methods

Data obtained were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago, USA) 15.0 for windows . Kruskal – Waliis test used for comparisn of the occurrence of PONV across the groups, Bonferroni test used for listing the significant treatment groups , Chi –square test used for Gender distribution and ANOVA test used for comparing Age , Weight, Pulse rate , MAP, Duration of anesthesia across the treatment groups. $P < 0.05$ was considered statistically significant.

Results

The patients were randomly divided into 3 groups of 30 patients each. Group I received Metoclopramide 0.25 mg/kg , Group II received Ondansetron 100 mcg/ kg and Group III received Granisetron 40 mcg/kg slowly Intravenously .

With reference to age between three groups, significance was measured using analysis of variance

(two tailed, a = 0.05) across the treatment groups. As p-values (.8791, 0.4006 and 0.4285) are >0.05, we concluded that the age difference is not significant across treatment groups (table 1). Regarding the weight across three groups, significance was measured using analysis of variance (two tailed, a= 0.05) across the treatment groups. As p-values (.9972, 0.2029, 0.6119 and 0.8205) are >0.05, it was concluded that the weight difference is not significant across treatment groups.

There was no significant change in the pulse rate (beats/min) values at pre-operative, 1 min, 5 min and 10 min across treatment groups (p-values (0.9305, 0.3222, 0.5908 and 0.6554) are >0.05) which is based on significance measured using analysis of variance (two tailed, $\alpha = 0.05$) across the treatment groups.

There was no significant change in the MAP values at pre-operative, 1 min, 5 min and 10 min across treatment groups ss p-values (0.3199, 0.7142, 0.2613 and 0.1472) are >0.05 , which is based on significance measured using analysis of variance (two tailed, $\alpha = 0.05$) across the treatment groups .

Incidence of nausea and/or vomiting during 0-3 hrs after surgery is 24%, 12% and 12% in Groups I, II, and III respectively, with a P value of 0.47 (Table 2). The incidence of nausea and/or vomiting during 3-24 hrs after surgery is 44%, 20% and 8% in Groups I, II, and III respectively, with a statistically significant P value (0.01) by Kruskal Waliis Test. The only statistically significant result of the present study, which is the difference in occurance of PONV between Group I and Group III with a P value of 0.026 by Bonferroni Test (Table 3) .

Overall incidence of nausea and/or vomiting during 0-24 hrs after surgery is 48%, 28% and 16% amongst Groups I, II, and III respectively, with a P value of 0.07.

Postoperatively the recovery score was noted . From Table 4 , it is found that the recovery score of 9 , which was considered to be adequate for discharge from the

Table 1: Summary of age (yrs) across treatment groups by gender

Gender	Statistics	Metoclopramide (n = 25)	Ondansetron (n = 25)	Granisetron (n = 25)	p-value*
Male	N (%)	11(44)	14(56)	13(52)	
	Mean	8.5	8	8	0.8791
	SD	3.7	2.4	2.9	
	Median	8	8	8	
	95% CI for Mean	(6,11)	(6.6,9.4)	(6.3,9.7)	
	Range (Min, Max)	(5,15)	(5,13)	(5,13)	
Female	N (%)	14(56)	11(44)	12(48)	
	Mean	10.1	10.2	8.5	0.4006
	SD	3.3	3.6	3.4	
	Median	10	10	7.5	
	95% CI for Mean	(8.2,12.1)	(7.8,12.6)	(6.3,10.7)	
	Range (Min, Max)	(5,15)	(5,15)	(5,15)	
Overall	N (%)	25(100)	25(100)	25(100)	
	Mean	9.4	9	8.2	0.4285
	SD	3.5	3.1	3.1	
	Median	10	9	8	
	95% CI for Mean	(8,10.9)	(7.7,10.3)	(7,9.5)	
	Range (Min, Max)	(5,15)	(5,15)	(5,15)	

* p-value obtained using ANOVA (two tailed, $\alpha = 0.05$).

Table 2: Comparison of occurrence of nausea & vomiting across treatment groups

Nausea & Vomiting at	Statistics	Metoclopramide (N = xx) N (%)	Ondansetron (N = xx) N (%)	Granisetron (N= xx) N(%)	p-value*
0 – 3 hrs	N (%)	25(100)	25(100)	25(100)	
	Mean	0.32	0.2	0.2	0.4770
	Median	0	0	0	
3 - 24 hrs	N (%)	25(100)	25(100)	25(100)	
	Mean	0.56	0.28	0.08	***0.0110***
	Median	0	0	0	
0 - 24 hrs	N (%)	25(100)	25(100)	25(100)	
	Mean	0.64	0.44	0.24	0.0760
	Median	0	0	0	

* p-value obtained using **Kruskal-waliis test** (two tailed, $\alpha = 0.05$)

PACU was achieved by majority of the patients at the end of 40 minutes. So it is concluded the all the three antiemetic agents in the study have no significant effect on the recovery from anesthesia.

Out of 25 subjects in metoclopramide group, 6 (24%) subjects reported with at least one side effect. 4 (16%) subjects reported headache, 1 (4%) subject reported dizziness, 2 (8%) subjects reported drowsiness and 2 (8%) subjects reported extra pyramidal (Table 5).

Table 3: Listing significant treatment groups

Nausea & Vomiting at	Comparison Group	Test Statistic	p-value*
3 – 24 hrs	Metoclopramide vs Granisetron	2.2190	*0.0265* ˙

*p-value obtained using Bonferroni (Dunn) test (two-tailed, α= 0.05) ˙= p value is statistically significant

Table 4: Summary of post anesthesia recovery score (PARS) across the treatment groups

PARS (min)	Score	Metoclopramide (N= 25) N (%)	Ondansetron (N= 25) N(%)	Granisetron (N= 25) N(%)
0 min	6	6(24)	5(20)	3(12)
	7	14(56)	13(52)	13(52)
	8	5(20)	7(28)	9(36)
	9	0(0)	0(0)	0(0)
	10	0(0)	0(0)	0(0)
20 min	6	0(0)	0(0)	0(0)
	7	2(8)	2(8)	0(0)
	8	13(52)	12(48)	14(56)
	9	10(40)	11(44)	11(44)
	10	0(0)	0(0)	0(0)
40 min	6	0(0)	0(0)	0(0)
	7	0(0)	0(0)	0(0)
	8	4(16)	3(12)	3(12)
	9	16(64)	17(68)	16(64)
	10	5(20)	5(20)	6(24)
60 min	6	0(0)	0(0)	0(0)
	7	0(0)	0(0)	0(0)
	8	0(0)	0(0)	0(0)
	9	11(44)	9(36)	7(28)
	10	14(56)	16(64)	18(72)

Table 5: Summary of adverse effects/complications by treatment group

Side Effects/Complications	Metoclopramide (N= 25) N (%)	Ondansetron (N= 25) N(%)	Granisetron (N= 25) N(%)
No. of Side Effects	4	3	1
No. of Subjects with at least One Side Effect	6(24)	5(20)	2(8)
Headache	4(16)	4(16)	2(8)
Dizziness	1(4)	1(4)	0(0)
Drowsiness	2(8)	1(4)	0(0)
Extra Pyramidal	2(8)	0(0)	0(0)

Discussion

The incidence of PONV in children undergoing tonsillectomy is sufficiently high (up to 70%) to warrant the use of effective antiemetic prophylaxis [2].

The most extensively used antiemetic for the last thirty years for the treatment of PONV is Metoclopramide. Recently many investigators have demonstrated the effectiveness of Ondansetron,a selective 5-HT3 antagonist, for PONV with less side effects. Granisetron is a new 5-HT3 antagonist with higher selectivity and is 5-10 times more potent antiemetic agent than Ondansetron.

The present study compared the properties of the above three drugs in patients undergoing tonsillectomy under GA.

The selected 75 patients belonged to either sex in the age group of 5-15 years with a physical status I and II. The patients were divided randomly into 3 groups of 25 patients each. All patients received GA.

Group I patients received Metoclopramide, Group

II patients Ondansetron and Group III patients received Granisetron i.v. in the doses of 0.25mg/kg, 100mcg/kg and 40mcg/kg respectively, prior to the induction of anesthesia, which were shown to be the effective antiemetic doses based on previous studies [6,7].

The use of volatile anesthetic agents has been purposefully avoided because in one study by Apfel et al., they suggested that Volatile agents may be the main cause of early PONV [8].

The present study has shown that the pulse rate , MAP, and the post anesthesia recovery are not significantly affected by any of the antiemetic agents used .

The P values for pulse rate at preoperative period, 1min, 5min, 10min are 0.93, 0.32, 0.59, 0.65 respectively, all of which are statistically insignificant.

The P values for MAP at preoperative period, 1min, 5min and 10min are 0.31, 0.71, 0.26, 0.14 respectively, all of which are statistically insignificant.

The Post Anesthesia Recovery Score of 9, which was considered as adequate for discharge of the patient from PACU, was achieved by majority of the patients in all the 3 groups at the end of 40 minutes postoperatively. The above results concur the finding of previous studies [9,10].

Previous studies suggest that Risk of POV increases with duration of surgery and anaesthesia, possibly because of greater accumulation of emetogenic anaeshetic angents [5]. In the present study the mean duration of anesthesia for Group I , II and III was 40.4, 42.8 and 41.6 minutes respectively and the difference amongst the 3 Groups was insignificant.

The common side effects of the traditional antiemetic agents like Headache, Dizziness, Drowsiness, Extrapyramidal effects, dirrhoea, constipation etc. have been compared amongst the 3 Groups .

We found that the number of patients with at least 1 side effect were 24%, 20%, and 8% amongst the Gr I, II and III respectively.

The incidence of Headache was seen in 16% of patients from Gr I and II each as compared to 8% from Gr III. Dizziness was observed in 1 (4%) patient from Gr I and II as compared to 0% in Gr III. Drowsiness was seen in 8% patients from Gr I as compared to 4% in Gr II & 0% in Gr III. Extrapyramidal effects in the form of Dystonia were found in 2 (8%) patients only from Gr I .

This concludes that Granisetron causes much less side effects as compared to both metoclopramide and Ondansetron and the Extrapyramidal side effects can occur with Metoclopramide .

The monitoring of nausea and vomiting during 0-3 hrs and 3-24 hrs after tonsillectomy and it's scoring (0=no nausea and vomiting, 1= only nausea and 2= vomiting) in the present study is similar as in a study by Fujii et al [11].

In a study conducted by Fujii et al (1996) [12] using Granisetron 40 mcg/kg i.v. in children undergoing strabismus surgery and Tonsillectomy , incidence of PONV was 12% in 24 hrs after the surgery which can be compared with the incidence of 16% in our study.

As per Matti Aapro [13], Granisetron is a potent and highly selective 5-HT3 antagonist that has little or no affinity for other receptors, acharacteristic that is thought to underly the favorable side effect and the safety profiles of this agent. In our study also Granisetron caused the least side effects as compared to Metoclopramide and Ondansetron.

Thus, the present study indicates that Granisetron in a dose of 40 mcg/kg is more effective than Metoclopramide in the long term prevention of PONV in the children undergoing tonsillectomy under GA. This result is similar to the one obtained in a study conducted by Fujii et al [11] in patients undergoing major gynecological surgeries.

Conclusion

Metoclopramide, Ondansetron and Granisetron when administered intravenously in the doses of 0.25 mg/kg, 100 mcg/kg and 40 mcg/kg , do not have significant effect on the vital parameters like pulse rate and MAP in children undergoing tonsillectomy under General anesthesia. Our study showed that Granisetron is highly effective in the long term prevention of PONV in children undergoing Tonsillectomy as compared to Metoclopramide and is associated with minimum side effects and higher patient satisfaction as compared to both Metoclopramide and Ondansetron.

References

1. Lawrence S. Friedman, Kurt J. Isselbacher : Nausea, vomiting and Indigestion In; Harrison's "Principle of Internal Medicine" 14th edition ; United States of America; McGraw Hill companies; 1998; Chapter 41: 230.
2. C. M. Bolton, P.S Myles, T. Nolan, and J. A Sterne:

Prophylaxis of Postoperative Vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis; British Journal of Anesthesia 2006; 97(5):593-604.

3. Gordon Yuill and Carl Gwinnutt. Postoperative Nausea and Vomiting. In : Keith G. Allman, Iain H. Wilson editor- "Oxford Hand book of Anaesthesia" Second edition , Oxford University press, 2006: 40: 1050- 54.
4. Cohen MM, Cameron CB, Duncan PG . Pediatric anesthesia morbidity and mortality in the perioperative period. Anesthesia Analgesia 1990; 70:160- 7.
5. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992; 77:162-84.
6. Watcha Mehernoor F, Bras, Paul J. Cieslak, Gary D Pennant, John H. The Dose- Response Relationship of Ondansetron in Preventing Postoperative Emisis in Pediatric Patients Undergoing Ambulatory Surgery. Anaesthesiology 1995; 82(1):47-52.
7. Cieslak, Gary D, Watcha Mehernoor F, Phillips, Michael B, Pennant, John H. The Dose- Resoponse Relation and Cost-effectiveness of Granisetron for the prophylaxis of Pediatric Postoperative Emesis. Anaesthesiology 85(5):1076-1085.
8. C C Apfel , P.Kranke, M. H. Katz, C. Geopfert, T. Papenfuss, S. Rauch, R. Heineck, C. A. Greim and N. Roewer. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: A randomized controlled trial of factorial design. British Journal of Anaesthesia 2002; 88(5):659-668.
9. Pankaj Jay Pasricha , Treatment Of Disorders Of Bowel Motility and Water Flux ; Antiemetics; Agents used in Biliary and Pancreatic Disease In; Laurence L. B., John S. L. ,Keith L. P. Editor , "Goodman & Gilman's The Pharmacological Basis Of THERAPEUTICS' Eleventh Edition , McGraw Hill Companies , U.S.A , 2006; 37:1001-1003.
10. Paul F. White and Alejandro Recart Freire. Ambulatory (Outpatient) Anesthesia. In: Ronald D. Miller Edited "Miller's Anesthesia' sixth Edition, ELSEVIER Churchill Livingston, 2005; 68:2597-99.
11. Y Fujii , H Tanaka , H Toyooka . Reduction of Postoperative Nausea and Vomiting with Granisetron. Canadian Journal Of Anesthesia 1994; 41:291-294.
12. Y Fujii, H Tanaka and H Tayooka. Granisetron reduces vomiting after strabismus surgery and tonsillectomy in children. Canadian Journal of Anaesthesia 1996 ; 43:35-38.
13. Matti Aapro. Granisetron: An Update on its Clinical use in the Management of Nausea and Vomiting. The Oncologist, Alpha Med Press 2004; 9(6):673-686.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.6

Comparison of Intrathecal Adjuvants with Levobupivacaine in Lower Limb Surgeries

Richa Chandra*, Mahesh Kashyap, Nivedita*****

Abstract

Background and Aim: Studies and research are ongoing to find appropriate adjuvants tointrathecal local anaesthetic agents to make them more effective and economical. In view of the same we undertook a study with Levobupivacaine,being a newer agent with more cardiac stability and compared the outcomes with 3 adjuvants.

Settings and Design: After approval from the hospital ethical committee, a randomized double blind study was conducted among 90 healthy, American Society of Anesthesiologists ASA I and II patients, scheduled forlower limb surgeries.The study wasdone over a period of one year.

Materials and Methods: Spinal block was administered in L3 and L4 intervertebral space, using 0.5% Levobupivacaine 12mg. Adjuvants added in group 1- Fentanyl 25 mcg, in group 2- Dexmedetomidine 10mcg and in group 3 - Clonidine 30mcg. Anaesthetic level achieved was T10. Onset time to achieve sensory, motor blockade, and their regression time was noted. Hemodynamic changes and requirement for other analgesic drugs was also noted.

Results: 90 patients were enrolled in our study. The data was recorded and analysed using statistical analysis.

Conclusion: To conclude, Levobupivacaine with Dexmedetomidine, gavebetter result for intra and postoperativeregionalanaesthesia without any adverse effects.

Keywords: Adjuvants; Intrathecal; Levobupivacaine; Dexmedetomidine; Fentanyl; Clonidine.

Introduction

Spinal anaesthesia is an accepted technique for lower limb surgeries. Anaesthesiologists are searching for such compounds for intrathecal use which can provide good relaxation, less hemodynamic disturbances and prolonged analgesia. Levobupivacaine (an Sisomer of Bupivacaine) is the most recent such addition [1]. It has less adverse CVS and CNS side effects. Studies on using adjuvants with Levobupivacaine are relatively few.Adding adjunct allows reduction in dose of Levobupivacaine and provides CVS stability.

Fentanyl and Clonidine are being used in spinal anaesthesia to improve the quality of anaesthesia blockade and for prolongation of post operative analgesia [2].

A newer alpha 2 agonist, Dexmetodomidine, is on theway to be added in the list of adjuvants. In our study, we compared the effects of various adjuvants added to Levobupivacaine.

Material and Methods

After approval from hospital's ethical committee, we selected 90 patients in our institute, aged 18 years – 55 years. Patients with American Society of Anaesthesiologists (ASA) physical status I and II, posted for lower limb surgeries,closed procedures (e.g. Tibia and Femur interlocking,arthroscopies) during the period between Oct 2013 to Feb 2014, were selected through closed envelope technique. Design of the study was a prospective randomized double blind study. We excluded, patients with American Society of Anaesthesiologists (ASA) physical status III / IV/V; patients with BMI > 30 and <20; patients on any alpha adrenergic blocker drugs e.g. Prazosin, and H/O drug allergy to the drugs, used in the

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Received on 20.12.2016
Accepted on 28.12.2016

study. Completegeneral physical examination and laboratory examination (completeblood count, fasting blood sugar, S.Urea, S.Creatinine, S.electrolytes, PT/ PTT,ECG and CXR)weredone to rule out any abnormality. The patients were admitted, one day prior tosurgery. They werecounseled about the regional anesthesia and informed consent was taken.

Tab Alprazolam 0.25 mg was prescribed night before and at 6 AM, on the day of surgery,with sips of water, to allay anxiety.For aspiration prophylaxis, Inj. Ondansetron 4mg IV was givenhalf an hour before the surgery.

In operation room, standard monitors,i.e., ECG, SPO_2, NIBP, HRf were attached to the patients. All patients were preloaded with RL 500 ml. After ensuring all aseptic precautions, and local skin infiltration of 2 ml of 2% Lignocaine, lumbar puncture was done with 27G Quincke spinal needle at L3-L4 space. A third observer injected the drug after ensuring free flow of clear CSF. Oxygen through facemask was given to each patient.After following

Bromage Zero	the patient has free movement of legs and feet
Bromage 1	the patient is just able to flex knee with free movement of feet.
Bromage 2	the patient is unable to flex knee, but free movement of feet.
Bromage 3	the patient is unable to move the leg and feet

exclusion criteria, 90 patients were randomized into 3 groups by a computer generated list.

Ingroup 1-Levobupivacaine 0.5% 12 mg + 25 mcg Fentanyl, ingroup 2-Levobupivacaine 0.5%12mg + 10mcg Dexmedetomidine andin group 3-Levobupivacaine 0.5% 12mg +Clonidine 30mcg were administered.In group2- 0.4 mland in group 3-0.3mlpreservative freenormal saline was added to make volume in all groups the same.The drug was prepared by the third observer,who was unaware about the study.

After the block, the time of sensory block up toT10 and grade 3Bromage motor block was assessed before the start of surgery[3]. Time was set at zero when the subarachnoid block was administered.

Hypotension[SBP fall> 30% from baseline or < 90mm Hg] and bradycardia [HR<50 bpm] were noted. The other adverse effects viz. nausea, vomiting, shivering, pruritus, sedation and respiratory depression were noted.

Time of recovery of S_1dermatome and complete recovery from motor block, i.e. Bromage 0 was also noted.Vital parameters were also noted.

Results

SPSS statistical software(16.0) was usedfor data analysis. In this study p value< 0.05 has been considered as statistically significant. To calculate the sample size, a power analysis of α=0.05 and β=0.80, showed that 30 patients per study group were needed. Datas are expressed as mean and standard deviation. For comparing, the two main groups,

Table 1: Comparison of demographic data amongst groups

	Group1	Group 2	Group 3	p value		
				B/T group 1 and 2	B/T 2 and 3	B/T 1 and 3
Age in years	46.6±6.91	39±15.47	38.2±9.76	0.403	0.928	0.127
Height in cm	166.5±3.30	165±4.35	161±1.29	0.650	0.320	0.076
Weight in Kg	68.25±3.11	63.5±2.72	61.75±2.13	0.086	0.432	0.05
BMI[Kg/M²]	24.57±0.165	23.35±0.65	23.67±1.05	0.176	0.772	0.104

Abbreviation-B/t-Between

Student t test was applied. For qualitative assessment, Chi Square test was done.

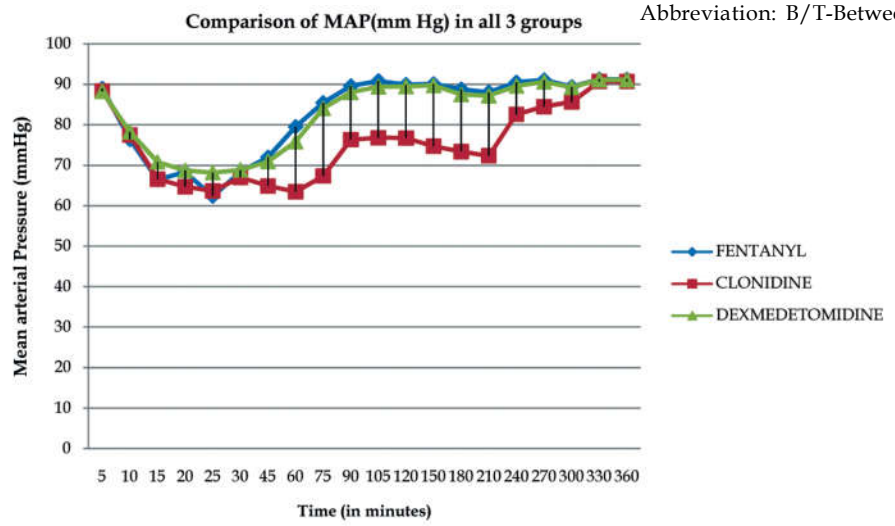
Demographic data, in all groups are comparable, because p value is not significant.

Time to achieve sensory level up to T10 dermatome level and time to achieve complete motor block i.e.Bromage grade 3 were found to be significantly longer in group 3. (p value< 0.05 shown in chart). Time for complete reversal of sensory block or regression time to S1 was significantly longerin group 2 approx 470±5.38 minutes [p<0.05]. Time for complete regain of motor block orBromage 0 was also significantly longerin group 2. There is no statistical difference, between the groups relative to baseline MAP and HR values.Study was done up to 480

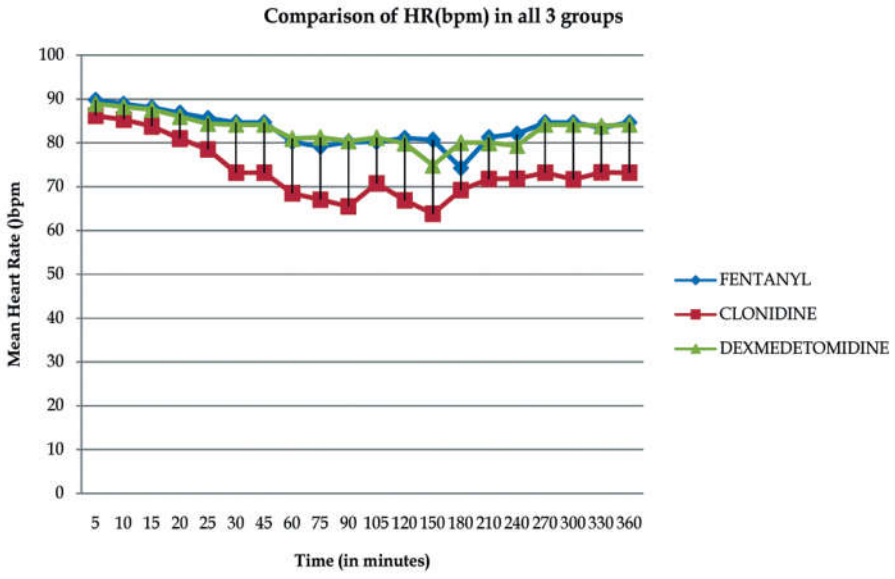
Table 2: Comparison of Spinal Block Characteristics amongst groups

	Group 1	Group 2	Group 3	p value B/T group 1 & 2	p value B/T Group2 & 3	p value B/T Group 1 & 3
Time to onset of sensory block	2.84±0.96	4.17±1.11	6.28±1.2	0.00	0.00	0.00
Time to onset of motor block	2.5±0.59	2.94±0.95	7.95±0.55	0.051	0.00	0.00
Time to achieve sensory level up to T10	5.25±0.87	5.04±0.84	7.94±1.02	0.396	0.000	0.00
Time to achieve Bromage3	6.12±0.80	6.17±0.67	8.44±0.78	0.746	0.00	0.00
Time to regression to S1	257.96±4.29	470±5.38	309±3.52	0.00	0.00	0.00
Time to achieve Bromage 0	215.73±4.36	422.33±5.24	286±7.070	0.00	0.00	0.00

Abbreviation: B/T-Between



Graph 1:



Graph 2:

minutes.

Although, group 3 showed slight fall in values, but that is not significant statistically.

Three patients in group 1, 4 patients in group 2 and 8 patients in group 3developed hypotension. It was managed with inj.Ephedrine and IVfluids[p >0.05]. Four patients in group 1, three patients in group 2 and six patients in group 3 developed bradycardia. It responded well to inj. Atropine 0.6 mg [p>0.05]. Only patients of group 1(Fentanyl) had pruritus, which was absent in Dexmedetomidine group. It was found to be significant [p<0.05]. Incidence of nausea, in all three groups were very low and statistically non significant. Mild sedation was significantly present,in group 2and 3 [p<0.05]

Discussion

Levobupivacaine is a

longer acting local anaesthetic, with pharmacological structure similar to Bupivacaine and with a larger safety margin. Levobupivacaine has less inotropic effects and produces less prolongation of QTc interval, than Bupivacaine.It also has less depressant effect on AV conduction and QRS duration. Glacer C. compared it with racemic Bupivacaine in elective hip replacement cases and demonstrated thatLevobupivacaine is less cardio and neurotoxic[4].

Availability of relatively few studies of Levobupivacaine with adjuvants prompted us to compare effects of adding different adjuvants to Levobupivacaine. Fentanyl as an intrathecal adjuvant, is being used for years. The addition of Fentanyl 15mcg demonstrated sparing effect on requirement of Levobupivacaine with least hemodynamic variations[2]. It was found in some studies that time taken for maximum sensory and motor block was shorter in Bupivacaine + Fentanyl group in caesarean sections than in Levobupivacaine + Fentanyl group[5]. Fentanyl group showed shorter anesthesia phase than Dexmedetomidinegroup but was associated with side effects like pruritus.

Dexmedetomidine, a novel α_2 agonist potentiates local anaesthetic action, prolongs postoperative analgesia and has dose dependent sedative effect.The stimulation of α_2 receptor, decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter releaseleading to its various effects such as hypotension, brady cardia, sedation and analgesia[6,7,8]. Studies by Shubhi M. et al and collegues have shown the prolongation of spinal block by intrathecal 5mcg and 10 mcg, Dexmedetomidine has no effect on BP or HR[9,10]. Keshav and his collegues used Dexmedetomidine 10 mcg with intrathecal Bupivacaine without significant hypotension[11]. Al Mustafa et al, added 5 and 10 mcg Dexmedetomidine to intrathecal Bupivacaine 12.5 mg for urological procedures.They noted shorter onset and prolonged duration of block without significant side effects[12]. We did not get statistically significant hypotension in our study, as we were using Levobupivacaine, which as discussed earlier has least cardiotoxiceffects.Also by its nature Local anaesthestics reduce BP by decreasing the sympathetic outflow.But the intrathecal local anaesthetics, already producemaximum blockade of sympathetic outflow so intrathecalDexmedetomidine does not have scope to lower down BP. This explains, the absence of large variations in haemodynamic profiles in our study even if we used large amount of drug intrathecally[13,14]. Group 2 showed more prolongation of anaesthesia blockade than other groups.

Clonidine, a selective partial α_2 agonist is successfully being used to prolong sensory and motor block of local anaesthetics.Its effect is mediated through the activation of postsynaptic α_2 receptors in substsansiagelatinosa of spinal cord. Sethi et al and collegues demonstrated prolongation of the effect of intrathecal Bupivacaine by addition of Clonidine in gynaecological surgeries [15]. In our study, Group 3 developed same height of block after little duration of time($p<0.05$), but the effect did not last for a longer duration in comparison to Dexmedetomidine group. Niemi et al, used very high concentration of Clonidine intrathecally [3mcg/kg], which resulted in profound hypotension[16]. Van Tuijl I et al showed significant out come when used Clonidine in a very low concentration [15mcg][17]. We used very low dose 30mcg Clonidine, which had no significant effect on HR and BP butwith mild sedation. The effect of Clonidine lasted less than the Dexmedetomidine group but longer than the Fentanyl group.

So, to conclude, Levobupivacaine with Dexmedetomidine provides a better choice for intraoperative an aesthesia as well as for postoperative analgesia without any adverse effects.

Conclusion

There is a constant search for intrathecal adjuvant which can prolong the blockwithout causing hemodynamic disturbances.In our study, Dexmedetomidine group showed significant prolongation of spinal block than other groups without causing significant hemodynamic disturbances.

References

1. Update on LA: focus on levo B. Crina L Burlacu andDonal J Buggy. TherClinRisk Manag. Apr 2008; 4(2):381-392, published online Apr 2008.
2. G. Edward Morgan Maged S Mikhail, Regional Anaesthesia and Pain Management in Clinical Anaesthesia. 3rd Edition, New York Mcgrow Hill 2002.p.29.
3. ThakurA, Bhardwaj M, KaurK, DurejaJ, HoodaS, TaxakS, Intrathecal Clonidine as an adjuvant to hyperbaric Bupivacaine in patients undergoing inguinal herniorraphy:A randomized double blind study, Journal of Anaesthesiology, Clinical Pharmacology 2013; 29(1):66-70.

3. Glaser C, Morhofer P, Zimfer G, Heinz M, Sitzwohl C, Levobupivacaine versus racemic Bupivacaine for SA, Anaesth Analg, 2002 Jan; 94(1):194-8.
4. AggenTurAggen Turkmen, DonduGencMoralar, Ahmet Ali, AyselAltan,Comparison of the anaesthetic effects of intrathecalLevobupivacaine and Fentanyl and Bupivacaine + Fentanyl during caesarean section. MEJAnaesth 2012; 21(4).
5. Gentler R, Brown HC, Mitchell DH, Dexmedetomidine a novel sedative analgesic agent Proc,(BaylUniv Med Cent) 2001 Jan; 14(1):13-21.
6. Venn R, Hell J, Ground R, Respiratory effects of Dexmedetomidine in the surgical patient requiring intensive care, crit care. 2000; 4(5):302-308.
7. Ahmed SobhyBaruni, HodaAlsaid Ahmad Egg, Dexmedetomidine as supplement to low dose Bupivacaine spinal anaesthesia for knee Arthroscopy, Egyptian J of Anaesthesia, 2014 April; 30(2):149-153.
8. SubhiM et al, AlGhanem S et al, Marsad I M et al, effect of adding Dexmedetomidine versus Fentanyl to intrathecalBupivacaine on spinal block characteristics in gynaecological procedures, A double blind controlled study, American J of Applied Sciences 2009; 6(5): 882-887.
9. Mariann A. Haselman, CRNA, MSNA, Dexmedetomidine, A useful adjunct to consider, in some high risk situations, AANA Journal. Oct 2008; 76(5):335-339.
10. KeshavGovindRao,Manoj Kumar Chaurasiya, Pawan Kapoor, Aparna Shukla, Randomized controlled double blind study to compare, Dexmedetomidine 5mcg and 10mcg as an adjuvant to intrathecal Bupivacaine; International journal of scientific research 2013 Dec 2(12). ISSN. 2277-8179.
11. Al mustafa MM, Abu Halawah SA, Aloweidi AS, Murshidi MM,Ammari BA, Awwad ZM et al; effect of Dexmedetomidine added to spinal Bupivacaine for urological procedures; Saudi med J 2009; 30:365-7.
12. Klimmschaw, Chairi A, Kraft P, Plattner O, Talisimk Meyer N, Weinstabl C, Schneider B - Haemodynamic and analgesic effect of Clonidine added respectively to continuous epidural and spinal blocks, anaesthanalg, 1995; 80(2):22.
13. Hula EA Eid MD, Mohammad A Shafie, HendYoussuf,doserelated prolongation of hyperbaric Bupivacaine,spinalanaesthesia by Dexmedetomidine, AIN Shams journal of anaesthesiology, 2011 July; 4(2):83-95.
14. Sethi B.S., Samuel Mary, Sreevastav D, Efficacy of analgesic effects of low dose intrathecal Clonidine as adjuvant to Bupivacaine, Indian J of Anaesthesia, 2007; 51(5):415-419.
15. NiemiL, Effects of intrathecal Clonidine on duration of Bupivacaine SA, hemodynamics and postoperative analgesia in patients undergoing knee arthroscopy, Acta AnaesthesiolScand 194; 38:724-8.
16. Van Tuijl I et al,Intrathecal low dose hyperbaric Bupivacaine Clonidine combination in outpatient knee arthroscopy ;a randomized controlled trial Acta Anaesthesiol Scand, 2008; 52(3):343-9.

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Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.7

Effect of Clonidine and Nitroglycerine Infusion on Haemodynamic and Intraocular Pressure in Laparoscopic Cholecystectomy

Sarita Kumari*, Prakash Kumar Dubey**

Abstract

Background: In comparison to open surgery laparoscopic cholecystectomy is beneficial. Nevertheless, pneumoperitoneum and the alteration because of patient position causing pathophysiological offers limitation in anaesthetic management. We designed a study to observe the changes on heart rate and blood pressure, intraocular pressure and end-tidal carbon dioxide pressure due to use of clonidine and nitroglycerin during laparoscopic cholecystectomy.

Method: The study included 60 patients belonging to American Society of Anesthesiologists class I-II, planned for elective laparoscopic cholecystectomy were randomly divided into 2 groups: Clonidine infusion was given in group 1 at the rate of 1.5 µg/kg/hr and Group II received nitroglycerine infusion at the rate of 0.5 µg/kg/min (30µg/kg/hr). The parameters observed included mean arterial blood pressure, heart rate, end tidal CO_2, and intraocular pressure.

Results: The groups were comparable with no significant differences in gender and age. Heart rate of the patients were observed at preinduction, at intubation and after intubation at at interval of 5 minutes onwards upto reversal. Heart rate comparison after 15 minutes onwards upto reversal between group I and II showed statistically significant difference. Mean arterial pressure comparison between group I and II showed insignificant difference. Mean IOP at the time of induction in group I and II was 16.27±3.06 and 18.13±2.80 respectively, which was significant statistically. ETCO2 difference between the groups was not statistically significant.

Conclusion: The findings in our study suggested that clonidine surpass nitroglycerin in effectiveness with regard to prevent hemodynamic parameters changes and IOP induced by insufflations of CO2 in laparoscopic cholecystectomy. Also there is no significant hypotension requiring stopping of infusion or further treatment.

Keywords: Clonidine; Nitroglycerin; Laparoscopy; Cholecystectomy; Intraocular Pressure**.**

Introduction

The benefits of laparoscopy cholecystectomy has made it the gold standard for treatment of cholelithiasis [1]. Laparoscopy however requires CO2 for pneumoperitoneum.

Pneumoperitoneum causes physiological changes comprising of increase in arterial pressure and increase in pulmonary and systemic vascular resistance (PVR and SVR) early after the beginning of intra-abdominal insufflation with minor change in heart rate (HR).Studies have shown a reduction of 10% to 30% in cardiac output[2-4]. Any major alteration in arterial pressure can be detrimental for increase chances of adverse events in patients with pre-existing ischemic cardiac disease, essential hypertension, or increased intra-ocular or intra-cranial pressure.

Both pneumoperitoneum and patient positioning can synergistically increase the problems encountered during laparoscopic surgeries. [2,3]. Stimulation of the sympathetic nervous system by pneumoperitoneum and hypercapnia cause vasopressin and catecholamine release[5,6]. Drugs like beta-blockers, α_2 adrenergic agonists and opioids are used often to overcome the pneumoperitoneum induced

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Received on 19.12.2016

Accepted on 22.12.2016

circulatory response [2,7,8].

Clonidine has 9-12 hrs of half life and is a selective α_2 adrenergic agonist. It has central sympatholytic effect and causes fall in the blood pressure and hear rate with decreased cardiac output and systemic vascular resistance. In addition it nullifies the surgical stimuli induced and reduces the anesthetic and narcotic drug doses [9].

Intraocular pressure (IOP) normal range varies from 10-22 mm Hg andmaintained by several factorswhich includes the volume of intraocular fluid such as blood, venous congestion of the orbital veins, aqueous humor, the lens and the vitreous [10]. There is increase in IOP during laparoscopic surgerydue to physiological changes such as increase of blood pressure, end tidal carbon dioxide pressure and central venous pressure, which are the results of the postural changes and increased pressure in intrathoracic compartment [11]. The effects of nitroglycerine (NTG)on IOP have been studied with variable results [12-15].

Therefore, we designed randomized cross sectional to study the changes in heart rate, blood pressure , end tidal carbon dioxide ($EtCO_2$) pressure, and IOP associated with clonidine and nitroglycerin during laparoscopic cholecystectomy.

Methodology

Sixty patients(n=60) [American Society of Anesthesiologists class I or II] undergoing elective laparoscopic cholecystectomy were included in the study. The study was conducted after approval from the Institutional Ethics Committee. We excluded the patients who were younger than 20 years and older than 65 years; having acute or chronic opthalmic disease; pre-existing ocular hypertension and chronic lung diseases. This trial was registered by with Central Trial Registry of India (www.ctri.nic.in) having the registration number ***CTRI/2015/01/005434***

The patients were randomly divided into 2 groups: Group I received clonidine infusion at the rate of 1.5 µg/kg/hr and Group II received nitroglycerine infusion at the rate of 0.5 µg/kg/min (30µg/kg/hr). Randomization of the patients was achieved using a computer generated table.

Tablet alprazolam 0.5mg and tablet ranitidine 150 mg orally in night before surgery as pre-medication. All baseline readings were taken in the operating theater monitors displaying heart rate, electrocardiogram, noninvasive blood pressure, oxygen saturation, and $EtCO_2$ pressure. Patients were given intravenous pentazocine in a dose of 0.5 to 0.7 mg/kg body weight. After preoxygenation, the patients were induced with injection propofol 2mg/kg. Tracheal intubation was facilitated with vecuronium in dose of 100µg/kg body weight. Anaesthesia was maintained with oxygen, N_2O, isoflurane along with intermittent positive pressure ventilation (IPPV) and intermittent vecuronium. After induction and beforecreating pneumoperitonium infusion was started.

Rate of infusion was decreased to half if the value of mean arterial blood pressure decreases by 20% of baseline value, rate of infusion was doubled if the value of mean arterial blood pressure increases by 20% of baseline value. Infusion was terminated if the value of mean arterial blood pressure becomes less than 60mmHg. Infusion was stopped in all patients before reversal of neuromuscular blockade. Ringer lactate was administered at the rate of 15ml/kg in 1st hour followed by 7.5ml/kg/hr till the end of surgery to all patients.

The parameters observed were heart rate, mean arterial blood pressure, $EtCO_2$ pressure, and IOP. The heart rate, mean arterial blood pressure were measured just before induction, after induction, and therafter every 5 minutes until reversal. The $EtCO_2$was also observed every 5 minutes after induction until reversal. IOP was measured before induction, after startingthe infusion and 15minute thereafter, by Schiotz tonometer.

The mean and standard deviation of the parameters studied during observation period were calculated for two treatment groups and compared using Student t test. Intragroup comparison was done with Paired t- test. The critical value of 'p' indicating the probability of significant difference was taken as<0.05 for comparisons.

Results

There were no significant differences between two groups with respect to age and gender. Table 1 shows patient's heart rate in 2 groups. The patient's heart rate was observed preinduction, at the time of intubation and after intubation at every 5 minutes onwards upto reversal. The comparison of heart rate between group I and II showed statistically significant difference after 15 minutes onwards upto reversal.

Table 2 compares intergroup mean arterial pressure. Intergroup comparison of mean arterial

pressure between group I and II showed no significant difference.

Table 3 shows comparison of inter group IOP. At the time of pre induction mean IOP between group I and II was statistically not significant. At intubation mean IOP between group I and II was 16.27±3.06 and 18.13±2.80 respectively. At the time of reversal mean IOP in group I and II was 14.07±2.51 and 14.87±2.06 respectively (p = 0.184).

Table 4 compares intergroup $EtCO_2$ which is not significant. The mean change in $EtCO_2$ at 5 minutes between group I and II was 40.77±3.14 and40.80±2.14 respectively and at the time of reversal mean $EtCO_2$ was 34.27±1.17 and 34.77±1.07 respectively.

Table 1: Intergroup comparison of heart rate

Time interval	Group 1 Mean±SD	Group 2 Mean±SD	t-value	p-value
Preinduction	76.07±16.98	71.00±16.65	1.167	0.248
Induction	77.97±14.28	73.03±16.01	1.259	0.213
5min	74.60±14.43	76.50±16.08	-0.482	0.632
10min	71.87±13.42	78.27±15.47	-1.711	0.092
15min	69.50±13.74	80.23±15.54	-2.833	0.006
20min	67.53±13.14	83.47±15.41	-4.308	<0.001
25min	66.83±12.30	86.07±15.93	-5.147	<0.001
30min	62.65±12.25	87.67±13.27	-6.262	<0.001
35min	64.73±11.51	91.47±14.89	-5.499	<0.001
40min	62.83±13.23	90.90±19.02	-4.072	0.001
Reversal	65.77±10.38	94.00±15.70	-8.214	<0.001

Table 2: Intergroup comparison of mean arterial pressure (MAP)

Time interval	Group 1 Mean±SD	Group 2 Mean±SD	t-value	p-value
Preinduction	82.60±9.05	79.53±8.13	1.380	0.173
Induction	82.00±8.32	78.13±7.76	1.861	0.068
5min	103.47±133.84	75.60±7.43	1.139	0.260
10min	77.17±7.34	72.90±7.32	2.253	0.028
15min	74.87±7.00	71.30±6.95	1.979	0.053
20min	72.53±6.61	69.27±7.28	1.818	0.074
25min	70.34±6.80	66.97±8.02	1.729	0.089
30min	68.50±6.45	67.83±6.63	0.337	0.738
35min	65.20±5.69	66.00±6.09	-.371	0.713
40min	63.33±4.11	62.00±4.89	0.694	0.496
Reversal	65.80±6.33	63.87±6.01	1.213	0.230

Table 3: Intergroup comparison of intraocular pressure (IOP)

Time interval	Group 1 Mean±SD	Group 2 Mean±SD	t-value	p-value
Preinduction	17.80±1.90	18.50±2.06	-1.366	0.177
Induction	16.27±3.06	18.13±2.80	-2.464	0.017
5min	-	-	-	-
10min	-	-	-	-
15min	14.73±2.76	16.03±2.37	-1.955	0.055
20min	-	-	-	-
25min	-	-	-	-
30min	14.05±2.97	14.95±1.93	-1.145	0.259
35min	-	-	-	-
40min	-	-	-	-
Reversal	14.07±2.51	14.87±2.06	-1.346	0.184

Table 4: Intergroup comparison of end- tidal carbon dioxide($EtCO_2$)

Time interval	Group 1 Mean±SD	Group 2 Mean±SD	T-value	P-value
Preinduction	-	-	-	-
Induction	-	-	-	-
5min	40.77±3.14	40.80±2.14	-.048	0.962
10min	39.30±2.43	39.57±1.97	-.465	0.643
15min	37.73±2.10	37.87±1.83	-.262	0.794
20min	35.80±1.86	36.33±1.70	-1.155	0.253
25min	35.62±1.49	35.41±1.52	0.521	0.604
30min	35.00±1.29	35.14±1.76	-.294	0.771
35min	35.40±1.29	35.27±1.10	0.303	0.764
40min	33.83±0.93	34.40±0.96	-1.392	0.179
Reversal	34.27±1.17	34.77±1.07	-1.723	0.090

Discussion

In recent years, laparoscopic surgery has become a common clinical practice with laparoscopic cholecystectomy being the most frequent. From anesthetic point of view an appraisal of the complication of hemodynamic alterations due to pneumoperitoneum, increase in intra-abdominal pressure and procedure related are essential. For upper abdominal laparoscopic surgery general anesthesia is the choice of anesthesia. Protection of airway is done by tracheal intubation and intermittent positive pressure ventilation(IPPV) and for normocarbia control of pulmonary ventilation is required. To control these haemodynamic changes which could be devastating present study was done to compare effects of clonidine and nitroglycerine.

In group I clonidine showed significant decrease in heart rate($p<0.05$). Clonidine, when used as intravenous infusion, intramuscular or orally, maintains haemodynamic stability during pneumoperitoneum by minimizing the heart rate variability as found in other studies [16-18].

In clonidine group out of 30 patients, heart rate was increased in 15 patients (50%) as response to intubation. However, heart rate fell significantly after 10 minutes of intubation ($p <0.05$). In our study Clonidine onset of action was more than 5 minutes. Fall in heart rate was observed after 20-30 minutes which was statistically significant. The peak plasma concentration of clonidine occur after 30 minutes. Heart rate was slightly increased during reversal as before reversal clonidine infusion was stopped.

In nitroglycerin group after intubation upto reversal increase in heart rate was observed which was statistically significant ($p<0.05$). The onset of action was observed to be 1-3 minutes. Nitroglycerine infusion was used in low dose in our study. As NTG at low doses preferentially dilate the veins more than the arterioles, it causes fall in mean arterial pressure, a decrease in blood pressure and might increases heart rate. Venodilation decrease size of both ventricles and end-diastolic pressures, however there is only minor change in systemic vascular resistance. Studies have shown that intravenous NTG causes vasodilation in coronaries before any changes in systemic haemodynamic. Also in another studythe heart rate began to augment after 1min in the healthy subjects after sublingual administration which became normal within 30minute [19-21].

After15 minutes of intubation and up to reversal heart rate difference between both groups was found statistically significant, as nitroglycerine causes rise in heart rate wheras clonidine attenutes heart rate (Table 1). Both clonidine and NTG caused decrease in mean arterial pressure however the difference was not significant (Table 2). Similar studies have shown the effect of premedication with clonidine in maintaining perioperative haemodynamic stability.

NTG has vasodilator effect on both veins and arteries. NTG nullify the rise in MAP and SVR . In laparoscopic surgery NTG infusion causes decrease in after load which cause marked haemodynamic improvement as it causes vascular smooth muscle relaxation. NTG infusion was stopped in 6 patients out of 30 (20%) because MAP fall less than 60mmHg. None of the patient in clonidine group developed hypotension.

Nitroglycerine decreases IOP by preventing increase of SVR and modulating aqueous humor dynamics. Preinfusion and postintubation rise in IOP in both groups due to intubation response. In laparoscopic cholecystectomy low dose nitroglycerin infusion might be beneficial to decrease IOP at the time of pneumoperitoneum. There was fall in IOP by both clonidine and nitroglycerine (Table 3) which is consistent with studies done elsewhere [22,23].

There is significant decrease in $EtCO_2$ by both clonidine and nitroglycerine infusion which persisted upto reversal. The fall in $EtCO_2$ was due to decrease in blood pressure that can decreases lung perfusion.

The findings of our study suggested that, clonidine was found more effective than nitroglycerine preventing change in haemodynamic parameter and IOP. Comparative studies between clonidine and NTG are sparse. Limitations of the study includes low sample size. More studies with large population is needed to validate this result.

References

1. Cunningham AJ, Brull SJ. Laparoscopic Cholecystectomy: Anesthetic implications. Anaesth Analg. 1993; 76:1120–33.
2. Joris J.Anesthetic management of laparoscopy.In – Miller's Anesthesia5th ed. New York: Churchill Livingstone; 1994.p.2011–2029.
3. Wabha RW, Beique F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy.Can J Anaesth 1995; 42:51-63.
4. Sharma KC, Brandstetter RD, Brensilver JM, Jung LD. Cardiopulmonary physiology and pathophysiology as a consequence of laparoscopic

surgery. Chest 1996; 110:810-5.

5. Naude GP, Ryan MK, Pianim NA, Klein SR, Lippmann M, Bongard FS. Comparative stress hormone changes during helium versus carbon dioxide laparoscopic cholecystectomy.J Laparoendosc Surg 1996; 6:93-8.
6. O' leary E, Hubbard K, Tormey W et al. Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitonium and changes in position.Br J Anaesth 1996; 76:640-644.
7. Koivusalo AM, Scheinin M, Tikkanen I, et al. Effects of esmolol on haemodynamic response toCO_2 pneumoperitoneum for laparoscopic surgery. Acta Anaesthesiol Scand 1998; 42:510-7.
8. Lentschener C, Axler O, Fernandez H, et al. Haemodynamic changes and vasopressn release are not consistently associated with carbon dioxide pneumoperitoneum in humans.Acta Anaesthesiol Scand 2001; 45:527-35.
9. Kalra NK, Verma A, Agarwal A, Pandey HD. Comparative study of intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy.J Anaesthesiol Clin Pharmacol 2011; 27:344-48.
10. Herlich A. Open-Eye Injury and Intraocular Pressure. In: Clinical Cases in Anesthesia. 2nd ed Philadelphia, PA: Churchill Livingstone; 1995: 187–190.
11. Mowafi HA, Al-Ghamdhi A, Rushood A. Intraocular pressure changes during laparoscopy in patients anaesthetized with propofol total intravenous anaesthesia versus isoflurane inhaled anaesthesia. Anesth Analg. 2003; 97:471–474.
12. Zurakowski D, Vorwerk CK, Gorla M, et al. Nitrate therapy may retard glaucomatous optic neuropathy, perhaps through modulation of glutamate receptors. Vision Res. 1998; 38:1489–1494.
13. Hessemer V, Schmidt KG. Influence of the vasodilator drug isosorbide dinitrate on ocular circulation.Arch Ophthalmol. 1997; 115:324–327.
14. Kotikoski H, Moilanen E, Vapaatola H, Aine E. Biochemical markers of theL-arginine-nitricoxide pathway in the aqueous humour in glaucoma patients. Acta Ophtalmol Scand. 2002; 80:191–195.
15. Wizemann AJ, Wizemann V. Organic nitrate therapy in glaucoma. Am J Ophtalmol. 1980; 90: 106–109.
16. Malek KJ, Knor J, Kurzova A, Lopourova M. Adverse haemodynamic changes during laparoscopic cholecystectomy and their possible suppression with clonidine premedication.Comparison with intravenous and intramuscular premedication. Rozhl Chir. 1999; 78:286–291.
17. Yu HP, Hseu SS, Yien HW, Teng YH, Chan KH. Oral clonidine premedication preserves heart rate variability for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 2003; 47(2):185–190.
18. Tripathi DC, Shah TS, Dubey SR, Doshi SM, Raval PV. Hemodynamic stress response during laparoscopic cholecystectomy effect of two different doses of intravenous clonidine premedication. J Anaesth Clin Pharmacol. 2011; 27:475–480.
19. Vatner SF, Higgins CB, Millard RW, Franklin D. Direct and reflex effects of nitroglycerin on coronary and left ventricular dynamics in conscious dogs. J Clin Invest. 1972; 51(11):2872–2882.
20. Lahtela JT, Sotaniemi EA. Effect of short-acting nitroglycerin on heart rate: evaluation by a self-monitoring device. Br J Clin Pharmacol. 1989; 28 (5):605–607.
21. Moon HS, Lee SK, Choi YS, In CB, Choi EJ. The effect of nitroglycerin on hemodynamic changes during laparoscopic low anterior resection. Korean J Anesthesiol. 2011; 61(5):388–393.
22. Sen S, Ugur B, Aydin ON. The effects of low dose intravenous nitroglycerin infusion on intraocular pressure in laparoscopic cholecystectomy. Turkiye Klinikleri J Anest Reanim. 2006; 4:101–105.
23. Sung CS, Lin SH, Chan KH, Chang WK, Chow LH, Lee TY. Effect of oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Sin. 2000; 38:23–29.

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Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.8

Comparison of Midazolam and Propofol for BIS Guided Sedation during Regional Anaesthesia

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Abstract

Bispectral Index (BIS) was introduced by Aspect Medical Systems, Inc in 1994 as a novel measure of level of consciousness by algorithmic analysis of patient's encephalogram during anaesthesia. Besides providing an idea about the hypnotic state of the patient, it also enables titration of anaesthetic agents so as to avoid adverse effects as awareness and side effects of over doses. The ideal sedative medication should provide an early titrable level of sedation, predictable amnesia, decreased anxiety and a rapid recovery with minimal side effects.

In the present study, 60 patients of either sex belonging to ASA grade I and II between age range of 20-60 years posted for elective operative procedures performed under spinal anaesthesia were selected.

All these patients were preanaesthetically evaluated and written valid consent was obtained. All monitors were attached and baseline parameters as pulse rate, mean arterial pressure, respiratory rate and SpO_2 were noted. These 60 patients were divided into 2 equal groups of 30 patients each. In Group M, Midazolam 1% intravenous infusion in 5% Dextrose was started in dose of 0.5mg/kg/hr till BIS value more than 75 was maintained with infusion via syringe pump at 65-85 range and

In group P, Propofol 1% infusion in 5% Dextrose was started in dose of 6mg/kg/hr. Intraoperatively, mean pulse rate, mean arterial pressure, respiratory rate, SpO_2 were monitored and noted at various time intervals. These patients were monitored intra and postoperatively for any side effects These patients were evaluated for time taken to reach required level of sedation, time taken for recovery, dose required for level of sedation, haemodynamic stability and Alderate score. It was observed that, there was no significant difference in groups M and P at various time intervals but there was statistically significant difference in mean pulse rate, mean arterial pressure amongst the groups at various time intervals, When compared to baseline readings. This difference was more significant in Propofol group as compared to Midazolam group. BIS value in both groups at various time intervals, there was significant difference. Mean time taken to reach required level of sedation was significantly greater in group M as compared to group P. Mean time taken for recovery in group M was significantly greater as compared to group P. The incidence of dreadful complications was comparatively less in both groups. Mean Alderate score on arrival in recovery room in both groups was significant and insignificant at 1 hour.

Keywords: Regional Anaesthesia; Bispectral Index; Midazolam; Propofol; Less Side Effects.

Introduction

Monitored Anaesthesia care has been new concept developed in modern era of Anaesthesia practice. It has replaced old trend of standby practice for critical ill patients, radio diagnostic procedures, ophthalmic procedures or along with local anaesthesia procedures [1].

Conscious sedation is a minimally depressed level of consciousness that retains the patient's ability to maintain the airway and response to appropriate physical stimulation, verbal command [2]. With conscious sedation only some of the centers in medullary reticular formation and thalamus are depressed in dose dependent manner [3]. Thus, the level of

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Received on 09.12.2016
Accepted on 19.12.2016

sedation additionally provides the benefit of prevention of preservation of protective airway reflexes as in monitored anaesthesia care [3].

Regional anaesthesia techniques most popularly administered has its benefits as less chances of airway compromise, aspiration, facilitation of postoperative analgesia, utility in some medical conditions and operation theater pollution [4].

The concept of monitored anaesthesia care has come to highlight the fact that a vigilance on patient's vital parameters, level of sedation and regional anaesthesia monitoring are as important as in general anaesthesia [5]. From olden days to recent era there was a need of system which measures the depth and level of anaesthesia useful for titration of high dose or low dose administration of anaesthesia drugs [1].

Bispectral Index (BIS) was introduced by Aspect Medical Systems, Inc in 1994 as a novel measure of level of consciousness by algorithmic analysis of patient's encephalogram during anaesthesia and got FDA approval in 1996 [7]. Besides providing an idea about the hypnotic state of the patient, it also enables titration of anaesthetic agents so as to avoid adverse effects as awareness and side effects of over doses. The ideal sedative medication should provide an early titrable level of sedation, predictable amnesia, decreased anxiety and a rapid recovery with minimal side effects.

Propofol has many ideal properties of sedation/hypnosis for use for sedation/analgesia. The context sensitive halftime of Propofol remains short even after prolonged intravenous infusion (in contrast to Midazolam) and it is easily titrable drug which has an excellent recovery profile. Midazolam is short acting produces sedation, anxiolysis and amnesia, with side effects as significant respiratory depression and prolonged psychomotor impairment [9].

Regional anesthesia is becoming more popular even for day care surgery. Many patients prefer being sedated during operative procedures under regional anesthesia. Sedation increases patient's acceptance for regional anesthesia and improve patient's well being.

The present study was aimed to compare the efficacy of Midazolam and Propofol as sedative using Bispectral Index (BIS) in patients undergoing operative procedures under spinal anaesthesia to optimize patient comfort.

Material and Method of Study

The present study was a prospective, randomized single blind study carried out to evaluate the efficacy of Midazolam and Propofol in terms of haemodynamic stability, dose requirement as adjuvant to spinal anaesthesia and side effects. 60 patients belonging to ASA grade I and II of either sex with age range between 20-60 years posted for elective operative procedures below umbilicus were studied.

The demographic data was as shown in Table 1.

Table 1: Showing demographic data

Variables	Group M	Group P	t value	p value	Significance
Age in years	41.43 ±9.69	38.40 ± 11.27	1.11	0.26	NS
Height in cm	158.5 ± 7.01	151.7 ± 7.11	0.98	0.33	NS
Weight in Kg	57.10 ± 6.47	55.33 ± 6.01	1.09	0.28	NS

Mean age in Group M (Midazolam) was 41.43 ± 9.69 years and in Group P (Propofol) was 38.40 ± 11.27 years. Mean height in Group M was 158.5 ± 7.01cm and in Group P was 156.7 ± 7.15cm. Mean weight was 57.10 ± 6.47 kg In group M and 55.33 ± 6.01 kg in Group P. All these parameters were not statistically significant in both groups.

Sex distribution was as shown in Table 2.

Table 2: Showing sex distribution

Gender	Group M	Group P	X^2	p value	t value
Male	17(56.67%)	16(53.33%)			
Female	13((43.33%)	14(46.67%)	0.06	0.79	NS
Total	30(100%)	30(100%)			

In group M, there were 17 male (56.67%) and 13 female patients (43.33%). In group P, there were 16 (53.35%) male and 14 (46.67%) female patients. There was no significant difference in sex distribution in both groups.

All these patients were preanaesthetically evaluated for fitness according to ASA grading as

shown in Table 3.

There was no significant difference as far as ASA grading I and II was concerned in both groups.

All these patients were posted for various elective operative procedures which can be performed under spinal anaesthesia as shown in Table 4.

The distribution of operative procedures in 2 groups was almost identical and there was no significant difference.

In both groups, mean total duration of operative procedure as time start of operation to the end of operation was noted as shown in Table 5.

Mean duration of surgery was 83.00 ± 11.85 minutes in group M and 80.07 ± 15.30 mints in group P. In group M, maximum duration of surgery was 108 minutes and minimum duration was 64 minutes. In group P, maximum duration of surgery was 114 minutes and minimum 55 minutes. The difference in both groups was statistically significant.

All these patients were monitored for changes in vital parameters Intraoperatively. Preoperative (Baseline) mean pulse rate and mean arterial pressure were noted as shown in Table 6.

Table 3: Showing distribution according to ASA grading

ASA Grade	Group M	Group P	X^2	p value	t value
I	24(80%)	25(83.3%)			
II	6(20%)	5(16.6%)	0.11	0.74	NS
Total	30(100%)	30(100%)			

Table 4: Showing operative procedures in both groups

Type of Surgery	Group M	Group P	Total
Vaginal Hysterectomy	8(26.67%)	9(30%)	17(28.33%)
# Femur Shaft	6(20%)	5(16.67%)	11(18.33%)
# Tibia-Fibula	4(13.33%)	5(16.67%)	9(15%)
Inguinal Hernia	9(30%)	8(26.67%)	17(28.33%)
Incisional Hernia	3(10%)	3(10%)	6(15%)
Total	30(100%)	30(100%)	60(100%)

Table 5: Showing Mean Duration of Surgery

Mean Duration in Minutes	Group M	Group P	t value	p value	Difference
Mean Duration	83.00 ± 11.85	80.07 ± 15.30	0.83	0.43	NS

Table 6: Showing preoperative mean pulse rate and mean arterial pressure

Preoperative	Group M	Group P	T value	P value	Difference
Pulse rate Beats/min	83.57 ± 8.65	82.90 ± 10.95	0.27	0.79	NS
Mean arterial pressure	80.40 ± 4.53	82.27 ± 4.88	1.54	0.13	NS

Table 7: Showing mean pulse rate at various time intervals

Time Interval	Group M	Group P	T value	P value	Difference
Preop	83.40 ± 8.07	82.50 ± 10.98	0.36	0.72	NS
2 min	82.40 ± 8.07	79.0 ± 10.81	1.38	0.17	NS
5/6 min	76.67 ± 7.96	73.5 ± 9.90	1.35	0.18	NS
10 min	76.17 ± 7.95	73.88 ± 9.51	1.00	0.31	NS
30 min	74.23 ± 8.65	72.80 ± 9.51	0.61	0.54	NS
60 min	80.40 ± 8.76	75.76 ± 9.08	1.98	0.08	NS
90 min	83.82 ± 9.90	87.18 ± 10.63	0.81	0.42	NS

In group M, preoperative mean pulse rate was 83.57 ± 8.45 and mean arterial pressure was 80.40 ± 4.53 mm of Hg. In group P, mean pulse rate was 82.90 ± 10.95 and mean arterial pressure was 82.27 ± 4.88 mm of Hg. These preoperative mean pulse arte and mean arterial pressure were not statistically significant.

Intraoperatively, mean pulse rate and mean arterial pressure at various time intervals were noted in both groups as shown in Table 7.

It was observed that, in group M mean pulse rate

was 83.40±8.07 beats/min (at preoperative) gradually decreased to 74.23±8.65 beats/min at 35 minutes. In group P, initial mean pulse rate 82.50 ± 10.98 beats/min gradually decreased to 75.33 ± 10.25 beats /min at 25 minutes. The difference in mean pulse rate at various time intervals was not statistically significant at all time intervals. When mean pulse rate at various time intervals was compared to preoperative pulse rate, it was highly significant with p value <0.01 at 5 minutes and continued to remain till 45 minutes. At 60 minutes the difference was statistically significant p value <0.05 to become non significant at 60 minutes onwards. In groups P, when preoperative mean pulse rate was compared with various time intervals, it was observed that, the difference was highly significant with p value <0.01 at 5 minutes and continued till 45 minutes except 10 and 15 minutes. Again it was statistically significant with p value <0.05 at 60 and 75 minutes and not significant at 90 minutes.

Mean arterial pressure at various time intervals was as shown in Table 8.

In group M, mean arterial pressure at preoperative was 80.27 ± 4.32 mm of Hg decreased to 73.17 ± 6.21 mm at 60 minutes and in group P from 82.07 ± 4.91 mm gradually decreased to 68.37 ± 4.64 mm at 60 minutes.

In group M, maximum mean arterial pressure was 80.32 ±6.77 at 90 minutes and minimum was 73.17 ± 6.21 mm around 60 minutes. In group P, maximum mean arterial pressure was 82.07± 4.91 at preoperative and minimum 68.37±4.64 at 60 minutes. In both groups mean arterial pressure was not statistically significant upto 25-30 minutes but became highly significant at 30 minutes and continued upto 90 minutes. In group M, mean arterial pressure at preoperative reading when compared to various time intervals, at 2 minutes it was not significant but highly significant at 5 minutes and continued to remain high upto 60 minutes, It became significant at 75 minutes and non significant at 90 minutes. In group P, mean arterial pressure at various time intervals upto 90 minutes was highly significant when compared to preoperative readings.

Bispectral index (BIS) value at various time intervals was as shown in Table 9.

Table 8: Showing mean arterial pressure at various time intervals

Time Interval	Group M	Group P	t value	p value	Difference
Preop	80.27 ± 4.32	82.07 ± 4.91	1.51	0.14	NS
2 min	78.27 ± 4.31	78.57 ± 4.91	-0.22	0.83	NS
5/6 min	75.30 ± 4.29	75.00 ± 4.50	0.26	0.79	NS
10 min	76.20 ± 4.50	74.07 ± 4.39	1.86	0.07	NS
30 min	74.23 ± 4.83	68.87 ± 5.15	4.15	0.00	HS
60 min	73.17 ± 6.21	69.00 ± 4.69	2.90	0.00	HS
90 min	78.57 ± 6.10	70.73 ± 4.32	3.60	0.00	HS

Table 9: Showing BIS at various time intervals in both groups

Time Interval	Group M	Group P	t value	p value	Difference
Preop	97.70 ± 0.75	97.30 ± 1.23	1.52	0.13	NS
2 min	94.07 ± 1.45	91.50 ± 2.06	7.54	0.00	HS
5/6 min	85.20 ± 3.53	75.93 ± 3.06	10.86	0.00	HS
10 min	76.87 ± 3.19	72.03 ± 0.91	7.93	0.00	HS
15 min	72.20 ± 0.89	71.67 ± 0.89	2.18	0.03	Significant
25 min	71.83 ± 0.87	70.30 ± 1.51	4.80	0.00	HS
35 min	70.13 ± 0.97	70.17 ± 1.74	-0.10	0.91	NS
45 min	69.20 ± 1.30	71.00 ± 1.72	-4.57	0.00	HS
60 min	71.87 ± 1.59	71.86 ± 2.86	0.02	0.99	NS
90 min	76.50 ± 2.53	74.36 ± 3.04	1.92	0.07	NS

Table 10: Showing incidence of side effects

Side Effects	Group M	Group P	P value	Association
Nausea & Vomiting	4(13.33%)	2(6.66%)	0.67	NS
Restlessness	2(6.66%)	4(13.33%)	0.67	NS
Pain in Arm	0(0%)	2(6.66%)	0.49	NS
Awareness	6(20%)	5(16.67%)	0.99	NS
Hypotension	4(13.33%)	6(20%)	0.73	NS
Bradycardia	4(13.33%)	7(23.37%)	0.51	NS

In group M, BIS value at preoperative level was 97.70 ± 0.75 which gradually decreased to 69.20 ± 1.30 at 45 minutes. In group P, initial BIS value was 97.30 ± 1.23 which gradually decreased to 70.17 ± 1.74 at 35 minutes. There was statistically significant difference in BIS value at 2, 5, 10, 25, 35, 45 minutes when compared to preoperative value in both groups.

Mean time required to reach level of sedation was 10.83 ± 2.26 mint in group M an 6.40 ± 1.2 mints in group P which was significantly less where p>9.48, t 0.00

Mean time required for recovery (BIS value ≥ 90) was 18.03 ± 4.27 mints in group M and 10.13 ± 1.78 mints in group P, significantly less f=9.35, p 0.00

Intraoperatively and postoperatively, all patients were monitored to note side effects related to drugs or technique of anaesthesia and the incidence of side effects was as shown in Table 12.

Overall, the incidence of intraoperative and postoperative side effects / complications was not significant in both groups. Only 23.33% of patients in group P had bradycardia and 20% had hypotension.

Mean Alderate score was noted in both groups. In group M on arrival in recovery room, Alderate score was 8.03 ± 0.32 and after 1 hour it was 9.07 ± 0.25. In group P, Alderate score on arrival was 8.33 ± 0.61 and at 1 hour was 9.20 ± 0.41. The difference was significant at arrival and not significant at 1 hour in both groups.

Discussion

Regional anaesthesia offers many advantages over general anaesthesia with some disadvantages as pain at puncture site, fear of pin prick and recall of procedure. These factors stress the importance of sedation with analgesia, anxiolysis and amnesia [8].

Conscious sedation term is used for sedation as for therapeutic or diagnostic procedures and monitored anaesthesia care for sedation to supplement local or regional anaesthesia [10]. Sedation has been shown to increase patient's satisfaction during regional anaesthesia and may be considered as means of increase in patient's acceptance for regional anaesthesia technique [8].

Bispectral index (BIS), is a score derived from the frontal EEG. The property algorithm to determine this score was developed empirically by a computer aided search for statistical correlation between EEG characteristics and state of consciousness. It provides additional information for standard monitoring techniques that helps to guide the administration of sedative / hypnotic agents. It helps to titrate the level of sedation so that minimum drugs can be used to maintain desired level of sedation [9].

A dose related sedative effect has been demonstrated and non-dose related anxiolysis with Propofol. Amnesia is less with Propofol as compared to Midazolam. Propofol has quicker onset of action, quick induction, easy alteration of sedation level and early recovery. In high doses it causes severe hypotension and bradycardia with some haemodynamic instability. It is ideal agent for sedation during regional anaesthesia [9].

Midazolam has rapid onset of action, produces sedation, excellent amnesia but depresses respiration and arterial pressure only in high doses. It has no specific analgesic action.

In group M, intravenous infusion of Midazolam 1% was started with 0.5mg/kg/hr till BIS value reached upto 75 and titrated infusion was continued to maintain BIS in range of 65-85 via syringe pump. In group P, intravenous infusion of Propofol 1% was started with 6mg/kg/hr till BIS reached 75 and continued with titrated doses to maintain BIS value in range of 65-85. Our technique of administration of drugs was in accordance with Win Ni Ni etal (2005) [10]., Khurana P etal (2009) [3] and Patki P etal (2011) [11].

In group M, mean age of patients was 41.43 ± 9.69 years, mean height was 158.5 ± 7.01 cm and mean weight was 57.11 ± 6.47 kg. In group P, mean age of patients was 38.47 ± 11.27 years, mean height was 156.7 ± 7.15 cm and mean weight was 55.33 ± 6.01 kg. There was no statistical difference in these demographic data in both groups. All operative procedures performed were below umbilicus under general surgery or gynecology.

In group M, mean duration of surgery was 83.00 ± 11.85 mints and in group P was 80.07 ± 15.30 mints and there was no significant difference in both groups as far duration of surgery was concerned. Our observations were in accordance with Win Ni Ni etal (2005) [10], Khurana P etal (2009)3 and Patki A etal (2011) [11]. All preoperative vital parameters were almost similar in both groups and there was no statistical significant difference.

In group M, mean BIS value was 98.43 ± 0.57 where as in group P mean BIS value was 98.27 ± 0.69 and the difference was not significant. These observations were similar to studies of Atanassoff PG etal (1993)

[12], Win Ni Ni etal (2005) [10] and Patki A etal (2011) [11].

Overall, in between groups comparison of mean pulse rate at various time intervals revealed the difference was not significant at all time intervals. But the comparison of mean pulse rate at various time intervals with base line readings within same group showed significant difference in both groups. In between groups, In group P when mean arterial pressure was compared, there was no significant difference upto 30 minutes but it became highly significant at 35 minutes and continued to remain upto 90 minutes. The changes in mean arterial pressure between 2 groups being statistically significant at various time intervals indicated haemodynamic stability in group M as compared to group P.

In the present study, In group M mean BIS value at preoperative was 97.70 ± 0.75 which gradually decreased to 69.20 ± 1.30 at 45 minutes. In group P, BIS value decreased from 97.30 ± 1.23 to 70.17 ± 1.74 at 35 minutes. The difference in mean BIS value in both group at various time intervals was statistically not significant at baseline value but became highly significant at 5 minutes and continued to remain till 15 minutes, then at 25, 45 and 90 minutes. Our observations were comparable with studies of Conard B etal (1900) [13], Hofmann C etal (1999) [14], Gasoarovic S etal (2003) [15], Win Ni Ni etal (2005) [10], Hidaka S etal (2005) [16] and Khurana P etal (2009) [3]. They explained that cardiovascular effects of both drugs minimal when given in slow intravenous infusion with titrated doses. Both of these drugs have cardiac autonomic nervous system depression action during combined spinal-epidural anaesthesia. They observed that, Propofol to be more potent than Midazolam in resulting symatholytic activity during regional anaesthesia. Our observations can be explained on above grounds as we have used minimum titrated doses of both drugs.

In group M, mean time taken to reach required level of sedation was 10.83 ± 2.26 minutes and in group P it was 6.4 ± 1.2 minutes. The difference was statistically highly significant as more time was required in group M as compared to group P. In group M, mean time required for recovery (BIS) was 18.03 ± 4.27 and in group P it was 10.13 ± 1.78 mints and the difference was statistically significant. The of recovery was more in group M as compared to group P. Fanard L etal (1988) [17], Wilson E etal (1990) [18], Pratila MG etal (1993) [19] Atansssoff PG etal (1993) [12], Takeshita M etal (1998) [20], Gasparovic S etal (2003) [15], Yaddanapudi S etal (2007) [21], Khurana P etal (2004) [3], Patki A etal (2011) [11], Weinbroum AA etal (1997) [22], Sasaki T etal (2001) [23] and Nishiyama M etal 2004) [24] have all observed that recovery was faster with Propofol as compared to Midazolam. Our observations correlate to above authors.

In group M, mean maintenance dose for sedation was 0.12 ± 0.12 mg/kg/hr while in group P was 2.19 ± 0.31 mg/kg/hr. The dose requirement of Propofol was more as compared to Midazolam. Above authors also quotes less dose requirement with Midazolam than Propofol.

The incidence of dreadful side effects Intraoperatively as well as postoperatively was negligible in both groups as the doss used were therapeutically titrated and low doses. Many of the authors observed that Midazolam produced less side effects with effective amnesia while Propofol was associated with less postoperative sedation, drowsiness, confusion and amnesia with more rapid recovery.

In present study, on arrival in recovery room, mean Alderate score was 8.03 ± 0.32 in group M and 8.33 ± 0.61 in group P. The difference was significant. At one hour, mean Alderate score was 9.07 ± 0.25 in group M and 9.20 ± 0.41 in group P and the difference was not significant. Our observations were corresponding to Dortwine R etal (1988) [25], Murry LU etal (1989) [7], Wilson E etal (1990) [18], Conard B etal (1900) [13] and Pratik MG etal (1993) [19]. They noted Propofol to be superior to Midazolam due to shorter recovery time. With Propofol there is significantly faster restoration of higher mental functions as compared to Midazolam.

Summary

In the present study, 60 patients of either sex belonging to ASA grade I and II between age range of 20-60 years posted for elective operative procedures performed under spinal anaesthesia were selected. The patients with overall contraindications for spinal anaesthesia with central nervous system disorders were excluded from study.

All these patients were preanaesthetically evaluated and written valid consent was obtained. All monitors were attached and baseline parameters as pulse rate, mean arterial pressure, respiratory rate and SpO_2 were noted. Intravenous infusion was started with Ringer lactate and under all aseptic precautions spinal anaesthesia with 0.5% Bupivacaine 3-5ml was injected in subarachnoid

space. These 60 patients were divided into 2 equal groups of 30 patients each. In Group M, Midazolam 1% intravenous infusion in 5% Dextrose was started in dose of 0.5mg/kg/hr till BIS value more than 75 was maintained with infusion via syringe pump at 65-85 range. In group P, Propofol 1% infusion in 5% Dextrose was started in dose of 6mg/kg/hr till BIS d" 75 and titrated to maintain BIS value in range of 65-85. Intraoperatively, mean pulse rate, mean arterial pressure, respiratory rate, SpO_2 were monitored and noted at various time intervals. These patients were monitored intra and postoperatively for any side effects as nausea, vomiting, shivering, bradycardia, hypotension, respiratory depression etc. and treated accordingly. These patients were evaluated for time taken to reach required level of sedation, time taken for recovery, dose required for level of sedation, haemodynamic stability and Alderate score. It was observed that, there was no significant difference in groups M and P at various time intervals but there was statistically significant difference in mean pulse rate, mean arterial pressure amongst the groups at various time intervals. When compared to baseline readings. This difference was more significant in Propofol group as compared to Midazolam group. BIS value in both groups at various time intervals, there was significant difference. Mean time taken to reach required level of sedation was significantly greater in group M as compared to group P. Mean time taken for recovery in group M was significantly greater as compared to group P. The incidence of dreadful complications was comparatively less in both groups. Mean Alderate score on arrival in recovery room in both groups was significant and insignificant at 1 hour.

Conclusions

From the present study, it was concluded that Midazolam and Propofol both drugs are effective sedative agents during spinal anaesthesia. And can be easily titrated to maintain desired BIS value. The time taken to reach required level of sedation (BIS d" 75) was earlier with Propofol as compared to Midazolam.

The mean dose required to maintain level of sedation was 0.12 ± 0.02 mg/kg/hr for Midazolam and 2.19 ± 0.31 mg/kg/hr for Propofol. The mean time required for recovery was earlier with Propofol than Midazolam. Midazolam provided better haemodynamic stability as compared to Propofol as mean arterial pressure was significantly decreased in Propofol group than Midazolam group. The incidence of dreadful side effects was less in both groups. So both of these are equivalent as far efficacy is concerned during regional anaesthesia (spinal anaesthesia) for BIS control.

References

1. American Society of Anaesthesiologists Task Force on Sedation and Analgesia bu non-anaesthesiologists. Practice guidelines for sedation and analgesia by non-anaesthesiologists. Anaesthesiology 2002; 96: 1004-17.
2. Drummond JC; Monitoring depth of Anaesthesia, Anaesthesia: 2000; 93:876-882.
3. Khurana P, Agrawal A, Verma R K, Gupta P K, Comparison of Midazolam and Propofol for BIS guided sedation during regional anaesthesia. Indian J Anaesth 2009 Dec; 53:662-666.
4. Kalkmn Cor J, Drummond J C, Monitors of depth of anaesthesia Quo Vadis? Anaesthesiology, 2002 April; 96:784-787. Ibrahim A E, Juile K Taraday, Evan D Kharasch Bisepectral index monitoring during sedation with Sevoflurane, Midazolam and Propofol. Anaesthesiology 2001; 95:1151-1159.
5. Jaffrey C Sigl, Nassib G Chamoun An introduction to Bispectral analysis fr the electroencephalogram. Journal of Clinical Monitoring, 1994 Nov; 10: 392-404.
6. Murray L Urquhart, Paul F White, Comparison of sedative infusions during regional anaesthesia – Methohexital, Etomidate and Midazolam Anaesth Analg, 1989; 68:249-254.
7. Hoehener D, Blumenthal S, Borgeat A Sedation and regional anaesthesia in adult patients. Br. J Anaesth 2008:100, 8-16 Sandler N A, Hodges J, Sabino M Assessment of recovery in patients undergoing intravenous conscious sedation using Bispectral analysis. J Oral Maxillofac. Surg, 2001 Jun; 59:603-611.
8. Win Ni Ni, Haruhisa F, Hikaru K and Masahiro U The different effects of intravenous Propofol and Midazolam sedationon haemodynamic and heart rate variability. Anaesth Analg, 2005;101:97-102.
9. Patki A, Shelgaonkar VC, A comparison of equisedative infusion of Propofol and Midazolam for conscious sedation during spinal anaesthesia. A prospective randomized study. J Anaesthesiol Clin Pharmacol. 2011 Jan-March; 27:47-53.
10. Atanassoff P G, Alon E, Pasch T., Recovery after Propofol, Midazolam and Methohexitone as an adjuvant to epidural anaesthesia for lower abdominal surgery. Eur J Anaesthesiol. 1993 July; 10:313-318.
11. Conard B, Larsen R, RathgeberJ, Lange H, Stuber H, Crozier T., Propofol infusion for sedation in regional

anaesthesia. A comparison with Midazolam. Anaesth Intensivther Notfallmed, 1990 Jun; 25:186-192.

12. Hofmann C, Kiesslich R, Brackertz A, Jung M., Propofol for sedation in gastroscopy – a randomized comparison with Midazolam. Z Gastroentero, 1999; July; 37:589-595.
13. Gasparovic S, Rustemovic N, Opacic M, Bates M, Petrovecki M., Comparison of colonoscopies performed under sedation with Propofol or with Midazolam or without sedation. Acta Med Austrica, 2003; 30:13-16.
14. Hidaka S, Kawamoto M, Kurita S, Yuge O Comparison of the effects of Propofol and Midazolam on the cardiovascular autonomic nervous system during combined spinal an epidural anaesthesia. J Clin Anaesth 2005 Feb; 17:36-43.
15. Fanard L, Steenberge A, Demeire X, Van Der Pul F Comparison between Propofol and Midazolam as sedative agents for surgery under regional anaesthesia. Anaesthesaia, 1988 March; 43 (suppl.): 87-89.
16. Wilson E, David A, Mackenzie N, Grant I S., Sedation during spinal anaesthesia – comparison of Propofol and Midazolam. Br J Anaesth 1990 Jan; 64:48-52.
17. Pratila M G, Fischer M E, Alagesan R, Reinsel R A, Pratilas D., Propofol versus Midazolam for monitored sedation – comparison of intraoperative and recovery parameters. J Clin Anaesth 1993 Jul-Aug; 5:268-274.
18. Takeshita M, Karaba T, Tanaka N, Kondou O, Watanabe Y, Takasaki M., Sedative and hypnotic properties of porpofol during epidural or spinal anaesthesia. Masui. 1998 Sept; 47:1099-1103.
19. Yaddaanapudi S, Batra Y K, Balagopal A, Nagdeve N G., Sedation in patients above 60 years of age undergoing urological surgery under spinal anaesthesia – comparison of Propofol and Midazolam infusion. J Postgrad Med. 2007 Jul-Sep; 53:171-175.
20. Weinbroum A A, Halpern P, Rudick 'V, Sorkine P, Freedmann M, Geller E Midazolam versus Propofol for long term sedation in the ICU – a randomized prospective comparison. Intensive Care Med. 1997 Dec; 23:1258-1263.
21. Sasaki T, Kato H., The effects of conscious sedation by Propofol on respiration during abdominal hysterectomy under spinal anaesthesia. Masui. 2001 May; 50:491-495.
22. Nishiyama T, Yokoyama T, Hanaoka K., Sedation guidelines for Midazolam infusion during combined spinal and epidural anaesthesia. J Clin Anaesth 2004 Dec; 16:568-572.
23. Dertwinkel R, Nolte H., Continuous sedation for regional anaesthesia with Propofol and midazolm. A Comparative study Reg Anaesth 1988 Oct; 11: 84-89.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.9

Modified Transversus Abdominis Plane (TAP) Block for Postoperative Analgesia Following Cesarean Delivery

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Abstract

Introduction: Adequate postoperative pain relief after Caesarean delivery (CD) improves ambulation, breastfeeding and infant weight gain. The analgesic efficacy of the TAP block has been confirmed and used for postoperative analgesia following CD. We studied the analgesic efficacy and safety of TAP by using Loss of Resistance (LOR) technique, as part of a multimodel analgesic regimen, in the first 24 h after caesarean delivery.

Materials and Methods: 60 patients of ASA physical status I-II, undergone Cesarean delivery under spinal anaesthesia were divided into two groups. Group T (n=30) patients received bilateral TAP block at the end of surgical procedure with 0.25% Bupivacaine (maximum dose of 2mg/kg). Group C patients received only conventional analgesic regime.

Results: In Group T, patients who received TAP block required less analgesics and the time to require a first analgesic requirement was longer than the Group C. In Group C the patients required rescue analgesics much earlier than Group T. The mean VAS score in Group T was 1.54+0.41 Vs 4.02+0.24 in control group which was statistically significant (P <0.01). The TAP block significantly reduced the incidence of sedation (7% Vs 61%).

Conclusion: We would like to conclude that administration of TAP block as a part of the multimodal analgesia provides effective analgesia and results in reduction of analgesic drugs requirement following Cesarean delivery.

Keywords: Cesarean Delivery; TAP Block; LOR Technique; Postoperative Analgesia.

Introduction

Effective postoperative analgesia improves or facilitate early ambulation, and even improve the postoperative outcome by the prevention of postoperative morbidity like ineffective cough, atelectasis etc [1]. The major contribution towards postoperative pain after abdominal surgeries is from the abdominal wall [2]. Inadequate postoperative pain relief after Caesarean delivery(CD) can negatively impact ambulation, breastfeeding, and even maternal bonding [3], while effective analgesia improves ambulation, breastfeeding and infant weight gain [4]. Neuraxial anaesthesia has become the anaesthetic technique of choice in CD because of its safety and reduction in maternal morbidity [5].

The technique of analgesia must provide safe, effective analgesia, with minimal side effects for the mother and her child. The analgesic efficacy of the TAP block has been confirmed in several studies [6-9], and had been used for postoperative analgesia following CD [10]. Even though several studies shown the analgesic efficacy of the TAP block [9,11], others found no analgesic benefit [12,13].

We studied the efficacy of TAP block, as part of a multimodel analgesic regimen, would result in decreased opioid consumption and improved analgesia in the first 24 h after caesarean delivery.

Methods

We have enrolled 60 patients after approval from hospital ethics committee for a prospective nonrandomised study. Patients were of ASA physical status I – II. All patients were scheduled to undergo Caesarean delivery via a Pfannentiel incision under spinal anaesthesia. Patients were excluded if there was a history of

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Received on 22.12.2016
Accepted on 28.12.2016

relevant drug allergy, or treatments with opioids. They were divided into two groups. Group T (n=30) and Group C (n=30). All patients received Inj. Ranitidine 50mg intramuscularly 1 hour before the procedure. Group T received TAP block with 0.25% bupivacaine (20 ml), to a maximum dose of 2mg/kg for both side together. The TAP block was performed on both sides. Group C patients received conventional analgesic regime.

All patients received a standard spinal anaesthesia block (SAB) consisting of 10mg of Bupivacaine heavy 0.5% with fentanyl 25 microgram. Patients also received rectal diclofenac 100mg. Prophylactic antiemetic was (Injection Metoclopramide 10mg intravenously) given.

The TAP block was performed at the end of procedure by one investigator using the following technique. A modified Loss of Resistance (LOR) technique was used to locate the TAP. Even though the literature describes the block to be performed in the 'Lumbar triangle – Petit's triangle', we have used modified approach to achieve TAP block (Figure 1 and 2) [29]. We adopted the technique described by Dr. Shiv kumar Singh by using the Loss of Resistance technique (LOR). The investigator standing on the same side of the block to be given, the iliac crest & lower most point of costal margin were palpated. In the mid-axillary line, a point midway between the costal margin and iliac crest was marked. After necessary sterile preparation and draping, an 18G Toughy needle is connected with a syringe loaded with 10 ml of local anaesthetics (LA). Once the skin barrier is breached, the needle is advanced through the external Oblique, and a first 'pop' sensation is felt when the needle enters the plane between External oblique & internal oblique muscles. Further advancement of the needle results in a second 'pop' after it passes through IO fascia into the TAP. At this point after careful aspiration to exclude vascular puncture a test dose of 1ml of 0.25% Bupivacaine was injected. After confirming the negative test dose, 20 ml of the drug is injected in 3 ml aliquots. The TAP block was then performed on the other side in the same manner described above. The maximum total dose of Bupivacaine administered was 2mg/kg, including both sides. All patients were transferred to the PACU. A standard postoperative analgesic regimen consisting of Inj. Diclonefac 75 mg i.m 8th hourly combined with Inj. Tramadol 1mg/kg i.v12th hourly. Inj. Paraacetamol 1 g i.v infusion was given as a first rescue analgesic followed by Inj. Tramadol 50 mg i.v as a second rescue analgesic.

The severity of pain was assessed by using Visual Analogue Scale (VAS). The patient was asked to score the severity of pain between no 1 to 10.The presence and severity of pain (VAS score), nausea, vomiting and sedation were assessed at periodic intervals. These assessments were performed at 2, 4, 6, 12, and 24 hour intervals after TAP block. All patients were asked to give score for pain at rest as well as on movement (knee flexion). VAS on movement was assessed at 12 and 24 hour after surgery. The sedation was scored by using Modified Ramsay Sedation Scale (Table 5). Inj. Ondansetron 4 mg i.v was given for nausea and vomiting. The study period was up to 24 hours after TAP block.

The primary outcome measure in this study was first to evaluate analgesic efficacy of modified TAP for postoperative pain as a multimodal regime following Cesarean delivery. Secondary outcome measures include the success rate and safety profile of modified approach of TAP block.

Statistical Analysis

All the variables are expressed in terms of mean and standard deviation. Chi-square test and Student t test were used to analyse the statistical significance, where p value of <0.05 was considered to be significant.

Results

We have enrolled sixty patients for this study. 30 patients received TAP block (Group T) and another 30 patients (Group C) were received conventional analgesic regime. There was no difference in demographic variables (age, weight and height etc) between both groups (Table 1). The TAP block was performed in all patients in first attempt and without any complications. The TAP block reduced the pain score at all the time intervals (Graph 1). In Group T, patients who received TAP block required a less analgesics and the time to require a first analgesic requirement was longer than the Group C. In Group C the patients required rescue analgesics much earlier than Group T (Table 2).

The mean VAS score (Table 3) in Group T was 1.54+0.41 Vs 4.02+0.24 in control group which was statistically significant ($P<0.01$). Postoperative VAS pain scores at rest and on movement were reduced after TAP block (Table 4). The sedation score of 2 (Lightly sedated) was higher in Group C patients when compared with Group T patients (61% in group C, 7% in group T) which was statistically significant

Table 1: Demographic variables

Variables	Control	Tap	P Value
Age	31 ± 6.7	32 ± 4.6	Ns
Weight	69 ± 6.3	68 ± 8.2	Ns
BSA	1.6 ± 1.3	1.6 ± 1.3	Ns

Table 2: Requirement of rescue analgesics in both groups

Timing	Rescue Analgesia Control	Tap	T value	P value
0 - 30 M	0	0	NS	NS
30 - 60 M	0	0	NS	NS
60 - 90 M	8 (26%)	1 (3%)	6.36	0.011
90 - 120 M	8 (26 %)	0	9.18	0.002
2 - 4 HR	12 (39%)	0	9.22	0.0023
4 - 6 HR	20 (65%)	0	15.08	0.0001
6 - 12 HR	30 (97%)	17 (55%)	14.86	0.0001
12 - 24 HR	30 (97%)	12 (39%)	23.91	0.000001

Table 3: Mean comparison of vas score

Vas Score	N	Mean	SD	F value	P value
TAP block	30	1.54	0.41	581	<0.01
Control	30	4.02	0.24		

Table 4: Vas on movement

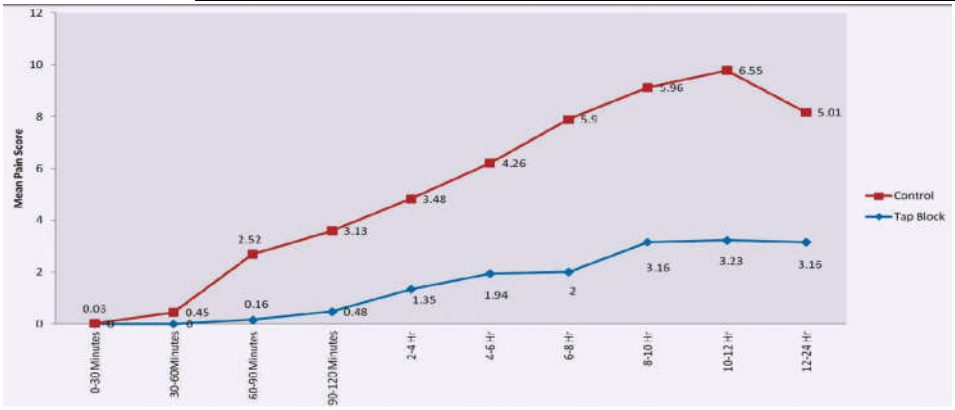
Hours	Control	Tap	T value	P value
4-6 hours	5.9 ± 1.0	2 ± 1	15.27	<0.00001
6-12 hours	6.5 ± 0.5	3.2 ± 1.2	13.44	<0.00001

Table 5: Modified ramsay sedation scale

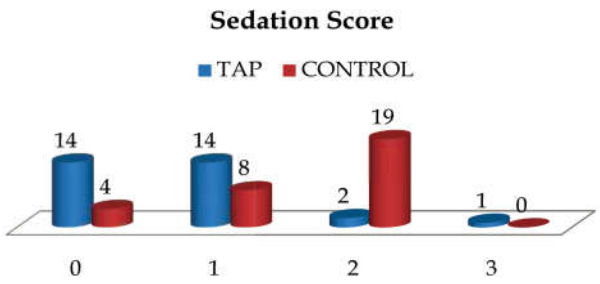
Score	Clinical Response
0	Paralyzed, Unable to evaluate
1	Awake
2	Lightly sedated
3	Moderately sedated, follows simple commands
4	Deeply sedated, responds to nonpainful stimuli
5	Deeply sedated, responds to painful stimuli
6	Deeply sedated, unresponsive to painful stimulli

Table 6: Sedation score

Score	Sedation Score Control	Tap	T Value	P Value
0	4 (13%)	14 (45%)	7.82	0.005
1	8 (26%)	14 (45%)	2.5	0.111
2	19 (61%)	2 (7%)	20.8	0.000005
3	1(3%)	0	1.01	0.3133



Graph 1: VAS Score at different intervals in both groups



Graph 2: Sedation score

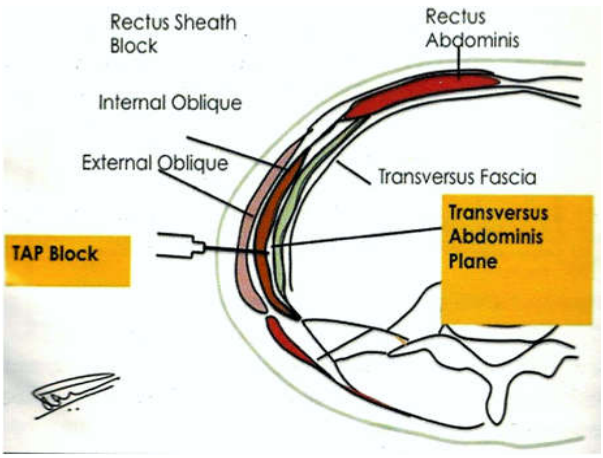


Fig. 1:

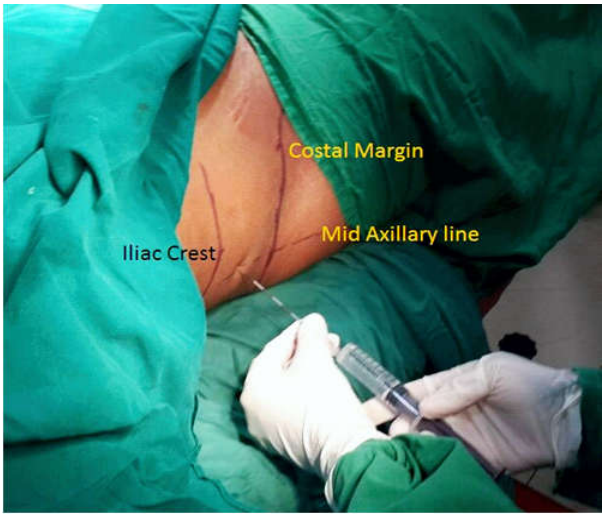


Fig. 2:

(P = 0.00005) (Table 6, Graph 2). There was no difference in the incidence of nausea or vomiting between two groups.

Discussion

A recent meta-analysis suggested that TAP block constitutes an effective analgesic option capable of reducing 24 h opioid consumption, 24 h rest pain scores, and PONV in parturient undergoing Caesarean Delivery who receive a multimodal analgesic regimen that excludes Intrathecal morphine [14]. Reduction in opioid analgesics is generally desirable in CD. Although opioid analgesics can be taken safely by lactating women, some opioids can result in significant exposures and toxicity in infants [25], including the risk of neurobehavioural depression in the breastfed newborn [16]. Some trials suggest a potential role of TAP block as a part of the post-caesarean multimodal analgesic settings [17,18]. We have not performed a TAP block with saline to avoid the possibility of potential harm as well as it might predispose the parturients to the unnecessary risks [19-22].

The analgesic regimen for post CD shoul provide safe, effective analgesia, with minimal side effects for mother and her child.Our study demonstrated that TAP block when administered as a part of a multimodal analgesic regimen reduced the first 24 hour analgesic requirements and parients who received the TAP block had reduced pain scores. Even the first requirement for analgesic supplementation also delayed.

The neuraxial blockade with long acting opioids produce effective analgesia, but they are associated with a frequent incidence of side effects, particularly nausea, vomiting, and pruritus, which reduce overall patient satisfaction [1]. The Hydrophilic opioids can spread rostrally which may result in delayed maternal respiratory depression [23].

Due to the presence of so many limiting factors for the administration of neuraxial blockade with the long acting opioid like morphine and the possibility of systemic opioids like meperidine secreting into breast milk and produce transient adverse neurobehavioral effects in the neonate [24], there is a considerable potential for TAP block to be a part of multimodal regimen for postcesarean delivery analgesia.

As the abdominal wall is a major contributor to acute postoperative pain after abdominal surgery [25], field blocks like TAP block [26] can provide effective analgesia for a variety of abdominal surgical procedures [26,27].

We had shown that TAP provides effective analgesia for post-CD parturients when given as a part of a multimodal analgesic regimen. And our study also demonstrated that a single-shot TAP block can produce effective analgesia for up to 24 hours. The reason for the prolonged duration of analgesic effect after TAP blockade may relate to the fact that the TAP is relatively poorly vascularised, and

therefore drug clearance may be slowed [28]. Even the TAP block improved the pain score during movement (knee flexion), suggesting that TAP block will allow the early ambulation of the patients.

Recently people prefer to perform the regional nerve blocks under Ultrasound guidance. Studies also suggest that using ultrasound may improve safety of performing nerve blocks, but the main limiting factor will be the non-availability of Ultrasound machine. Still these blocks can be performed safely and effectively. The Loss of Resistance (LOR) technique relies on using blunt or short bevelled needles, which provide a good feedback (pops or clicks) when they pass through fascial planes. Before feeling the loss of resistance, it is always nice to feel the bounce on the fascia. We have adopted the technique described by Shiv kumar singh and S.M. Gulyam Kuruba [29]. We have shown that TAP block can be performed safely and effectively by this modified approach using LOR technique. To our knowledge our study is the first one to study the the safety and analgesic efficacy of this modified approach with LOR technique even though it has been described in the literature.

We have a few limitations to our study. First it is a non-randomized study and the number of patients may not be large enough to assess the safety of the procedure. But none of the patient had any complication related to either the procedure related (like peritoneal puncture) or drug related. We didn't have a control group with USG guided TAP block to have a comparative data. We would like to conclude that administration of TAP block as a part of the multimodal analgesia provides effective analgesia and results in reduction of analgesic drugs requirement following Caesarean delivery. It can be done safely with LOR technique.

Acknowledgement

We sincerely acknowledge the contribution of Mr. Musthafa and Ms. Gomathy Jeeva for their statistical work for the preparation of this manuscript.

References

1. Farragher RA, Laffey JG. Postoperative pain management following cesarean section. In: Shorten G, Carr D, Harmon D, et al., eds. Postoperative pain management: an evidence-based guide to practice. 1st ed. Philadelphia, PA: Saunders Elsevier, 2006; 225–38.
2. Netter FH. Back and spinal cord. In: Netter FH, ed. Atlas of human anatomy. Summit, New Jersey: The Ciba-Geigy Corporation, 1989; 145–55.
3. Leung A. Postoperative pain management in obstetric anesthesia—new challenges and solutions. J Clin Anesth 2004; 16:57–65.
4. Hirose M, Hara Y, Hosokawa T, Tanaka Y. The effect of postoperative analgesia with continuous epidural bupivacaine after cesarean section on the amount of breast feeding and infant weight gain. Anesth Analg 1996; 82:1166–9.
5. Hawkins JL, Koonin LM, Palmer SK, Gibbs CP. Anesthesia-related deaths during obstetric delivery in the united states, 1979–1990. Anesthesiology 1997; 86:277–84.
6. Rafi AN. Abdominal field block: a new approach via the lumbar triangle.Anaesthesia 2001; 56:1024–6.
7. Belavy D, Cowlishaw PJ, Howes M, Phillips F. Ultrasound-guidedtransversus abdominis plane block for analgesia after caesarean delivery. Br J Anaesth 2009; 103:726–30.
8. Niraj G, Searle A, Mathews M, et al. Analgesic efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing open appendicectomy. Br J Anaesth 2009; 103:601–5.
9. El-Dawlatly AA, Turkistani A, Kettner SC, et al. Ultrasound-guided transversus abdominis plane block: description of a new technique and comparison with conventional systemic analgesia during laparoscopic cholecystectomy. Br J Anaesth 2009; 102:763–7.
10. McDonnell J, Curley G, Carney J, et al. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg 2008; 106:186–91.
11. Baaj J, Alsatli R, Majaj H, Babay Z, Thallaj A. Efficacy of ultrasoundguided transversus abdominis plane (TAP) block for postcesarean section delivery analgesia—a double-blind, placebo- controlled, randomized study. Middle East J Anaesthesiol 2010; 20:821–6.
12. Costello J, Moore A, Wieczorek P, Macarthur A, Balki M Carvalho JCA. The transversus abdominis plane block, when used as part of a multimodal regimen inclusive of intrathecal morphine, does not improve analgesia after cesarean delivery. Reg Anesth Pain Med 2009; 34:586–9.
13. McMorrow RCN, Ni Mhuircheartaigh RJ, Ahmed KA, et al. Comparison of transversus abdominis plane block vs spinal morphine for pain relief after Caesarean section. Br J Anaesth 2011; 106:706–12.
14. F. W. Abdallah, S. H. Halpern and C. B. Margarido. Transversus abdominis plane block for postoperative analgesia after Caesarean delivery performed under spinal anaesthesia? A systematic review and meta-analysis.

15. Ito S, Lee A. Drug excretion into breast milk—overview. Adv Drug Deliv Rev 2003; 55:617–27.
16. Wittels B, Glosten B, Faure EA, et al. Postcesarean analgesia with both epidural morphine and intravenous patient-controlled analgesia: neurobehavioral outcomes among nursing neonates. Anesth Analg 1997; 85:600–63 .
17. Kanazi G, Aouad M, Abdallah F, et al. The analgesic efficacy of subarachnoid morphine in comparison with ultrasound-guided transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg 2010; 111:475–81.
18. Loane HH. A randomized controlled trial comparing intrathecal morphine with transversus abdominis plane block for postcesarean delivery analgesia. Int J Obstet Anesth 2012; 21:112–8.
19. McGuirk S, Fahy C, Costi D, Cyna AM. Use of invasive placebos in research on local anaesthetic interventions. Anaesthesia 2011; 66:84–91.
20. Jarman J, Marks N, Fahy CJ, Costi D, Cyna AM. Anaesthetists' risk assessment of placebo nerve block studies using the SHAM (serious harm and morbidity) scale. Anaesthesia 2012; 67:361–6.
21. Lancaster P, Chadwick M. Liver trauma secondary to ultrasoundguided transversus abdominis plane block. Br J Anaesth 2010; 104:509–10.
22. Farooq M, Carey M. A case of liver trauma with a blunt regional anesthesia needle while performing transversus abdominis plane block. Reg Anesth Pain Med 2008; 33:274–5.
23. Dahl JB, Jeppesen IS, Jorgensen H, Wetterslev J, Moiniche S. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. Anesthesiology 1999; 91:1919–27.
24. Wittels B, Scott DT, Sinatra RS. Exogenous opioids in human breast milk and acute neonatal neurobehavior: a preliminary study. Anesthesiology 1990; 73:864–9.
25. Joris J, Cigarini I, Legrand M, et al. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. Br J Anaesth 1992; 69:341–5.
26. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. Anaesthesia 2001; 56:1024–6.
27. Johns NN, O'Neill S, Ventham NT, Barron F, Brady RR, Daniel T. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominalsurgery: a systematic review and meta-analysis.Colorectal Dis 2012; 14:635–42.
28. Abdallah FW, Chan VW, Brull R. Transversus abdominis plane block: the effects of surgery, dosing, technique, and timing on analgesic outcomes. A systematic review. Reg Anesth Pain Med 2012; 37: 193–209.
29. Shiv Kumar Singh and Gulyam Kuruba S.M. The Loss of Resistance Nerve Blocks. ISRN Anesthesiology 2011.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.10

Study on the Incidence of Perioperative Arrhythmias in Lower Segment Caesarean Section Patients Under Spinal Anaesthesia

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Abstract

Background: Lower segment caesarean sections [LSCS] are the most common emergency or elective cases we come across. Majority of these cases are done under regional anaesthesia. Perioperative cardiac arrhythmias in these cases are common because of the altered physiology of pregnancy and anaesthesia. Significantly most of these arrhythmias are benign. However, some arrhythmias during spinal anaesthesia can cause sudden vascular collapse and lead to increased peri-partum morbidity and mortality. There are few case reports reported but the incidence of intraoperative arrhythmias is not well established. So this study on the incidence of arrhythmias during spinal anaesthesia in LSCS patients was undertaken.

Methodology: We conducted this prospective study for a period of one year between august 2014 to august 2015. 957 patients underwent LSCS under spinal anaesthesia in this one year period. Out of which 68 patients were excluded as they had non-pregnancy related complications. 158 patients with pregnancy related complications like eclampsia, pre-eclampsia, gestational DM and gestational HT were also excluded. 10 cases got excluded as they had inadequate block so converted to GA. The study group included 721 patients.

Results: 101 patients i,e 14% of them out of 721 patients developed arrhythmias peri-operatively. Bradycardia was seen in 39[5.40%] patients followed by ventricular ectopics in 30 [4.16%] patients.

Conclusion: Arrhythmias under anaesthesia are quite common. Most of these perioperative arrhythmias revert back spontaneously. Only few of them needs treatment and most of them have stable haemodynamics. The surgeons should be gentler and the anesthesiologists should be vigilant. Continuous, close monitoring of the patient is mandatory.

Keywords: Lower Segment Caesarean Sections [LSCS]; Perioperative Arrhythmias; Spinal Anaesthesia.

Introduction

Arrhythmias under anaesthesia are frequently encountered by anaesthesiologist's. However life-threatening arrhythmias are not so common. Adversecardiovascular events can occur during arrhythmias. Although the incidence is higher during cardiac surgery and in cardiac patients, intra-operative dysrhythmias do occur innon-cardiac patients undergoing non-cardiac surgery. The incidence is higher in general anaesthesia compared to spinal anaesthesia. Relatively minor fluctuations in haemodynamic parameters due to arrhythmias cannot have significant long-term co-morbidity. However major intra-operative dysrhythmias can cause sudden cardiovascular collapse altering the perfusion of vital organs like brain, heart and kidneys [1].

The incidence of perioperative arrhythmias are not well established during LSCS [Lower segment caesarean sections].A wide range of cardiac arrhythmias can be observed during perioperative period and they usually have multifactorial origin. A large number of these perioperative arrhythmias have stable haemodynamics and can be successfully managed. Most common causes of these perioperative arrhythmias are electrolyte imbalance, hypercapnia, hypoxia, hypothermia and hypotension [1].

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Received on 12.12.2016
Accepted on 28.12.2016

Methodology

This prospective study was conducted in the Department of Anaesthesiology; MVJ MC & RHfor a period of one year between august 2014 to august 2015. The hospital ethical committee approval for the study protocol was obtained.Written informed consent was obtained from all the patients who were enrolled for the study. Pre anaesthetic check-up was carried out as and when required with a detailed history, general examination and systemic examination, airway assessment, spinal column examination. The following laboratory tests were done - Hemoglobin, Urine analysis, Blood sugar, Blood grouping and Rh typing. Both emergency and elective LSCS patients of ASA I and IIwho received spinal anaesthesia were included in the study. Patients with previous history of arrhythmias, epilepsy, asthma, hypertension, diabetes mellitus, thyroid dysfunction, with valvular heart disease and other cardiac diseases were excluded from the study. Failed spinal or due to other reason if patient was given general anaesthesia they were also excluded from the study. Patients with pregnancy related complications like eclampsia, pre-eclampsia, gestational hypertension and gestational diabetes mellitus were also excluded from the study group.

Inside the OT IV line was secured with 18g cannula. Basal recording of pulse, ECG, blood pressure and SpO2 were recorded. After preloading with 500 mL of lactated Ringer's solution, spinal anaesthesia was administered using a 25-G Quincke spinal needle between L3- 4 intervertebral space under all aseptic precautions. 2 mL of 0.5% hyperbaric bupivacaine was injected intrathecally in lateral position after confirming free CSF flow. Oxygen was administered at 4 L/min through a simple face mask during perioperative period. Right lateral wedge was given to all patients. Intraoperative monitoring included 5 leads electrocardiography [ECG] -lead II, pulse oximetry [SpO2], noninvasive blood pressure[NIBP]. Rhythm and rate were monitored and any deviation from normalwas considered as arrhythmia. ECG was closely monitored and whenever arrhythmias occurred, the ECG was recorded. After baby extraction all patients received 5 units of oxytocin in each bottle of intravenous fluids. Ergometrine when required was given as intramuscular injection. Prostodin (15-methyl PG F2-alpha) acts as a smooth muscle stimulant and is a recognized second-line agent for use in the management of postpartum uterine atony unresponsive to oxytocin/ergometrine was given asintramuscular injection whenever required. Hypotension was defined as mean arterial pressure less than 20% of the baseline reading. Ephedrine 6 mg and crystalloids were administered intravenously whenever hypotension occurred. Atropine 0.6 mg was administered intravenously when heart rate went below 50/min. Xylocard 1mg/kg was given when the rate went above 160/min. Carotid massage on one side was also done for tachycardia more than 160/min. The results are shown as mean (±SD) and proportions are expressed as a percentage.

Results

957 patients underwent LSCS under spinal anaesthesia in this one year period between august 2014 to august 2015. Out of which 68 patients were excluded as they had non-pregnancy related complications. 158 patients with pregnancy related complications like eclampsia, pre-eclampsia, gestational DM and gestational HT were also excluded. 10 cases got excluded as they had inadequate block so converted to GA. The study group included 721 patients. 101 patients i,e 14% of them developed arrhythmias in the peri-operative period. Bradycardia was recorded in 39[5.40%] patients and

Table 1: Characteristics of patients

	Age (yrs)	Height (cm)	Weight (kg)
Mean ± SD	26.5±5.4	153.03±5.08	56.3±6.7
Range	18--29	140--162	45--82

Table 2: Perioperative incidence of arrhythmias

	Number of pt	Percentage
Bradycardia	39	5.40%
A-V blocks	9	1.24%
SVT	15	2.08%
Atrial ectopic	6	0.83%
Ventricular ectopic	30	4.16%
AF	2	0.27%
Total	101	14%

A-V-atrioventricular, SVT-supra ventricular tachycardia, AF-atrial fibrillation

Table 3: Patients receiving ergometrine and prostodin

	Number of pt	Percentage
ergometrine	272	37.72%
prostodin	196	27.18%

ventricular ectopics in 30[4.16%] patients. Supra ventricular tachycardia in 15 [2.08%] patients, atrioventricularblocks in 9 [1.24%], Atrial ectopic in 6 [0.83%] and atrial fibrillation in 2 [0.27%] patients were recorded.

Discussion

Spinal anaesthesia has been considered as safest regionalanesthesia technique for LSCS. Arrhythmias during spinal anesthesia i,e the incidence of peri-operative arrhythmias is not well established. There are very few case reports and the studies are almost not there in the literature. In this prospective study the incidence of arrhythmias during spinal anesthesia in LSCS patients was done.The incidence of arrhythmias during spinal anesthesia for Cesarean section was 14%,101 cases in our study. Most of them wereBradycardia and Ventricularectopics, followed by supra ventricular tachycardia. Although these arrhythmias were transient and recovered spontaneously few of them needed medication and they responded to the treatment. Out of these 39 patients developed bradycardia, out of which 20 were during baby extraction when uterus was pressed from above, which reverted back immediately without any treatment. 9 cases immediately after spinal anaesthesia when the patient was turned supine which was treated with inj atropine. 6 cases developed bradycardia when they were doing tubectomy, we treated only 3 cases other 3 reverted without treatment. 2 cases when they externalised the uterus for massaging, needed inj atropine and the other 2 cases developed when injProstodin was given which reverted back without treatment. Ventricular ectopics were seen in 30 patients out of whom 22 patients developed it when uterus was externalised for suturing as most of them were stable hemodynamically and less than 6 per minute we did not treat them. 3 cases were associated with bradycardia during tubectomy which was treated with atropine. 5 cases were during manual placental extraction. Supra ventricular tachycardia in 15 patients, 10 cases were after injmethergin and 5 cases after inj atropine. Atrioventricular block in 9 patients was associated with bradycardia, one case of ventricular ectopic and one case of A-V-atrioventricular block continued inspite of medication. These two cases were referred to cardiologists for further management. Most of our patients remained hemodynamically stable.All the possible causes of the perioperative cardiac arrhythmias under anaesthesia like hypoxia, hypercarbia, electrolyte abnormality acid-base imbalance, stress, and pain have been ruled out in our cases. All patients were given oxygen by mask and the blood pressure was maintained with in the normal range. Fluctuations in cardiac output, extraction of baby, placental expulsion andmedications may be the major cause of arrhythmias in over patients.

Spinal anaesthesia causes sympathetic block leading to decreased sympathetic outflow [2,4]. This causes peripheral vasodilation andfall in blood pressure. This leads to decrease in the cardiac output. If patient develops bradycardia at this stage there will be further fall in the cardiac output leading to ischemia. This needs immediate and prompt treatment. These patients will develop metabolic acidosis and electrolyte imbalances which can precipitate arrhythmias, further leading to hemodynamic instability and cardiac arrest. Surgical stimulation like handling the ovaries, peritoneal traction, massaging the uterus, giving traction to the umbilical cord to bring out the placenta and dilating the cervix can lead to perioperative arrhythmias [3,4]. A large number of these intraoperative arrhythmias can be successfully managed by observation and elimination of the implicated stimuli mentioned above.

Oxytocin bolus causes tachycardia and hypotension [5,6]. Peripheral vasodilatation and reduced myocardial filling time decreases the cardiac output causes hypotension.Tachycardia can have detrimental effects in these patients as they develop ischemia due to reduced coronary diastolic filling time increased workload and hypotension. Ergometrine [7] causes coronary vasoconstriction and hypertension and increases the risks of myocardial ischemia and pulmonary oedema.Side effects of Prostodin[PG F2-alpha] are related to its effects on smooth muscles. They include nausea, vomiting, diarrhoea, bronchospasm, and systemic hypertension. Anaesthesiologist should be vigilant during administering these drugs as potentially dangerous arrhythmias can develop.

In pregnancy heart rate increases by 25%, thus sinus tachycardia, more during the third trimester, is quite common. Ectopic beats and non sustained arrhythmia were encountered in more than 50% of pregnant women investigated for palpitations [8]. Perioperative cardiac arrhythmias are relatively

frequent in both normal adults and pregnant women. The possible precipitating factors are hypoxia, hypercapnia, myocardial infarction, catecholamines, electrolyte abnormalities, acid-base imbalance, drug toxicity and adverse drug reactions. The sudden appearance of any new arrhythmia, regardless of hemodynamic consequences, is of concern and warrants attention. But compared to normal adult during pregnancy there are some physiological changes which increases the chances of perioperative cardiac arrhythmias during normal pregnancy. These physiological changes which occur during pregnancy, during anesthesia can further increase the incidence of arrhythmias in these patients. Fifty per cent increase in intravascular volume with its peaks at third trimester, Progressive decrease in systemic vascular resistance. 30-40% increase in cardiac output, 15% increase in heart rate, beginning at 8 weeks of gestation and peaking at approximately 34 weeks.Cardiac output is increased as well, with an average of 6.7 L/min in the first trimester and ≤8.7 L/min in the third trimester. This is the result of a 35% increase in stroke volume and a 15% increase in heart rate. The increase in plasma volume causes stretching of atrial and ventricular myocytes, and this may result in early after depolarizations, shortened refractoriness, slowed conduction, and spatial dispersion through activation of stretch-activated ion channels.Several hypothetical mechanisms have been invoked to explain the increased propensity for arrhythmias during the pregnancy. These include hemodynamic, autonomic, hormonal, and emotional changes related to pregnancy leading to increased plasma catecholamine concentrations and adrenergic receptor sensitivity, atrial stretch, and end diastolic volumes due to intravascular volume expansion [8]. Progesterone can cause selective cardiac depressant effect. Estrogen may alter the actomyocin-ATPase relationships in the myocardium and increase myocardium contractility. Although there are no relevant studies on the effect of sex hormones on the cardiac tissue, however, studies say that estrogens increase the number of β-adrenergic receptors in the myocardium and the α-adrenergic receptors in platelets [10,11]. Lower segment caesarean sections [LSCS] patients with altered physiology because of pregnancy are more prone during anaesthesia. If not recognised and treated timely they are at high risk in post-operative period for further complications like stroke, myocardial infarction, congestive cardiac failure, severe ventricular dysrhythmias, renal failure and cardiac arrest [1,6,10].

The resting ECG of a pregnant woman will be slightly different to that of a non pregnant woman.The increase in heart rate can lead to decreased PR, QRS and QT intervals. The electrical axis can be shift to the left because of the gravid uterus, and ectopics (premature atrial/ventricular beats) are quite common during pregnancy. There may be a Q wave and inverted T wave in the inferior leads.4 to 14 percent of women develop nonspecific ST segment and T-wave changes which typically resolve after delivery.The incidence of APBs and VPBs was found to be 56 and 59 percent, respectively. During labor, APBs and VPBs were detected in 90 and 50 percent of women, respectively. Stretch of the chambers particularly the left atrium produces cardiac conduction abnormalities. Supraventricular tachycardias and ventricular extrasystoles are common during pregnency,while many arrhythmias which occur during pregnancy are benign and self-limited [12].

Somboonviboon W [13]et al conducted a prospective cross sectional study from November 1, 2004 to July 31, 2005 on 722 parturients undergoing caesarean section under spinal anaesthesia.The current study evaluated factors associated to the incidences of hypotension or bradycardia.Incidence of hypotension and bradycardia were 52.6% and 2.5%. There results indicated that the incidence of hypotension after spinal anesthesia for cesarean section increased with amount of estimated blood loss > 500 mL and analgesic level > T4. Adding intrathecal morphine 0.2 mg (0.2 mL) to local anesthetics increased incidence of bradycardia.

Shen CL [14], et al studied 254 healthy women undergoing Cesarean section under spinal anesthesia prospectively. There results showed first degree atrioventricular block in nine patients (3.5%), second degree atrioventricular block in nine (3.5%), severe bradycardia(heart rate < 50 beats/min) in seventeen (6.7%), multiple VPC in three (1.2%) patients. The height and weight of patients with severe bradycardia, multiple VPCs, or atrioventricular block were not different from those of the other patients. However, the age of patients in the potentially dangerous arrhythmias group was greater than that in the other group (P = 0.006). They concluded that the incidence of arrhythmias as well as hypotension during spinal anesthesia for Cesarean section was higher than expected. Although most of these arrhythmias were transient and recovered spontaneously, they might unexpectedly occur and sometimes need immediate and prompt treatment.

Lewis NL [15] et al in the UK registry of high risk obstetric anaesthesia: arythmias, cardio-myopathy,

aortic stenosis, transposition of great arteries and marfan's syndrome reported as follows. In UK registry of high-risk obstetric anaesthesia which was set up in late 1996 to collect reports of high-risk pregnancy. They pooledthem into a central database. At the time of analysis for this paper i,e December 31, 2001, 308 cardiorespiratory reports were received. The five most common conditions, occurring in 125 cases (41% of the total), were arrhythmias (43 cases), cardiomyopathy (26 cases), aortic stenosis (24 cases), transposition of the great arteries (18 cases) and Marfan's syndrome (14 cases).

A wide range of cardiac arrhythmias can be observed in perioperative period. A large number of these perioperative arrhythmias revert back spontaneously. Most of them have stable haemodynamics and can be successfully managed. Administering oxytocic drugs should be in infusion as stat can causepotentially dangerous arrhythmias. The probable causes of these perioperative arrhythmias are acute blood lose, hypotention, bradycardia and tachycardia.Surgical causes like handling the ovaries, pushing hardly the abdomen during baby extraction, externalizing the uterus, massaging the uterus, giving traction to the umbilical cord to take out the placenta and dilating the cervix can also lead to perioperative arrhythmias. Most of them can be avoided, the surgeons should be gentler and the anesthesiologists should be more vigilant. Due to reduced cardiopulmonary reserve in pregnancy perioperative arrhythmias can lead to major cardiovascular complications.

Conclusion

In the current study, we analyzed the incidence of perioperative incidence of arrythmias during cesarean under spinal anesthesia. Spinal anaesthesia is an excellent regional technique which provides good operating conditions for caesarean section. Anesthesiologists caring pregnant women must remember that perioperative arrhythmias may occur without any warning signal and timely intervention is the only key for maternal safety. Continuous, close monitoring of the patient is mandatory.

References

1. Stoelting RK, Hines RL, Marschal KE, editors. 5th ed. Philadelphia: Saunders/Elsevier; 2008. Stoelting's Anesthesia and co-existing disease.
2. Greene N, Brull S. 4th ed. Baltimore: Williams and Wilkins; 1992. Physiology of Spinal Anesthesia.
3. Coventry DM, McMenemin I, Lawrie S. Bradycardia during intra-abdominal surgery. Modification by pre-operative anticholinergic agents. Anesthesia. 1987; 42:835–9.
4. Shen CL, Hung YC, Chen PJ, Tsao CM, Ho YY. Mobitz type II AV block during spinal anesthesia. Anesthesiology. 1999; 90:1477–8.
5. Charbit B, Funck-Brentano C, Benhamou D, Weissenburger J. Effects of oxytocin on Purkinje fibres.Br J Anaesth. 2012; 108:1039–1041.
6. David H. Chestnut, ýCynthia A Wong, ýLawrence C Tsen Chestnut's Obstetric Anesthesia: Principles and Practice- 2014.
7. Hung MJ, Cheng CW, Yang NI, Hung MY, Cherng WJ. Coronary vasospasm-induced acute coronary syndrome complicated by life-threatening cardiac arrhythmias in patients without hemodynamically significant coronary artery disease. Int J Cardiol. 2007; 117:37–44.
8. Shotan A, Ostrzega E, Mehra A. Incidence of arrhythmias in normal pregnancy and relation to palpitations, dizziness, and syncope. Am J Cardiol 1997; 79:1061–64.
9. Urmila Palaria1, Mohd A Rasheed1, Geeta Jain2, AK SinhaAnesthetic management of Wolff-Parkinson-White syndrome in a pregnant patient posted for emergency caesarean section. Anesthesia essays and researches : 2013; 7(3):408-410.
10. Roberts JM, Insel PA, Goldfien A. Regulation of myometrialadrenoreceptors and adrenergic response by sex steroids. MolPharmacol 1981; 20: 52-8.
11. Metz A, Stump K, Cowen PJ, Elliott JM, Gelder MG, Grahame-Smith DG. Changes in platelet alpha 2-adrenoceptor binding post partum: Possible relation to maternity blues. Lancet 1983; 1:495-8.
12. Carruth J E, Mivis S B, Brogan D R. The electrocardiogram in normal pregnancy. Am Heart J 1981; 102:1075–78.
13. Somboonviboon W, Kyokong O, Charuluxananan S, Narasethakamol A. Incidence and risk factors of hypotension and bradycardia after spinal anesthesia for cesarean section. J Med Assoc Thai. 2008; 91:181–7.
14. Shen CL, Ho YY, Hung YC, Chen PL.Arrhythmias during spinal anesthesia for Cesarean section.Can J Anaesth. 2000 May; 47(5):393-7.
15. Lewis NL, Dob DP, Yentis SM. UK registry of high risk obstetric anaesthesia: arythmias, cardio-myopathy, aortic stenosis, transposition of great arteries and mairfare syndrome. IJOA 2003; 12:28-34.
16. SouvikMaitra, Dalim Kumar Baidya, and

SulagnaBhattacharjeeNear fatal bradycardia during cesarean section under spinal anesthesia: "High spinal" may not be only risk factor. Saudi J Anaesth. 2014 Nov; 8(Suppl 1):S118–S119.

17. Jang YE, Do SH, Song IA. Vasovagal cardiac arrest during spinal anesthesia for Cesarean section — A case report. Korean J Anesthesiol. 2013; 64:77–81.
18. Ou CH, Tsou MY, Ting CK, Chiou CS, Chan KH, Tsai SK. Occurrence of the Bezold-Jarisch reflex during Cesarean section under spinal anesthesia — A case report. ActaAnaesthesiol Taiwan. 2004; 42: 175–8.
19. SeemaKalra and NitinHayaranArrhythmias following spinal anesthesia for cesarean delivery - Is Wenckebach common?J Anaesthesiol Clin Pharmacol. 2011 Oct-Dec; 27(4):541–543.
20. Gowda R M, Khan I A, Mehta N J. Cardiac arrhythmias in pregnancy: clinical and therapeutic considerations. Int J Cardiol 2003; 88:129–133.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.11

Comparative Study of Isoflurane and Sevoflurane as an Inducing Agent in Paediatric Group

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Abstract

In the present study pediatric patients of ASA g-1 & ASA-II were selected and divided in two groups each consisting of 30 patients. Induction done by Isoflurane is labelled as "Group-A" and sevoflurane as "Group-B".

The aim of study was to compare the induction and emergence from anaesthesia, complications during induction and post operative period and haemodynamic stability intraoperatively, In the present study, It was observed that mean pulse rate remain stable in sevoflurane and increased in isoflurane.

The mean induction time for isoflurane was 130 seconds as compared to sevoflurane 106 seconds. The complications like bradycardia, hypotension were more with sevoflurane, whereas breathholding, coughing, laryngospasm and salivation were more in isoflurane. In sevoflurane mean recovery time was 84 seconds and in isoflurane it was 110 seconds.

Postoperative pain and crying was same in both groups. In conclusion, induction and emergence from sevoflurane is rapid and pleasant than isoflurane.

Keywords: Anaesthesia; General Paediatrics; Induction Agent; Sevoflurane; Isoflurane.

Introduction

In paediatric age group, anaesthesiologist usually prefer anaesthetic techniques more likely to be associated with a rapid induction and emergence such type of induction is fulfilled by inhalational anaesthesia: halothane, isoflurane and sevoflurane anaesthetic agents. In this study we have studied to evaluate the use for induction and emergence from anaesthesia, complication during induction and postoperative period and haemodynamic stability. Sevoflurane is a newer inhalational inducing agent of anaesthesia, this is because of its low blood gas solubility, more depth of anesthesia, less airway irritation and profound respiratory depression with maintained cardiovascular stability.

Methods

Patients of physical status as a grade I & II undergoing elective surgical procedures like fiuid hernia, appendicitis, circumcision and cleft lips of age 4 to 5 years were selected and divided into two groups and were labelled as group 'A' and group 'B'. Informed consent was obtained preoperatively. All patients were premedicated with Inj Glycopyrollate 0.004 mg/kg before induction. In group "A", induction was done with 50% O_2, 50% N_2O and isoflurane and in group "B" induction was done with 50% O_2, 50% N_2O and sevoflurane by using modified Jackson Rees Circuit. Induction in group A was carried out by increasing the concentration of isoflurance from 0.5 to 3 to 3.5% while the group' B the concentration of sevoflurane was increased from 1% to 5-6% in a stepwise manner till loss of eyelid and eyelash reflexes with maintained regular breathing.

The time required for induction of anaesthesia was noted and patients were observed for complications like breathholding, coughing, laryngospasm, salivation, tachycardia, bradycardia and hypotension. All patients were intubated under the effect of inj. i.v. succinylcholine 2 mg/kg. Maintenance of anaesthesia was done with 50% O_2, 50% N_2O and isoflurane 1 to 1.5% and sevoflurane 2 to 2.5% with controlled ventilation. The long acting muscle relaxant was

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Received on 22.12.2016

Accepted on 28.12.2016

not given because time required for operative procedures was very short, it was 20 to 25 min. Intraoperative monitoring of pulse, blood pressure, SPO_2 and $ETCO_2$ was done. At the end of surgery, isoflurane, sevoflurane and N_2O stopped and patients were observed for time required for recovery. Postoperatively temperature, pulse, blood pressure, SPO_2, $ETCO_2$ noted and patients were also observed for complications like nausea, vomiting, pain, crying, respiratory movements, hypothermia, shivering and cyanosis.

Observation

Table 1: Demographic Comparison of two groups

Sr. No.	Name of drug	Age in Years	Sex		Weight (kg)
			Male	Female	
1	Group A (Isoflurane)	4-5	20	10	10-14
2	Group B (Sevoflurane)	4-5	20	10	10-14

Table 2: Showing incidence of various complication during

Sr. No.	Group A (Isoflurane) Number/Percentage	Group B (Sevoflurane) Number/Percentage	Complication
1	6 (20%)	1 (3.33%)	Breath holding
2	2 (6.66%)	0 (0.0%)	Coughing
3	7 (20.33%)	5 (16.66%)	Salivation
4	1 (3.33%)	4 (13.33%)	Bradycardia
5	4 (13.33%)	0 (0.0%)	Tachycardia
6	1 (3.33%)	3 (10%)	Hypotension
7	3 (10%)	0 (0.0%)	Laryngospasm

Table 3: Showing statistical changes in mean induction time

Sr. No.	Name of Drug	Mean Induction time (Seconds)	S. D.	t- Value	p- Value
1	Group A (Isoflurane)	130	+/- 20.30	4.20	P < 0.01
2	Group B (Sevoflurane)	106	+/- 12.20		

Table 4: Showing statistical changes in mean recovery time

Sr. No.	Name of Drug	Mean Recovery time (Seconds)	S. D.	t- Value	p- Value
1	Group A (Isoflurane)	110	+/- 30.20	3.99	P < 0.01
2	Group (Sevoflurane)	84	+/- 22.40		

Results

In this study 60 patients were compared in respect with age, sex and body weight (Table 1). Table 2 showing the incidence of respiratory complications like breathholding, coughing and laryngospasm during the induction were higher in the isoflurane group whereas bradyclirdia and hypotension were more with sevoflurane group.

The mean induction time with isoflurane was 130 (+/- 20.30) sec. and in sevoflurance was 106 (+/- 12.20) sec. Induction was faster with sevoflurane as compared to isoflurane which was highly significant stastically ($P < 0.01$) (Table 3). In sevoflurance group mean pulse rate/min remain stable and in isoflurance group mean pulse rate/min. increase which was statistically significant ($P < 0.05$). In sevoflurane group mean arterial pressure decreased and in isoflurane group, there was no significant change in mean arterial pressure which was statistically highly significant ($P < 0.01$). No significant changes in arterial oxygen saturation (SPO_2) were noted in both groups. Mean recovery time in sevoflurane was 84 (+/- 22.40) which was shorter than isoflurane group. 110 (+/- 30.20) sec and was statistically highly significant ($P < 0.01$) (Table 4).

Discussion

Inhalation induction by mask is the commonly used technique in paediatric anaesthesia because it can be achieved relatively easily and rapidly in most

children. Sevoflurane is one of the newer addition to inhalational anaesthesia agents and its use as induction agent is well documented in children.

In this study group sevoflurane was well accepted by 29 patients. (96.67%). The significantly short induction time (106 +/- 12.20 sec.) was the main advantage. While in isoflurane group 6 in 30 patients started breathing, 2 patients coughing, 7 salivation, 1 bradycurdia, 4 tachycardia and 1 hypotension as compared to sevoflurane, 1 in 30 patients started breath holding, 5 salivation, 4 bradycardia and 3 patients hypotension. 3 in 30 patients in isoflurane had laryngospasm. So mask was kept away from the face and slowly brought closer and the concentration of isoflurane was gradually increased which look significantly longer induction time. (130 +/- 20.30 sec.)

Dash field et al, sloan MH et al, had quoted induction time of 54 sec and 34 sec. respectively. They had taken children in the age group of 7 years and above could easily follow the command for single breath vital capacity induction. In this study group age was 4 to 5 years and weight was 10-14kg, so explanation of the methodology for single breath vital capacity induction was not possible. The induction of anaestesia was smooth in sevoflurane group. The incidence of coughing (6.66%) and laryngospasm (10%) was noted in isoflurane group which is similar to the result obtained by Dashfield et al.

Sevoflurane did not alter the heart rate and it remained stable and unchanged from awake baseline throughout anaesthetic period and even lower heart rates were noticed compared with isoflurane. 4 Patients developed, bradycardia, but it returned to nomal after decreasing the concentration of sevoflurane. Same findings described by Ebert TJ et al. In sevoflurane group mean arterial pressure decrease more than isoflurane group. Ebert TJ et al showed that sevoflurane decreased blood pressure to a greater extent than did isoflurane. Mean recovery time in sevoflurane was 84 +/- 22.40 sec and in isoflurane 110 +/- 30.20 sec. Frink EJ et al found that more rapid emergence occurred after sevoflurane anaesthesia (7.5 min) compared with isoflurane anaestesia (18.6 min.) From the present study it is concluded that induction and emergence from sevoflurane anaesthesia is rapid and pleasant and is associated with less complications like breathholding, laryngospasm, coughing as compared with isoflurane anaesthesia.

References

1. Ti LK, Pua HL, Lec TL. Single breath vital capacity nhalational anaestetic induction in adults isoflurane versus sevoflurane. Can J Anaesth 1998; 45:949-53.
2. Dashfield AK, Birt DJ, Thurlow J, Kestin IG, Longton JA. Recovery characteristics using single breath 8% sevoflurane or propofol for induction of anaethesia in day case arthroscopy patients. Anaethesia 1998; 53:1062-6.
3. Yasuda N, Targ AG, Eger EI II : Solubility of I-653, sevoflurane, isoflurane and halothane in human tissue. Anesth, Analg 1989; 69:370-373.
4. Sloan MH, Conard PF,, Karasunky PK, Gross JB, Sevoflurane versus isoflurane : induction and recovery charachteristics with single breath inhaled induction of anaesthesia. Anesth Analg 1996; 82: 585-32.
5. Ebert TJ, Robinson BJ, Uhrich TD, Machenthun A, Pichotter PJ. Recovery from sevoflurane anaesthesia: a comparison to isoflurane and propofol anaesthesia. Anesthesiology 1998; 89:1524-31.
6. Doi M, Ikeda K : Respiratory effect of sevoflurane. Anesth Analg 1987; 66:241-4.
7. Inada T. Inada K : Respiratory effect of sevoflurane. Anesth Analg 1987 ; 66:241-4
8. Mori N, Suzuki M. Sevoflurane in paediatric anaesthesia ; effect on respiration and circulation during induction and recovery. Paed Anaesth 1996; 6:95-102.
9. Ebert TJ, Harkin CP, Muzi M : Cardiovascular respones to sevoflurane : A review. Anesth Analg 1995; 81:S11.
10. Frink Jr. EG, Malam TP. Atlas M et al : comparison of sevoflurane and isoflurane in healthy patient. Anesth Analg 1992; 74;241-5.

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Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.12

Are We Performing Hand Hygiene: A Lifesaving Skill Correctly?

Nishith Govil*, Shalini Dadu, Vinay Rai***, Parag Kumar***

Abstract

Introduction: This question is asked invariably just like being asked during CPR's correct method and right timing of practicing hand hygiene to avoid a loss of life to hospital acquired infection (HAI). Are we doing enough? Are we reminding others enough? Aim: This study is done to assess the level of knowledge; attitudes and practices among health care worker in ICU with regard to hand hygiene and to suggest documented and globally accepted recommendation for betterment in present practices and to improve compliance.

Methodology: 100 nurses were selected by stratified random sampling technique and given a questionnaire consisted of standard precautions for hand hygiene. Next we intervene with an education module explaining all the measures that should be followed to control nosocomial infection and correct indications and methods for hand hygiene then we study the impact of education and measure any change in the level of compliance and attitude among different health care worker. Objectively we compared the result of skin swab culture from the dorsum of nurse's hands for presence of endogenous microbial flora before and after the educational intervention.

Statistical analysis: Descriptive statistics were used to summarize the data obtained.

Result and conclusion: If the measures followed for hand hygiene are continuously pursued and upgraded, the infection level can be further reduced. This can be done by giving training, conducting awareness programme, providing asses of healthcare worker to standard requirements of hand hygiene and implementation of infection control programs.

Keywords: Hand Hygiene; ICU; Lifesaving Skill.

Introduction

This question is asked invariably just like being asked during CPR – correct method and right timing of practicing hand hygiene to avoid a loss of life to hospital acquired infection (HAI). Are we doing enough? Are we reminding others enough? To know the answers of these questions we conducted a observational study to assess the knowledge, attitude and practices among health care worker (HCW) in the role of hand hygiene in preventing HAI in a teaching medical school.

Nosocomial infections affect both developed and resource-poor countries and are a significant economical and morbidity burden both for the patient and for public health [1]. Prolonged stay not only increases direct costs to patients but also indirect costs due to lost work. A study by Coella R et al [2] showed that the overall increase in the duration of hospitalization for patients with surgical wound infections was 8.2 days, ranging from 3 days for gynecology to 9.9 for general surgery and 19.8 for orthopaedic surgery. The increased use of antibiotics, need for isolation and the use of additional laboratory and other diagnostic studies also contribute to costs. Hospital-acquired infections divert resource allocation for primary and secondary health care to the management of potentially preventable conditions.

The WHO study [1] has shown that the highest prevalence of nosocomial infections occurs in intensive care units and in acute surgical and orthopaedic wards. There are various modes of acquiring nosocomial infections but direct transmission from one patient to another by way of health

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Received on 22.12.2016
Accepted on 28.12.2016

care workers (HCWs) who have not washed their hands between patients or HCWs who do not practice control measures such as hand disinfection or glove use is the most common cause. Despite knowing the significance of hand hygiene compliance of HCWs with the recommended hand hygiene practices remains low. Causes of poor compliance are lack of awareness among HCW and the organization, cost containment, logistical barriers and other reasons like dryness of skin, being too busy, and wards being full and understaffed. At many places lack of access to sinks, running water and alcohol-based handrub is likely to contribute to lower rates of compliance in hand hygiene

The importance of hand hygiene is universally acknowledged by organizations such as the Joint Commission, World Health Organization (WHO) and Centers for Disease Control (CDC) which recommend hand hygiene practices and interventions to improve hand hygiene compliance in order to reduce health care-acquired infections [3,4].

This study is done to identify priorities area for change, guide the preparation and revision of ongoing action plans. Finding out details about the baseline knowledge of HCW, prevailing practices and hand hygiene compliance rates ideally should be completed by the hand hygiene programme coordinator at speciûed follow-up intervals when an update is necessary to maintain the required hand hygiene infrastructures.

Objective

1. To assess the level of knowledge, attitudes and practices among health care worker in ICU with regard to hand hygiene.
2. To suggest documented and globally accepted recommendation for betterment in present practices and to improve compliance.

Methodology

The study was done over a period of one month in the two surgical ICU of a tertiary hospital associated with a teaching medical college after taking due permission from the research committee, medical superintendent and ICU in charge This is a Descriptive Prospective study where 100 ICU nursing staff of either sex was enrolled and data collection was done by interviewing them through semi structured questionnaire. After collecting the data, it was analyzed by using percentage analysis and bar graphs to reach a conclusion.

100 nurses were selected by stratified random sampling technique from the directory for each ICU. For our survey we use the instrument "Hand Hygiene Knowledge Questionnaire for Health- Care Workers" prepared by infection control experts from WHO according to international guidelines on standard hand hygiene practices. The questionnaire consisted of three main domains, with 21 close-ended items i.e., students' demographic profile (10 items), knowledge (5 items), and following standard precautions for hand hygiene (6 items).

Prior to the study, participants were given a brief introduction to the purpose of the study, after which their consent was sought and obtained. All the participants completed and returned the Questionnaire giving a response rate of 100%. After the collection of filled questionnaire feedbacks were taken from them about their current hand hygiene practices in ICU in preventing nosocomial infection

Next day we intervene with an education module explaining all the measures that should be followed to control nosocomial infection and correctindications andmethods for hand hygiene. Then we again distribute the questionnaire at different time intervals to study the impact of education and measure any change in the level of compliance and attitude among different health care worker. Objectively we compared the result of skin swab culture from the dorsum of nurse's hands for presence of endogenous microbial flora before and after the educational intervention. These cultures were collected from the hands of all the nurses during their working hours in the ICU while giving medical care to the patients.

We have conducted our study in the Surgical ICU of our hospital which has the capacity to intake 24 patients for postoperative care as well as patients of trauma and other surgical emergencies. Majority of patients are admitted for a prolong stay with Foley's catheter, central lines or peripheral IV cannulas, drains and have to undergo regular dressing changes by the doctors and nursing staffs. Patient's mobilization during nursing care or dressings or for recuperation as well as their waste management is also carried out by nursing staff and ward aides.

Statistical Analysis and Results

We used a data capturing form to collect subjects' sociodemographic characteristics, their understanding of nosocomial infection and their main source of information.Descriptive statistics were used to summarize the data obtained. Questions were

asked regarding practices followed for hand hygiene, compliance of hand hygiene and HCW's knowledgeand interest in upgrading their knowledge about nosocomial infections were assessed. A response rate of 100% was achieved through close follow-up among the participants.

Profiles of 100 nursing staff randomly sampled to participate in our studycomprised of 28 males (28%) and 72 females (72%). Their mean age was 23.5 ± 1.20 years. Their education background with respect to qualifications and working experience in ICU were similar.

Of the staff interviewed, 80% of the nursing staff has not received any formal training in hand hygiene in the last three year. The knowledge they have got is generally acquired from their colleagues and seniors. Also what they have learned during their internship and professional course has not been updated anytime with respect to hand hygiene as well as others measures undertaken to reduce incidence of hospital acquired infection. 38% of the respondents use hand rub as a method of hand hygiene in comparison to soap and water wash because it takes less time to sterilize their hands with alcohol based preparation, washing area is far from their service area and due to other factors discussed later.

Majority of health care worker (26%) consider that "Health-care workers' hands when not clean" is the main route of cross-transmission of potentially harmful germs between patients in a health-care facility. "Patients' exposure to colonized surfaces" is perceived as the second most common (12%) cause of spreading HAI. 40% of the participated staff feels that "The hospital's water system" is the most frequent source of germs responsible for health care-associated infections while only 32% feels that germs already present on or within the patient is the major source of germs.

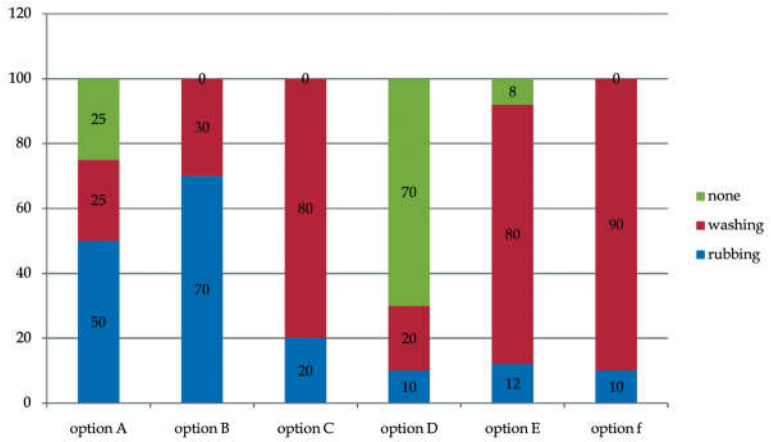
Respondents gave varying answers in response to the question that which hand hygiene action prevents transmission of germs to the patient. Majority feel that "Before touching a patient" and "Immediately before a clean/aseptic procedure" are absolute indications to perform hand washing followed by hand rub with an alcohol based solution. Similarly for the question that which hand hygiene action prevents transmission of germs to the health care worker. Consensus was that "Immediately after a risk of body fluid exposure" and "after touching a patient" exposes the health worker to risk of contamination

A short glossary of terms like hand washing, hand rubbing etc. were provided to nursing staff before they filled the questionnaire. Almost above 90% believe that alcohol based hand rubbing is more rapid, more effective against germs but cause more irritation to the skin than soap and water based hand washing. Surprisingly and correctly 90% of respondents feel that handwashing and hand rubbing are to be done in sequence to protect from the germs present in water

Majority of the staff believed that giving more time for hand rub will be more effective against germs and so around 50% believe that 1 minute is the minimal time needed for alcohol-based handrub to kill most germs on your hands as against 20 seconds (only 25%). Lastly, almost 96 % feels that wearing jewellery and damaged skin are associated with increased likelihood of colonization of hands with harmful germs. Rubbing is the preferred of hand hygiene method before performing a sterile procedure or touching a patient while washing is the preferred method when exposure to blood or bodily fluid occurs.

Varying response was obtained (Table 1) for the query related to their daily working "Which type of hand hygiene method is required in the following situations?" which showed that their knowledge is based on their own assumptions and not on formal protocols.

Which type of hand hygiene method is required in



the following situations?

Option A:before palpation of the abdomen

Option B: before giving an injection

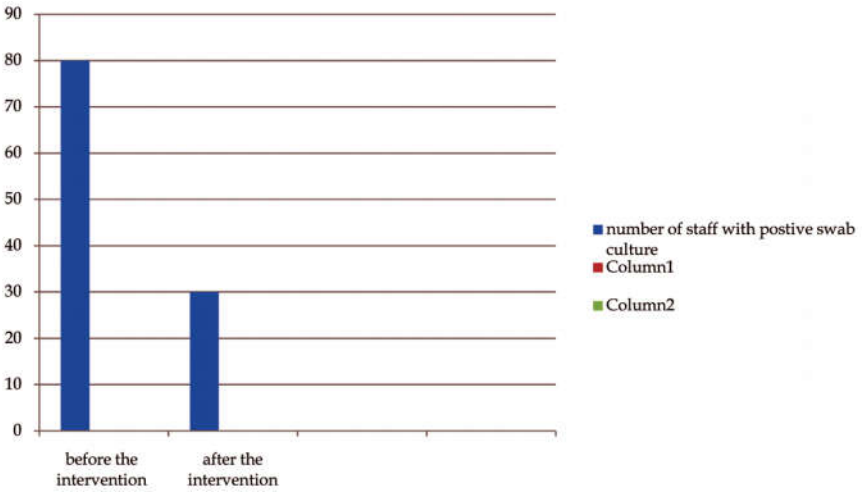
Option C: after emptying a bedpan

Option D: after removing examination gloves

Option E: after making a patient's bed

Option F: after visible exposure to blood

Results of skin swab culture from the dorsum of hand where positive culture means growth of endogenous microbial flora.



Discussion

WHO (2002) Definitions [1]of HAI states thatany infection acquired in hospital by a patient who was admitted for a reason other than that infection or an infection occurring in a patient which was not present or incubating at the time of admission. For most bacterial infections the onset of symptoms more than 48-72 hours after admission and within 10 days after hospital discharge are defined as nosocomial or hospital acquired. When the incubation period is unknown, an infection is called nosocomial if it develops any time after admission. Surgical site infections (SSI) are considered nosocomial if the infections occur within 30 days after the operative procedure or within 1 year if a device or foreign material is implanted.

Common Routes of transmission of HAIare by direct contact – hands andindirectly by contaminated or unsterilized instruments, airborne contacts of dust particles, spores and common vehicle spread. In 1999, Dancer [5]depicts that many microorganisms associated with hospital-acquired infections display two particular features; firstly, they are pathogens of well-established medical importance and secondly, they can withstand the rigorous sterility of the hospital environment. Some pathogens originate from the patient's own flora, especially those who are immunocompromised and others can survive only in human tissues and thus rely upon person-to-to person spread in order to disseminate. In 2009, the WHO published guidelines for proper hand-hygiene[3] protocol and how to design a multi-faceted, multi-modal intervention to increase proper hand hygiene with special focus on individual factors such as normative beliefs (peer behavior), perceived control, and attitude (awareness of being observed) to decrease the spread of nosocomial infection.

A 2008 systematic review [6] addressed studies evaluating the impact of hand hygiene interventions and its impact in reduction of HAI. Interventions included multifaceted initiatives, introduction of new hand-hygiene products, implementation of practices and policies, direct surveys and electronic monitoring. Eighteen of 31 included studies (58%) reported a statistically significant reduction in healthcare-associated infections with the intervention compared with the control group.

However progress in decreasing HAI is stopped by decrease of compliance with the standard protocols. Some Observed risk factors for poor adherence to recommended hand-hygiene practices are Physician status (rather than a nurse), Nursing assistant status (rather than a nurse), Male sex, working in an ward with high patient load rather than ICU and activities with low risk of cross-transmission. Self-reported factors by nurses for poor adherence with hand hygiene are handwashing agents causing irritation and dryness, sinks are inconveniently located, lack of soap and paper

towels, being too busy, understaffing, patient needs taking priority. And lastly lack of knowledge of guidelines/protocols, beliefs that glove use obviates the need for hand hygiene, forgetfulness, no role model from colleagues or superiors, skepticism regarding the value of hand hygiene, disagreement with the recommendations and lack of scientific information of definitive impact of improved hand

Hand Hygiene Knowledge Questionnaire for Health-Care Workers

Period Number*

- The knowledge required for this test is specifically transmitted through the WHO hand hygiene training material and you may find the questions more difficult if you did not participate in this training.
- Tick **only one answer** to each question.
- Please read the questions carefully before answering. Your answers will be kept confidential.
- **Short Glossary:**

Alcohol-based handrub formulation: an alcohol-containing preparation (liquid, gel or foam) designed for application to the hands to kill germs.

Facility: health-care setting where the survey is being carried out (e.g., hospital, ambulatory, long-term facility, etc).

Handrubbing: treatment of hands with an antiseptic handrub (alcohol-based formulation).

Handwashing: washing hands with plain or antimicrobial soap and water.

Service: a branch of a hospital staff that provides specified patient care.

Ward: a division, floor, or room of a hospital for a particular category or group of patients (it corresponds to the smallest segmentation of the health-care facility; one service can include multiple wards).

1. **Personal ID**:**
2. **Date:**
3. **Facility:**
4. **Service**:**
5. **Ward**:**
6. **City:****
7. **Country**:**

8. **Gender:** ☐ Female ☐ Male
9. **Age:** ☐ years
10. **Profession***:** ☐ Nurse ☐ Auxiliary nurse ☐ Midwife ☐ Medical doctor ☐ Resident ☐ Technician ☐ Therapist ☐ Nurse student ☐ Medical student ☐ Other

11. * To be completed by the data manager.
** **Optional**, to be used if appropriate, according to the local needs and regulations.
*** **Technicians**: radiologist, cardiology technician, operating room technician, laboratory technician
Therapist: physiotherapist, occupational therapist, audiologist, speech therapist
Others: dietician, dentist, social worker, etc.

1. **Department (please select the department which best represents yours):**

☐ Internal medicine ☐ Surgery ☐ Intensive care unit ☐ Mixed medical/surgical

☐ Emergency unit ☐ Obstetrics ☐ Paediatrics ☐ Long-term/rehabilitation

☐ Outpatient clinic ☐ Other

2. **Did you receive formal training in hand hygiene in the last three years?** ☐ Yes ☐ No

3. **Do you routinely use an alcohol-based handrub for hand hygiene?** ☐ Yes ☐ No

4. **Which of the following is the main route of cross-transmission of potentially harmful germs between patients in a health-care facility? (*tick one answer only*)**

a. ☐ Health-care workers' hands when not clean

b. ☐ Air circulating in the hospital

c. ☐ Patients' exposure to colonised surfaces (i.e., beds, chairs, tables, floors)

d. ☐ Sharing non-invasive objects (i.e., stethoscopes, pressure cuffs, etc.) between patients

5. **What is the most frequent source of germs responsible for health care-associated infections? *(tick one answer only)***

a. ☐ The hospital's water system

b. ☐ The hospital air

c. ☐ Germs already present on or within the patient

d. ☐ The hospital environment (surfaces)

6. **Which of the following hand hygiene actions prevents transmission of germs *to the patient*?**

e. Before touching a patient ☐ Yes ☐ No
f. Immediately after a risk of body fluid exposure ☐ Yes ☐ No
g. After exposure to the immediate surroundings of a patient ☐ Yes ☐ No
h. Immediately before a clean/aseptic procedure ☐ Yes ☐ No

7. **Which of the following hand hygiene actions prevents transmission of germs *to the health-care worker*?**

i. After touching a patient ☐ Yes ☐ No
j. Immediately after a risk of body fluid exposure ☐ Yes ☐ No
k. Immediately before a clean/aseptic procedure ☐ Yes ☐ No
l. After exposure to the immediate surroundings of a patient ☐ Yes ☐ No

8. **Which of the following statements on alcohol-based handrub and handwashing with soap and water are true?**

a. Handrubbing causes skin dryness more than handwashing ☐ True ☐ False

b. Handrubbing is more effective against germs than handwashing ☐ True ☐ False

c. Handwashing and handrubbing are recommended to be performed in sequence ☐ True ☐ False

1. **What is the minimal time needed for alcohol-based handrub to kill most germs on your hands?** ***(tick one answer only)***

   d. ☐ 20 seconds

   e. ☐ 3 seconds

   f. ☐ 1 minute

   g. ☐ 10 seconds

2. **Which type of hand hygiene method is required in the following situations?**

h.	Before palpation of the abdomen	☐ Rubbing	☐ Washing	☐ None
i.	Before giving an injection	☐ Rubbing	☐ Washing	☐ None
j.	After emptying a bedpan	☐ Rubbing	☐ Washing	☐ None
k.	After removing examination gloves	☐ Rubbing	☐ Washing	☐ None
l.	After making a patient's bed	☐ Rubbing	☐ Washing	☐ None
m.	After visible exposure to blood	☐ Rubbing	☐ Washing	☐ None

3. **Which of the following should be avoided, as associated with increased likelihood of colonisation of hands with harmful germs?**

n.	Wearing jewellery	☐ Yes	☐ No
o.	Damaged skin	☐ Yes	☐ No
p.	Artificial fingernails	☐ Yes	☐ No
q.	Regular use of a hand cream	☐ Yes	☐ No

Thank you very much for your time!

WHO acknowledges the Hôpitaux Universitaires de Genève (HUG), in particular the members of the Infection Control Programme, for their active participation in developing this material.

hygiene on health-care–associated infection rates.

A study by Boyce [7] in 2011 with the focus on "Monitoring health care workers' compliance with hand hygiene practices"recommends using validated methodology for monitoring compliance which include patient-observations, measuring of hand hygiene product consumption and electronic hand hygiene compliance monitoring systems (e.g. real-time location systems or video monitoring). Similarly the Joint Commission created a monograph for health care organizations to properly measure hand hygiene compliance using three measurement methods i.e. surveys, measuring product use and directly observing hand hygiene performance. Comprehensive content for the monograph came from the Consensus Measurement in Hand Hygiene Project and published review literature [8].

In response to feedbacks in removing the flaws and additional perceived barriers that come to our notice from the respondents of our study are lack of active participation in hand-hygiene promotion at institutional level, lack of role model, lack of motivation and rewarding for compliers with hand hygiene and lastly lack of HCW's concern for own individual safety from protection from HAI. Similar views are echoed in a 2010 review [9] that a successful hand hygiene educational program has several key features which include reinforcement of hand hygiene

messages, health care workers' perceived importance of hand hygiene and its role in prevention of healthcare-associated infections, monitoring and feedback of hand hygiene practices. Further practical education tools, role-modeling by senior staff, supportive infrastructure, multimodal interventions and teaching methodology should be progressive that include local culture, priorities and available resources to make a significant change.

The Institute for Healthcare Improvement, in collaboration with the CDC, the Association for Professionals in Infection Control and Epidemiology, and the Society of Healthcare Epidemiology of America, created a how-to guide [10] on improving hand-hygiene among health care workers for organizations withfour key aims to improve knowledge, implement knowledge, to ensure the availability of hand hygiene products at the point of care and to ensure that competency and compliance in hand hygiene is regularly verified, monitored and appropriate feedback loops are in place. The CDC has given guideline [11] that provides suggestions and rationale for proper hand hygiene techniques and indications for glove use, interactive tools, educational, motivational and promotional posters aiming to demonstrate and remind proper hand-hygiene practice.

A 2010 Cochrane systematic review (updated 2007 review) [12] included randomized controlled trials, controlled clinical trials, controlled before and after studies, and interrupted time series analyses from 1980-2009 found insufficient evidence that hand-hygiene interventions improve hand hygiene in the hospital setting. Four studies were included with one study finding a statistically significant improvement in hand hygiene 4 months post-intervention, two studies finding a statistically significant increase in product use which was sustained at one site for 2 years, and one study finding no effect in the intervention compared with the control group 3 months post-intervention. However in our study data regarding culture of microbial flora from HCW's hand collected confirmed presence of compliance with regard to hand hygiene after one month. Not included in this study but we have planned for check of compliance at every 3 months interval by same parameter of skin swab culture till one year.

After our intervention in form of knowledge and reminders skin swab culture showing growth in 30 % of the nurses shows that level of compliance is still not satisfactory, long term follow up with constant reminder is necessary to instill the desire to perform.. An interesting study by Irene Okran [13] concluded that HCWs have knowledge of HAIs' preventive methods however, implementation of these knowledge through compliance were poor resulting in 54.9% washing hands always with water, 53.5% washing always with soap and 71.9% disinfecting with alcohol rub.

Lastly an important consideration that we miss in our study is the role of patient and visitors in reducing HAI. A 2011 review by McGuckin and colleagues found evidence of the importance of patient engagement or empowerment in terms of patient participation, knowledge, observatory skills and a facilitating environment for their participation in hand hygiene improvement create a huge difference. The majority of patients agreed that they would ask their health care provider to wash their hands (80% to 90%). However later studies found little efficacy of patient empowerment interventions to improve health care worker hand hygiene [14].

Conclusion

Our study revealed that current physical facilities available in our hospital for infection control are good and meets the standard level although knowledge of the health care provider about hand hygiene is not based on formal training but is based on their own assumptions and prevailing practices. If the measures followed for hand hygiene are continuously pursued and upgraded, the infection level can be further reduced. This can be done by giving training, conducting awareness programme, providing asses of healthcare worker to standard requirements of hand hygiene and implementation of infection control programmes. Besides healthcare provider, the awareness about infection control should also be developed among visitors and patient's attendant. All available material, efforts, skill and knowledge should be directed towards achieving the common objective of decreasing the incidence of hospital acquired infection.

Following limitation is felt after conducting this study:

In order to assess the efficacy of education programme we did not observe for the change in compliance long term with hand washing procedures in nursing staff after imparting them education. Further studies are needed to study the impact of interventions on the level of change in attitude and practices at different interval of time.

Well-developed tools are available for implementing hand hygiene interventions, although studies are needed to know high-quality evidence demonstrating which interventions are most effective.

New strategies, such as patient engagement in hand-hygiene interventions, are an emerging area with only a few studies assessing their effectiveness, and need further research on how best to implement them effectively.

Many factors potentially influenced the response of participants in this study ranging from different levels of entry of HCW into the observation phase of program, extent of physical contact with patients, training in hands-on techniques and general patient handling practices.

Finally, research may be directed toward understanding the effectiveness of specific elements of hand hygiene interventions. Interventions should be multimodal, addressing HCW's knowledge, attitudes and beliefs regarding hand hygiene, as well as strategies for behavioral change, and should ideally be tailored to institutional needs as well as different health care situations. Health care administrators embarking on a hand hygiene intervention should take advantage of the tools developed by the CDC and the WHO. This calls for a review of health care curricula to pave the way for more pragmatic infection control teaching in all our health care programs.

Recommendations

Following recommendations are based on the analysis of by Pittet D [15] and Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force [16]. CDC MMWR October 25, 2002 / Vol. 51 / No. RR-16

1. Prepare an action plan to implement these recommendations, involving all key health-care providers who will make system change happen. Ensure an adequate infrastructure and continuous supply of hand hygiene products at the right time and at the right location. Consider a timeframe and potential costs for meeting these requirements.
2. Each point of patient care will have sinks for handwashing with safe and clean running water. Soap and alcohol based handrub with single-use towel (paper or cloth) for hand drying should be made available;
3. Where taps are not present, water "flowing" from an already ûlled container with a tap is required. Access to water without touching the tap with soiled hands is preferred.
4. Alcohol-based handrub, meeting the recognized standards for antimicrobial efûcacy (ASTM or EN standards) should be well tolerated for skin, economical and are purchased in adequate quantities.
5. Durable and reusable Dispensers should be made available at the point of care. They should be well-functioning and reliably contain alcohol-based handrub.
6. All health-care workers require full training and education on the importance of hand hygiene, the "My 5 Moments for Hand Hygiene" approach and the correct steps for hand washing and hand rubbing.
7. By spreading clear messages with a user-centered approach, training and education aims to induce behavioral change and ensure that compliance is deep-rooted and maintained. As hand hygiene improvement start occurring, regular education updates and competence checks to all existing and new starts health-care workers is required.
8. A top-down direction to training is needed whereby the hand hygiene programme coordinator will identify the individual's role as trainers and observers. The trainer should have knowledge of infection control policy and familiar with the tools available for surveillance of infection control
9. Activities to train trainers and observers should be led by the hand hygiene programme coordinator, who should have experience of delivering health-care at the bedside and taken part in the facility preparedness.
10. Basic educational sessions for trainers, observers and health-care workers should focus on: background to WHO Patient Safety and the First Global Patient Safety Challenge; Deûnition, impact and burden of HCAI; Major patterns of transmission of health care-associated pathogens, with a particular focus on hand transmission; Prevention of HCAI and the critical role of hand hygiene; WHO Guidelines on Hand Hygiene in Health Care and their implementation strategy and tools, including why, when and how to perform hand hygiene in health care.
11. Reminders in the workplace are the most important tools to prompt and remind health-

care workers about the importance, appropriate indication and procedures for performing hand hygiene. Reminders also inform patients and their visitors of the standard of care that they should expect from their health-care provider with respect to hand hygiene.

12. Posters are the most common reminder and include WHO-branded standard posters to visualize the "My 5 Moments for Hand Hygiene" approach and the correct method of hand washing and hand rubbing. How to Hand wash Poster should be displayed beside each sink (which ideally should coincide with each point of care)
13. Other types of reminders are pocket leaûets, stickers posted at the point of care, special labels including prompting slogans stuck on alcohol-based handrub dispensers and badges with the hand hygiene logo.
14. A pocket leaûet summarizing the key messages to be distributed in the clinical settings where the hand hygiene improvement programme is being implemented. SAVE LIVES: Clean Your Hands Screensaver for computer screens to be displayed on computers used by health-care workers at the facility.
15. Local adaptation of the WHO reminders certainly facilitates local uptake of the strategy by using the best terminology and images according to the culture. Health-care workers will also have access to local hand hygiene guidelines or standard operating procedures.
16. Ensure that the reminders displayed are always in good condition, regularly updated and refreshed changing the images and the slogans regularly.
17. A problem-solving approach should be employed to apply theoretical principles. Facilities should consider implementing a system of checking on the competence of all health-care workers who have received hand hygiene training. This could take the form of an annual training course or a practical hand hygiene demonstration workshop to conûrm competence in relation to correct hand hygiene techniques at the correct moments. Utilizing the hand hygiene knowledge survey will also fulfil the purpose of checks on competence.

Refrences

1. Prevention of hospital-acquired infections A practical guide 2nd edition World Health Organization Department of Communicable Disease, Surveillance and response WHO/CDS/CSR/EPH/2002.12
2. Coella R et al. The cost of infection in surgical patients: a case study. J Hosp Infect, 1993, 25:239–250.
3. World Health Organization. WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge. 2009. [November 22, 2011].
4. Centers for Disease Control and Prevention. Hand Hygiene in Health Care Settings: Hand hygiene basics. May 19, 2011. [November 16, 2011].
5. Dancer S J. Mopping up hospital infection. Journal of hospital infection; 1999.p.85-90.
6. Backman C, Zoutman DE, Marck PB. An integrative review of the current evidence on the relationship between hand hygiene interventions and the incidence of health care-associated infections. Am J Infect Control. 2008; 36(5):333–48.
7. Boyce JM. Measuring healthcare worker hand hygiene activity: current practices and emerging technologies. Infect Control Hosp Epidemiol. 2011; 32(10):1016–28.
8. Joint Commission. Measuring Hand Hygiene Adherence: Overcoming the challenges. 2009.
9. Mathai E, Allegranzi B, Seto WH, et al. Educating healthcare workers to optimal hand hygiene practices: addressing the need. Infection. 2010; 38(5):349–56.
10. Institute for Healthcare Improvement. How-to Guide: Improving Hand Hygiene. 2006.
11. Centers for Disease Control and Prevention. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR. 2002; 51(16).
12. Gould DJ, Moralejo D, Drey N, Chudleigh JH. Interventions to improve hand hygiene compliance in patient care. Cochrane Database Syst Rev. 2010; 9:CD005186.
13. Irene Ocran, Daniel Nii Aryee Tagoe. Knowledge and attitude of healthcare workers and patients on healthcare associated infections in a regional hospital in Ghana. Asian Pac J Trop Dis 2014; 4(2):135-139.
14. McGuckin M, Storr J, Longtin Y, Allegranzi B, Pittet D. Patient empowerment and multimodal hand hygiene promotion: a win-win strategy. Am J Med Qual. 2011; 26(1):10–7.
15. Pittet D. Improving compliance with hand hygiene in hospitals. Infect Control Hosp Epidemiol 2000; 21:381–6.
16. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. CDC MMWR 2002 Oct 25; 51(16).

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.13

Comparison of Various Parameters after Induction of Spinal Anaesthesia for Caesarean Section in Sitting and Lateral Position

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Abstract

Background: Hypotension is one of the common complications in patients undergoing surgeries under spinal anesthesia. This phenomenon is comparatively more in pregnant women undergoing caesarean section under spinal anesthesia due to anatomical variations in the spinal cord and physiological changes in pregnant women. Maternal position may influence the spread of the local anaesthetic drug. So, in this study we have aimed to compare incidence of hypotension and various other parameters like onset of sensory and motor blockade, total number of mephentermine incremental doses (5mg/dose) required in each group to correct hypotension after induction of spinal anesthesia in sitting and lateral position for caesarean sections.

Methods: Seventy American Society of Anesthesiologists physical status I and II patients undergoing elective caesarean section were randomnly divided into two groups by closed envelope technique to receive spinal anaesthesia in the lateral position (Group L) or the sitting position (Group S). In Lumbar (L3-4) interspace, lumbar puncture was done after taking aseptic precautions, plain bupivacaine 0.5% heavy 10 or 12 mg according to the height was injected after confirming free flow of cerebro-spinal fluid. After this, they were placed in the supine position immediately with right wedge providing for left lateral uterine displacement to avoid supine hypotension syndrome. Maternal blood pressure was measured every minute for 5 minutes, every two min for 10 min and 5-minutely thereafter. Hypotension was defined as a fall in systolic blood pressure >20% of the baseline value or a value <90 mmHg.

Results: Statistical studies showed that number of patients who received spinal anesthesia in lateral position had significantly more incidences of hypotension (19 incidences) compared to those who received in sitting position (10 incidences) with P value being (P= 0.048). And also there was faster onset (average time) of action (sensory and motor) in Group L (5 minutes for sensory and 6.2 minutes for motor) than compared to Group S (7 minutes for sensory and 7.4 minutes for motor) but not statistically significant (P= 0.361 for sensory and 0.639 for motor). We also observed that, total number of incremental doses (5mg/dose) of mephentermine used were more in patients who received spinal anaesthesia in lateral position (n= 10 increments) than compared to those who received in sitting position(n=5 increments) but it was not statistically significant (P=0.145).

Conclusion: Spinal anesthesia given in lateral position of the patients for caesarean section causes significantly more incidences of hypotension than that given in sitting position. And there were no significant differences with respect to onset of sensory and motor block and mephentermine requirement between the groups.

Keywords: Spinal Anesthesia; Sitting Position; Lateral Position; Hypotension; Mephentermine.

Introduction

Spinal anesthesia is the preferred anesthesia technique for caesarean section as it produces adequate anesthesia, analgesia and adequate motor block while keeping the patient conscious [4]. Spinal anesthesia can be administered to patients in sitting and lateral

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Received on 10.11.2016
Accepted on 01.12.2016

position. There has been a consistent debate as to which position is better for inducing spinal anesthesia in caesarean section [11], and each position has its own advantages and disadvantages [1]. Some studies have preferred sitting position to be better, based on their results [12,13]. In sitting position the landmark identification is easier [2], while in lateral position the landmark identification might be difficult but sedated patients can be maintained in lateral position for long time comparatively [2]. Some studies have shown lateral position has lesser incidences of hypotension than sitting position and some studies have shown the opposite one [2].

Hence the present study was designed to compare the incidences of hypotension and various other parameters like onset of sensory and motor block, mephentermine requitement in the patients after induction of spinal anesthesia in sitting and lateral position for caesarean sections.

Materials and Methods

Seventy parturients (18-40 years, American society of anesthesiologist-ASA I and II) undergoing elective caesarean section(studied for 18 months) at P.E.S.I.M.S.R, Kuppam were considered, informed written consent was taken and subjects were randomly allocated into two groups by closed envelope technique before performance of spinal anesthesia. Group S(sitting) (n = 35) patients were placed in the sitting position, group L (n = 35) patients in the lateral position, after sub-arachnoid block was given, patients were put back to supine position. Sample size is determined this way, the range of time (minutes) to reach T4 sensory block is 5.5 minutes (Group L) and 6 minutes (Group S) and standard deviation worked out to be 1.4 and 1.5 respectively. Accordingly, 35 patients in each group achieved 80% power to detect mean difference of 1 with 5% level of significance.

Exclusion Criteria

Patients with significant cardiovascular diseases like mitral stenosis, ischemic heart diseases, respiratory, spinal problems, liver disorders, deranged renal functions and local infection. Surgery prolonged for more than 45 minutes, total blood loss more than 750ml.

Injection ranitidine 50 mg intravenous, 30 minutes before shifting to operation theatre was given as premedication. Patients were cannulated with 18G intravenous cannula, and preloaded with 20 ml/kg of Ringers lactate solution half an hour before intrathecal injection. In the operation theatre, pulse rate, blood pressure, electrocardiogram, and oxygen saturation were noted and parturients were appropriately positioned according to the groups allocated. Patients were positioned with the help of assistance. For the left lateral position, the legs were brought to rest on the abdomen after flexion, and chin touching the chest. For the sitting position, the legs were placed on the edge of the table and the feet supported down, a pillow was placed on her lap, and the arms wrapped around the pillow, resting on the flexed lower extremity.

Under aseptic measures lumbar puncture done at L3-L4 space with 25G Toughy needle, free flow of the cerebrospinal fluid was ascertained and 2ml (10 to 12mg based on the height) of 0.5% bupivacaine heavy was injected. The spinal needle was removed, and the patient turned to the supine position immediately. The sensory block was tested by the loss of sensation to touch.

Motor blockade was assessed by *modified Bromage scale:*

0 = no motor paralysis; 1 = not able to raise extended legs but able to flex at knee and ankles; 2 = not able to raise extended legs and flex the knees but able to move feet; 3 = unable to flex ankles or feet).

Observations

The time taken from the initiation of sub-arachnoid block to the achievement of sensory blockade up to T_4 dermatome was recorded. The time taken from the initiation of sub-arachnoid block to the achievement of maximum motor blockade (bromage score 3) is also noted. And average time calculated for sensory and motor onset for each groups. Maternal blood pressure was measured every minute for 5 min, every two min for 10 min and 5-minutely thereafter. Hypotension was noted when there was a fall in systolic blood pressure (SBP) >20% or a systolic pressure value of <90 mmHg. The total number of incidences of hypotension in each group was noted and recorded. Injection mephenteramine 5 mg IV (intravenous) increments were used to return SBP > 90 mmHg and the total number of times of such mephenteramine increments used were recorded in each group. The results obtained from the study were statistically analyzed using one way ANOVA for continuous data and Chi-square test for categorical data using SPSS version 16. A P value of <0.05 was considered significant.

Results

Study design consists of two groups of 35 patients each, Group L (spinal anesthesia given in left lateral position of patients), Group S (Spinal anesthesia given in sitting position of patients).

Table 1: Weight (kilograms) distribution of patients

Variables	Group L	Group S	P Value
Weight (kilograms)	53+/-5.6	53.4+/-4.3	0.9348

Weight distribution statistically matched in the two groups

Table 2: Age distribution of patients

Age in years	Group L		Group S		P value
	No	%	No	%	
18-20	7	20	6	17.14	0.758
21-30	15	42.85	16	45.71	0.809
31-40	13	37.14	13	37.14	1.000
Total	35	100.0	35	100.0	
Mean ± SD	27.51±6.19		27.68±5.17		

Age distribution matched in the two groups

Table 3: Incidence of hypotension, Vasopressors requirement and other spinal anesthesia parameters

	Group L	Group S	P Value
Total Incidences of hypotension in the groups	19	10	0.048*
Total number of Mephentermine increments required in the groups(5mg/dose)	10	5	0.145
Average time in minutes to reach maximum bromage score of 3 from the initiation of spinal anaesthesia	6.2	7.4	0.639
Average time in minutes to reach T4 level of sensory block from the initiation of spinal anaesthesia.	5	7.0	0.361

*statistically significant

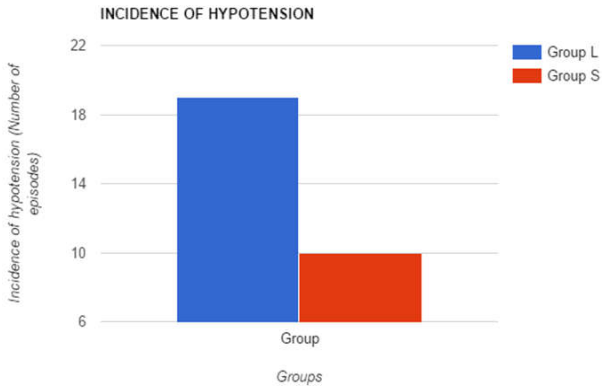

Fig. 1: Incidence of hypotension

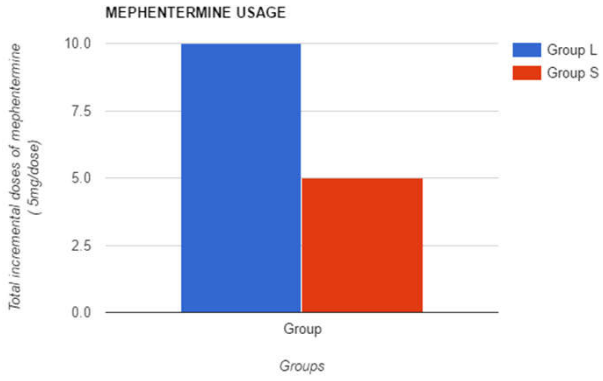

Fig. 2: Mephentermine increments

Discussion

Spinal anesthesia under sitting and lateral position may influence the spread of local anesthetic drug and consequently the blockade [3]. Normally, reduced systemic vascular resistance is compensated by increase in cardiac output, but in patients under spinal anesthesia this compensatory method is lost

leading to hypotension [4]. In sitting position the landmark identification is easier [7], while in lateral position the landmark identification might be difficult but sedated patients can be maintained in lateral position for long time comparatively.

Mendonca et al. have shown that hypotension was less frequent among mothers placed in the left lateral position (64%) than among those placed in the tilted supine position (90%) [5]. Studies done by Inglis A, Daniel M showed that mothers in lateral group required more ephedrine than sitting [6].

Coppejans HC, Hendrickx E et al in 2006 showed that, performing a CSE(combined spinal epidural) technique for cesarean delivery in the sitting position was easier and caused less severe hypotension [7].

In our study, the incidences of hypotension was significantly more in patients who were given spinal anesthesia in lateral position (19 times) than those who were given in the sitting position (10 times) with P value being 0.048 which is significant. The average time to reach T4 sensory level block and maximum bromage score is less in patients who were given spinal anesthesia in lateral position(5 minutes and 6.2 minutes respectively) than those who were given in sitting position(7 minutes and 7.4 minutes respectively), but not significant(P= 0.361 and 0.639 respectively) In this study, total number of mephentermine (vasopressor) incremental requirement (5mg/dose) to increase the systolic blood pressure to greater than 90mmhg in patients having hypotension, were more in patients in whom spinal anesthesia were given in lateral position (n=10) than those patients who were given spinal anesthesia in sitting position(n=5) but not statistically significant. (P=0.145) Age, weight were statistically matched such that they will not interfere with the results in our study.

Conclusion

Spinal anesthesia given in lateral position of the patients for caesarean section causes significantly more incidence of hypotension than that given in sitting position. And there were no significant differences with respect to onset of sensory and motor block and mephentermine requirement between the groups.

References

1. David J. Birnbach,Ingrid M. Browne.Anesthesia for Obstetrics. In: Miller RD, ed. Anesthesia. 7th ed. Churchill Livingstone, An Imprint of Elsevier, 2009. p.2203-40.
2. Kelly JD, Mccoy D, Rosenbaum SH, Brull SJ. Haemodynamic changes induced by bupivacaine heavy (hyperbaric) during lateral decubitus or supine spinal anaesthesia. Eur J Anaesthesiol 2005; 22:717-22.
3. Zohar E, Nog Y, Laboritck I, Fredman B. Intrathecal anesthesia for elderly patient undergoing short transurethral procedure: a dose finding study. AnesthAnalg 2007; 104:552-4.
4. Thomas DG, Robson SC, Redfern N, et al. Randomized trial of ephedrine bolus or phenylephrine bolus for maintenance of arterial pressure during spinal anaesthesia for Caesarean section. Br J Anaesth. 1996; 76:61–65.
5. Mendonca C, Griffiths J, Ateleanu B, Collis RE. Hypotension following combined spinal-epidural anaesthesia for Caeserian section. Left lateral position versus tilted supine position. Anaesthesia. 2003; 58:428–31.
6. Inglis A1, Daniel M, McGrady E. Maternal position during induction of spinal anesthesia for caeserian section. A comparison of right lateral position and sitting position. Anaesthesia. 1995 Apr; 50(4) 363-5.
7. Coppejans HC1, Hendrickx E, Goossens J, Vercauteren MP. The sitting versus right lateral position during combined spinal epidural anesthesia for ceserian section: block features and severity of hypotension. Anesth Analg. 2006 Jan; 102(1):243-7.
8. Hallworth SP1, Fernando R, Columb MO, Stocks GM. The effect of posture and baricity on the spread of intrathecal bupivacaine for elective ceserian section. Anaesth-Analg. 2005; 100:1159-1165.
9. Chumpathong, S., Chinachoti, T., Visalyaputra, S., Himmunngan, T. Incidence and risk factors of hypotension during spinal anaesthesia for caesarean section at Siriraj hospital. J Med Assoc Thai. 2006; 89: 1127–1132.
10. Gori, F., Corradetti, F., Cerotto, V., Aldo Peduto, V. Influence of positioning on plain levo-bupivacaine spinal anaesthesia in cesarean section. Anesthesiol Res Pract. 2010; pii212696.
11. Stephen P Hallworth, Roshan fernando et al. Effect of posture and baricity on the spread of intrathecal bupivacaine for elective caesarean delivery. Anaesth-Analg. 2005; 100:1159-1165.
12. Ece Dumanlar Tan, Berrin Gunaydin. Comparison of maternal and neonatal effects of combined spinal epidural anaesthesia either in sitting or lateral position during elective caesarean section. Turk J Anaesthreanim. 2014; 42:23-32.
13. G Hocking, JAW Wildsmith. Intrathecal drug spread. BJA 2004; 93(4):568-578.
14. Russell IF. A comparison of cold, pinprick and touch for assessing the level of spinal block at caesarean section. International Journal of Obstetric Anesthesia 2004; 13:146–52.
15. Robert H Riffenburg (2005), Statistics in Medicine, second edition, Academic press. 85-125.
16. John Eng (2003), Sample size estimation: How many Individuals Should be Studied? Radiology 227: 309-313.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.14

Nalbuphine as an Intrathecal Adjuvant is a Good Alternative to Fentany l

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Abstract

Background: 0.5% Bupivacaine used in subarachnoid block provides about 3 hours of analgesia. Opioids morphine and Fentanyl are used as adjuvant to produce extended postoperative analgesia. Nalbuphine is an agonist antagonist and does not require a narcotic license, which is a must for procuring other opiods. This study was carried out to evaluate the efficacy of Nalbuphine versus Fentanyl as intrathecal adjuvant.

Material and Methods: Hundred ASA 1-3 patients posted for elective Total Abdominal Hysterectomy were included in this study and were randomly divided into two groups of fifty each. Group FB received 15mg of 0.5% Bupivacaine and 25 mcg of Fentanyl. Group NB received 15mg 0.5% Bupivacaine and 1mg Nalbuphine.

Results: The onset of sensory blockade, time to attain peak sensory block and complete motor block was significantly faster in Group FB($p<0.001$). The duration of motor block was comparable in both the groups. The time for sensory block to regress by two segments was significantly longer in Group NB, 97.72±9.50 minutes, than in Group FB, 88.88±9.48 minutes. The time to first analgesic requirement in Group NB was 460.78±77.98 minutes compared to 283.44±78.97 minutes in Group FB($p<0.001$). No statistical difference was seen in terms of adverse effects. *Conclusion:* Time for sensory level to regress by two segments and the post operative analgesia time is longer with Nalbuphine. So, Nalbuphine is a good adjuvant in spinal anaesthesia especially in centres without narcotics license.

Keywords: Nalbuphine; Intrathecal Adjuvant; Fentanyl; Bupivacaine; Analgesia.

Introduction

Total abdominal hysterectomy (TAH) is preferably done under regional anaesthesia. Spinal anaesthesia is the technique of choice as it is less cumbersome compared to general anaesthesia. There is good stress response, less blood loss and good muscle relaxation. Hyperbaric Bupivacaine used alone gives analgesia for 2-3 hours only. Additives used with Bupivacaine can enhance the intensity and duration of the post operative analgesia. Intrathecal opioids have been widely used as adjuncts, resulting in a longer duration of analgesia and good patient satisfaction [1-4].

Intrathecal opioids bind to pre and postsynaptic opioid receptors in lamina 1 and 2 of the dorsal horn. The mu and delta opioid receptor activation causes G protein mediated K channel opening while kappa opioid receptor activation causes Ca++ channel closure. These events lead to a fall in intracellular Ca++ levels, reducing the release of excitatory neurotransmitters and hence antinociception.

Fentanyl has been used extensively intrathecally as it has no significant side effects [5]. It is a potent synthetic mu receptor agonist. Fentanyl has structural similarities to local anaesthetics. It has local anaesthetic action on the primary afferent sensory C nerve fibres causing analgesia.

Nalbuphine hydrochloride is a synthetic opioid structurally related to oxymorphine and is an agonist antagonist opioid. It has agonist action at kappa receptors and is antagonist at mu receptors [6,7]. So, while giving good analgesia, it is devoid of opioid related adverse effects [8,9].

We conducted this study to compare the effects of Nalbuphine and Fentanyl as adjuvants to intrathecal 0.5% Bupivacaine in patients undergoing TAH.

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Received on 09.12.2016
Accepted on 16.12.2016

Material and Methods

On obtaining the departmental ethical committee approval and written informed consent, hundred patients ASA 1-3 patients, aged 30-65 years posted for elective TAH were included in this study. This was a prospective randomised double blind study. A thorough pre-anaesthetic check up followed by a series of lab investigations like haematocrit, coagulation profile, electrocardiogram, chest X-ray, blood sugars, electrolytes were conducted. Patients with contraindication for spinal anaesthesia were excluded from this study. The patients were randomly allocated to two groups of fifty each by computer generated programme. Group FB received 15mg of 0.5% Bupivacaine (3ml) and 25 mcg of Fentanyl (0.5ml) and Group NB received 15mg 0.5% Bupivacaine (3ml) and 1mg Nalbuphine(0.5ml)

All patients were familiarized with the visual analogue pain scale- 0 being no pain and 10 worst pain imaginable. They were also briefed about the pin prick method of sensory assessment and lower limb movement for motor block assessment. We kept the patients nil by mouth for 8 hours prior to surgery. No sedative or analgesic was given preoperatively. A good peripheral intravenous access was secured with 18 g cannula and preload was done with 10ml/ kg ringer lactate solution. Intraoperative monitoring included non-invasive blood pressure, electrocardiogram, pulse oximetry. Under strict sterile precautions spinal anaesthesia was administered with the patients in the sitting posture at L_{3-4} interspace in the midline with 26 gauge spinal needle. The drug was loaded and handed over by the assistant. The anaesthesiologist was not aware of what the adjuvant was being given. The patients were immediately made supine with 10 degree Trendelenburg tilt. Any fall in heart rate below 50 per minute was treated with atropine 0.6mg. Fall in systolic blood pressure below 20% baseline was managed by 6mg intravenous ephedrine in increments. We looked for any signs of respiratory depression and were equipped with oxygen supplementation and assisted ventilation.

We compared the characteristics of the subarachnoid block between the two groups. After the intrathecal instillation of the drugs, the time for sensory block to reach T10 dermatome, the umbilicus was noted as 't10'. The time for the loss of sensation to reach T6 dermatome, the peak sensory level was taken as 't6'. The time for complete motor block, 'tm', was taken as inability to flex the knee (Bromage 3). The time for the sensory level to fall from T6 to T8 dermatome, 't8' was also recorded. The time for effective analgesia, i.e. the time for the first request of rescue analgesia was taken as 'ta'. Duration of motor block, i.e time to reach Bromage 1; just able to move knees was noted as 'dm'. Any untoward events were looked and noted. Rescue analgesic given was injection diclofenac 75 mg intramuscularly.

Statistical Methods

The statistical analysis was performed by STATA 11.2 (College Station TX USA). Students t-test were performed for to find the significance difference between the age, height, weight, onset of sensory blockade, peak sensory blockade, time to attain complete motor block, 2 Segment Regression of Sensory Level(t8)[Min], duration of motor block, time to first analgesic with the treatment groups (Fentanyl and Nalbuphine) and its expressed as mean and standard deviation, Chi square or fisher exact test were used to measure the association between the adverse event and ASA grade with the treatment groups. $P<0.05$ considered as statistically significance.

Results

We compared the effects of intrathecal Fentanyl and Nalbuphine as adjuvant to 0.5%Bupivacaine in patients undergoing TAH. 100 patients took part in this randomized study. In group FB, 50 patients received 25 mcg Fentanyl and 3 ml 0.5%bupivacine intrathecally. The rest, group NB received 1mg Nalbuphine and 3ml 0.5% Bupivacaine.

The demographic profile of both groups were not statistically different (Table 1). The onset of sensory block was faster in group FB (3.09±0.47 minutes), than in group NB(4.20±0.52 minutes) (p value <0.001). Time to attain peak sensory blockade was faster in group FB, 6.31±0.58 minutes than in group NB, 6.76±0.54 minutes. The difference was statistically significant (p value<0.001) (Table 2). Time for complete motor block was 6.85±0.66 minutes in group FB, while it was 7.93±0.67 minutes in group NB, with statistically significant difference (p<0.001)(Table 2). The time to two segments sensory level regression was longer in Group NB, 97.72±9.50 minutes, while it was 88.88±9.48 minutes in Group FB. The difference was statistically significant (p<0.001) (Table 3). The duration of motor block in Group FB was 136.24±12.23 minutes and was comparable to 129.78±24.07 minutes in Group NB. The difference was not statistically significant (p=0.096). The time to first

analgesic requirement was 460.78±77.98 minutes in Group NB while in Group FB, it was 283.44±78.97 minutes, with statistically significant difference (p<0.001) (Table 3). There was no statistical difference in the adverse events in the two groups (p=0.240). Two patients and one in Group FB developed hypotension and pruritus respectively. Nausea was seen in two patients in either group (Table 4, 5). No active intervention was required. None developed respiratory distress.

Table 1: Demographic profile

	Fentanyl	Nalbuphine	P-Value
	Mean ± SD	Mean ± SD	
Age	52.26 ± 8.13	50.34 ± 8.55	0.252
ASA Grade			0.910
I	27 (54%)	29 (58%)	
II	18 (36%)	16 (32%)	
III	5 (10%)	5 (10%)	
Height	155.92 ± 9.04	157.88 ± 6.26	0.211
Weight	57.32 ± 6.95	58.06 ± 4.65	0.534

Table 2: Characteristics of spinal anaesthesia

	Fentanyl Mean ± SD	Nalbuphine Mean ± SD	P-Value
Onset of sensory blockade (t10) min	3.09 ± 0.47	4.20 ± 0.52	<0.001
Peak Sensory Blockade(t6) [Min]	6.31 ± 0.58	6.76 ± 0.54	<0.001
Time to attain complete motor block(tcm)	6.85 ± 0.66	7.93 ± 0.67	<0.001

Table 3: Regression of block with Nalbupine and Fentanyl

	Fentanyl Mean ± SD	Nalbuphine Mean ± SD	P-Value
2 Segment Regression of Sensory Level(t8)[Min]	88.88 ± 9.48	97.72 ± 9.50	<0.001
Duration of Motor Block (dm)[Min]	136.24 ± 12.23	129.78 ± 24.07	0.096
time to first analgesic (ta) [min]	283.44 ± 78.97	460.78 ± 77.98	<0.001

Table 4: Total Adverse events with Nalbuphine and Fentanyl

	Fentanyl	Nalbuphine	Total	P-Value
Yes	5 (10%)	2 (4%)	7 (7%)	
No	45 (90%)	48 (96%)	93 (93%)	0.240
Total	50	50	100	

Table 5: Types of adverse effects with Nalbuphine and Fentanyl

	Fentanyl	Nalbuphine	Total
Hypotension	2 (4%)		2
Nausea	2 (4%)	2 (4%)	4
Pruritis	1 (2%)		1
Nil	45 (90%)	48 (96%)	93
Total	50	50	100

Discussion

Intrathecal opioids have a significant place in management of acute post operative pain. The presence of intrinsic opioid apparatus in human body has popularized their use both intrathecally and epidural. Liposolubility of opioids determine their spinal selectivity. The more liposoluble ones like Fentanyl and Sufentanyl have short duration of analgesia (1-4 hours) compared to water soluble morphine which produces analgesia for nearly 24 hours post operatively [10]. However, morphine is associated with a higher incidence of adverse effects. Lipophilic opioids given intrathecally tend to sequestrate in the epidural fat and are rapidly cleared from plasma. This does not let them to get a good concentration at the site of action. This explains the limited intensity and duration when given intrathecally. The analgesic property of the intrathecal opioids is attributed to spinal selectivity. The lipophilic ones due to their good vascular uptake and

redistribution rapidly reach higher concentration in the brain as well [10]. As they are devoid of sympathetic and motor block while enhancing analgesia, opioids are good adjuncts. Early post operative ambulation is possible as the volume of Bupivacaine gets reduced [11,12].

Nalbuphine is a lipophilic opioid with agonist action at the kappa opioid receptor and antagonist at the mu receptor. Unlike morphine, it has a short duration of action due to its liposolubility and rapid plasma clearance [13]. Nalbuphine interferes in the nociceptive pathway by post synaptic inhibition of interneurons and output neuron of spinothalamic tract. Its analgesic potency is equivalent to morphine on weight basis and causes respiratory depression in same degree as equianalgesic morphine dose, but has a ceiling effect. Doses above 30 mg do not aggravate respiratory depression.

There is limited data on comparison of spinal effects of Nalbuphine and Fentanyl.

Our study groups had subjects with similar age group, ASA grading, height and weight. The onset of sensory block was earlier in group FB compared to group NB. The time to achieve peak sensory level as well as complete motor block was earlier in group FB than group NB. This can be attributed to the fact that Fentanyl is more lipid soluble and a rapid tissue uptake compared to Nalbuphine. H M Gomaa et al [14] compared the effects of intrathecal Nalbuphine and Fentanyl in caesarean patients and concluded that there was no significant difference in onset and duration of sensory and motor block but the onset of motor block was faster with Fentanyl. We observed that the duration of motor block in the two groups in the two groups was not significantly different. Also the time for sensory block to fall by two segments i.e., from T6 to T8 level was lesser in group FB compared to group NB. Again the pharmacokinetics of Fentanyl explains it. This was consistent with H M Gomaa et al [14] study.

The time of first analgesic requirement was lower in group FB than Group NB. Postoperative analgesia was more prolonged with intrathecal Nalbuphine than Fentanyl. Gupta et al [15] studied the two drugs intrathecally and observed that 2mg Nalbuphine extended the duration of sensory block and extended post operative analgesia more than Fentanyl. Culebras et al [16] also studied these drugs intrathecally in caesarean patients and concluded that Nalbuphine prolonged analgesia without any side effects. Mukerjee et al [17] studied 0.2mg, 0.4 mg, and 0.8mg Nalbuphine and came the conclusion that a higher dose intrathecally resulted better analgesia without any adverse effects. No significant side effects were encountered. We also observed no major side effects. Two patients and one in group FB developed hypotension and pruritus respectively. Two patients in both the groups complained of nausea. Catherine O Hunt et al [4] used intrathecal Fentanyl in caesarean patients and concluded that a good sensory block was achieved but pruritus developed with high doses. M S Khanna et al [18] found incidence of pruritus and respiratory depression with use of intrathecal Fentanyl. In a study, it was found that intrathecal Nalbuphine was associated with lesser incidence of pruritus compared to morphine [19].

Pruritus is mainly in the face and is a known opioid side effect. Its cause is the presence of a type of C fibres mediating the itch response linked to central receptor network. Quite a number of mu opioid and 5HT3 receptors are located in and around the trigeminal nucleus

We did not encounter respiratory depression in any of our patients in either groups. This was because this risk is seen more in geriatric population, concomitant chronic sedative usage or co existing respiratory disease. All these factors were excluded in our study groups.

Thus, we conclude that Nalbuphine is a good intrathecal adjuvant, providing intense and extended postoperative analgesia without any significant adverse effects.

Nalbuphine being antagonist as well is devoid of the usual opioid side effects. Unlike Fentanyl and other opioids, it is not included under the Narcotic Act, making it available in the pharmacy on prescription. So in centres where Fentanyl is difficult to procure, Nalbuphine may be used as intrathecal adjuvant.

References

1. RousselJR, Heindel L. Effects ofintrathecal Fentanyl on duration of Bupivacaine spinal blockade for outpatient knee arthroscopy. AANA J 1999; 67: 337 43.
2. Förster JG, Rosenberg PH. Clinically useful adjuvantsin regional anaesthesia. CurrOpin Anaesthesiol 2003; 16:477 86.
3. Singh H et al. Intrathecal Fentanyl prolongs sensory Bupivacaine spinal block. Can J Anesth. 1995; 42: 987-91.
4. Catherine O Hunt et al. Perioperative analgesia with subarachnoid Fentanyl-Bupivacaine for cesarean delivery. Anesthesiology. 1989; 71:535-540.

5. Chavada H, Mehta PJ, Vyas AH. A comparative study of intrathecal Fentanyl and suFentanyl with Bupivacaine heavy for postoperative analgesia. Int J Anesthesiol 2009; 20:2–8.
6. Zarr GD, Werling LL, Brown SR, Cox BM. Opioid ligand binding sites in the spinal cord of the guinea-pig. Neuropharmacology 1986; 25:47-80. [PubMed].
7. De Souza EB, Schmidt WK, Kuhar MJ. Nalbuphine: An autoradiographic opioid receptor binding profile in the central nervous system of an agonist/ antagonist analgesic. J PharmacolExpTher 1988; 244: 391-402. [PubMed].
8. Lin ML. The analgesic effect of subarachnoid administration of tetracaine combined with low dose of morphine or Nalbuphine for spinal anesthesia. Ma ZuiXueZaZhi 1992; 30:101-5. [PubMed].
9. Fournier R, Gamulin Z, Macksay M, Van Gessel E. Intrathecal morphine versus Nalbuphine for post-operative pain relief after total hip replacement. Anesthesiology 1998; 89:867. [PubMed].
10. Bujedo B M, Santos S G, Azpiazu A V. A review of epidural and Intrathecal opioids used in treatment of postoperative pain. J Opioid Manag 2012; 8(3) 177-92.
11. Tawfik MO. Mode of action of intraspinal opioids. Pain Rev. 1994; 1:275–94.
12. Terajima K, Onodera H, Kobayashi M, Yamanaka H, Ohno T, Konuma S, et al. Efficacy of intrathecal morphine for analgesia following elective cesarean section: Comparison with previous delivery. J Nippon Med Sch. 2003; 70:327–33.
13. Chaney MA. Side effects of intrathecal and epidural opioids. Can J Anesth. 1995; 42:891–903.
14. Gomaa H M, Mohamed N Net.al.A comparison between post-operative analgesia after intrathecal Nalbuphine with Bupivacaine and intrathecal Fentanyl with Bupivacaine after cesarean section. Egyptian Journal of Anaesthesia. 2014 Oct; 30(4):405-410.
15. Gupta K, Rastogi B et.al. Intrathecal napbuphine versus intrathecal Fentanyl as adjuvant to 0.5% hyperbaric Bupivacaine for orthopaedic surgery of lower limbs under sabarachnoid blocks: A comparative evaluation. Indian J Pain 2016; 30:90-5.
16. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA. Advantages of intrathecal Nalbuphine, compared with intrathecal morphine, after cesarean delivery: An evaluation of postoperative analgesia and adverse effects. AnesthAnalg 2000; 91:601 5.
17. Mukherjee A, Pal A, Agrawal J, Mehrotra A, DawarN.IntrathecalNalbuphine as an adjuvant to subarachnoid block: What is the most effective dose? Anesth Essays Res 2011; 5:171 5.
18. M S Khanna et al. Comparative evaluation of Bupivacaine plain versus Bupivacaine with Fentanyl in Spinal Anaesthesia in Geriatric patients. Indian J Anaesth. 2002; 46(3):199-203.
19. Hea Jo Yoon et al. A comparison of analgesic effects and side effects of intrathecal Morphine, Nalbuphine and a Morphine Nalbuphine mixture for pain relief during a caesarian section. Korean Journal of Anaesthesiology. 2002 May; 042(05):627-633.

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Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4116.15

Comparison of Dexmedetomidine Versus Esmolol to Decrease the Stressor Responses during Tracheal Intubation and Immediately Thereafter

Pradeep R.*, Chandrashekar Tolla**

Abstract

Context: Endo-tracheal intubation following laryngoscopy may cause sympathetic stimulation by releasing catecholamines and may result in complications like hypertension, tachycardia, cardiac arrhythmias, cerebro-vascular accidents, which can be detrimental to the patient's life. Many drugs and techniques are being tried to reduce the stressor responses to intubation over years, and Dexmedetomidine and esmolol are the newer drugs.

Aims: This study was aimed at comparing dexmedetomidine versus esmolol in attenuating hemodynamic responses during and immediately after tracheal intubation.

Settings and Design: This study was a randomised prospective double-blind controlled study.

Subjects and Methods: Ninety patients posted for surgery under general anesthesia were divided into three groups, D and E and C with thirty patients in each group. Group-D patients received the first study drug dexmedetomidine 0.5 µg/kg, Group-E patients received the second study drug esmolol 1 mg/kg and Group-C patients received 0.9% 20ml saline as intravenous over 5 minutes before anaesthesia induction. The subject's Systolic blood pressure, diastolic and mean arterial blood pressures with heart rate were measured at 1st, 3rd 5th, 7th, 10th minute post- intubation.

Statistical Analysis: The statistical methods employed were descriptive and inferential methods for the analysis of the obtained data.

Results: A statistically significant differences were seen in the period between endo-tracheal intubation and at 3 minute post intubation in Group D. The heart rate, systolic, diastolic pressure and mean arterial pressures showed statistically significantly lesser increase in dexmedetomidine group ($P<0.05$) than compared to other two groups at immediate post intubation and till 3minutes thereafter.

Conclusions:

Dexmedetomidine is more efficient than esmolol in reducing the stressor responses to tracheal intubation and immediately (< 3minutes) thereafter.

Keywords: Dexmedetomidine; Esmolol; Hemodynamics; Intubation; Laryngoscopy.

Introduction

During general anaesthesia airway control is provided by endo-tracheal intubation. Laryngoscopy and intubation leads to mechanical and chemical stimuli. Mechanical and chemical stimuli may cause undesired responses in cardiovascular (tachycardia, arrhythmias) and respiratory systems (bronchospasm, laryngospasm), which reaches its peak within 1 minute and ends by 5 to 10 minutes after intubation [4]. Chemical stimuli are mediated through release of sympathetic neurotransmitters (catecholamines) which causes tachycardia, hypertension, arrhythymias. The degree of these responses is related to how deep the anaesthesia plain is? The deeper the plain, lesser is the stressor response. Patient's age and association with diabetes mellitus or heart disease can also influence the pressor responses [6]. Some measures which can be taken to reduce the reflex responses are; using lignocaine 4% spray, opioid drugs, using inhalation anesthetics to deepen the plain of anaesthesia, before laryngoscopy and intubation.

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Received on 01.12.2016
Accepted on 13.12.2016

Dexmedetomidine is a selective α_2 adrenergic agonist. It produces sedation, anxiolysis, and analgesia due to its effect on central nervous system to reduce sympathetic outflow. Esmolol is a β receptor blocker (cardio-selective) that has quick onset of action and is of shorter duration[6]. It is cardio-selective because it inhibits β_1 receptors of the heart and not β_2, but at large doses it can inhibit β_2 receptors also which are present in the bronchial smooth muscles and vascular walls [7].

In our study, we have compared the effects of dexmedetomidine versus esmolol in attenuating hemodynamic responses during and after endo-tracheal intubation.

Methods

Ninety patients posted for elective surgery (general surgery) under general anaesthesia and who were in ASA I and II groups and aged between 20 and 60 years were taken as the subjects for the study. The study was conducted at P.E.S. Medical college and hospital, Kuppam, Andhra Pradesh. Informed consent was taken from the each subject. The present study was a prospective, double blind and randomized controlled study.

Exclusion Criteria

Patients in whom difficult airway and possible difficult intubation was expected, who had Ischemic heart disease, obstructive pulmonary diseases (COPD), diabetes mellitus, hypertension etc and who were using any medications for cardiac diseases were excluded.

All included patients were explained about the procedure and informed written consent was taken. In the pre-operative room intravenous line was secured with 20Gauge cannula and 8 mL/kg/hour Ringer's lactate infusion was initiated. After shifting to operation room, the patients were premedicated with with 0.01 mg/kg intravenous (i.v) midazolam, 0.08 mg/kg glycopyrrolate. The following monitors were connected, Electro Cardio Gram to monitor heart rate (HR) and rhythm, non-invasive blood pressure to monitor systolic blood pressure, diastolic and mean arterial pressure (SAP, DAP and MAP respectively), and pulse oximeter to monitor peripheral oxygen saturation (SpO_2) .

The patients were grouped into three groups randomly by closed envelope technique. The blindness of the study was maintained as the anaesthesiologists preparing the medications and administering them were different. Group D (n = 30) received 0.5 ìg/kg dexmedetomidine with infusion over 5 minutes, Group C (n = 30) received 20 ML 0.9% normal saline and Group E received 1 mg/kg esmolol over 5minutes before anaesthesia induction. Then, 5 mg/kg thiopental sodium and 0.1 mg/kg vecuronium intravenous was given. Laryngoscopy and intubation were performed. Those patients in whom failure of intubation was seen within 30 seconds were excluded. All patients received 50%O_2 (2.5 L/min), 50% N_2O (2.5 L/min) and 1 MAC Isoflurane during maintenance of anaesthesia. Arterial blood pressure, Heart Rate were noted before induction, after the patient is induced, noted before intubation and at 1st, 3rd, 5th, 7th and 10th minute post intubation for all subjects. The measurements taken before induction were designated as base level measurements and all others were compared with those levels.

The Surgery was allowed to commence once the data collection is over. The patients were artificially ventilated using pressure controlled ventilation and end tidal CO_2 levels were maintained between 30 and 35 mm Hg. During the procedure the above said parameters were recorded with 5 min intervals. After the surgery, the subjects were transferred to recovery room and monitored for an hour and then shifted to post-operative room.

Statistical Analysis

The statistical software SPSS 10.0 was used for statistical analysis. Quantitative data was compared using ANOVA and student's t test and the results were presented in mean, standard deviation. Qualitative data was compared using Chi-square test. After the pilot study, we came to know that a 20% of difference should be the detectable difference (minimum) of means in the groups studied. The standard deviation (SD) was also kept at (average difference of 20% among the groups). The α value was 0.05 and the power of the study was 0.80(80%). The sample size calculated for each group was 24 patients, so we included 30 patients in each group. The data when compared was not significant if ($p > 0.05$), significant ($p < 0.05$) in a confidence interval of 95%. To reject null hypothesis the significant level was taken as $P<0.05$.

Results

All the patients completed the study. The demographic parameters of the patients with respect

to age (years), body weight (kilograms), male and female ratio, American Society of Anaesthesiology status, Mallampatti Class were statistically comparable (P> 0.05) among the groups (Table 1).

As soon as the intubation was over, immediately the heart rate increased in all the three groups. But the mean increase was statistically minimal in Group D compared to other two groups at immediate post-intubation (P= 0.0004) and 3 minutes after intubation (P=0.0027) (Table 2).

The mean systolic blood pressure in Group D increased by significantly lesser extent than Groups C and E at immediate post intubation (P< 0.001) and at 3rd minute(P=0.001), and at 5th minute(P=0.003)

Table 1: Patient's characteristics

Variables	Group C	Group E	Group D	P value
Age (years)	44.11+/-8	45+/-7.6	45.7+/-8.8	0.800
Weight (kg)	53+/-5.6	53.4+-4.3	53+/-4.9	0.9348
Height(cm)	153.25+/-7.9	153.9+/-4.4	153.8+/-7.4	0.946
BMI(kg/sqm)	22.65+/-1.5	22+/-1.6	22.7+/-2	>0.05
Sex(male: female)	10:20	10:20	12:18	0.823
ASA status I/II	8/22	8/22	9/21	0.946
MP grade I/II	7/23	7/23	8/22	0.941
Baseline SpO2	98.2+/-0.5	99.3+/-0.6	98.23+/-0.58	0.815

Values are mean+/-SD, BMI: Body mass index; ASA: American society of anaesthesiologists; MP: Mallampati; SpO2: Oxygen saturation; SD: Standard deviation

Table 2:

HR (/Minutes)	Group C	Group E	Group D	P value
Baseline	80+/-4	82+/-4	84+/-4	0.762
After study drug	80+/-6	76+/-2	80+/-4	0.727
After induction	80+/-6	76+/-2	80+/-4	0.727
After intubation	104.8	90	85	0.0004*
3rd min	102.5	90	84	0.0027*
5th min	96	88	82.6	0.079
7th min	88.5	84	78	0.219
10th min	82	80	78	0.832

HR- Heart Rate

Table 3:

Mean SAP(mmhg)	Group C	Group E	Group D	P value
Baseline	122+/- 9.5	121.5+/-11.0	121.4+/-4.5	0.985
After study drug	126+/-12.8	131+/-17.5	127.5+/-15	0.710
After induction	114+/-6	114+/-12	122+/-13.8	0.439
After intubation(1 min)	166+/-13.5	156+/-13	125+/-18.6	0.0001***
3rd min	142+/-18.47	148+/-21.9	117+/-12.7	0.0001***
5th min	133.80+/-16.4	132+/-22.2	111.15+/-11.6	0.003*
7th min	124+/-12.8	125+/-18	111+/-12.3	0.078
10th min	122+/-12.5	120.5+/-18.5	114.2+/-14.3	0.461

Values are mean+/-SD, *significant,**highly significant,***extremely significant
SD: Standard deviation, SAP: Systolic arterial pressure.

Table 4:

Mean DAP(mmhg)	Group C	Group E	Group D	P value
Baseline	78+/-8.7	77.8+/-8.7	79.2+/-8.75	0.980
After study drug	76+/-8.7	77.5+/-8.4	81.4+/-14	0.688
After induction	78+/-5.3	72.3+/-10.5	78.1+/-13.4	0.517
After intubation(1 min)	100.5+/-18.5	94.5+/-10.8	79.37+/-16.22	0.0001***
3rd min	97.8+/-11.7	84.5+/-13.5	76.3+/-12.9	0.0003**
5th min	81+/-10	78+/-8.7	71.7+/-12.2	0.305
7th min	80.2+/-21.3	72+/-10.4	71.6+/-10.3	0.323
10th min	75+/-9.4	70.5+/-11.8	70.7+/-11.9	0.766

Values are mean+/-SD, *significant,**highly significant,***extremely significant
SD: Standard deviation, DAP: Diastolic arterial pressure.

Table 5:

Mean MAP(mmhg)	Group C	Group E	Group D	P value
Baseline	92.3+/-9.4	92.5+/-8	93.5+/-6.5	0.962
After study drug	91.5+/-10	95+/-11.8	96.5+/-13.6	0.781
After induction	88.4+/-6.2	87.6+/-14	96.6+/-14	0.371
After intubation(1 min)	122+/-16	116.5+/-10	95.4+/17.6	<0.0001***
3rd min	107+/-11.8	104.5+/-15	91+/-11.8	0.034*
5th min	99+/-10.5	95.3+/-12	85+/-12.3	0.140
7th min	93+/-8.4	89.4+/-11.4	84+/-11	0.486
10th min	93+/-8.4	88+/-11.5	85.3+/-11.7	0.560

Values are +/-SD, *Significant,**Highly significant, ***Extremely significant
***Extremely significant, SD Standard deviation.

post intubation. Esmolol didn't prevent the increase in SAP at immediate post- intubation, but the increase was lesser than that in patients in Group C (Table 3).

The DAP increased to significantly lesser extent in Group D than that in Groups C and E at immediate post intubation (P=0.0001), and at 3rdminute (P=0.003)(Table 4).

The baseline MAP was comparable in all the studied groups, both before and post induction. The MAP increased in all the studied groups post intubation, but it was to significantly lesser extent in Group D at immediate post intubation (P=0.0001) and at 3rd minute (P= 0.034) post intubation (Table 5).

Discussion

Endo-tracheal intubation may lead to many systemic effects in the body like, cardiovascular responses in the form of hypertension, tachycardia, arrhythmias. These responses may be detrimental to the patients, especially on those patients who have cardiac and cerebro-vascular diseases [8]. Thus, preventing the excessive increase in sympathetic activity post intubation is very important. Dexmedetomidine, is a selective α_2 adrenergic agonist, and esmolol, is a short acting β receptor blocker which are used to reduce the stress responses.

Among the β– receptor blocking drugs, esmolol has some special features like, quick onset of action, and faster elimination and it is cardio-selective [8]. There are many reports showing its effects on HR and arterial blood pressure after endo-tracheal intubation when it was compared with placebo [9]. Miller *et al* [9] showed that esmolol 100mg bolus effectively controlled the stress response to tracheal intubation. Liu *et al*. used esmolol infusion to control intubation responses, showed that it prevented increase in heart rate and systolic blood pressure prior to and post intubation, when compared to the placebo group [10].

In this study we found that the hemodynamic parameters increased after intubation in all the groups but the response was minimal and significantly lower in dexmedetomidine group when compared to other groups after intubation. The increase in heart rate after intubation was 1.19% in dexmedetomidine group (P=0.0004) when compared to 9.75% in Group E and 31.25% in Group C. And it was also lower for Group D at 3rd minute (P=0.0027).

With respect to increase in SBP and DBP in Group D at 1 minute and 3rd minute it was significantly less(P=<0.0001) when compared to Group E and Group C.

In a study done by Ugur et al [12], he observed that esmolol 1.5mg/kg along with fentanyl 1µg/kg and 1.5 mg/kg lidocaine given 2 minute before intubation prevented the raise in the heart rate.

Scheinin *et al*. [13][3] showed that dexmedetomidine 0.6µg/kg decreased stress response to intubation in individuals. Keniya *et al*. showed that pre-medication with dexmedetomidine 1.0 µg/kg decreased the cardiovascular responses to endo-tracheal intubation post induction of anaesthesia [14].

The α_2 adreno-receptors plays important role in autonomic nervous system. The α_2 –adrenergic-receptors are found on the blood vessels, where their stimulation leads to vasoconstriction and there are also seen in the presynaptic sympathetic terminals, where they inhibit adrenaline and nor-adrenaline release [15]. α_2 -adrenoceptors in the central nervous system produces sedation on activation, cause reduction in sympathetic outflow such that the Vagal activity takes predominance. This can result in a decrease in HR and cardiac output, hence the use of α_2 agonists used before intubation can decrease the stress responses, and hence its use in our study is substantiated [15].

Patient's characteristics like age, sex and others were statistically matched such that they will not

influence the result of the study.

No complications in the form of hypotension, bradycardia, arrhythmias were found in any of the groups studied.

Conclusion

Dexmedetomidine is more efficient than esmolol in attenuating the hemodynamic responses to tracheal intubation and immediately (< 3minutes) thereafter.

References

1. Siddareddigari Velayudha Reddy, Donthu Balaji, Dexmedetomidine versus esmolol to attenuate the hemodynamic response to tracheal intubation: A double-blind clinical study. Int J Appl Basic Med Res. 2014 Jul-Dec; 4(2):95–100.
2. Nermin Gogus, Belgin Akan, The comparison of the effects of dexmedetomidine, esmolol and fentanyl in preventing hemodynamic response to tracheal intubation. Rev Bras Anestesiol.2014; 64(5):314-319.
3. Kovac AL. Controlling the hemodynamic responses to laryngoscopy and intubation. J Clin Anesth. 1996; 8:63–79.
4. B. Yavascaoglu, F.N. Kaya, M. Baykara. A comparison of dexmedetomidine and esmolol in attenuating the intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation. Euro J Anaesthesiol, 2008; 25:517–519.
5. N. Bhana, K.L. Goa, K.J. McClellan. Dexmedetomidine Drugs, 2000; 59:263–268.
6. S. Gupta, P. Tank. A comparative study of efficacy and fentanyl for attenuating pressure during laryngoscopy and intubation. Saudi J Anaesth, 2011; 5:2–8.
7. A.M. Hussain, S.T. Sultan. Efficacy of fentanyl vs esmolol in the prevention of haemodynamic response to intubation. J Coll Physicians Surg Pak, 2005; 15:454–457.
8. Sum CY, Yacobi A et al. Kinetics of esmolol, an ultra-short-acting $beta_2$ blocker, and of its metabolite. Clinical Pharmacol Ther. 1983; 34:427–34.
9. Miller DR, Martineau RJ, Wynands JE, Hill J. Bolus administration of esmolol for reducing the haemodynamic responses to tracheal intubation: The Canadian Trial. Can J Anaesth. 1991; 38:849–58.
10. Liu PL, Gatt S et al. Esmolol for control of increase in heart rate and blood pressure due to tracheal intubation after administering thiopentone and succinylcholine. Can Anaesth Soc J. 1986; 33:556–62.
11. Y.U. Adachi, M. Satomoto, H. Higuchi. Fentanyl decreases the hemodynamic response to endotracheal intubation more than that due to laryngoscopy. Anesth Analg, 2002; 95:233–237.
12. Kindler CH, Schumacher PG, Schneider MC et al. Effects of intravenous lignocaine and or or esmolol on hemodynamic responses to laryngoscopy and intubation: A controlled double-blind clinical trial. J Clinical Anesth. 1996; 8:491–6.
13. Scheinin B, Lindgren L, Randell T et al. Dexmedetomidine decreases sympatho-adrenal responses to intubation and reduces the need for fentanyl and thiopentone. Br J Anaesth. 1992; 68: 126–31.
14. Keniya VM, Ladi S et al. Dexmedetomidine attenuates sympatho-adrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth. 2011; 55:352–7.
15. Yildiz M, Tavlan A et al. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Peri-operative haemodynamics and anaesthetic requirements. Drugs R D. 2006; 7:43–52.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.16

The Efficacy of Fentanyl as Adjuvant in Ultrasound Guided Oblique Subcostal Transversus Abdominis Plane Block

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Abstract

Background: Ultrasound guided oblique subcostal transversus abdominis plane block is associated with a wider area of spread (T7-L1). The aim of this study was to assess the efficacy of adding fentanyl to 0.25% bupivacaine in bilateral oblique subcostal transversus abdominis plane block preemptively in patients undergoing laproscopic cystectomy.

Method: 100 patients posted for laproscopic ovarian cystectomy were randomly allocated in two equal groups. Group BF received preoperatively 20 ml of 0.25% bupivacaine and 1 mcg fentanyl(1ml) on each side oblique subcostal block and group B received 20 ml bupivacaine with 1ml normal saline. We assessed opioid requirement, the time of first demand of rescue analgesia and twenty four hour morphine requirement.

Results: There is a statistically significant difference in the intraoperative fentanyl requirement between the two groups. Group BF required 16.4016.26mcg of intraoperative fentanyl while Group B required 59.8019.05mcg fentanyl ($p<0.001$). There is a significant difference in the mean VAS score in the two groups. The time of first demand of rescue analgesia was earlier in Group B; 5.961.09hrs compared to 11.182.28 hrs in Group BF ($p<0.001$). The total 24 hour morphine requirement in Group BF was significantly lower 0.581.01mg compared to Group B i.e. 4.621.63mg ($p<0.001$).

Conclusion: 1mcg/kg fentanyl used as a supplement in bilateral TAP block reduced the need for systemic opioid intra and post operatively and prolonged analgesia in laproscopic ovarian cystectomy patients.

Keywords: Fentanyl; Bupivacaine; Ultrasound Guided Transversus Abdominis Plane Block; Laproscopic Surgeries.

Introduction

Laproscopic surgeries are preferred to open surgeries due to minimal invasiveness, less tissue handling, less patient discomfort, early patient recovery and discharge. Laproscopic ovarian cystectomy is associated with moderate pain in the immediate postoperative period. Systemic opiods are the conventional post operative pain management modality but have side effects of nausea, vomiting, sedation and pruritus. These days ultrasound guided regional blocks have helped to block the pain afferents more superiorly and so reduced the use of narcotics. In laproscopic surgeries, the major component of pain originates from the abdominal wall incision [1]. Transeversus abdominis plane (TAP) block is a regional analgesic technique that blocks neural afferents of antero lateral abdominal wall. Rafi [2] and McDonnel [3] were the first to describe this block. Hebbard et al [4] described its ultrasound approach. Three approaches described are – the subcostal, midaxillary, and lumbar triangle of Petit [5]. The oblique subcostal approach was associated with a larger area of spread T7-T11, where as it was only T10-L1 with the other two approaches [6].

Local anaesthetics used alone give analgesia for few hours only, however adjuncts have been combined with local anaesthetics to improve the duration and quality of peripheral nerve block. Fentanyl is an opiod that has been successfully used as adjuvant to local anaesthetics to prolong the analgesia [7]. Very few studies are done on the use of fentanyl in oblique subcostal TAP block given pre emptively in laproscopic gynaecologic surgeries. In this study, we have assessed the

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Received on 22.12.2016
Accepted on 28.12.2016

efficacy of fentanyl as adjuvant to bupivacaine in oblique subcostal TAP block in laproscopic cystectomy patients given preoperatively.

Materials and Methods

This double blind study was done on 100 ASA 1 and 2 patients posted for laproscopic ovarian cystectomy after obtaining approval from faculty ethical committee. Patient refusal, coagulation disorders, local infection at the site of block, allergy to local anaesthetics, chronic use of pain medications were the exclusion criteria done.

A detailed pre anaesthetic check up was done. The preoperative investigations included were haemoglobin, blood sugar levels, serum electrolytes, urea, creatinine, liver function tests, coagulation profile, chest X-ray and pulmonary function tests. We explained them visual analogue pain scale for pain assessment 0-10, 0 meaning no pain and 10 meaning worst pain imaginable.

The patients were randomized using a computer generated program and allocated to 2 groups- Group BF and Group B. Group BF received on each side 20 ml 0.25% bupivacaine and 1mcg/kg (1ml)of fentanyl while Group B received 20 ml 0.25% bupivacaine and 1ml normal saline before the incision. All patients were premedicated with Injection glycopyrrolate and Injection midazolam 0.03 mg/kg. Monitoring included noninvasive blood pressure, heart rate, pulse oximetry and end tidal CO2 (Et CO2).

Induction was with injection fentanyl 2mcg/kg, propofol 1-2 mg/kg and vecuronium 0.1mg/kg intravenously. Tracheal intubation was done with endotracheal tube no.7 mm ID. Maintenance of anaesthesia was with N2O, O2(FiO2 0.35) and sevoflurane(1-1.2 MAC). After intubation, oblique subcostal TAP block was performed. We placed the linear probe below the xiphisternum and moved it laterally along the subcostal margin. The rectus abdominis and transversus abdominis muscles were identified. A 22 gauge 150 mm stimuplex needle was inserted in plane through the rectus abdominis muscle 2-3 cm medial to the probe. Once the tip was visualised between the rectus muscle and transversus abdominis muscle and negative aspiration confirmed the drug was injected and hydrodissection demonstrated. The drug injectant was loaded by another Anaesthetist and handed to the investigator. The block was repeated on the other side as well. Ventilatory settings were adjusted to maintain ETCO2 between 35-40 mmHg and SpO2-95-100%. A PEEP of 5 cm H2O was used in all patients. All patients were placed in dorsal lithotomy position. Umbilical incision was made and CO_2 was insufflated through the port. Intra abdominal pressure was not to exceed 20 cm Hg. Two secondary ports were placed 5 cm superior and lateral to the pubic symphisis. Any 20% rise of heart rate or blood pressure necessitated repeating intravenous fentanyl at 25mcg increments and this was recorded.

The cases were all done by the same surgical team and was completed in 60-75 minutes. At the end of procedure, patients were reversed with Neostigmine 50 mcg/kg and atropine 0.01mg/kg. All patients were extubated uneventfully and kept in PACU for 24 hours. Postoperatively pain scores were assessed for 24 hours and whenever VAS≥3, intravenous Morphine 2mg was administered. Hemodynamic monitoring and any adverse effects were looked for. The time for the first requirement of morphine and the cumulative dose of morphine for 24 hours were noted.

Statistical Methods

The statistical analysis was performed by STATA 11.2 (College Station TX USA). Shapiro wilk test has been used to check normality, Mann Whitney test were used to find the significance difference between the pain score with treatment groups, Students t-test were performed to find the significance difference between the age, height, weight, intra operative fentanyl used, time of first dose of morphine, total 24 hours morphine required with the treatment groups and those expressed as mean and standard deviation. $P<0.05$ considered as statistically significance.

Results

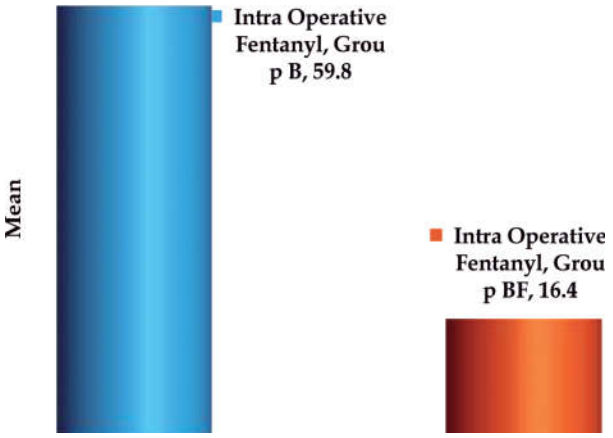
One hundred patients took part in this study and were randomly assigned to the two groups.All

Table1: Patient demography

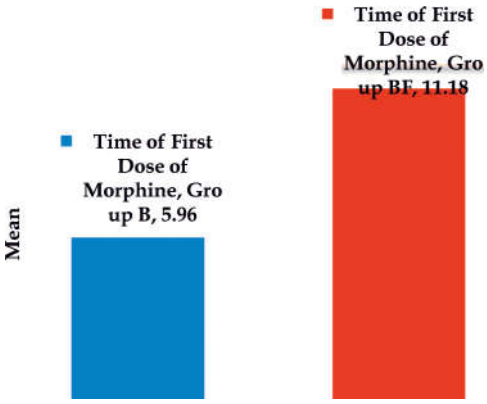
Height	**155.92 ± 9.04**	**157.88 ± 6.26**	**0.211**
Weight	57.32 ± 6.95	58.06 ± 4.68	0.534
	Group B Mean ± SD	**Group BF Mean ± SD**	**P-Value**
Age	42.76 ± 8.63	41.80 ± 8.42	0.575

Table 2: Intraoperative and postoperative Opiod requirement

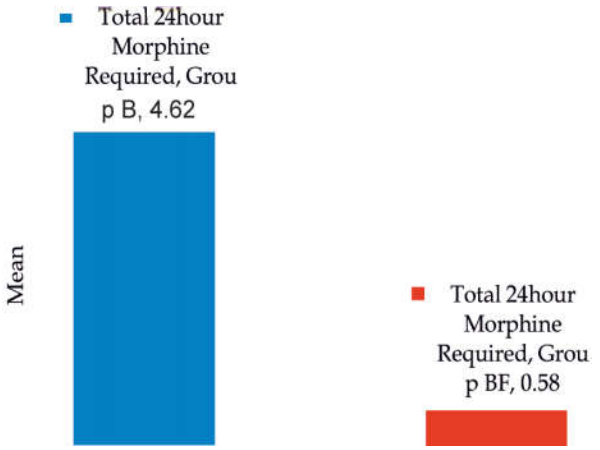
	Group B Mean ± SD	Group BF Mean ± SD	P-Value
Intraoperative fentanyl	59.80 ± 19.05	16.40 ± 16.26	<0.001
Time of 1st dose of morphine	5.96 ± 1.09	11.18 ± 2.28	<0.001
Total 24 hour morphine required	4.62 ± 1.63	0.58 ± 1.01	<0.001



Graph 1: Intraoperative Fentanyl



Graph 2: Time of first dose of Morphine



Graph 3: Total 24 hour Morphine required

ultrasound guided oblique subcostal TAP block were performed as described without any complications. Patient characteristics and perioperative data are shown in Table 1. There were no differences in patient demography.

There is a statistically significant difference in the intraoperative fentanyl requirement between the two groups. Group BF required 16.40±16.26 mcg of intraoperative fentanyl while Group B required 59.80±19.05 mcg fentanyl (p<0.001).

Also there is a significant difference in the mean VAS score in the two groups. P<0.001 for 8 hours.

Table 3: Mean Pain Score

Time	Group B Mean ± SD	Group BF Mean ± SD	P-Value
0 minutes	0.66 ± 0.74	0.16 ± 0.36	<0.001
2 hours	2.04 ± 1.47	0.96 ± 0.49	<0.001
4 hours	2.60 ± 1.19	1.26 ± 0.49	<0.001
6 hours	2.62 ± 1.01	1.60 ± 0.50	<0.001
8 hours	3.10 ± 1.03	1.82 ± 0.44	<0.001
10 hours	2.38 ± 1.14	1.98 ± 0.51	0.007
12 hours	1.90 ± 0.84	1.80 ± 0.40	0.803
14 hours	1.86 ± 1.03	1.96 ± 0.78	0.365
16 hours	2.14 ± 0.93	2.34 ± 0.96	0.284
18 hours	1.72 ± 0.81	1.82 ± 0.99	1.000
20 hours	1.52 ± 0.76	1.50 ± 0.81	0.739
22 hours	1.24 ± 0.62	1.32 ± 0.51	0.234
24 hours	1.12 ± 0.48	1.14 ± 0.35	0.446

	0 Min	2 Hrs	4 Hrs	6 Hrs	8 Hrs	10 Hrs	12 Hrs	14 Hrs	16 Hrs	18 Hrs	20 Hrs	22 Hrs	24 Hrs
Group B	0.66	2.04	2.6	2.62	3.1	2.38	1.9	1.86	2.14	1.72	1.52	1.24	1.12
Group BF	0.16	0.96	1.26	1.6	1.82	1.98	1.8	1.96	2.34	1.82	1.5	1.32	1.14

Graph 4: Mean pain score

The time of first demand of rescue analgesia i.e. morphine was earlier in Group B; 5.96±1.09 hours compared to 11.18±2.28 hours in Group B ($p<0.001$). The total 24 hour morphine requirement in Group BF was significantly lower, 0.58±1.01mg compared to Group B i.e. 4.62±1.63mg ($p<0.001$).

Discussion

This study shows that fentanyl supplemented with 0.25% bupivacaine in bilateral oblique subcostal TAP block given pre emptively in patients undergoing laproscopic ovarian cystectomy prolonged analgesia and decreased requirement of systemic opiod both intraoperatively and postoperatively.

TAP blockade has been rapidly evolving and recently has been modified to the oblique subcostal approach which provide wider sensory blockade and is suitable for surgeries both superior and inferior to umbilicus [8]. The efficacy of TAP block in providing analgesia in various abdominal surgeries is very encouraging [9-13]. Ultrasound guided TAP block has advantages of being performed accurately and safely in a short time as the procedure is implemented by watching real time image.Also the target site has no vital anatomical structure like large vessels and spinal cord [14].

Our study has revealed that pre emptive oblique subcostal TAP block with fentanyl performed has reduced intraoperative systemic opioid requirement. The wider and more extensive spread of the drug via oblique subcostal approach has resulted in a better sensory coverage.

Opiates have anti-nociceptive effect at the central and / or spinal cord level [15]. In animals peripheral opioid receptors have been reported [16-18]. Fentanyl has been shown to extend the dose of analgesia when added to local anaesthetics in brachial plexus block [19] and axillary block [20]. But Fletcher et al [21] found no increase in duration of analgesia when fentanyl was added to lidocaine for axillary block. These differences may be due to variations in technique or opioid used. Li Zhong Wang et al concluded that 50 mcg of fentanyl added to 0.375% ropivacaine in ultrasound guided TAP block did not improve analgesia following caesarean delivery. This may be due to a lower dose of fentanyl used and also due to the limitation of TAP block to somatic pain only.

Fentanyl acts directly on peripheral nervous system [18]. Activation of peripheral opioid receptors results in opioid antinociception. Primary afferent tissues (here, intercostal T7-T11, subcostal T12, iliohypogastric and ilioinguinal nerves L1) contain opioid binding sites.Fentanyl may diffuse through the nerve sheath and potentiate the action of local anaesthetics.Fentanyl is reported to have a local anaesthetic action as well [23]. These are the ways to explain the mechanism of fentanyl to intensify the peripheral block with local anaesthetics. None of the patients had any adverse effects.

Further research is required to study any changes occurring to the pH of local anaesthetic agent upon the addition of fentanyl causing any delayed onset. The block has to be performed in awake patients and in surgeries involving motor innervation and onset of motor and sensory block is to be assessed. Also a comparison between all additives including buprenorphine, dexamethasone, dexmedetomidine has to be studied.

Thus we conclude that 1mcg/kg fentanyl used as a supplement inTAP block performed preemptively on each side of abdomen reduced the need for systemic opioid intra and post operatively and prolonged analgesia in laproscopic ovarian cystectomy patients.

References

1. Tran TMN, Rozen W, Ashton M, Barrington M, Ivanusic J, Taylor G. Redefining the course of the intercostal nerves: a new understanding of the innervation of the anterior abdominal wall. Clin Anat, 2008; 21:325–333.
2. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. Anaesthesia 2001; 56:1024-6.
3. McDonnell JG, O'Donnell BD, et al. The regional abdominal field infiltration technique computerised tomographic and anatomical identification of a novel approach to the transversus abdominis neurovascular fascial plane. Anaesthesiology 2004; 101:A899.
4. Hebbard P, Fujjiwara Y, Shibata Y, et al. Ultrasound-guided transversus abdominis plane block. Anesth Interns Care 2007; 35(4):616-7.
5. Milan Z, Tabor D, McConnell P, Pickering J, Kocarev M, du Feu F, et al. Three different approaches to transversus abdominis plane block: a cadaveric study. Medicinski Glasnik 2011; 8:181-4.
6. Sivapurapu V, Vasudevan A, Gupta S, et al. Comparison of analgesic efficacy of transversus abdominis plane block with direct infiltration of local anesthetic into surgical incision in lower abdominal gynaecological surgeries. J Anaesthesiol Clin Pharmacol 2013; 29(1):71-5.
7. W.P.Gormley, J.M.Murray, J. P. H. Fee, and S. Bower, "Effect ofthe addition of alfentanil to lignocaine during axillary brachialplexus anaesthesia," British Journal of Anaesthesia, 1996; 76(6):802–805.
8. Chen CK, Phui VE. The efficacy of ultrasound-guided oblique subcostal transversus abdominis plane block in patients undergoing open cholecystectomy. South Afr J Anaesth Analg 2011; 17(4):308-310.
9. McDonnell JG, O'Donnell BD, Curley GCJ, et al. The analgesic efficacy of transversus abdominis block after abdominal surgery: a prospective randomised controlled trial. Anaesth Analg. 2007; 104:193-197.
10. McDonnell JG, Curley GCJ, Carney J, et al. The analgesic efficacy of transversus abdominis block after caesarean delivery. Anaesth Analg. 2008; 106: 186-191.
11. Carney J, McDonnell JG, Ochana A, et al. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. Anaesth Analg. 2008; 107:2056-2060.
12. Belavy D, Cowlishaw PJ, Howes M, Phillips F. Ultrasound-guided transversus abdominis plane block for analgesia after Caesarean delivery. Br J Anaesth. 2009; 103:726-730.
13. Langford L, Bosenberg M, Bosenberg A. Transversus abdominis plane block as an alternative analgesic for children undergoing appendicectomy: a preliminary report. S Afr J Anaesthesiol Analg. 2008; 14:23.
14. Hyun-Jung Shin, Sang Tae Kim, Kyoung Hoon Yim, et al. Preemptive analgesic efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing gynecologic surgery via a transverse lower abdominal skinincision. Korean J Anesthesiol. 2011 Nov; 61(5):413-418.
15. Yaksh TL. Multiple opioid receptor systems in brain and spinal cord. Eur J Anaesthesiol. 1984; 1:171–99. [PubMed: 6152613].
16. Stein C. Peripheral mechanisms of opioid analgesia. Anesth Analg. 1993; 76:182–91. [PubMed: 8380316].
17. Sibinga NE, Goldstein A. Opioid peptides and opioid receptors in cells of the immune system. Annu Rev Immunol. 1988; 6:219–49. [PubMed: 2838048].
18. Fields HL, Emson PC, Leigh BK, Gilbert RF, Iversen LL, et al. Multiple opiate receptor sites on primary afferent fibres. Nature. 1980; 284:351-3. [PubMed: 6244504].
19. Shirish G. Chavan, Alka R. Koshire, Prasad Panbude. Effect of addition of fentanyl to local anesthetic in brachial plexus block on duration of analgesia. Anesth Essays Res. 2011 Jan-Jun; 5(1):39–42.
20. Siamak Yaghoobi, Mahyar Seddighi, Zohreh Yazdi, et al. Comparison of Postoperative Analgesic Effect of Dexamethasone and Fentanyl Added to Lidocaine through Axillary Block in Forearm Fracture. Pain Research and Treatment Volume 2013, Article ID 761583, 6 pages.
21. Fletcher D, Kuhlman G, Samii K. Addition of fentanyl to 1.5% lidocaine does not increase the success of axillary plexus block. Reg Anesth. 1994; 19:183–8. [PubMed: 7999653].
22. Li Zhong Wang, Xia Liu, Ying Fa Zhang, et al. Addition of fentanyl to the ultrasound-guided transversus abdominis plane block does not improve analgesia following cesarean delivery Experimental and therapeutic medicine 2016; 111: 1441-1446.
23. Gissen AJ, Gugino LD, Datta S, Miller J, Covino BG. Effects of fentanyl and sufentanil on peripheral mammalian nerves. Anesth Analg. 1987; 66:1272–6. [PubMed: 2961289].

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.17

A Comparative Study between Intrathecal Clonidine and Buprenorphine with Intrathecal Bupivacaine for Lower Abdominal Surgeries

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Abstract

Purpose: Subarachnoid (spinal) block is a safe and effective alternative to general anesthesia when the surgical site is located on the lower extremities, perineum (eg, surgery on the genitalia or anus), or lower body wall (eg, inguinal herniorrhaphy). In no other way, can an anaesthesiologist obtain so much of an effect for the introduction of a small quantity of the drug. Likewise a properly chosen adjuvant to local anaesthetic agent produces the best way to achieve a good quality regional block.

Aim of Study: To compare the effect of intrathecal Clonidine 75 micrograms (µg) and Buprenorphine 150 µg with 2.5ml (12.5mg) of intrathecal 0.5% hyperbaric Bupivacaine. With regards to: 1) Sensory characteristics, 2) Motor characteristics, 3) Hemodynamic stability and 4) Side effects.

Methodology: A prospective randomized experimental study were performed on 50 patients posted for lower abdominal surgery belonging to ASA I and aged between18-60 years after obtaining an informed consent and ethical clearance.

Result: Addition of 150 µg Buprenorphine significantly enhances the onset of sensory block (90±15 secs) and motor block (150±15 secs) than compared to Clonidine onset of sensory block(150±20 secs) and motor block(210±20 secs) (p<0.05). Hemodynamic was well maintained with buprenorphine group. And addition of Buprenorphine 150µg to intrathecal Bupivacaine(0.5%) produces prolonged analgesia (526±96) than compared to the Clonidine group of 362±36mins (p<0.05) with no serious adverse effect noted perioperatively in either groups.

Conclusion: The addition of Buprenorphine to intrathecal Bupivacaine (0.5%) prolongs the duration of post operative analgesia than compare to clonidine. Buprenorphine has faster onset of sensory and motor blockade than compare to clonidine.

Keywords: Clonidine; Buprenorphine; Hyperbaric; Lower Abdominal Surgery Analgesia; Bromage Scale [1].

Introduction

Spinal anaesthesia may be defined as the temporary interruption of transmission of the nerve impulses across the nerve fibers by injecting drug into the sub arachnoid space. It is safe and satisfactory if performed with the knowledge of its physiological consequences and in many instances, it is the method of choice in view of patient's condition and produces an ideal operating condition and post operative pain relief.

Bupivacaine has been used since 1963; Bupivacaine is more potent than Lignocaine and has longer duration of action. Its disadvantage is a slow onset of action and decreased motor block [2]. Hyperbaric Bupivacaine 0.5% is extensively and the only local anaesthetic used intrathecally in India. Peri--operative hemodynamic status and post operative pain relief are important issues with bupivacaine. Many adjuvants are commonly used to overcome these demerits. So our concern is to choose an ideal adjuvant with Bupivacaine which provides a stable intraoperative condition, prolonging the post operative analgesia with minimal side effects.

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Received on 06.12.2016
Accepted on 19.12.2016

Clonidine is a selective alpha (α) 2 agonist agent, routinely used as a premedicant for general anaesthesia. Its use decreases the requirement of analgesics and anaesthetic drugs intraoperatively. Intrathecally clonidine produces analgesia by indirectly inhibiting the activity of wide dynamic range (WDR) neurons [2,3].

Buprenorphine is a semi synthetic, highly lipophilic opioid which was originally derived from thebaine, one of the most chemically reactive opioid alkaloids. Buprenorphine, a partial opiate agonists which posses high analgesic potency, long duration and low acute toxicity [4,16]. Buprenorphine binds to substantia gelatinosa of the dorsal horn of the spinal cord and produces presynaptic and (post synaptic) inhibition of neuronal cell excitation [5].

Keeping the pharmacological and economical profile of both clonidine and buprenorphine, we performed a double blind randomized study in our institute for comparing the effects of clonidine and buprenorphine with intrathecal bupivacaine. The chief aims of this pharmacological comparison were to observe the effects on duration of analgesia, hemodynamic parameters with addition of these adjuncts.

Materials & Methods

Over a period of 5 months duration, a double blinded prospective randomized study was performed in our institute. Ethical committee clearance was obtained for our study. All patients belonging to the following inclusion criteria were randomly divided into two groups (Group BB and Group BC): sample size: 50.

Inclusion Criteria

All patients aged between a) 18-60 years, b) ASA Grade I and II c) Patients posted for lower abdominal surgeries.

Exclusion Criteria

a) Patients with local sepsis, b) Patients with bleeding diathesis, c) Patients with raised intracranial pressure(ICP), d) Patients with any co-morbid diseases like ischemic heart disease (IHD), hypertension, bronchial asthma, diabetes mellitus and morbidly obese patients.

Group BB (n=25) received 2.5 ml of 0.5% hyperbaric Bupivacaine along with 0.5 ml of Buprenorphine (150 µg). And Group BC (n=25) received 2.5 ml of 0.5% hyperbaric Bupivacaine + (75µg) 0.5 ml of Clonidine. The study was double blinded, spinal anesthesia was given by the anesthesiologist with the study drug, who was not involved in the patients monitoring. The patients and the monitoring anesthesiologist were blinded to the study solutions. Ethical committee clearance and patients consent were obtained. All the patients were evaluated on the previous day of surgery; the procedure was explained to each patient and informed consent was taken. All the patients were premedicated with ranitidine 150 mg, Alprazolam 0.5 mg orally on previous night. On the day of surgery, patient's basal pulse and basal blood pressure were recorded. A peripheral intravenous line with 18 gauge cannula was secured in one of the upper limbs. Patients were preloaded with 500 ml of Ringer lactate solution. Lumbar puncture was performed with 23 gauge spinal needle (Quincke's) using a midline approach with the patients in the left or right lateral decubitus position. The lumbar 3-4 inter space was chosen for all the patients and when a free flow of clear cerebrospinal fluid was obtained, the study drug was administered at a rate of not more than 0.3ml per second.

Immediately after the injection the needle was withdrawn, the patient turned supine, supplemented with oxygen through simple face mask and allowed to remain so until the maximum level of sensory blockade was achieved and the change in position if required was then allowed. Assessment of the sensory and the motor blockade were done at the end of each minute till the maximum level achieved. Measurements of blood pressure, pulse rate, respiratory rate, and arterial oxygen saturation were obtained at regular intervals of 2 mins for initial 20 mins and 5 mins thereafter.

Sensory block was assessed using a short beveled 22 gauge needle and was tested in the midclavicular line on chest, trunk and legs on either side. Analgesia was defined as loss of the sensation to pinprick and, Anaesthesia as loss of sensation of touch. The following were observed: 1) Time of onset of analgesia: defined as time taken from the injection of the drug to onset of analgesia at T10 level, 2) Maximum level of analgesia achieved. 3) Time taken for achieving maximum level of analgesia, 4) Total duration of analgesia: defined as the time taken from the onset of analgesia to the point where the patient complained of pain in the operated site requiring rescue analgesics, if VAS [visual analogue scale]>5.

Motor blockade: Was assessed using (Bromage 1965) Bromage scale :

0: full movement of leg.

1: inability to raise the extended leg (just able to move knees)

2: inability to flex the knee (able to move feet only)

3: inability to flex the ankle joint (unable to move feet or knees)

During recovery, motor blockade was assessed as follows:

0: No movement, complete paralysis.

1: Flickering movement

2: Movement with gravity

3: Movement against gravity

4: Movement against resistance

5: Normal power.

The following parameters were noted : a)Time taken for onset of motor blockade: defined as the time taken for complete inability to flex both the lower limbs at hip joint, b) Quality of motor blockade assessed by Bromage scale [1] c) Total duration of surgery.

Intra operative complications like fall in blood pressure, variation in pulse rate, complaints like nausea, vomiting, pruritus, sweating were noted at 2^{nd},5^{th},10^{th} and every 15 mins till surgery. Similarly in post operatively complaints like nausea, vomiting, pruritus, and any other side effects associated with study drug were noted, treated and tabulated.

Incremental titrated doses of Mephentermine (i.v) 3 mg were given to patients whose systolic blood pressure fell below 30% of basal systolic blood pressure or below 90mmHg of systolic blood pressure-hypotension [6]. Bradycardia (<60 beats/min) was treated with injection Atropine 0.6mg. Nausea and vomiting were treated with injection Ondensetron (i.v).

Post operatively, the patients were observed for the duration of analgesia by using visual analogue scale scoring system of 0 to 10, with no pain being 0 and most severe pain being 10 and post operative complications if any were noted. Patients were given rescue analgesia once the visual analogue scores was more than 5, time taken for complete recovery of motor power was also noted.

At the end of the study, the data was complied systematically and was subjected to statistical analysis using student 't' test and SPSS version 10.0 for windows. Value of $p<0.05$ was considered significant.

Results

The groups were comparable with respect to age, weight, sex and duration of surgery. There was no statistically significant difference in either of the groups, ($p>0.05$) (Table 1).

Sensory characteristics are tabulated (Table 2). Group BB shows early onset of sensory loss (90±15 secs) with same segment higher block (T4) than the Group BC. Block regression was significantly slower with addition of intrathecal Buprenorphine and the mean total duration of analgesia was prolonged to nearly 9 hours in Group BB than compared to nearly 7 hours in Group BC (Graph 1).

Motor characteristics are tabulated (Table 3). Group BB shows early onset of motor block (150±15 secs) and early regain of motor power (170±40mins) than compared to Clonidine group motor block onset (210±20 secs) and duration of motor blockade (210±50 mins). With the dosage used of 150µg of Buprenorphine and 75µg of Clonidine there was no sedation, sweating or other serious complications like respiratory depression were observed in either groups.

In our study (Graph 2), intra operative blood pressure was well maintained in either of the groups. Intraoperative need of vasopressor was more with Group BC compared to Group BB. In Group BC ten patients exhibited hypotension with SBP< 80 mmHg. It occurred 15- 30 min after SAB four patients required intravenous Mephentermine to maintain SBP at or above 100 mmHg. In Group BB, eight patients manifested hypotension, out of eight three patients required additional vasopressor mephentermine to balance the sympathetic tone. Hypotension was associated with bradycardia was also noticed in 3 patients in group BC and 2 patients in group BB. It

Table 1: Demography

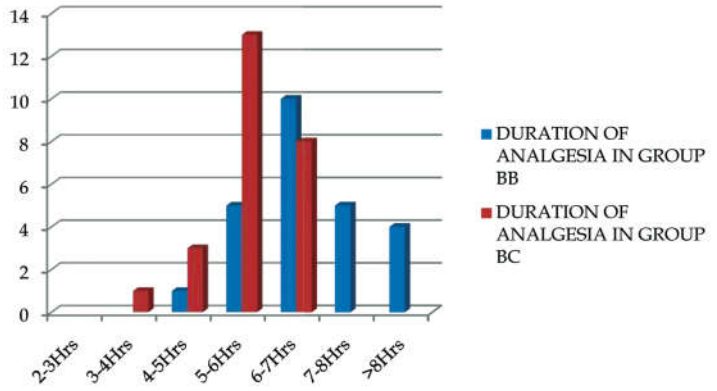
	Group BB	Group BC	*P* Value
Mean Age	28.72	37.6	>0.05
Mean Weight	56.36Kg	52.3Kg	>0.05
Male:Female Ratio	18:07	11:14	0.1
Duration of Surgery FOR 45-60mins	20	20	>0.05
Duration of Surgery FOR 60-120mins	5	5	>0.05

Table 2: Sensory charateristics

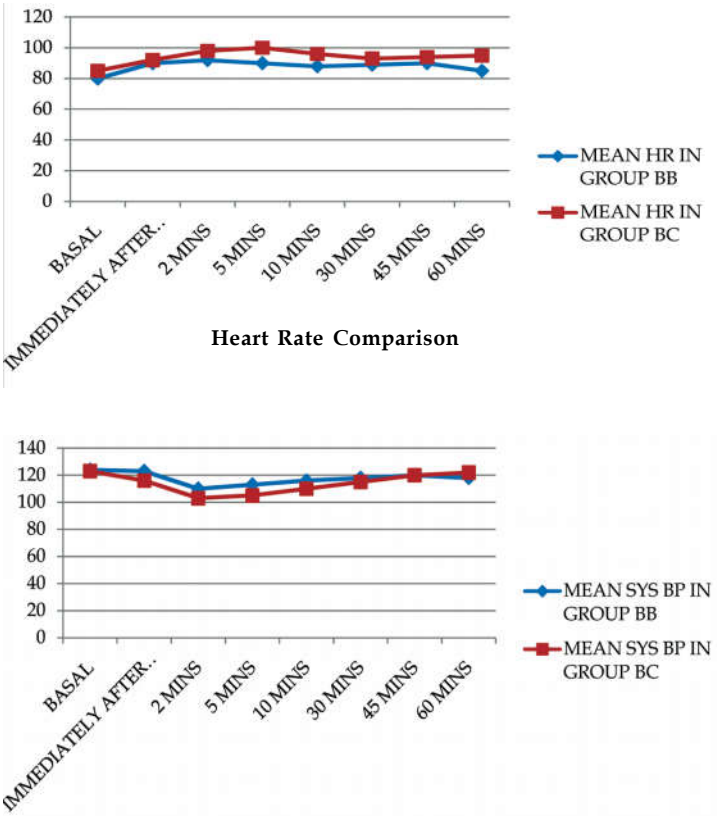
	Group BB	Group BC	*P* value
Mean Onset Time	1mins 38secs	2mins 40secs	<0.05
Mean Max Level Obtained	T4	T4	
Mean Time For Achieving Mean Max Level	5.28±2.2mins	6.12±3.2mins	<0.05
Mean Total Duration Of Analgesia	526.8±25 mins	362±36 mins	<0.05

Table 3: Motor characteristics

	Group BB	Group BC	*P* value
Mean Time Required To Attain Max Motor Blk	150±15secs	220±40secs	<0.05
Quality Of Motor Blockade	Bromge grade III→ 100%	Bromage grade III→100%	
Duration Of Motor Blockade	170±40mins	210±50mins	<0.05



Graph 1: Duration of post operative analgesia



Graph 2: Hemodynamic changes – group bb and group bc

responded to i.v. Atropine 0.6mg.

Subsequently in all these patients there were no further changes in SBP or HR. No patients of either group had sedation, nausea and vomiting post dural puncture headache or transient neurological symptoms at the post operative follow up.

Discussion

Clonidine, a partial α_2 adrenergic agonist, has antinociceptive properties. Clonidine produces spinal cholinergic activation: Cholinergic interaction in spinal α_2 adrenergic receptors which are located on descending nor-adrenergic pathways produces nor-adrenaline release that causes analgesia directly and also it releases acetylcholine (Ach) to produce analgesia. Clonidine also blocks Aδ and C- fibers at lamina V, thereby producing analgesia [2,7,8]. Clonidine has been used orally, epidurally and intrathecally to prolong the analgesia provided by local anaesthetics when given intrathecally or epidurally [3]. Clonidine has been used in varying doses from 15µg to 300µg intrathecally by various authors. Recently it has been established that with local anaesthetics, the maximum dose of intrathecal Clonidine to be 1-2µg/kg [3]. Higher doses of sole Clonidine is said to produce marked sedation as well as hemodynamic disturbances. Plateau effect of analgesic effect of Clonidine is seen around a dose of 150µg [9,10]. In view of this, in the present study we selected a dose of 75µg of Clonidine.

Our hospital protocol includes routine use of Buprenorphine as intrathecal

additive to produce post operative analgesia. Buprenorphine being a lipid soluble and non ionized drug passes rapidly via the arachanoid granulation into the venous and lymphatic vessels which allow minimal increase of CSF concentration with minimal risk of respiratory depression [11]. In addition Buprenorphine, because of its high affinity for opiate receptors is likely to produce greater duration of analgesia than other lipophilic agents [5].

In the present study, we noticed that in Group- BB onset time for sensory blockade was earlier compared to Group- BC, showing that Buprenorphine enhances action of spinally administered local anaesthetics. However, there was no clinically significant difference in the maximum level of sensory blockade achieved in both the groups.

Clonidine is believed to prolong the motor blockade produced by local anaesthetic agents [2]. Clonidine produces local vasoconstriction by acting on vascular smooth muscle (α-receptors), which decreases absorption of local anaesthetics from sub arachanoid space thereby prolonging the duration of action [12,13,14]. The motor blockade of Buprenorphine is by potential direct inhibition of motor activity by administration of Buprenorphine through by opioid receptor activity at substantia gelatinosa[5]. Buprenorphine enhanced motor block from spinal bupivacaine may be useful in the clinical setting. Many lower abdominal surgical procedures require muscle relaxation, and spinal bupivacaine with other adjuncts provides only modest motor block [11]. In our study the mean time for motor block onset was significantly faster in Buprenorphine group than compared to Group BC, similarly the mean time taken for maximum motor blockade was clinically and significantly faster in Buprenorphine group than compared to Group BC. This concurs with the study result conducted by Manika Sen [15].

Clonidine after neuraxial administration affects arterial blood pressure in a complex manner because of opposing actions at different sites. The α_2 adrenergic agonism produces sympathicolysis and reduces the blood pressure through effects on brainstem nuclei and on sympathetic pre-ganglionic neurons. However, these effects are counteracted by direct vasoconstriction resulting from the effect of α_1 and α_2 adrenergic agonistic actions on the peripheral vasculature [2,13].

On other hand, in group BB also the variation in hemodynamic parameter mimics that of group BC which was uneventful. The peripheral vasodilatation leading to noticeable hypotension caused by intrathecal local anaesthetics was counter balanced by addition of opioid adjuncts like fentanyl, Buprenorphine etc acting on mu receptor at substantia gelatinosa[5,16].

Pruritus was observed in 4 patients of Buprenorphine group, which was observed near the tip of the nose and the area around it. However, none of the patients described it as a disturbing complaint. Capogna G, Celleno D, Tagariello V [17] observed increased incidence of nausea, vomiting and pruritus with increase dose of Buprenorphine (300 micrograms)

In the present study, in Group-BB the total duration of analgesia was significantly higher compared to Group-BC. This ability of intrathecal Buprenorphine to prolong analgesia without any side effects has many fold advantages. It provides adequate post-operative analgesia. In unexpected prolongation of superficial surgical procedures, maintenance of analgesia provides additional time for the surgeon to complete the surgery without resorting to alternative anaesthesia [2,17].

Conclusion

The use of intrathecal Buprenorphine significantly hastens the onset of sensory and motor block along with a good quality of surgical relaxation. And Intrathecal Buprenorphine significantly produces prolongation of analgesia. Both the adjuncts manifests with no significant side effects.

References

1. Bromage PR. Philadelphia: WB Saunders; 1978.p.144.
2. Eisenach JC, De Kock M, Klimscha W. Alpha(2)-adrenergic agonists for regional anesthesia: a clinical review of Clonidine. Anesthesiology 1996; 85: 655–74.
3. Stephan Strebel, MD, Jurg A. Gurzeler MD, et al. Small dose intrathecal Clonidine and isobaric bupivacaine for orthopedic surgery: A dose response study. Anesthesia and Analgesia 2004; 99:1231-1238.
4. D Celleno and G Capogna: Spinal Buprenorphine for post operative analgesia after cesarean section-Acta Anaesthesiology Scand 1989; 33;236-238.
5. Michael J Cousins, Laurence E Mather: Intrathecal and epidural administration of Opioids-Anesthesiology 1984; 61;276-310.
6. Bria M. Coates, Monica S. Vavilala, MD, Christopher D. Mack, MS et al. The Influence of Definition and Location of Hypotension on Outcome Following

Severe Pediatric Traumatic Brain Injury. Crit Care Med 2005; 33(11):2645-2650.

7. Philip JS, Allan RM, et al. The efficacy of Intrathecal Morphine and Clonidine in the treatment of pain after spinal cord injury. Anesthesia and Analgesia 2000; 91:1493-1498.
8. I. van Tuijl, W.A.van Klei, et al . The effect of addition of intrathecal Clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after Caesarean section: a randomized controlled trial. British Journal of Anaesthesia 2006; 97(3): 365-370.
9. Filos KS, Goudas LC, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal Clonidine in humans: a dose response study. Anesthesiology 1994; 81:591-601.
10. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal Clonidine as a sole analgesic for pain relief after cesarean section. Anesthesiology 1992; 77:267–274.
11. D Celleno and G Capogna: Spinal Buprenorphine for post operative analgesia after cesarean section- Acta Anaesthesiology Scand 1989; 33;236-238.
12. Chiari A, Eisenach JC: Spinal anesthesia: Mechanisms, agents, methods, and safety. Reg Anesthesia and Pain Medicine 1998; 23:357–362.
13. De kock M, Gautler P, Fanard L, Hody JL, Lavand'homme P Intrathecal Ropivacaine and Clonidine for ambulatory knee arthroscopy. A dose response study. Anesthesiology 2001; 94:574-578.
14. Hassenbusch SJ, Gunes S, Wachsman S, Willis KD. Intrathecal Clonidine in the treatment of intractable pain: a phase I/II study. Pain Medicine 2002; 3(2): 85-91.
15. (Mrs.) Manika Sen (Basu): Intrathecal Buprenorphine for post operative analgesia in orthopedic surgery- J Indian Medical Association 1992 Jan; 90(1);5-6.
16. Michael J Cousins, Laurence E Mather: Intrathecal and epidural administration of Opioids- Anesthesiology 1984; 61;276-310.
17. Capogna G, Celleno D, Tagariello V, Loffreda-Mancinelli C: Intrathecal Buprenorphine for post operative analgesia in the elderly patient- 1988 Feb; 43(2);128-130.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.18

Study on Effectiveness of EMLA Cream in Attenuation of the Hemodynamic Response to Venepuncture

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Abstract

Context: The anxiety related to venepuncture can result in a hemodynamic stress response leading to increase in heart rate and blood pressure of the patient.
Aims: To evaluate the efficacy of eutectic mixture of local anesthetic (EMLA) cream in attenuating the hemodynamic response to venous cannulation.

Settings and Design: 200 patients undergoing elective operative procedures belonging to ASA grade I and II aged 18-60 years were selected and were divided into two groups.

Methods and Material: EMLA cream was applied for 60 minutes in 100 group I patients with an occlusive dressing and in remaining 100 group II patients, normal saline was applied before cannulation. Heart rate and blood pressure was recorded prior and during cannulation.

Statistical Analysis Used: Data analysis was done by Z-test.

Results: There was no significant difference in heart rate, systolic blood pressure, diastolic blood pressure among group-I and group-II before cannulation. There was statistically significant difference in heart rate among group-I and group-II during cannulation ($z=5.05$, $p<0.01$). There is significant difference in systolic blood pressure among group-I and group-II during cannulation ($z=5.28$, $p<0.01$). Significant difference of diastolic blood pressure among group-I and group-II patients was noticed during cannulation ($z=2.65$, $p<0.01$).

Conclusions: The hemodynamic stress response to venous cannulation was significantly low in patients with EMLA cream when compared to the control group. The effective time of application of EMLA cream in producing adequate analgesia to venous cannulation was found to be 60 minutes. No significant local side effects of EMLA cream were seen.

Keywords: Eutectic Mixture of Local Anaesthetic Cream; Hemodynamic Response; Venepuncture.

Introduction

Venous cannulation is the most commonly performed invasive procedure in hospital patients [1]. It is painful and associated with a high incidence of vasovagal reactions and pressor responses in patients [2]. The nociceptive apparatus associated with skin can often produce fear of medical procedures, causing discomfort, pain and anxiety, which sometimes lead to vasovagal attacks [3]. The needle prick can also make a patient uncooperative and the anxiety caused can result in a hemodynamic stress response leading to increase in heart rate and blood pressure of the patient [4]. Different pharmacological agents have been used to obtund this response. The major step in pharmaceutical research on topical drugs came with a discovery that a specific mixture of crystalline bases of lidocaine and prilocaine had a lower melting point than the melting point of the individual drugs. This combination is termed a eutectic mixture and such a combination of local anesthetics is a liquid at room temperature and the individual components are crystalline solids [5].

The eutectic mixture of local anesthetics (EMLA) cream consists of an oil in water emulsion of a eutectic mixture of lignocaine base 2.5% and prilocaine base 2.5% with a thickener (carbopol) added to obtain suitable consistency [6].

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Received on 31.12.2016
Accepted on 03.01.2017

With the advent of EMLA cream, effective topical anesthesia of intact skin is now claimed to be feasible without the need for subcutaneous injections or exposure to high concentrations of local anesthetics [5]. Hence a study was conducted to evaluate the efficacy of eutectic mixture of local anesthetic (EMLA) cream in attenuating hemodynamic response to venous cannulation.

Subjects and Methods

Ethical Committee approval was obtained before starting the study. A total of 200 patients undergoing elective operative procedures belonging to American society of Anesthesiologist (ASA) grade I and II were selected. The patients belonged to either sex and were of the age group between 18 and 60 years. The purpose and procedure of the study was explained to all the patients and informed and written consent was taken.

A routine pre-operative evaluation was done for all patients and the following patients were excluded:

- Patients with known hypersensitivity to EMLA cream or any other local anesthetics.
- Patients with methemoglobinemia or on drugs that may cause methemoglobinemia.
- Patients with mental illness.
- Patients with open wounds on dorsum of hand.

Investigations included routine haemogram, urine analysis, blood sugar and other specific tests like ECG, chest X-ray, blood urea, serum creatinine etc. as required for respective patients and surgeries.

Procedures

The patients were selected randomly and were divided into two groups.

Group-I: Patients applied with EMLA cream before intravenous cannulation.

Group-II: Patients applied with placebo (normal saline) before intravenous cannulation.

After explaining the procedure, a suitable vein on the dorsum of the hand was selected. In group-I patients, EMLA cream 1.5 to 2 gm/ 10 cm^2 area was applied over the site of cannulation in a thick layer. This layer was then covered with an occlusive dressing. EMLA cream was applied for a minimum period of 1 hour. The occlusive dressing was removed just before the intravenous cannulation. The area was then wiped dry with gauze. Heart rate and blood pressure was recorded prior to cannulation. After disinfecting with spirit, intravenous cannulation was performed with 18 gauge IV cannula. Heart rate and blood pressure was recorded during cannulation.

In group-II, normal saline was applied over the site of cannulation and was covered with an occlusive dressing for a minimum period of 1 hour. The occlusive dressing was removed just before the intravenous cannulation. Heart rate and blood pressure were recorded prior to cannulation. After disinfecting with spirit, intravenous cannulation was performed with 18 gauge IV cannula. Heart rate and blood pressure were recorded during cannulation.

Results

The two groups were compared with respect to age, sex, heart rate, systolic and diastolic blood pressure. Data analysis was done by Z-test.

Age difference among male and female was statistically insignificant in group-I ($z=1.22$, $p>0.05$) (Table 1) and group-II ($z=1.93$, $p>0.05$) (Table 2).

There was no significant difference in heart rate among group-I and group-II before cannulation ($z=1.49$, $p>0.05$) (Table 3). There was statistically significant difference in heart rate among group-I and group-II during cannulation ($z=5.05$, $p<0.01$) (Table 3). The mean heart rate before and during cannulation in group-I showed no significant change whereas significant change was noted in group-II.

There was no significant difference in systolic blood pressure among group-I and group-II before cannulation ($z=0.89$, $p>0.05$) (Table 4). There is

Table 1: Age and sex wise distribution of cases in group-I

Age	Sex		Total
	Male	Female	
18 – 27	15	19	34
28 – 37	13	14	27
38 – 47	13	06	19
48 – 57	10	08	18
58 – 67	01	01	02
Total	52	48	100.00
Mean	36.54	33.75	35.20
SD	10.43	12.25	11.84

Table 2: Age and sex wise distribution of cases in group-II

Age	Sex		Total
	Male	Female	
18 – 27	13	13	26
28 – 37	17	17	34
38 – 47	17	09	26
48 – 57	07	03	10
58 – 67	04	00	04
Total	58	42	100
Mean	37.37	33.28	35.30
SD	11.23	9.84	10.68

Table 3: Comparison of heart rate variation before and during cannulation in group-i and group-II

	Group	No. of cases	Mean±SD	Test value 'z'	'p'	Remarks
Before cannulation	Group-I	100	79.36±7.88	1.49	>0.05	Insignificant
	Group-II	100	77.76±7.25			
During cannulation	Group-I	100	79.86±8.11	5.05	<0.01	Highly significant
	Group-II	100	85.46±7.62			

Table 4: Comparison of systolic blood pressure before and during cannulation in group-i and group-II

	Group	No. of cases	Mean±SD	Test value 'z'	'p'	Remarks
Before cannulation	Group-I	100	117.78±7.63	0.89	>0.05	Insignificant
	Group-II	100	118.66±6.15			
During cannulation	Group-I	100	117.92±7.60	5.28	<0.01	Highly significant
	Group-II	100	123.20±6.58			

Table 5: Comparison of diastolic blood pressure before and during cannulation in group-I and group-II

	Group	No. of cases	Mean±SD	Test value 'z'	'p'	Remarks
Before cannulation	Group-I	100	76.40±6.70	0.098	>0.05	Insignificant
	Group-II	100	76.32±5.32			
During cannulation	Group-I	100	76.42±6.10	2.65	<0.01	Highly significant
	Group-II	100	78.57±5.42			

significant difference in systolic blood pressure among group-I and group-II during cannulation ($z=5.28$, $p<0.01$) (Table 4).

Significant difference of diastolic blood pressure among group-I and group-II patients was noticed during cannulation ($z=2.65$, $p<0.01$) (Table 5).

Discussion

EMLA (Eutectic Mixture of Local Anesthetic) cream is a 5% mixture of two local anesthetics, lignocaine and prilocaine. Using a eutectic mixture, Frederick Broberg discovered that equal parts of lignocaine and prilocaine produced adequate analgesia after topical application to the skin [7].

A total of 200 patients of either sex belonging to the age group 18-60 years posted for elective surgeries were selected. They were divided into two groups i.e., group-I and group-II with 100 patients in each group. The efficacy of eutectic mixture of local anaesthetic cream in attenuating the hemodynamic response to venous cannulation was evaluated. Before intravenous cannulation, EMLA cream was applied in group-I patients and placebo (normal saline) was applied in group-II patients. Both the groups were compared regarding age and sex and there was no statistical difference with respect to these variables. The venous cannulation causes increase in heart rate and blood pressure due to anxiety and pain. The hemodynamic response to venous cannulation such as the heart rate, systolic and diastolic blood pressure was recorded before and during cannulation. We observed that the mean heart rate in group-I patients before and during cannulation showed no significant change whereas in group-II patients, the mean heart rate before and during the cannulation showed significant change. The difference in heart rate among group-I and II patients during cannulation ($z=5.05$, $p<0.01$) was statistically significant.

The systolic blood pressure and diastolic blood pressure did not show any significant change in group-I patients before and during cannulation, whereas in group-II patients, there was significant change in systolic blood pressure and diastolic blood pressure.

There was statistically significant difference in systolic blood pressure ($z=5.28$, $p<0.01$) and diastolic blood pressure ($z=2.65$, $p<0.01$) among group-I and group-II patients during cannulation. The above observations in our study reveal that the EMLA cream is efficient in attenuating the haemodynamic response to venous cannulation. Similar finding was appreciated by Lindh V et al [8] (2000) in newborn infants on application of EMLA cream during venepuncture. Tak JH, Van Bon WHJ [9] (2006) compared the effect of EMLA cream and a placebo cream on reported pain and observed distress associated with venepuncture. They concluded that EMLA cream reduces pain and distress from venepuncture. Study by Norbert Griessinger [10] (1995) showed that the application of EMLA cream can be a very useful measure to facilitate venepuncture in patients with reflex sympathetic dystrophy as it avoids any haemodynamic alterations. In this study, we applied the EMLA cream for a minimum period of 60 minutes as per the recommendations made in various studies. Significantly lower pain scores for EMLA cream at 60 minutes was also demonstrated in a study by Smith AJ and Stacey MR [11] (1996).

Another study by Vaghadia H, Al-Ahlan OA, Nevein K [12] (1997) showed that EMLA patch when applied to the skin for 60-90 minutes before venous cannulation reduced the pain of venepuncture and also reduced vasovagal side effects. Hallen B, Olsson G et al [6] (1984) conducted a study to assess the effect of application of EMLA cream and their study also revealed that the effect of cream became evident at about 60 minutes for venepuncture. A study by Noor M Gajraj and John H Penant [5] (1994) on various uses of EMLA cream in adults and children concluded that EMLA cream is a safe, effective, topical anesthetic for use in a variety of clinical settings. It is particularly helpful in venepuncture and intravenous cannulation. In our study, only 2% of patients had blanching at the site of EMLA cream application. There were no other side effects.

Conclusion

In our study, we have proved that the application of EMLA cream for venous cannulation prevented a significant rise in blood pressure and heart rate. The effective time of application was found to be 60 minutes. EMLA cream has been found to be efficacious as a topical analgesic prior to venepuncture. The main advantage being in its single dosage and easy application. The minor disadvantages include cost of EMLA cream and requirement of a rather long application time up to one hour. The cost factor could be overlooked considering the efficacy of EMLA cream in producing dermal analgesia especially in children and anxious adults.

References

1. Langham BT, Harrison DA. Local anesthetics: Does it really reduce the pain on insertion of all sizes of venous cannula?. Anesthesia.1992; 47:890-1.
2. Pavlin DJ, Links S, Rapp SE, Nessly ML, Keyes HJ. Vaso-vagal reactions in an ambulation surgery center. Anesthesia Analgesia.1993; 76:931-5.
3. Raveh T, Weinberg A, Sibirsky O, Caspi R et al. Efficacy of the topical anesthetic cream, EMLA in alleviating both needle insertion and injection pain. Annals of Plastic Surgery. 1995 Dec; 35(6):576-579.
4. Griessinger N, Sittl R. EMLA cream for venepuncture in patients with reflex sympathetic dystrophy. Anesthesia Analgesia. 1995; 81:424-435.
5. Noor M Gajraj, John H. Pennant et al. Eutectic mixture of local anesthetics (EMLA) cream. Anesthesia Analgesia. 1994; 78: 574-83.
6. Hallen B, Olsson G, Uppfeldt A. Pain free venepuncture – Effect of timing of application of local anesthetic cream. Anesthesia. 1984; 39:969-972.
7. Juhlin I, Evers H, Broberg F. A lidocaine-prilocaine cream for superficial skin surgery and painful lesions. Acta Derm Venereol (Stockh). 1980; 60:554-546.
8. Lindh V, Wiklund U et al. Assessment of the effect of EMLA cream during venepuncture in the newborn by analysis of heart rate variability. Pain. 2000; 86(3): 247-254.
9. Manner T, Kanto J, Lisalo E, Lindberg R, Viinamaki O, Seheinin M. Reduction of pain at venous cannulation in children with a eutectic mixture of lidocaine and prilocaine (EMLA cream): Comparison with placebo cream and no local premedication. Acta Anesthesiol Scan. 1987; 31(8):735-9.
10. Griessinger N, Sittl R. EMLA cream for venepuncture in patients with reflex sympathetic dystrophy. Anaesthesia Analgesia 1995; 81(2):432-3.
11. Smith AJ, Stacey MR. Topical ibuprofen for skin analgesia prior to venepuncture. Anesthesia. 1996; 51:495-497.
12. Vaghadia H, Al-Ahlan OA, Nevin K. EMLA patch for intravenous cannulation in adult surgical outpatiens. Canadian Journal of Anesthesia. 1997; 44(8):798-802.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.19

Comparative Study of Post Operative Analgesia with Epidural Clonidine and Epidural Normal Saline Using Combined Spinal Epidural Technique

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Abstract

Introduction: Epidural anaesthesia/analgesia with adjuvant is the preferred method for intra and postoperative pain relief in lower abdominal and lower limb surgeries but search for ideal adjuvant without any side effect goes on. Alpha (α_2) adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia.

Aim: It is a comparative study of post operative analgesia with epidural Clonidine and epidural normal saline in patients undergoing lower abdominal and lower limb surgeries using combined spinal epidural technique.

Materials and Methods: The present study was undertaken during the period of May 2015 to October 2016. 100 patients posted for elective major lower abdominal and lower limb surgeries were selected and allocated randomly into two groups. Each group has 50 patients. Group 1:-Patients received intrathecal 0.5% Hyperbaric Bupivacaine + epidural Clonidine 1µg/kg or 50µg whichever is lower, diluted to 10ml with normal saline. Group 2:- Patients received intrathecal 0.5% Hyperbaric Bupivacaine + epidural 10ml normal saline. Quality of analgesia, duration of analgesia and duration of motor blockade between the two groups were compared. Patient vitals like pulse rate, blood pressure, respiratory rate, SPO_2 and ECG were monitored during the study. During the study patients were observed for the side effects like nausea, vomiting, hypotension, bradycardia and dryness of mouth.

Results: In present study majority of patients were in the age group between 31-50 yrs in both the groups and most of them weigh between 61-70 kgs. Total abdominal hysterectomy cases were majority cases observed in both groups. Quality of analgesia is excellent in both the groups and none of the patients complained of severe pain. Mild pain was observed in most of the cases in both the groups. The average time taken for 2 segment regression is more in Clonidine group compared to control group. The total duration of analgesia is more in Clonidine group compared to control group. The time taken for 1st movement i.e. beginning of motor recovery is more in Clonidine group compared to control group. Mean pulse rate, systolic BP and diastolic BP changes are statistically significant in Group 1. Complications observed in Group 1 were nausea & vomiting in 7 patients, hypotension in 7 patients, bradycardia in 1 patient, sedation in 1 patient, dry mouth in 2 patients. Hypoxia and bleeding were not reported.

Conclusion: Quality of analgesia is excellent in patients receiving Clonidine when compared to placebo group. Total duration of analgesia and motor blockade is significantly prolonged in Clonidine group compared to placebo group. Minimal side effects like mild hypotension, mild sedation and dryness of mouth were seen in Clonidine group which does not require any active intervention.

Keywords: Epidural Analgesia; Bupivacaine; Clonidine.

Introduction

Epidural anaesthesia provides both intra and post operative pain relief in various lower abdominal and lower limb surgeries. Epidural Bupivacaine has been used extensively for providing adequate postoperative pain relief in patients undergoing lower abdominal surgeries [1]. Many techniques and drug regimens,

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Received on 27.12.2016
Accepted on 30.12.2016

with partial or greater success, have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anesthesia [2-4]. Neuraxial anaesthesia and analgesia provide solid analgesic effect by inhibiting nociceptive transmission from peripheral to central nervous system, but their analgesic advantages might be limited by the short half life of current local anaesthetics. The analgesic duration can be prolonged by increasing the dose of local anaesthetics; however the risk of accompanied systemic neurotoxicity can be increased [5]. Therefore, adjuvant can be added to local anaesthetics to prolong the analgesic duration and to limit the dose requirement of local anaesthetics. Recently, several neuraxial adjuvants, including Clonidine, opioids, dexamethasone, ketamine, magnesium sulphate and midazolam have demonstrated the synergistic analgesic effect with local anaesthetics with varying degrees of success. But the search for ideal adjuvant for a particular local anaesthetic goes on [6]. Alpha 2-adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic, anesthetic sparing and hemodynamic stabilizing properties [7]. Clonidine, an α_2-adrenergic agonist added to a solution of bupivacaine and morphine has analgesic properties [8]. It also has a synergistic effect on local anesthetics and has been effectively used for postoperative analgesia. It has been used epidurally in different doses 18.75 mcg/h, 10, 15, and 20 mcg/h (Peach) and 6 mcg/kg/h (De Koch) [9]. The objective of present study is to evaluate the effect of spinal bupivacaine in combination with either epidural Clonidine or epidural normal saline administered by combined spinal epidural technique on postoperative outcome in patients undergoing lower abdominal or lower limb surgeries.

Material and Methods

This is "A Comparative study of Post operative analgesia with epidural Clonidine and epidural normal saline in patients undergoing lower limb and lower abdominal surgeries using combined spinal epidural technique". The study was undertaken at Prathima Institute of Medical Sciences, Karimnagar during the period of May 2015 to October 2016.

Patients selected for the study were between age groups 25 to 60 years, who had no complicating systemic disorders {ASA I and II}. 100 patients were divided into two groups of 50 each according to the drug they received. In Group 1 patients received epidural Clonidine 1μg/kg or 50μg whichever is lower, diluted in normal saline, the total volume injected was 10ml and in Group 2 the patients received 10ml of normal saline epidurally; in both the groups 0.5% Hyperbaric Bupivacaine was injected into subarachnoid space; the volume was determined by the type of surgery. Epidural drug was given after 15min after positioning the patient supine.

All the selected patients were thoroughly examined and investigated to rule out any systemic disorders. All patients were explained about the procedure and informed consent was taken.

Equipment used: Sterile gown and gloves, Sterile drape, Syringes: 2cc, 5cc, 10cc, insulin syringe {for Clonidine}, Loss of resistance syringe, Combined spinal epidural needle {18G Touhy combined spinal epidural needle and 27G sprotte spinal needle}, 18G epidural catheter with filter and sterile steel bowl.

Monitors used: Pulse oximeter, NIBP monitor, ECG, visual analogue scale for pain assessment.

Drugs used: Bupivacaine hydrochloride- 0.5% hyperbaric solution sterile ampoule, Clonidine hydrochloride 150μg ampoule {Cloneon by Neon labs} and 0.9%Normal saline.

Anaesthesia machine, resuscitation equipment and drugs were checked and kept ready, before undertaking the procedure.

Procedure

Preoperative vital data such as pulse rate, SPO_2 and blood pressure were noted. Heart and lungs were examined. An intravenous line established with 18G IV cannula and Ringer lactate drip started before the procedure.

With the patient in sitting position, under aseptic precautions L2-L3 / L3-L4 interspace was identified with highest point of iliac crest as the anatomical landmark. Local infiltration of 2ml 1% lignocaine was given to facilitate introduction of epidural needle. Then 18G CSE needle was introduced and advanced gradually connecting it to Loss of resistance syringe and epidural space identified by loss of resistance to air. 27G sprotte spinal needle was inserted and after obtaining clear CSF 0.5% Hyperbaric Bupivacaine 3-4ml was injected. Spinal needle was removed and an 18G epidural catheter was inserted so that 3-4cm of catheter is inside the epidural space. Patient was made to lie in supine position and level of sensory and motor block was checked.

Intraoperatively, patient was monitored for pulse rate, SPO_2, blood pressure, ECG changes, blood loss,

urine output and adverse reactions. Any side effect due to the drugs administered was documented.

Patient was shifted to postoperative ward in a hemodynamically stable state and after 2 segment regression of sensory blockade was confirmed. In postoperative period all the vital parameters were monitored and regression of motor blockade and sensory blockade, duration of analgesia and side effects were noted. Duration of analgesia was calculated from the time of injection of intrathecal bupivacaine to first complaint of pain. Pain was treated with epidural tramadol injections. Analgesia is scored by visual analogue scale ranging from 0 to10.

Visual Analogue Scale scoring as follows 0- No pain; 1, 2, 3- mild pain; 4, 5, 6- moderate pain; 7, 8, 9- severe pain and 10- Worst ever felt pain.

Quality of Analgesia: Assessed as No analgesia/ complaints of severe pain; Minimal analgesia/patient uncomfortable with pain; Good analgesia/patient comfortable, but complains of mild pain and Excellent analgesia/no pain.

All the patients were observed for the following side effects like nausea & vomiting, hypotension, ECG rhythm changes, sedation, dry mouth, bleeding, hypoxia, giddiness and voiding difficulty throughout the study period and rescue medications given.

Results

This study includes 100 patients posted for elective lower limb or lower abdominal surgeries divided into 2 groups of 50 each. Group 1 received intrathecal Hyperbaric Bupivacaine and epidural Clonidine and Group 2 received intrathecal Hyperbaric Bupivacaine and epidural normal saline. The effect of recovery from neuraxial blockade and duration of analgesia was compared and contrasted.

Table 1: Comparasion of surgeries undertaken in both groups

Name of Surgery	Group 1	Group 2
Surgeries on hip joint	5	3
Surgeries on femur	12	13
Surgeries on leg	10	12
Total abdominal hysterectomy	15	16
Vaginal hysterectomy	4	2
Incisional hernia below umbilicus	2	3
Ovarian cystectomy	2	1

Table 2: Age and weight distribution among 2 groups

Age distribution in years	Group 1	Group 2
20-30	9	11
31-40	18	14
41-50	13	15
51-60	10	10
Weight in kgs		
40-50	11	8
51-60	1	14
61-70	18	19
71-80	9	9

In the present study, cases observed in Group 1 was 5 cases were hip joint surgeries, 12 cases were femur surgeries, 10 cases were surgeries on leg, 15 cases were total abdominal hysterectomy, 4 cases were vaginal hysterectomy, 2 cases were Incisional hernia below umbilicus and 2 cases were ovarian cystectomy where as in Group 2 was 3 cases were hip joint surgeries, 13 cases were femur surgeries, 12 cases were surgeries on leg, 16 cases were total abdominal hysterectomy, 2 cases were vaginal hysterectomy, 3 cases were Incisional hernia below umbilicus and 1 case was ovarian cystectomy.

In the present study age distribution in Group 1 was 9 patients were in 20-30 yr age group, 18 patients in 31-40 yr age group, 13 patients in 41-50 yr age group and 10 patients in 51-60 age group where as in Group 2 was 11 patients were in 20-30 yr age group, 14 patients in 31-40 yr age group, 15 patients in 41-50 yr age group and 10 patients in 51-60 age group.

The P value calculated by unpaired student t test is 0.765 {t value 0.29, df 98%}, which is more than 0.05, so it is not statistically significant. Age distribution in both the groups is comparable.

Weight distribution in Group 1 was 11 patients were between 40-50 kgs, 12 patients were in 51-60 kgs, 18 patients were in 61-70 kgs and 9 patients were in 71-80 kgs where as in Group 2 was 8 patients were between 40-50 kgs , 14 patients were in 51-60 kgs, 19 patients were in 61-70 kgs and 9 patients were in 71-80 kgs. The P value calculated by unpaired student t test is 0.707 {t value 0.376, df 98}, which is more than 0.05, so it is not statistically significant. Weight distribution in both the groups is comparable. (Table 2).

Table 3: Comparasion of quality, duration of analgesia, 2 segment regression and motor movement in both groups

Variable	Group 1	Group 2
	Quality of analgesia	
Mild pain	44	42
Moderate pain	6	8
Severe pain	0	0
2 Segment regression (in hrs)	1.45	1.3
Duration of analgesia	3.32	2.23
Time of first movement	2.54	2.43

Quality of analgesia is excellent in both the groups and none of the patients complained of severe pain. Complaints of mild pain in Group 1 was in 44 cases, Group 2 was in 42 cases while moderate pain in Group 1 was in 6 cases and in Group 2 was 8 cases. The calculated P value is > 0.05 and it is statistically insignificant.

The average time taken for 2 segment regression is more in Clonidine group compared to control group i.e., Mean Group1=1.45{0.3}, Group 2=1.30{0.03}. The calculated P value is <0.001 which is less than 0.05, so this is statistically significant.

The total duration of analgesia is more in Clonidine group compared to control group. So patients in Group1 are pain free for a longer time. The calculated P value is <0.0001 which is less than 0.05, which is highly statistically significant.

The time taken for 1st movement i.e. beginning of motor recovery is more in Clonidine group compared to control group. The calculated P value is <0.001 which is less than 0.05, and is statistically significant (Table 3).

Table 4: mean pulse rate, systolic and diastolic BP changes

Mean Values	Group 1	Group 2
Mean pulse rate changes	83.6{2.88}	85.76{3.81}
Mean systolic BP changes	108.2{5.87}	111.87{4.91}
Mean diastolic BP changes	71.25{3.96}	73.4{2.89}

Mean pulse rate, systolic BP and diastolic BP changes are statistically significant in both groups.

The calculated P value for mean pulse rate changes is 0.042 which is less than 0.05, and is statistically significant. The calculated P value for systolic BP changes is 0.028 which is less than 0.05, hence statistically significant. The calculated P value for diastolic BP changes is 0.019 which is less than 0.05, therefore statistically significant (Table 4).

Complications observed in Group 1 were nausea & vomiting in 7 patients, hypotension in 7 patients, bradycardia in 1 patient, sedation in 1 patient, dry mouth in 2 patients where as in Group 2 nausea &

Table 6: Comparasion of complications in both groups

Complication	Group 1	Group 2
Nausea &vomiting	7	8
Hypotension	7	5
Bradycardia	1	0
Sedation	1	0
Dry mouth	2	0
Hypoxia	0	0
Bleeding	0	0

vomiting in 8 patients, hypotension in 5 patients observed and bradycardia , sedation, dry mouth. Hypoxia and bleeding were not reported in either group (Table 5).

Discussion

This study is conducted to observe the effects of a combination of Bupivacaine spinal technique with epidural Clonidine in patients undergoing lower limb and lower abdominal surgeries comparing it with spinal Bupivacaine and epidural normal saline.

Clonidine is a selective partial agonist for α_2 adrenoreceptors. It is known to increase both sensory and motor block of local anaesthetics. It produces analgesia by mimicking the activation of descending noradrenergic pathways. Sympathetic hyperactivity may be reduced by the administration of epidural Clonidine through three mechanisms of action. First mechanism proposed is Clonidine may inhibit nociceptive neurotransmitter release in the dorsal horn and sympathetic outflow in the spinal cord intermediolateral column. Second is it may inhibit norepinephrine release from sympathetic terminals in the periphery. Third one is epidural Clonidine may also be reabsorbed into the systemic circulation where it reaches the α_2 adrenoreceptors of the dorsal horn and provides analgesia by increasing the antinociceptive threshold of the spinal cord which activates the descending noradrenergic pathway to inhibit small-diameter afferent-induced substance P release.

Clonidine blocks conduction of C and Aδ fibers and increases potassium conductance, intensifying the neural block of local anesthetics. It may also cause local vasoconstriction reducing removal of local anesthetic. Clonidine reduces blood pressure by inhibiting preganglionic sympathetic neural activity in the spinal cord. It can also reach the brainstem via systemic redistribution or cephalad spread in the cerebrospinal fluid, further contributing to decreased blood pressure. These same mechanisms may also be responsible for the noted decreases in HR after the administration of epidural Clonidine.

The present study was undertaken to evaluate the addition of Clonidine in epidural space to surgeries in which intrathecal bupivacaine is given. 100 patients were randomly allocated to two groups, 50 patients received 1μ/kg or 50μg Clonidine epidurally while others received same volume of normal saline. All the patients received intrathecal bupivacaine heavy. The effect on analgesia, sensory and motor blockade and duration was studied.

W.Scott Jellish et.al [10] in 2003 studied the effect of epidural Clonidine in combination with spinal bupivacaine in patients undergoing lumbar laminectomy procedures. They concluded that epidural Clonidine prolongs the time of sensory analgesia and motor blockade. Our study is in agreement with the former study. The duration of analgesia is 3.33 {S.D0.181} in Clonidine group compared to 2.29 {S.D 0.075} in control group.

M J Paech et.al [11] 1997 in their study on Epidural Clonidine infused 20 μg/hour improves analgesia during coughing when combined with epidural bupivacaine-fentanyl in patients undergoing lower abdominal surgery but is associated with hemodynamic changes and increased vasopressor requirement. Our study is in agreement with them that there is better postoperative outcome and decreased requirement of analgesics after Clonidine. But the hypotension incidence and requirement of vasopressors in our study was similar in both the groups.

Dobrydnjov et. al [12] in 2005 concluded low-dose intrathecal Clonidine provided a better quality of anesthesia and longer-lasting analgesia. Epidural Clonidine-ropivacaine infusion resulted in improved postoperative analgesia but was associated with a moderate decrease in blood pressure. The same result has been seen in our study and the hypotension was not alarming and required treatment with fluids and smaller doses of mephentermine only. Although Clonidine prolonged motor block in our patients, this increase was not clinically significant and did not require a prolonged PACU admission.

Andrew D. Farmery [13] in 2009 proved in his study that Low-dose epidural Clonidine significantly reduced the demand for morphine and reduced postoperative nausea with few side effects in patients undergoing decompressive spine surgeries. This is in agreement with our study where the incidence of nausea is similar in both test and control groups.

Bonhomme et al [14]. recently evaluated the effect of epidural small-dose morphine in combination with Clonidine for postoperative analgesia after lumbar disc surgery. They reported reduced pain with movement after surgery using small-dose Clonidine and morphine, which was not manifested when a combination of bupivacaine and Clonidine was used. Their patients experienced a frequent incidence of difficulty in initiating micturition (30%–45%) not seen in our population. This may be related to the fact that their patients received a general anesthetic in which both IV and epidural narcotics were given. Our patients received a spinal anesthetic with no

intraoperative narcotics. Urinary retention has not been noted with neuroaxial Clonidine administration and, in fact, it may actually hasten the time to first micturition after spinal anesthesia.

There were no statistical differences in the number of patients experiencing nausea or vomiting in either the PACU or during the 24-hour postsurgical period. In addition, there seemed to be no sedative effect of epidural Clonidine as demonstrated by no difference in Steward Recovery scores among the groups. This is one of the noted advantages of administering epidural Clonidine compared with other forms of analgesia.

Many previous studies have used intrathecal Clonidine combined with opioids and local anaesthetics for labor analgesia and orthopedic surgery. The combination of Clonidine with opioids developed problems like respiratory depression, pruritis, urinary retention and abuse liability. In our study sedation was seen in the Clonidine group but the respiratory depression and opioid related complications were not seen.

Conclusion

Quality of analgesia is excellent in patients receiving epidural Clonidine when compared to placebo group.

Total duration of analgesia and motor blockade is significantly prolonged in Clonidine group compared to placebo group. Minimal side effects like mild hypotension, mild sedation and dryness of mouth were seen in Clonidine group which does not require any active intervention.

References

1. Tziavrangos E, Schug SA; Regional anaesthesia and peri operative outcome. Current opinion in anaesthesiology 2006; 19(5):521-525.
2. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. Br J Anaesth. 2008; 100:8–16.
3. Helgeson LE. Sedation during regional anesthesia: Inhalation versus intravenous. Curr Opin Anaesthesiol. 2005; 18:534–9.
4. Némethy M, Paroli L, Williams-Russo PG, Blanck TJ. Assessing sedation with regional anesthesia: Inter-rater agreement on a modified Wilson sedation scale. Anesth Analg. 2002; 94:723–8.
5. Becker DE, Reed KL; Local anaesthetics: review of pharmacological considerations. Anesthesia progress, 2012; 59(2):90-102.
6. Ulke ZS, Senturk M; Non-analgesic effects of thoracic epidural anesthesia. Agriculture, 2007; 19(2):6-12.
7. Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists; Their pharmacology and therapeutic role. Anaesthesia 1999 Feb; 54(2): 146-65.
8. Ossipov MH, Suarez LJ, Spaulding TC. Antinociceptive interactions between alpha2-adrenergic and opiate agonists at the spinal level in rodents. Anesth Analg 1989; 68:194-200.
9. Mogensen T, Eliasen K, Ejlersen E, Vegger P, Nielsen IK, Kehlet H. Epidural Clonidine enhances postoperative analgesia from a combined low-dose epidural bupivacaine and morphine regimen. Anesth Analg 1992; 75:607-10.
10. Jellish WS, Abodeely A, Fluder EM, Shea J. The effect of spinal bupivacaine in combination with either epidural Clonidine and/or 0.5% bupivacaine administered at the incision site on postoperative outcome in patients undergoing lumbar laminectomy. Anesth Analg 2003; 96:874–80.
11. M J Paech, T J Pavy, C E Orlikowski,W Lim, and S F Evans: Postoperative epidural infusion: a randomized, double-blind, dose-finding trial of Clonidine in combination with bupivacaine and fentanyl Anesth Analg. 1997 Jun; 84:1323-1328.
12. I. Dobrydnjov, k. Axelsson, A. Gupta , A. Lundin , B. Holmstro m and B. Granath Department of Anesthesiology and Intensive Care, and 2 Department of Orthopedic Surgery, University Hospital, O¨ rebro, Sweden**.** Improved analgesia with Clonidine when added to local anesthetic during combined spinal-epidural anesthesia for hip arthroplasty: a double-blind, randomized and placebo-controlled study. Acta Anaesthesiol Scand 2005; 49:538-545.
13. Farmery HYPERLINK "https://www.ncbi.nlm.nih.gov/p ubmed/?term=Farm ery%20AD% 5BAuthor% 5D&cauthor=true&cauthor_ uid= 19151300".
14. Bonhomme V, Doll A, Dewandre PY, Brichant JF, Ghassempour K, Hans P. Epidural administration of low-dose morphine combined with Clonidine for postoperative analgesia after lumbar disc surgery. J Neurosurg Anesthesiol. 2002; 14:1–6.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.20

Evaluation of Fentanyl as an Adjuvant in Ultrasound Guided Supraclavicular Brachial Plexus Block

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Abstract

Background & Objectives: Supraclavicular brachial plexus blocks have been performed effectively using local anaesthetic agents alone for upper limb surgeries. The Primary objective of this study is to determine whether the addition of fentanyl to a supraclavicular brachial plexus block improves the success rate, block time, duration and quality of postoperative analgesia. Secondary objective is can fentanyl be recommended as a safe adjuvant to local anaesthetic agents for peripheral blocks.

Design & Methods: The study was conducted on ASA I-III patients who were randomly divided into Group I (Control) and Group II (Study). Patients in the control group received 20 ml 0.5% bupivacaine, 10 ml 2% lidocaine and 2 ml normal saline. The study group received 20 ml 0.5% bupivacaine, 10 ml 2% lidocaine and 2 ml fentanyl (100 μg). Onset times for sensory and motor block were recorded. Post-operatively patients were followed over a 24 h period at 2hr interval for any breakthrough pain, and the intensity of pain was determined using Verbal Rating Score (VRS) system.

Results: Fifty patients were studied with 25 in each group. The overall mean Verbal Rating Score for immediate postoperative pain in the fentanyl group was 2.6 compared to that of the control group which was 3.8 ($p<0.001$). 24 h post-operatively at 2hr intervals, the VRS ranged between 1 and 8; the mean VRS in control group was 5.7 while it was 3.8 in the study group ($p<0.001$). There was also a significant reduction in the incidence of breakthrough pain in the fentanyl group ($p<0.0001$) at the end of 24 hrs.

Conclusions: The study found that the addition of 100 μg fentanyl in supraclavicular brachial plexus block prolongs the duration of analgesia without any side effects. Fentanyl may be used as a safe adjuvant for supraclavicular brachial plexus blocks to improve the quality of analgesia.

Keywords: Fentanyl; Brachial Block; Ultrasound.

Introduction

All major upper limb surgeries are associated with severe postoperative pain [1]. The supraclavicular approach of the brachial plexus block has a high success rate including blockade of the ulnar and musculocutaneous nerve, which can be missed respectively with the interscalene and axillary approach [1,2]. At the level of the supraclavicular fossa, the plexus is most compactly arranged.

Antinociceptive effects of opioids at the central and/or spinal cord level are well known [3]. However, evidence from recent experimental studies have shown that by activation of peripheral opioid receptors by exogenous opioid drugs antinociception can be initiated [4,5]. Opioids are used as an adjuvant with local anaesthetic drugs to prolong analgesia during post-operative period. Fentanyl a synthetic opioid is approximately thirty times more potent than morphine because of its high lipophilicity. Fentanyl causes less nausea and decreased histamine release so less itching in relation to morphine. Fentanyl has been shown to be of benefit in central neuraxial blocks and other regional blocks by increasing the duration of pain relief [6,7]. Hence we decided to use fentanyl in this study because of its potent effect and relatively less systemic side

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Received on 25.12.2016
Accepted on 29.12.2016

effects.

The addition of narcotic analgesic in brachial plexus block has improved success rate and postoperative analgesia [8-12]. However the results are conflicting with some authors showing favorable response, whereas others have found no effect [13-15].

With this background, the current study was conducted to determine if addition of fentanyl as an adjuvant to the local anaesthetic agents during brachial plexus blocks would improve the quality of analgesia postoperatively.

Methods and Materials

Description of Study

The protocol of this prospective, randomized, double-blind study was approved by the Ethics Committee and the Institutional Review Board. All participants fulfilling inclusion criteria were explained about procedure, and written informed consent was obtained from them.

Sample Size was Calculated using the Following Formula

Desired power of study = 0.8

P value = 0.05

Effect size = 30% reduction in pain in the study group compared to control group.

The following formula was used to calculate the sample size which yielded 25 patients in each group.

$$n = \frac{2(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

(where p is the effect size, Z_{β} is the desired power, Z_{α} is the level of statistical significance)

Inclusion Criteria

1. ASA grade I, II, and III posted for elective operations on elbow, forearm and hand, ele
2. Age group: 17 to 70 years
3. Sex: Either gender.

Exclusion Criteria

1. ASA grades IV and V
2. Age below 17 or above 70 years
3. Patients who had history of significant neurological, psychiatric, neuromuscular disease as well as pregnant or lactating women.
4. Known hypersensitivity to local anaesthetic drugs and history of coagulation disorders
5. Local infection.

All enrolled patients received supraclavicular brachial plexus block which were performed by an experienced anaesthetist guided by sonographical images and nerve stimulator. A different anaesthetist assessed the patient during the postoperative period. Both the anaesthetists were blinded .

After standard anesthesia monitoring , Blocks were performed on all the patients in either lying or semi-supine position. The head of the patient was rotated either to right or left side, opposite to the side of block. All aseptic precautions were taken prior to performing the block. A 50 mm, 22 gauge Teflon-coated short-bevel peripheral nerve stimulator needle (Pajunk, Geisingen, Germany; or B. Braun Bethlehem PA), Stimuplex (Braun Germany) nerve stimulator and Ultrasound (Siemens, Acuson X 150) guidance was used during the procedure.

Subcutaneous injection of 2mL of 1% lidocaine was administered at the needle insertion site. After locating the end point and observing the response using ultrasound landmarks,using in plane approach and a distal motor response with an output lower than 0.5 mA, following negative aspiration the solution containing local anaesthetic combined with either fentanyl or normal saline was administered as follows:

Group I (control): bupivacaine 0.5% 20 mL + lidocaine 2% 10 mL + NS 2 mL

Group II (study): bupivacaine 0.5% 20 mL + lidocaine 2% 10 mL + fentanyl 2 mL (100μg).

Mild sedation was administered after evaluation of block was complete, so that constant verbal contact can be maintained with the patient.

Any clinical evidence suggesting local anaesthetic toxicity, in addition to possible side effects like nausea, vomiting, and systemic effects of fentanyl was recorded, which is routine after all regional anaesthetic techniques such as brachial plexus blocks.

Outcomes Measured Include the Following

- Time of onset of sensory and motor block of the area of distribution of the brachial plexus block.
- The duration of post block analgesia, defined as

the interval between block completion and requirement of first postoperative analgesic and incidence of post block neurologic and respiratory complication were recorded.

Evaluation of sensory block was performed every 5 minutes in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve over a 30 minute period after the completion of the block procedure. Onset of sensory blockade was determined by the pin prick method, and evaluation was made based on the findings when there is a dull sensation to pin prick along the distribution of any of the above nerves.

Rating of the block was quantified as, no block (sharp pin sensation felt), partial block (dull sensation felt), or complete block (no sensation felt).

The block was considered successful when there was complete loss of sensation to pin prick. Motor block was evaluated using forearm flexion-extension, thumb and second digit pinch, and thumb and fifth digit pinch, and scored as follows: no loss of force (no block); reduced force compared with the contralateral arm (partial block); incapacity to overcome gravity (complete block). Patients were assessed for sensory and motor blockade at regular intervals intraoperatively and postoperatively over period of 24 hours at 2hr intervals. Patients were instructed pre-operatively about use of the Verbal Rating Scale (VRS) for pain assessment. Where patients were asked to verbally rate their perceived pain intensity on a numerical scale from 0 to 10, with the zero representing "no pain" and the 10 representing the extreme pain ("the worst pain possible"). If any potentially surgical territory was not completely anaesthetised at the time of surgery around the elbow or wrist, general anaesthesia was induced and patients were excluded from the study.

During Postoperative Period Following Assessments was Made:

1. First analgesia for breakthrough pain
2. Duration of time- the regions of the arm remain insensible or weakened
3. Respiratory Rate

Table 1: Types of surgeries in the study subjects

Surgery	Frequency (%)
ORIF forearm bones	19 (38)
AV Fistula	18 (36)
K wiring	5 (10)
Exploration surgery	3 (6)
Excision of bony cyst	2 (4)
Tendon repair	1 (2)
Synovectomy	1 (2)
Ulnar artery repair	1 (2)

Results

Data were collected and entered in Microsoft Excel software. Statistical analyses were performed by using computer software package Statistical Package for Social Sciences (SPSS)-version 16.

Descriptive analyses of all the demographic as well as clinical parameters were done. The numerical variables were expressed in mean and standard deviation as well as median and interquartile ranges. The verbal rating Score which is ordinal scale were compared between the groups using Mann- Whitney U test. Chi-square test was used to analyse the difference between groups for categorical data such as gender, breakthrough pain etc. Statistical significance was fixed at the level of $p<0.05$.

A total of 50 patients who were scheduled for upper limb surgery were included in this study. The study compared intra-operative and post-operative analgesic effects after performing supraclavicular brachial plexus block using 0.5% bupivacaine and 2% lidocaine in Group I (control) and 0.5% bupivacaine, 2% lidocaine and 100 µg fentanyl in Group II (study).

The age of patients ranged from 17 to 70 with a mean of 44.5 [16.5 (SD)]. 60% of the study subjects were males. The gender was equally distributed between groups

Brachial plexus blocks were performed for different upper limb procedures. The denomination of surgeries is given in Table 1.

Majority of the patients (54%) did not receive any supplemental sedation during procedures, while in 46% of the patients mild sedation was provided with

midazolam.

Overall 58% of the patients did not have any breakthrough pain and 42% were recorded to have experienced it at the end of 24 Hrs.Those with pain were treated with Inj.Pethidine.

The onset time of sensory block ranged from 10-45 min, the median was 20 min. The onset time for motor block ranged between 15 to 60 min, the median was 24.5 min. The surgical duration ranged from 35 to 180 min, the median being 90 min. The Verbal Rating Score (VRS) during immediate post-operative period ranged between 1-6, the median was 3 and VRS after 24 hours ranged between 1-8, the median being 5.

Table II shows that the mean age in control group was 38.9 years where as in study group it was 50.2 years. The difference was statistically insignificant. The onset time for sensory block varied between 10 minutes to 45 minutes but the mean was 21 minutes in control group and in study group it was 20.5 minutes respectively. This was not much different between the groups and was statistically insignificant. The onset time for motor block ranged between 15 minutes to 60 minutes, however the mean motor block time in study group 25.8 minutes which was less when compared to control group which was 26.4 minutes but was statistically insignificant. The surgical duration varied between 35 minutes to 180 minutes which was based on the different type of surgeries. The statistical comparison of the surgical duration was insignificant in both groups. The Verbal Rating score (VRS) was in range of 1- 6 during post operative period but the mean in control group was 3.8 and study group was 2.6 which was statistically

Table 2: Comparison of variables between groups

Variable	Control group Mean (SD)	Study group Mean (SD)	P value
Age	38.9 (14.8)	50.2 (16.3)	0.015*
Onset time – sensory block (min)	21 (6.8)	20.5 (8.4)	0.470
Onset time- motor block (min)	26.4 (8.1)	25.8 (10.7)	0.470
Surgical duration (min)	96 (33.3)	86.4 (27.4)	0.445
VRS postoperative	3.8 (1.2)	2.6 (0.8)	0.001*
VRS 24 hours	5.7 (1.4)	3.8 (1.1)	<0.001*

VRS Verbal Rating Score for pain
*Statistically significant by Mann-Whitney U test

Table 3: Comparison of breakthrough pain

Study Group	Breakthrough pain		Total
	No	Yes	
I (Control)	4(mean-24hrs)	21(mean-12 Hrs)	25
II (Fentanyl)	25(mean-24hrs)	0	25
Total	29	21	50

Chi-square value 36.2; df: 1; p<0.0001

significant. The VRS 24 hours postoperative period at 2hr interval ranged between 1- 8 and the mean was 5.7 in control group and 3.8 in study group which was again statistically significant with p value <0.001. Vital parameters like pulse rate, systolic blood pressure, respiratory rate, and oxygen saturation did not show any significant fluctuation in both the groups.

14 patients in Control group received sedation and only 9 patients in study group received sedation, whereas 11 patients in control group and 16 patients in study group did not receive any sedation during surgical procedure. Even though sedation requirement in control group was higher compared to study group still the results were not statistically insignificant.

Table 3 shows the comparison of the incidence of breakthrough pain between the groups. There was statistically significant reduction in the incidence of breakthrough pain in the fentanyl group compared to the control group at the end of 24 hrs postoperative period. 25 patients in fentanyl group had no breakthrough pain where as only 4 patients in control group had no breakthrough pain. None of the patients in fentanyl group complained of breakthrough pain where as 21 patients in control group complained of breakthrough pain at mean of 12 hrs postoperatively. 75 mg of pethidine was administered intramuscularly to all the patients who complained of breakthrough pain, and VRS in these patients was >5.Surprisingly none of the patients in study group had breakthrough pain even after 24 hrs.

Discussion

This study demonstrates the efficacy of adding fentanyl as an adjuvant to local anaesthetic drug in ultrasound guided brachial plexus block for upper limb surgeries. A comparison was made to determine effect of fentanyl in prolonging the analgesia during immediate postoperative period and over 24 hr period in Group I (Control) and Group II (Study group). Statistically significant difference in analgesia was observed postoperatively using Verbal Rating Score. However, fentanyl did not prolong the onset time of the sensory and motor block according to our study.

Addition of fentanyl to lidocaine for brachial blocks improved the success rate of sensory blockade [7,9,16,17]. Morphine and buprenorphine are reported to cause analgesia with or without local anaesthetic drugs when used for brachial plexus block [18]. Studies performed using agents such as tramadol, clonidine, dexamethasone and dexmedetomidine as an adjunct in brachial blocks have demonstrated significant increase in sensory and motor blockade when used with local anaesthetic solution [19-22]. Study conducted by Karakaya et al [9] showed that the duration of sensory block, motor block and analgesia was longer when fentanyl was added to bupivacaine, the duration was almost double when compared to the group in which Bupivacaine alone was administered. Similar finding were demonstrated by Nishikawa et al. in their study where fentanyl was administered with lidocaine in epinephrine 1: 200000 for axillary blocks [23]. There was increase in success rate and the duration of blockade there by prolonging postoperative analgesia.

Some authors have postulated the mechanism of action by which fentanyl improved analgesia on peripheral administration. First, fentanyl could act directly on the peripheral opioid receptor. Secondly presence of primary afferent tissues (dorsal root) have known to contain opioid binding sites [9,10] and the presence of bi-directional axonal transport of opioid binding protein has been shown [24], so fentanyl may penetrate the nerve membrane and act at the dorsal horn. This could have also accounted for the prolonged analgesia. However, some authors have reported of fentanyl also has a local anaesthetic like action [9]; Gormley et al [11] suggested that alfentanil also prolonged postoperative analgesia by local anaesthetic action. In animals presence of peripheral opioid receptors has been reported [25-27]. As it is still unclear if functional opioid receptors exist in human peripheral tissue various studies were conducted in past to determine if addition of opioids to local anaesthetic drugs would improve the quality of regional blocks [10]. However, further studies are required comparing the effects of fentanyl on brachial plexus block using solution of different pH and quantity. But from our study 100 μg of fentanyl did prolong the sensory block significantly there by prolonging analgesia. However, not all studies confide with our findings.

Contradicting results were published by Fletcher et al. which showed no change in the success rate, onset time, or duration of analgesia when fentanyl was used for axillary brachial plexus block [13,15]. Study by Racz et al [14] demonstrated that addition of morphine to local anaesthetic solution neither changed the onset time nor quality of postoperative pain relief. Kanaya et al [27] in his study demonstrated that addition of fentanyl to axillary brachial plexus block prolonged the onset time of sensory block in every trunk; This effect was contributed due to change in pH on addition of fentanyl to the local anaesthetic solution [16-27]. It is well know that change in pH of an anaesthetic drug can alter the action of local anaesthetic. However there was no increase in onset time in our study.We had included different types of upper limb surgeries as mentioned in Table 1, so that the intensity of pain based on severity of procedure could be evaluated and efficacy of fentanyl in brachial blocks for different surgery could be determined on assessment using VRS. In other studies the choice of procedure was selective there by assessment of pain using subjective scoring system could be influenced by various factors [2].

Conclusion

Our sample size was relatively small, and this smaller sample size may contribute to the statistical misappropriations and may overstate the benefits from the addition of drugs to brachial plexus blocks.In conclusion, addition of fentanyl to local anaesthetic solution does prolong the sensory block there by prolonging the duration of analgesia which was evident in our study when assessed in immediate postoperative period and at regular intervals over a period of 24 hrs. However there was no increase in duration of motor blockade and neither did it affect the onset time after the block was performed.

References

1. Wedel D. J. Regional anesthesia and pain

management: reviewing the past decade and predicting the future. Anaesthesia Analgesia 2000; 90:1244-5.

2. Bruce B. G, Green A, Blaine T. A, Wesner L. V. Brachial plexus blocks for upper extremity orthopaedic surgery. J Am Acad Orthop Surg 2012; 20(1):38-47.
3. Yaksh T L. Multiple opioid receptor systems in brain and spinal cord. Part I. Eur J Anaesthesiology 1984; 1:171-99.
4. Stein C. Peripheral mechanisms of opioid analgesia. Anesthesia Analgesia 1993; 76(1):182-91.
5. Sibinga N. E, Goldstein A, Opioid peptides and opioid receptors in cells of the immune system. Annual Review Immunology 1988; 6:219-49.
6. Celleno D, Capogna G. Epidural fentanyl plus bupivacaine 0.125 per cent for labour analgesic effects. Canadian Journal of Anaesthesia 1988; 35(4): 375–78.
7. Abo EL Enin M. A, Amin I. E, Abd EL Aziz A. S, Mahdy M. M et al. Effect of fentanyl addition to local anaesthetics in peribulbar blocks. Indian Journal of Anaesthesia 2009; 53(1):57-63.
8. Brummett C. M, Williams B. A. Additives to Local Anesthetics for peripheral nerve blockade. Int Anesthesiology Clinics 2011; 49(4):104-16.
9. Karakaya D, Buyukgoz F, Baris S, Guldogus F, Tur A. Addition of fentanyl to bupivacaine prolongs anesthesia and analgesia in axillary brachial plexus block. Regional Anesthesia and Pain Medicine 2001; 26:434-8.
10. Gissen A. J, Gugino L. D, Datta S, Miller J, Covino B. G. Effect of fentanyl and sufentanil on peripheral mammalian nerves. Anesthesia Analgesia 1987; 66: 1272-76.
11. Gormley WP, Murray JM, Fee JP, Bower S. Effect of the addition of alfentanil to lignocaine during axillary brachial plexus anaesthesia. British Journal of Anaesthesia 1996; 76:802–5.
12. Axelsson K, Gupta A. Local anaesthesia adjuvants: neuraxial versus peripheral nerve block. Current Opinion in Anesthesiology 2009; 22(5):649-54.
13. Bouaziz H, Kinirons BP, Macalou D, Heck M et al. Sufentanil does not prolong the duration of analgesia in mepavacaine brachial plexus block: a dose response study. Anesthesia Analgesia 2000; 90:383-7.
14. Racz H, Gunning K, Della Santa D, Forster A. Evaluation of the effect of perineuronal morphine on the quality of postoperative analgesia after axillary plexus block: a randomized double- blind study. Anesthesia Analgesia 1991; 72:769-72.
15. Fletcher D, Kuhlman G, Samii K. Addition of fentanyl to 1.5% lidocaine does not increase the success of axillary plexus block. Regional Anesthesia 1994; 19: 183-8.
16. Nishikawa K, Kanaya N, Nakayama M, Igarashi M et al. Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. Anaesthesia and Analgesia 2000; 91:384-7.
17. Sindjelic R. P, Vlajkovic G. P, Davidovic L. B, Markovic D. Z et al. The addition of fentanyl to local anesthetics affects the quality and duration of cervical plexus block: A randomized controlled trial. Anesthesia and Analgesia 2010; 111:234-37.
18. Viel E. J, Elediam J. J, De La Coussaye J. E, D'Athis F. Brachial plexus block with opioids for postoperative pain relief: Comparison between buprenorphine and morphine. Regional Anesthesia 1989; 14:274-8.
19. Singh S, Aggarwal A. A randomized controlled double blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries. Indian Journal Anaesthesia 2010; 54(6):552-557.
20. Swami S. S, Keniya V. M, Ladi S. D, Rao R. Comparison of dexmedetomidine and clonidine as an adjuvant to local anaesthesia in supraclavicular brachial plexus block: A randomised double-blind prospective study. Indian Journal Anaesthesia 2012; 56:243-9.
21. Chattopadhyay S, Mitra L. G, Biswas B. N, Majumder P. Tramadol as an adjuvant for brachial plexus block. J Anaesth Clin Pharmacol 2007; 23(2):187-189.
22. Vieira P. A, Pulai I, Tsao G. C, Manikantan P et al. Dexamethasone with bupivacaine increases the duration of analgesia in ultrasound-guided interscalene brachial plexus blockade. Eur J Anaesthesiology 2010; 27(3):285-8.
23 Iwaszkiewicz K. S, Schneider J. J, Hua S. Targetting peripheral opiod receptors to promote analgesics and anti inflammatory actions. Front Pharmacology 2013; 24(4):132.
24 Koscielniak-Nielsen Z. J, Dahl J. B. Ultrasound guided peripheral nerve blockade of upper extremity. Current opinion Anaesthesiology 2012; 25(2):253-9.
25 Chan V. W. S., Perlas A Rawson R, Odukoya O. Ultrasound guided supraclavicular brachial plexus block: Anesthesia Analgesia 2003; 97:1514-7.
26 Sanchez R, Nielsen H, Heslet L, Iversen A. D. Neuronal blockade with morphine: A hypothesis. Anaesthesia 1984; 39:788-89.
27 Kanaya N, Imaizumi H, Matsumoto M, Namiki A, Tsunoda K. Evaluation of alkalinized lidocaine solution in brachial plexus blockade. Journal of Anesthesia 1991; 5:128-31.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.21

Study of Effect of Ramosetron and Granisetron in Prevention of Post Operative Nausea and Vomiting Following Laproscopic Cholecystectomy

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Abstract

Background: Post operative nausea and vomiting following laparoscopic cholecystectomy is a common complication. This study was designed to analyze and compare efficacy and adverse effect of ramosetron and granisetron in prevention of post operative nausea and vomiting following laparoscopic cholecystectomy.

Method: 100 patients of American Society of Anesthesiologists class I-II, aged 25 to 55 years scheduled for laproscopic cholecystectomy were included in study. Patients with history of smoking, drug or alcohol abuse, known allergy to granisetron or ramosetron, impaired kidney or liver function, motion sickness and history of previous post-operative nausea and vomiting, or those who received antiemetics within 24 hours before scheduled surgery, menstruating, pregnant or lactating women, or those on whom laparoscopic cholecystectomy was converted into open cholecystectomy were excluded from the study. 100 patients were divided into 2 groups of group A and Group B of 50 patients each. Group A patients received 2 mg of granisetron diluted to make 4ml in normal saline and group B patients received 0.3 mg of ramosetron diluted to make 4ml in normal saline given at the end of surgery

Results: No significant statistical difference seen immediately after extubation and 0 to 6 hrs and 6 to 12 hrs. but statistically significant result was observed 12 to 18 and 18 to 24 after surgery.

Conclusion: Ramosetron provides prolonged relief from post operative nausea vomiting as compared to granisetron in laproscopic cholecystectomy .

Keywords: Granisetron; Ramosetron; Laproscopic Cholecystectomy; Nausea Vomiting.

Introduction

Postoperative nausea and vomiting (PONV) is one of the most common complaints following anaesthesia and serious complications of clinical concern in the postoperative period and is often associated with increased morbidity of postoperative bleeding, wound dehiscence, fluid and electrolyte imbalance, delayed hospital discharge, and decreased satisfaction in surgical patients [1]. The main patient related factors are age, gender, history of motion sickness, previous nausea and vomiting, pregnancy , surgery within 1-7 days of menstrual cycle ,patients not smoking [2-6]. Laparoscopic cholecystectomy, a popular alternative to open cholecystectomy is associated with excessive episodes of nausea and vomiting in the postoperative period [7].

A variety of drugs are being used include include anticholinergics, phenothiazines, antihistamines, butyrophenones, benzamides and steroids. Some of these antiemetics are associated with adverse effects such as restlessness, dry mouth, sedation, hypotension, extrapyramidal symptoms and dystonic effects [8]. An ideal antiemetic should have quicker onset and longer duration of action and no or minimal undesired effects. The newer 5-HT3 receptor antagonists, is generally superior to the traditional antiemetic[2,4,8]. Therefore the present study was conducted to study the efficacy of a newer 5-HT3 receptor antagonists, ramosetron and its comparison with granisetron in prevention of postoperative nausea and vomiting following

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Received on 24.12.2016
Accepted on 29.12.2016

laparoscopic cholecystectomy. Granisetron is indicated in prevention of nausea and vomiting associated with surgery and anesthesia (i.e., PONV), and that associated with treatment of cancer by chemotherapy [4,7,8,9]. The dose in adults and children is i.v. 40 mcg/kg [2,4,8,9]. Adverse effects include decreased gastrointestinal motility, headache, diarrhoea, somnolence, dizziness.and dyspepsia [4,9].

Ramosetron, a newer antiemetic with adult dose of 0.3 mg intravenously once a day has high bioavailability and elimination half life of 9 hours. It makes it more potent with a longer duration of action than older 5-HT3 receptor antagonists [1]. Paediatric dose has been found to be 6 mcg/kg in 4-10 years of age[1]. Adverse side effects include headache, dizziness, diarrhoea, constipation, drowsiness, sedation, muscle pain[10].

Materials and Methods

This prospective randomized double blind study was conducted in the Department of Anaesthesiology at Indira Gandhi Institute of Medical Sciences, Patna, Bihar from September 2014 to July 2015. 100 patients divided in two groups of 50 each of ASA grade I and II, aged between 25 and 55 years who gave written informed consent years were included in the study. Sample size has been estimated based on an alpha error of 0.05 and a power of 80%. Patients with history of smoking, drug or alcohol abuse, known allergy to granisetron or ramosetron, impaired kidney or liver function, motion sickness and history of previous post-operative nausea and vomiting, or those who received antiemetics within 24 hours before scheduled surgery, menstruating, pregnant or lactating women, or those on whom laparoscopic cholecystectomy was converted into open cholecystectomy were excluded from the study. After approval by institutional ethical committee 100 patients were randomised using computer generated sequence into two groups of 50 each Group A: were to receive 2 mg of granisetron ; Group B: Patients were to receive 0.3 mg of ramosetron . Blinding was done by closed envelop technique On the day before the surgery all the patients were clinically evaluated, assessed and investigated .The study protocol was explained and written informed consent was taken from each participant. All patients received oral pantoprazole 40mg as pre anesthetic medication at 6AM on the day of surgery. In operation theatre after securing intravenous line, standard monitoring including ECG, NIBP and pulse oximetry were attached and base line parameters recorded. General anesthesia was induced with intravenous fentanyl 2mcg/kg, propofol 2 mg /kg followed by atracurium 0.5 mg/kg to facilitate insertion of endotracheal tube of appropriate size. A nasogastric tube was inserted and suction applied to empty stomach of air and other contents. Anaesthesia was maintained with isoflurane in a mixture of oxygen and nitrous oxide. Intra operative muscle relaxation was achieved with atracurium as required. Ventilation was mechanically controlled and adjusted to maintain $ETCO_2$ at 30-40 mm Hg with an Anaesthetic/Respiratory analyzer (Drager Fabius GS). During surgery patients were positioned in the reverse trendlenburg position with the right side of the table elevated. The abdomen was insufflated with carbon dioxide to an abdominal pressure of 10 to 14 mm Hg. Intraoperative monitoring including ECG, pulse oximetry, $ETCO_2$, systolic, diastolic and mean blood pressure were recorded after every 5 minutes**.** Boluses of injection fentanyl 1mcg/kg intravenously were given if the heart rate and blood pressure increased more than 30% of the preoperative baseline. Injection paracetamol 15mg/kg and diclofenac sodium aqueous 75 mg was given via intravenous infusion unless contraindicated and was given during maintenance also. Duration of anaesthesia, surgery and carbon dioxide insufflations was recorded as per the proforma .Drug was prepared by a trained nurse in 5 ml syringe diluted to 4 ml with normal saline, and given towards the end of the procedure. Patients enrolled in the granisetron group received 2 mg IV of granisetron and those in the ramosetron group received 0.3 mg IV of ramosetron towards the completion of the surgical procedure. After completion of surgery, neuromuscular blockade was reversed with neostigmine 0.04 mg/kg and glycopyrolate 0.01mg/kg. Before extubation of trachea, the nasogastric tube was again suctioned and then removed. When adequate spontaneous ventilation was established, muscle relaxation reversed and patient was following commands, tracheal extubation was done. The incidence of nausea and vomiting was recorded immediately after extubation and every 6 hours for a period of 24 hours by direct questioning to the patient or to his attendant by the same anesthetist. Nausea and vomiting were evaluated on a three point scale as per the proforma 0 =none; 1 =nausea; 2=vomiting Adverse effects, if any, were recorded in all patients. Student t test (unpaired two tailed) has been used to find the significance of age, weight and duration of anesthesia, surgery and CO_2insufflation between two groups. Chi square/ Fischer exact test has been used to find the significance

of incidence of nausea and vomiting between the two groups of patients. A p-value <0.05 was considered significant. Clinical Trials Registry India (CTRI) registration number is CTRI/2015/09/009815.

Results

There was no statistically significant difference (p > 0.05) among the groups in respect of age, weight, duration of anesthesia, surgery and duration of CO_2 insufflation (Table 1).

Immediately after extubation, 0-6 hours and 6-12 hours the difference of incidence of nausea was statistically insignificant but at 12-18 hours and 18-24 hours it was statistically insignificant (p value > 0.05) [Table 2a,b,c,d,e].

The most common side effects of the drugs in the two groups observed in our study were headache (12%in granisetron group and 10% in ramosetron group), and dizziness (6% in granisetron group and 4% in ramosetron group which was not statistical significant between the two groups.

Table 1: Demographic profile of patients

	Demographic Profile	Granise Tron	Ramose Tron	P value
1	Age (yrs)	40.14±8.42	39.76±8.64	0.8262
2	Weight (kg)	53.20±8.76	52.84±7.58	0.8269
3	Duration of Anesthesia (minutes)	46.48±7.14	46.36±4.15	0.8856
4	Duration of Surgery	34.54±3.66	34.02±2.80	0.4268
5	Duration of CO_2 Insufflation (minutes)	28.10±3.16 minutes	27.18±2.24 minutes	0.0962

Table 2: Post operative nausea and vomiting score at a) immediately after extubation, b) 0-6hours, c) 6-12 hours, d) 12-18hours, e) 18-24 hours.

Table 2a: Post operative nausea and vomiting score immediately after extubation

	Granisetron		Ramosetron		Pvalue	Remarks
PONV score	No	%	No	%		
Nausea	5	10	4	8	1.000	Not Significant
Vomiting	2	4	1	2	1.000	Not Significant
Rescue antiemetic required	2	4	1	2	1.000	Not Significant

Table 2b: Post Operative Nausea and Vomiting (Pony) score 0-6 hours after extubation

	Granisetron		Ramosetron		Pvalue	Remarks
PONV score	No	%	No	%		
Nausea	8	16	6	12	0.7742	Not Significant
Vomiting	4	8	2	4	0.6777	Not Significant
Rescue antiemetic required	1	2	2	2	1.000	Not Significant

Table 2c: Post operative Nausea and Vomiting (PONV) score 6-12 hours after extubation

	Granisetron		Ramosetron		P value	Remarks
PONV score	No	%	No	%		
Nausea	10	20	6	12	0.4139	Not Significant
Vomiting	4	8	2	4	0.6777	Not Significant
Rescue antiemetic required	3	6	1	2	1.6173	Not Significant

Table 2d: Post operative Nausea and Vomiting (PONV) score 12-18 hours after

	Granisetron		Ramosetron		P value	Remarks
PONV score	No	%	No	%		
Nausea	16	32	6	12	0.0283	Significant
Vomiting	10	20	2	4	0.0277	Significant
Rescue antiemetic required	8	16	1	2	0.0309	Significant

Table 2e: Post operative Nausea and Vomiting (PONV) score 18-24 hours after extubation

PONV score	Granisetron		Ramosetron		P value	Remarks
	No	%	No	%		
Nausea	18	32	8	16	0.0390	Significant
Vomiting	14	28	33	6	0.0064	Significant
Rescue antiemetic required	8	16	1	2	0.0309	Significant

Discussion

Despite the latest advances in anesthesia and the introduction of new class of antiemetics, almost one third of patients undergoing surgery suffer from postoperative nausea, vomiting, or both, and often rate PONV as worse than postoperative pain [6]. PONV is commonly experienced after general anesthesia in laparoscopic surgery , and its incidence ranges between 60% to 72%[11]. Its etiology after laparoscopic cholecystectomy is not known but probably associated with effect of intraperitoneal carbon dioxide insufflation on residual stretching and irritation of the peritoneum [12]. Although always self limiting and nonfatal PONV can cause significant morbidity,[13] Efforts are being made to reduce the chances of vomiting associated with anaesthesia and surgery. Many studies have been conducted to know the mechanism and causes of postoperative nausea and vomiting and to find out the safe and satisfactory antiemetic or emesis free anaesthesia. Multiple factors like patient related, surgery related, anesthesia related risk factors like use of volatile anesthetics,N2O, postoperative opioids, postoperative pain, and intraoperative hypovolemia have been found [14]. In our study we have standardized the factors that may play a role in the development or attenuation of PONV and also standardized the anesthetic technique for all the patients. There was no statistical difference between the two groups with respect to their demographic profile such as age, weight, height, sex, duration of anesthesia and surgery, We can therefore presume that the difference in effects between the two groups can be attributed to the drugs administered. PONV is classified as early, occurring up to 2 to 6 hours after surgery, or late, occurring up to 24-48 hours after surgery.The causative factors for early and late PONV may be different with use of volatile anesthetics being a main cause for early PONV [15].We have, therefore, chosen 6 h interval for our study design.

We found no statistically significant difference in the PONV scores in the two groups immediately after extubation, 0 to 6 hrs and 6 to 12 hrs hence proving that upto 12 hrs ramosetron is as effective as granisetron for preventing PONV which are similar as found by I Bhat et al and Waqar-ul-nisa et al [10,11].

We found a statistically significant difference in the PONV scores between the two groups 12-18 and 18 to 24 hours after extubation hrs which is same as results found by Bhat et al and Waqar-ul-nisa et al but differ from Newstar et al . who observed that the differences in the PONV scores were statistically insignificant during early (0-2 hrs) as well as 2 to 24 hrs [12].

The persistent response of ramosetron lasting over the period of 48 hrs after surgery may be a reflection of its more prolonged elimination half life of ramosetron (9 hours) and granisetron (4.9 hours) [16,17]. Ramosetron is 58 times more potent than granisetron, and its antiemetic effect lasts 10.7 times longer than that of granisetron in patients treated with cisplatin[18]. Ramosetron has a longer half life than that reported for granisetron (5.8 h for ramosetron and 3.1 – 3.2 h for granisetron)[13]. Because of these pharmacological properties, ramosetron is reported to be more potent with a longer duration of action than older 5-HT3 receptor antagonists [19,20]. The more potency and longer duration of action of ramosetron could be the reasons that gave us favorable results for ramosetron over granisetron .

The side effects of the drugs noticed during the study were headache (12% in granisetron group and 10% in ramosetron group) and dizziness (6% in granisetron group and 4% ramosetron group) were of mild nature and self limiting. The side effects observed in our study were similar to most of other studies [12]. The side effects were of mild nature and self-limiting. The differences of adverse effects in the two groups were found to be notsignificant ($P > 0.05$). There were certain limitations in this study i.e. the bias of gender was not eliminated from the study. Further, it may also be extrapolated to a larger sample size to overcome the possibility of beta error if any. However, our study suggested that Ramosetron is superior to granisetron in providing prolonged relief from postoperative nausea and vomiting .

Refrences

1. Won OK, Bon NK, Yong KK, Hae KK; Ramosetron for the prevention of postoperative nausea and vomiting : a meta-analysis. Korean J Anesthesiol. 2011; 61:405-12.
2. Ky Ho, J W Chiu. Multimodal antiemetic therapy and emetic risk profiling .Ann Acad Med Singapore 2005; 34:196-205.
3. Lindbald T, Bucklers DN, Forrest JB. The incidence of postoperative nausea and vomiting in women undergoing laparoscopy is influenced by the day of menstrual cycle. Can J Anesth 1991.p.382-98.
4. Alex SE, Mervyn M,Evan DK. Antiemetics. In: Alex S. Evers, Mervyn Maze, Evan D. Kharasch, Editor. Anesthetic pharmacology (physiologic principles and clinical practices), a companion to Millers anesthesia, 2nd edition: Cambridge University Press; 2013.p.842-54.
5. Lichtor JL. Ambulatory Anesthesia. In: GB Paul ,FC Bruce, KS Robert, editors; clinical anesthesia 6th ed. Philadelphia, PA:lippincott Williams and wilkins, a wolters Kluwer business 2009, 32:841.
6. Eun JK, JustinSK, Chung SK, Sang ML, Duck HC . Combination of antiernetics for prevention of post operative nausea and vomiting in high risk patients: J Korean Med Sci 2007; 22:878-82.
7. Jean LJ. Anesthesia for laparoscopic surgery .DM Ronald. Editor. MillersAnaesthesia. 7thed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010.p.2185-97.
8. Bruce DC, Bernadette KB. Gastrointestinal Diseases. AH Richard , JQ David.Editors. Textbook of Therapeutics Drug and Disease Management.8th ed . Philadelphia,Pa : Lippincott Williams & Wilkins, 2006 .p.1287-8.
9. Boston LR. Prokinetic and Antiemetic drugs. In:TN Hardman, L Lee editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics; 10 th ed. New York: McGraw-Hill 2001; 38:1029-30.
10. Bhat I, Farooq A, Waqar-ul-Nisa, Maqbool A, Ahmad A. Prevention Of Post-Operative Nausea And Vomiting In Females Following Laparoscopic Cholecystectomy: Is Ramosetron Superior To Granisetron?. The Internet Journal of Anesthesiology. 2013; 32: 2.
11. Waqar N, Farooqi A, Ahmad I, I Bhat, Buch V.Prevention of post-operative nausea and vomiting in females following thyroidectomy: a comparison between ramosetron and granisetron. JIARM issn 2014; 2:2320-5083.
12. Newstar S, Lairenlakpam DS, Nongthombam RS, Takhelmayum HS, Longjam ED. A comparative study between ramosetron and granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. JMEDSOC, 2013; 27:194-8.
13. Kang YK, Park YH, Ryoo BY, Bang YJ, Cho KS, Shin DB, *et al.* Ramosetron for the Prevention of Cisplatin induced Acute Emesis a Prospective Randomized Comparison with Granisetron.The Journal of International Medical Research. 2002; 30:220-9.
14. Gan TJ. Risk factors for postoperative nausea and vomiting. Anesth Analg. 2006; 102:1884-98.
15. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: (A randomized controlled trial of factorial design. Br J Anaesth. 2002b; 88:659-68.
16. Ansari MM, Siddiqui OA, Haleem S, Varshney R, Akhtar S, Khan FA. Comparison of ramosetron and ondansetron for control of post-operative nausea and vomiting following laparoscopic cholecystectomy. Indian J Med Sci. 2010; 64:272-80.
17. Kamato T, Ito H, Nagakura Y. Mechanism of cisplatin and m-chlorophenylbiguanide induced emesis in ferret. Eur J Pharma col. 1993; 238:369-76.
18. Feng YF, Pin Z, You JH, Yu LH, Mei ZZ, Gang C et al. Comparison of the selective serotonin-3 antagonist in treating acute chemotherapy induced emesis, nausea and anorexia: A single blind, randomized, crossover study.CTR. 2000; 6:12-19.
19. Kim SI, Kim SC, Baek YH, Ok SY, Kim SH. Comparison of Ramosetron with Ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. Br J Anaesth. 2009; 103:549-53.20.
20. Rabasseda X. Ramosetron, a 5-HT3 receptor antagonist for the control of nausea and vomiting; Drugs Today (Bare). 2002; 38:75-89.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.22

A Study on 'Comparison of Hemodynamic Changes between Clonidine and Dexmedetomidine as Adjuvants' with 0.5% Levobupivacaine in Axillary Brachial Plexus Block

Naveed Abrar*, Krishna D.*

Abstract

Introduction: The haemodynamic effects of alpha-2 adrenergic agonists are both central and peripheral. Stimulation of the peripheral sub-endothelial receptor causes vasoconstriction & the action is however transient.

Methodology: Group LC: (N=40) received 25ml of 0.5 % of Levobupivacaine + 1 µg/ kg of Clonidine. [Total volume of drug- 30 ml by adding sterile water for injection] Group LD: (N=40) received 25ml of 0.5% of Levobupivacaine + 1µg/ kg of Dexmedetomidine [Total volume of drug- 30 ml by adding sterile water for injection.

Results: In group LC, the mean SBP ranged from 117.15 ± 5.10 to 118.25 ± 6.93 mm of Hg, where as in group LD, the mean SBP ranged from 117.55 ± 5.44 to 119.10 ± 5.08 mm of Hg.

Conclusion: No significant difference in haemodynamic variables i.e., pulse rate, SBP, DBP and oxygen saturation were found.

Keywords: Clonidine; Dexmedetomidine; Pulse Rate; Blood Pressure.

Introduction

Clonidine hydrochloride, an imidazoline derivative was originally developed as a nasal decongestant and vasoconstrictor. Its hypotensive and bradycardia effects were first appreciated in 1962. It is a centrally acting adrenergic agonist that lowers blood pressure by decreasing basal sympathetic nervous system activity. It was introduced first for use as an antihypertensive agent [1]. Intravenous clonidine can cause a transient rise in blood pressure due to its ability to cause vasoconstriction via an alpha-2 agonist effect on vascular smooth muscle of skin and mucosa. This is followed by a decreased blood pressure due presumably to activation of CNS alpha-2 receptors, resulting in a decreased central outflow of impulses in sympathetic nervous system.

Although this is an area of intense current research interest, some evidence suggests that different mechanisms may be more important. Some of the antihypertensive effect of clonidine may also be due to diminished release of norepinephrine at sympathetic postganglionic nerve terminals due to activation of presynaptic alpha-2 receptors [2].

The haemodynamic effects of alpha-2 adrenergic agonists are both central and peripheral. Stimulation of the peripheral sub-endothelial receptor causes vasoconstriction. The action is however transient. However, stimulation of the alpha-2 adrenergic receptors of the neurons in the nucleus tractus solitaries causes inhibition of the nucleus of sympathetic neurons in the medulla. By this mechanism, alpha adrenergic agonists reduce the tonic activity of the baroreflex, decreasing atrial pressure and causing bradycardia. It is interesting to note that phasic activity of the baroreflex is preserved or perhaps even improved, so that any decrease in arterial pressure is followed by a significant increase in heart rate. In addition alpha-2 adrenergic agonists depress presynaptic sympathetic neurons in the lateral horn of the thoracic spinal cord [3]. It should be noted here that this effect is reversed by the local administration of cholinesterase inhibitor neostigmine. It is a result of this modality of action that intrathecal administration of clonidine causes more profound hypotension than after intravenous administration. Hypotension and bradycardia caused by Clonidine need to be reversed by fluids, vasoconstrictors (e.g. Phenylephrine) and Atropine respectively. Large doses may be needed.

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Received on 29.12.2016
Accepted on 04.01.2017

Dexmedetomidine is a relatively new drug approved at the end of 1999 by the Food and Drug Administration (FDA) for humans use for short-term sedation and analgesia. Dexmedetomidine is the dextrorotatory S-enantiomer of medetomidin [4]. Dexmedetomidine evokes a biphasic blood pressure response: A short hypertensive phase and subsequent hypotension. The two phases are considered to be mediated by two different α 2-AR subtypes: the α-2b AR is responsible for the initial hypertensive phase, where as hypotension is mediated by the α2a-AR. In younger patients with high levels of vagal tone, bradycardia and sinus arrest have been described which were effectively treated with anticholinergic agents (Atropine, Glycopyrrolate).

Methodology

Inclusion Criteria

- ASA Class I and II
- Age: 20 to 60 years

Exclusion Criteria

- Patient refusal
- ASA Class III and IV
- Patients with severe anemia, severe hypovolemia, shock, septicemia.
- Abnormal Clotting Time, Bleeding Time or patient on anticoagulant therapy.
- Local infection at the site of proposed puncture for axillary block.
- History of drug allergy to Local anaesthetics, Clonidine, or Dexmedetomidine

The procedure of the anaesthesia technique and the development of sensory and motor block were explained to the patient to ensure good co-operation. The ultrasound guided axillary brachial plexus (with all aseptic precautions) was performed in the operation theatre.

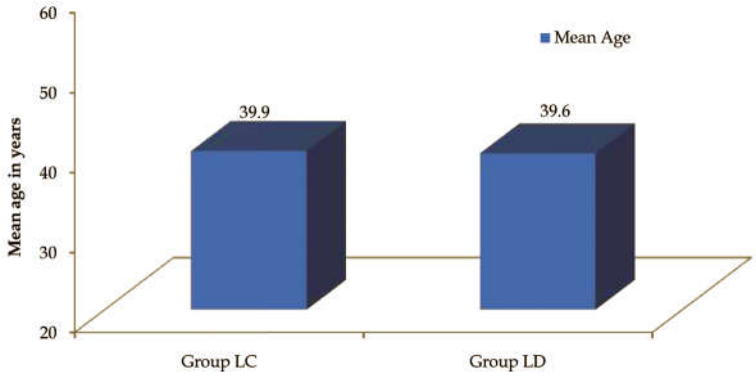
- *Group LC:* (N=40) received 25ml of 0.5% of Levobupivacaine + 1 µg/ kg of Clonidine

(The total volume of solution was made 30 ml by adding sterile water for injection)

- *Group LD:* (N=40) received 25ml of 0.5% of Levobupivacaine + 1µg/ kg of Dexmedetomidine

(The total volume of solution was made 30 ml by adding sterile water for injection)

Results



Graph 1: Mean age distribution (Yrs.)

Table 1: Pulse Rate (beats/min)

Time of assessment	Mean±SD		Mean Difference	t*Value	P Value	Significance
	Group LC	Group LD				
0 min	78.88±7.13	79.38±6.48	0.5	0.32	P>0.05	NS
5 min	78.22±6.62	78.92±6.18	0.7	0.48	P>0.05	NS
15 min	78.58±7.53	75.58±5.50	3.0	2.03	P>0.05	NS
30 min	79.42±6.34	76.90±6.78	2.52	1.72	P>0.05	NS
60 min	79.68±6.34	76.98±5.99	2.7	1.95	P>0.05	NS
2 hrs	79.22±5.84	77.42±5.14	1.8	2.08	P>0.05	NS
6 hrs	79.40±6.75	77.08±6.38	2.32	1.58	P>0.05	NS
12 hrs	79.35±5.99	76.98±6.11	2.37	1.75	P>0.05	NS

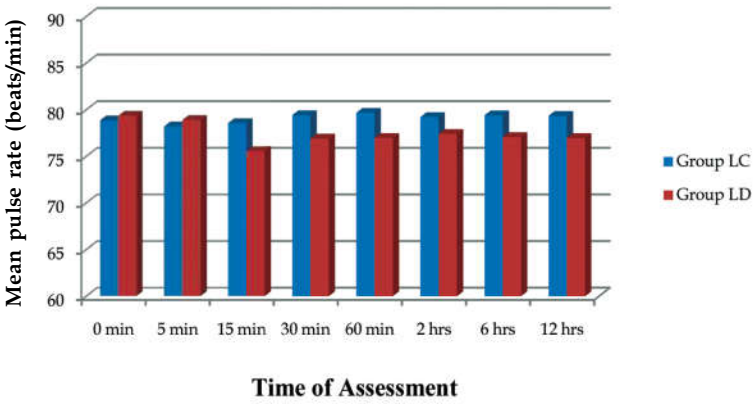
* Students unpaired't' test, NS- Non Significant

Pulse rate, Systolic BP, Diastolic BP, Oxygen saturation was recorded at 0 min, 5 min, 15 min, 60 min, 2 hours, 6 hours and 12 hours.

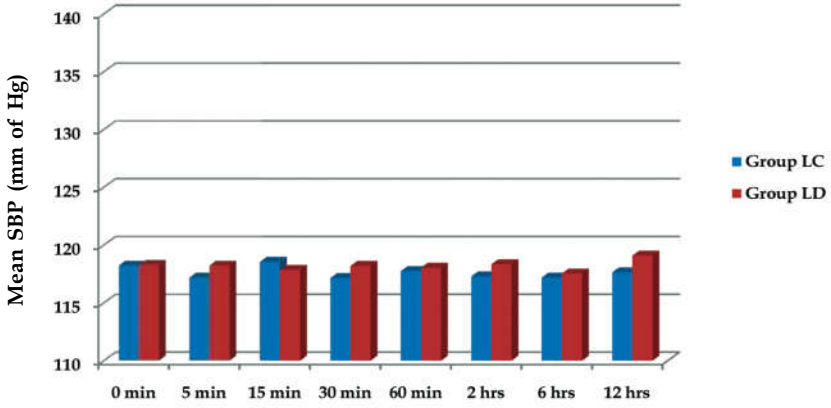
In group LC, the mean pulse rate ranged from 78.22 ± 6.62 to 79.68 ± 6.34 beats/min In group LD, the mean pulse rate ranged from 75.58 ± 5.50 to 79.38 ± 6.48 beats/min. The statistical analysis by student's unpaired't' test showed that there was no significant difference in pulse rate between the two groups (P >0.05).

In group LC, the mean systolic blood pressure ranged from 117.15 ± 5.10 to 118.25 ± 6.93 mm/Hg. In group LD, the mean systolic blood pressure ranged from 117.55 ± 5.44 to 119.10 ± 5.08 mm/Hg. The statistical analysis by student's unpaired 't' test showed that there was no significant difference in systolic blood pressure between the two groups (P >0.05)

In group LC, the mean systolic blood pressure ranged from 79.05 ± 5.81 to 80.15 ± 6.18 mm/Hg. In group LD, the mean systolic blood pressure ranged from 79.25±6.72 to 80.05±6.05 mm/Hg. The statistical analysis by student's unpaired 't' test showed that there was no significant difference in



Graph 2: Pulse rate (beats/min)



Graph 3: Systolic blood pressure (mm/Hg)

Table 2: Systolic blood pressure (mm of Hg)

Time of assessment	Mean±SD Group LC	Mean±SD Group LD	Mean Difference	t*Value	P Value	Significance
0 min	118.25±6.93	118.30±6.41	0.05	0.03	P>0.05	NS
5 min	117.20±5.83	118.25±5.92	1.05	0.79	P>0.05	NS
15 min	118.55±6.30	117.85±4.86	0.70	0.55	P>0.05	NS
30 min	117.15±5.10	118.20±5.48	1.05	0.88	P>0.05	NS
60 min	117.75±5.16	118.05±5.91	0.30	0.24	P>0.05	NS
2 hrs	117.30±4.38	118.35±6.51	1.05	0.84	P>0.05	NS
6 hrs	117.20±5.16	117.55±5.44	0.35	0.29	P>0.05	NS
12 hrs	117.65±5.56	119.10±5.08	1.45	1.21	P>0.05	NS

* Student's unpaired't' test, NS- Non Significant

systolic blood pressure between the two groups (P >0.05).

In group LC, the mean oxygen saturation ranged from 98.90±0.77 % to 99.02 ± 0.80 %. In group LD, the mean oxygen saturation ranged from 98.78±0.73 % to 98.92±0.79%. The statistical analysis by student's unpaired 't' test showed that there was no significant difference in oxygen saturation between the two groups (P >0.05).

Discussion

Brachial plexus block provides postoperative analgesia of short duration, even when a long acting local anaesthetic like Levobupivacaine is used alone. Various adjuvant drugs like opioids, Midazolam, Neostigmine, and Hyaluronidase have been evaluated in conjugation with local anaesthetics to prolong the duration of analgesia. But they were found to be either ineffective or produce an unacceptably high incidence of adverse effects. Alpha-

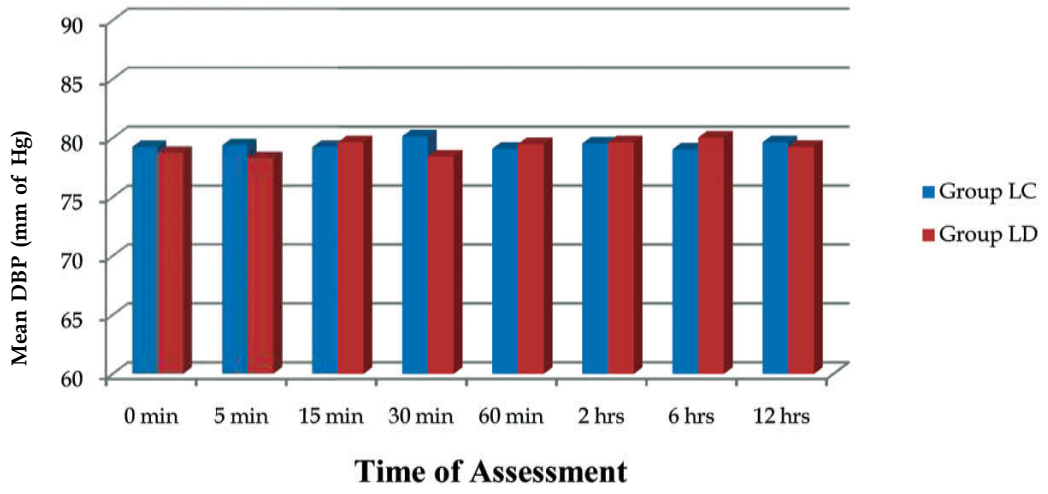
Table 3: Diastolic Blood Pressure (mm/Hg)

Time of assessment	Mean±SD Group LC	Mean±SD Group LD	Mean Difference	t*Value	P Value	Significance
0 min	79.25±5.11	78.75±6.05	0.50	0.39	P>0.05	NS
5 min	79.40±5.60	78.30±6.18	1.10	0.83	P>0.05	NS
15 min	79.25±6.62	79.65±6.68	0.40	0.26	P>0.05	NS
30 min	80.15±6.18	78.45±6.63	1.70	1.18	P>0.05	NS
60 min	79.10±6.02	79.50±6.30	0.40	0.29	P>0.05	NS
2 hrs	79.55±6.75	79.65±7.07	0.10	0.06	P>0.05	NS
6 hrs	79.05±5.81	80.05±6.05	1	0.75	P>0.05	NS
12 hrs	79.65±6.05	79.25±6.72	0.40	0.27	P>0.05	NS

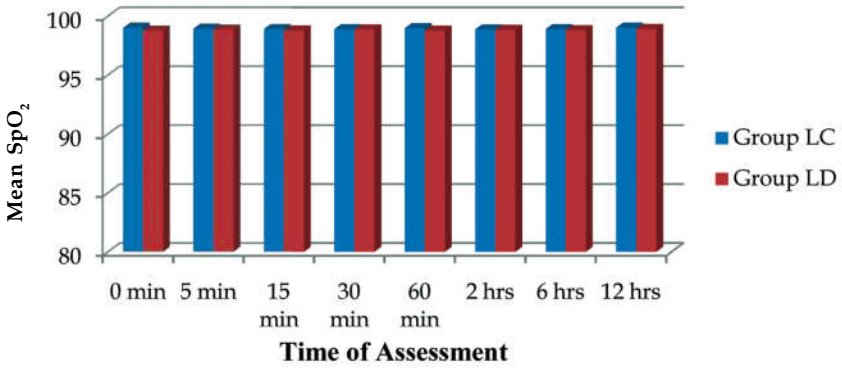
Table 4: Oxygen saturation (SpO_2%)

Time of assessment	Mean±SD Group LC	Mean±SD Group LD	Mean Difference	t*Value	P Value	Significance
0 min	99.02±0.80	98.80±0.79	0.22	1.26	P>0.05	NS
5 min	98.95±0.81	98.88±0.79	0.07	0.41	P>0.05	NS
15 min	98.92±0.79	98.80±0.79	0.12	0.70	P>0.05	NS
30 min	98.90±0.77	98.88±0.79	0.02	0.14	P>0.05	NS
60 min	98.98±0.80	98.78±0.73	0.20	1.16	P>0.05	NS
2 hrs	98.88±0.82	98.85±0.77	0.03	0.14	P>0.05	NS
6 hrs	98.90±0.77	98.82±0.78	0.08	0.43	P>0.05	NS
12 hrs	99.02±0.80	98.92±0.79	0.10	0.56	P>0.05	NS

* Students unpaired 't' test, NS- Non Significant



Graph 4: Diastolic Blood Pressure (mm/Hg)



Graph 5: Oxygen saturation (SpO_2%)

2 adrenergic agonists become popular because of their sedative, analgesic, antihypertensive, antiemetic actions in addition to reducing the anaesthetic drugs requirement. Alpha-2 adrenergic agonists have been tried either alone or in combination with other drugs, in epidural, intrathecal and peripheral injections, to prolong the duration of anaesthesia. There are many human studies on brachial plexus nerve blocks, which have demonstrated that increased duration of sensory and motor blockade can be achieved by adding Dexmedetomidine to local anaesthetics.

Aggarwal S et al. [5], compared the effects of adding Dexmedetomidine to Bupivacaine in supraclavicular brachial plexus block in fifty patients. They concluded that Dexmedetomidine added as an adjuvant to Bupivacaine for supraclavicular brachial plexus block significantly shortens the onset time and prolongs the duration of sensory and motor blocks and duration of analgesia. Patients in Dexmedetomidine group were adequately sedated with no adverse effects except bradycardia in one patient.

Other studies like Feroz Ahmad Dar et al. [6], and Kumar Das et al. [7], evaluated the effect of adding Dexmedetomidine to local anaesthetics for brachial plexus blockade in patients scheduled for elective forearm and hand surgeries. They found that sensory and motor block onset times were shorter, sensory and motor blockade durations were longer along with prolonged duration of analgesia with addition of Dexmedetomidine.

We have studied & compared the action of two $á_2$ agonists, i.e. Clonidine and Dexmedetomidine with Levobupivacaine in axillary brachial plexus block, so that along with increasing the duration of analgesia with a single shot axillary brachial plexus block, the longer duration of post-operative analgesia was to be achieved without significant clinical side-effects and hence we can avoid continuous catheterization.

The result of our study showed that the onset time of sensory and motor blockade was significantly faster in group LD. The duration of sensory and motor blockade and duration of analgesia were also prolonged significantly in group LD when compared with group LC. These results were consistent with other studies.

Harshavardhana HS et al. [8], did a study aiming to test the hypothesis that Dexmedetomidine produces a better analgesia, motor block and postoperative analgesia when added as an adjuvant to ropivacaine 0.5% in Supraclavicular brachial plexus block compared with Clonidine. They found that Dexmedetomidine prolonged the duration of sensory and motor block and enhanced the quality of block as compared with Clonidine when used as an adjuvant to ropivacaine in peripheral nerve block and concluded that Dexmedetomidine was a better adjuvant as compared to Clonidine.

Conclusion

Both groups were comparable with regards to Pulse rate, Systolic blood pressure, Diastolic blood pressure and Oxygen saturation. There was no statistically significant difference between the groups.

References

1. Zhang Y, Wang CS, Shi JH, Sun B, Liu SJ, Li P, Li EY. Perineural administration of dexmedetomidine in combination with ropivacaine prolongs axillary brachial plexus block. Int J ClinExp Med. 2014; 7(3): 680-5.
2. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine

prolongs axillary brachial plexus block. AnesthAnalg. 2010; 111(6):1548-51.

3. Kaygusuz K, Kol IO, Duger C, et al. Effects of Adding Dexmedetomidine to Levobupivacaine in Axillary Brachial Plexus Block. Current Therapeutic Research, Clinical and Experimental. 2012; 73(3):103-111.
4. Gandhi R, Shah A, Patel I. Use of dexmedetomidine along with bupivacaine for brachial plexus block. National journal of medical research. 2012; 2:67-69.
5. Agarwal S, Aggarwal R, Gupta P. Dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block. Journal of Anaesthesio, Clinical Pharmacology. 2014; 30(1):36-40.
6. Dar F A , Najar M R, Jan N .Dexmedetomidine Added to Ropivacaine Prolongs Axillary Brachial Plexus Block. International Journal of Biomedical and Advance Research. 2013; 4:719-722.
7. Biswas S, Das RK, Mukherjee G, Ghose T. Dexmedetomidine an Adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block: A Randomized Double Blind Prospective Study. Ethiop J Health Sci. 2014; 24:203–208.
8. Harshavardhan H.S. Efficacy of Dexmedetomidine Compared to Clonidine added to Ropivacaine in Supraclavicular Nerve Blocks: A Prospective Randomised Double Blind Study.Int J Med Health Sci. 2014 Apr; 3(2):127-32.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.23

Comparative Study between Modified Mallampathi and Extended Mallampathi and Thytomental Distance in Predicting Difficult Intubation in Obese Individuals

Sayeda Noor Huzefa*, Ramesh K.**

Abstract

Background: The modified Mallampati (MMP) classification is a standard method of oropharyngeal evaluation for predicting difficult laryngoscopy. Previous studies have demonstrated that the predictive value of the MMP is improved when thepatient's craniocervical junction is extended rather than neutral (Extended Mallampati Score, EMS). In the present study, we compared the predictive value of the MMP, EMS and thyromental score in the obese.

Methods: We performed a prospective study of adult patients with a Body Mass Index (BMI) 40 comparing the MMP and EMS. The performance of the MMP, EMS, and thyromental distance was compared forthe ability to predict difficult laryngoscopy, defined as a Cormack-Lehane grade of 3 or 4. Positioning and direct laryngoscopic techniques were not standardized.

Results: Hundred patients with a BMI >35 were evaluated withboth the MMP and EMS and received direct laryngoscopy. On average, craniocervical extension decreased the MMP class. Compared to the MMP, the EMS improved specificity and predictive value while maintaining sensitivity. Compared to the MMP and thyromental distance, an EMS class of 3 or 4 were statistically significant predictors of difficultlaryngoscopy in the obese. There was no difference in the incidence ofdifficult laryngoscopy or intubation in the obese compared to patientswith a BMI >35.

Conclusions: The EMS was Superior to the MMP in the Prediction of Difficult; Laryngoscopy in the Obese Population.

Keywords: Modified Mallampathi; Extended Mallampathi; Thyromental Distance; Cormac Lehane Grading; Obesity.

Introduction

The modified Mallampati (MMP) examination is astandard method of evaluating the airway for potentially difficult laryngoscopy [1-3]. As originally described, the MMP examination is performed with thepatient sitting upright, head neutral, tongue maximally protruded, and no phonation [3]. It has beendemonstrated that the predictive value of the examinationis dependent on the position of the cervicalspine:

Lewis et al. recommended that the MMP be performed with the patient sitting and with extension of the craniocervical junction [4].

Method

During the preanesthetic evaluation of the patient Anesthesia providers score adult patients using the standard MMP evaluation: sitting, head in neutral lposition, mouth open fully, tongue protruded maximally, no phonation and with the examiner eye toeye. The EMS is performed with the patient sitting, craniocervical junction extended, mouth openfully, tongue protruded maximally, no phonation, and the examiner eye-to-eye. MMP and EMS classification are scored as follows:

Class 1: Entire uvula clearly visible

Class 2: Upper half of uvula visible

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Received on 30.12.2016
Accepted on 04.01.2017

Class 3: Soft and hard palate clearly visible

Class 4: Only hard palate visible

Thyromental distance was measured along a straight line from the thyroid notch to the lower border of the mandibular mentum, with the head fully extended and the mouth closed [5].

Thyromental distance (T)

Grade 0: T _ 6.5 cm 0

Grade 1: T 5.5e6.4 cm 1

Grade 2: T < 5.5 cm

Informed written consent was obtained from all the participants. Hundred adultpatients aged 18 to 70 years, irrespective of sex, of the American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective surgeries under general were enrolled for the study. Patients with an obvious difficult airway (fractured mandible or cervical spine disorder, obstructive airway tumor, edentulous patients, mouth opening <3 cm etc.), or those who refused to participate, were excluded.

Results

Standard fasting guidelines were observed in all patients. Monitors for electrocardiogram (ECG) lead II and V, noninvasive blood pressure, heart rate and peripheral oxygen saturation were applied before induction. Following preoxygenation for 3 minutes, patient was premedicated with intravenous midazolam (0.02 mg/kg) and fentanyl (2 mg/kg) and induced with propofol. Muscle relaxant vecuronium bromide (0.1 mg/kg) was administered intravenously and ventilation continued for 3 minutes. Laryngoscopy was performed in sniffing position using a Macintosh laryngoscope and the best possible laryngoscopic view was obtained. Difficult laryngoscopy was defined as the view observed corresponding to Grade 3 or 4 of the Cormack and Lehane (CL) laryngoscopic view and attempts to intubation more than 2.

Table 1: Comaprison of difficult intubation between EMS,TMD and MMS

EMS	No. of pts	Difficulty	
1	23	E	20 (86.9%)
		D	3 (13.1%)
2	21	E	19 (90.5%)
		D	2 (09.5%)
3	6	E	2 (33.3%)
		D	4 (66.7%)
4	0	E	0
		D	0
TMD			
0	27	E	24 (88.8%)
		D	3 (11.2%)
1	18	E	14 (77.7%)
		D	4 (22.3%)
2	5	E	1(20.0%)
		D	4 (80.0%)
MMS			
1	21	E	20 (95.2%)
		D	1 (04.8%)
2	13	E	11(84.6%)
		D	2 (15.4%)
3	14	E	9 (64.2%)
		D	5 (35.8%)
4	2	E	0
		D	2 (100%)

EMS: Extended mallampathi score, TMD: Thyro mental distance, MMS: Modified mallampathi score, E: Easy intubation, D: Difficult intubation

Discussion

A major factor that has been considered to be related to the morbidity and mortality following

anesthesia isunexpected difficult intubation [6]. For this reason, itis necessary to investigate for a simple and accuratepredictive test. Increasedconsumption of oxygen and decreased functional residualcapacity in the morbidly obese population, accurate prediction of difficult laryngoscopy is especially important. The MMP examination has become astandard method of oropharyngeal evaluation, althoug has a single test it is thought to be of limited diagnostic value [7]. Indeed, there has been wide variationin the reported sensitivity and specificity of theMMP, as well as low positive predictive value. Thereare statistical reasons for such values. As Yentis hasnoted, positive predictive values will always be lowwhen the outcome of interest (such as difficult laryngoscopyor tracheal intubation) is relatively uncommon [8]. Other reasons for poor predictive value include anintrinsic lack of value to the test or poor execution of thetest.It has been established that the positive predictivevalue of the MMP is dependent on the position of thepatient. Lewis et al. studied 24 different sets of conditions in 213 patients, combining various body, head,and tongue positions [4]. They demonstrated that the position associated with the best positive predictivevalue of the MMP was the patient sitting, head extended, and tongue maximally protruded. This verywell designed study was not clinically realistic, however, as there were only two examiners for the patientsand laryngoscopic positioning and technique werestandardized. Mashour and Sandberg tested the EMSon the basis of these results, allowing multiple examinersand nonstandardized laryngoscopy [9]. In a studyof 60 patients, they found that performing the MMPwith the patient sitting and in craniocervicalextension improved the positive predictive value. This study was limited due to the relatively small number ofpatients and the detailed instructions given to theexaminers. Furthermore, since the examiners knew thehypothesis being tested and were the ones performing laryngoscopy, there was the potential for a Hawthorneeffect.

We demonstrate thatthe EMS is superior to the MMP in the prediction ofdifficult laryngoscopy in the morbidly obese population.The EMS predictions demonstrate better agreementwith Cormack-Lehane grades compared to the MMP (P _ 0.0001) obese patients. Our data show that EMS class 3 or 4 in the obese, compared to MMP and other standard methodsof airway evaluation is a better predictor of difficultlaryngoscopy Other commonly used bedsidetests, such as thyromental distance and mandibularprotrusion were not effective in predicting difficultlaryngoscopy in this study. Given the low sensitivityand predictive values of both Mallampati examinationswithin the morbidly obese population, furthertests need to be developed.

Our data agree with those of Brodsky et al. [10], in thatmorbid obesity is not an independent predictor ofdifficult direct laryngoscopy *per se* .

There are several limitations to our study. Therewas a heterogeneity of examiners and laryngoscopists, which creates the potential for inter-rater variability inthe evaluation of both oropharyngeal classifications.

Conclusion

In conclusion, we find that the EMS is a betterpredictor of difficult laryngoscopy than MMP in theobese population. The EMS is associated with loweroropharyngeal scores, improved specificity, and improved predictive value. This study, therefore, represents a validation of the EMS in obesepopulation in a routine perioperative setting.

References

1. Mallampati SR. Clinical sign to predict difficult trachealintubation (hypothesis). Can AnaesthSoc J 1983; 30(3 Pt 1):316–7.
2. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B,Friberger D, Liu PL. A clinical sign to predict difficulttracheal intubation: a prospective study. Can AnaesthSoc J1985; 32:429–34.
3. Samsoon GL, Young JR. Difficult tracheal intubation: a retrospectivestudy Anaesthesia 1987; 42:487–90.
4. Lewis M, Keramati S, Benumof JL, Berry CC. What is the bestway to determine oropharyngeal classification and mandibularspace length to predict difficult laryngoscopy? Anesthesiology 1994; 81: 69–74.
5. Lewis M, Keramati S, Benumof JL, Berry CC. What is the best way to determineoropharyngeal classification and mandibular space length to predict difficultlaryngoscopy? Anesthesiology 1994; 81: 69e75.
6. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, FribergerD, et al. A clinical sign to predict diffi cult tracheal intubation: A prospectivestudy. Can AnaesthSoc J 1985; 32:429-34.
7. Shiga T, Wajima Z, Inoue T, Sakamoto A. Predicting difficult intubationin apparently normal patients: a meta-analysis of bedside screeningtest performance. Anesthesiology 2005; 103:429–37.

8. Yentis SM. Predicting difficult intubation—worth while exercise or pointless ritual? Anaesthesia 2002; 57:105–9.
9. Mashour GA, Sandberg WS. Craniocervical extension improves the specificity and predictive value of the Mallampatiairway evaluation. AnesthAnalg 2006; 103:1256-9.
10. Brodsky J, Lemmens, HJM, Brock-Utne JG, Vierra M, Saidman LJ. Morbid obesity and tracheal intubation. AnesthAnalg 2002; 94:732–6.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.24

Clinical Study on Complications of Ketamine

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Abstract

Introduction: Intrathecally administered ketamine is advantageous as its beneficial effects on the cardiovascular system and respiratory functions may be combined with the analgesic effects of spinal anesthesia. The primary mechanism of action of the spinal anesthetic ketamine is noncompetitive blocking of the NMDA ionophore.

Methodology: 100 Patients were monitored continuously using sphygmo-manometer, pulse oximeter and electrocardiogram. After spinal anesthesia the patients pulse rate and blood pressure were recorded at 0, 5, 10, 20, 30, 45, 60, 90 and 120 minutes.

Results: The most common complication was nystagmus, which was present in all males and females, followed by sedation, which occurred in 45 males and 25 females. Only 4 patients had delirium reaction.

Conclusion: Intrathecal ketamine with adrenaline produces a reliable anesthesia, better operative conditions and patients comfort with minimal side effects.

Keywords: Ketamine; Complications; Blood Pressure.

Introduction

Spinal anesthesia or regional anesthesia is a potent anesthetic procedure. Additional modalities have been sought to increase the duration of block in spinal anesthesia [1]. Ketamine is an N-methyl-D-aspartate (NMDA) receptor blocker that has an anesthetic effect when injected intrathecally and has a synergic effect with bupivacaine. Ketamine also has potent analgesic properties [2,3].

Ketamine, an N-methyl-D-aspartate (NMDA) receptor blocker, has an anesthetic effect when injected intrathecally and is synergic with bupivacaine. Ketamine is a phencyclidine derivative with potent analgesic properties, which has various advantages over other local anesthetics, as it tends to stimulate the cardiovascular system and maintains respiratory response to carbon dioxide. Intrathecally administered ketamine is advantageous as its beneficial effects on the cardiovascular system and respiratory functions may be combined with the analgesic effects of spinal anesthesia. The primary mechanism of action of the spinal anesthetic ketamine is noncompetitive blocking of the NMDA ionophore [4,5].

Methodology

Inclusion Criteria

1. Patients of either sex
2. Patients with ASA grade-I and II.
3. Patients aged between 18-60 years.

Exclusion Criteria

Patients with severe systemic disease metabolic disorders, neurological, congenital or cardiovascular disease were excluded from this study.

Mode of Selection: Random.

Perioperative Period

On the eve of the surgery, all the patients were visited and a detailed examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous system and examination of spine for deformity, infection was carried out.Routine investigations like hemogram, total leucocyte count, differential leucocyte count, ESR, complete urine examination, random blood sugar, electrocardiogram, chest X-ray,

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Received on 30.12.2016
Accepted on 04.01.2017

blood grouping, blood urea, serum creatinine, etc. were done wherever necessary.

Intraoperative Periods

Once the patient was shifted to the operating room, the patients was connected to the routine monitors, which included electrocardiogram, non-invasive blood pressure and pulse oximeter. All resuscitation equipments like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephentramine was kept ready. The anaesthesia machine was also checked along with oxygen delivery system.

A wide bore intravenous access was obtained and secured. All patients were premediated with injection ranitdine 50mg, injection Odansetron, 4mg, injection diazepam 5mg intravenously. All patients were preloaded with 500ml of ringer lactate prior to spinal anesthesia.Baseline pulse rate, blood pressure, respiratory rate, SPO_2 were noted.

Under strict aseptic precaution lumbar puncture was performed in left lateral position by midline approach by using disposable quince spinal needle (22-25 G) at L3 L4 intervertebral space and injection ketamine 100mg (2ml) + injection adrenaline 0.1 mg (0.1ml of 1:1000) was injected intrathecally after free now of CSF.

Patients were monitored continuously using sphygmomanometer, pulse oximeter and electrocardiogram.After spinal anesthesia the patients pulse rate and blood pressure were recorded at 0, 5, 10, 20, 30, 45, 60, 90 and 120 minutes.

Following Parameters were Assessed

Assessment of sensory blockade

This was tested by pinprick method.

- Time of onset of sensory blockade – Time taken from injection of the drug into the sub-arachnoid space to loss of pinprick sensation.
- The time to achieve maximum sensory blockade. Time from injection of the drug to loss of pinprick sensation at highest dermatomal level.
- Duration of analgesia: it is the priod between the onset of analgesia and time of regression of analgesia by the two dermatomes.
- Degree of analgesia (sensory blockade): This was graded as follows:

Grade-I: Good analgesia, sedation were given only to relieve apprehension.

Grade-II: Inadequate, incomplete or patchy analgesia, supplementation was given with narcotics or N_2O/O_2/ halothane or ketamine intravenously.

Grade-III: Very poor analgesia, general anesthesia was given.

Assessment of Motor Blockade

- Time of onset of motor blockade: Time interval between injection of drug into subarachnoid space to the patients inability to lift the straight extended leg.
- Duration of motor blockade was recorded from onset time to the time when patient was able to lift extended leg.
- Degree of motor blockade: This was assessed by Bromage scale.

0 Full flexion of knee and feet, no motor blockade

1 Just able to flex knee, full flexion of feet, partial blockade.

2 Unable to flex knee, but some flexion of feet possible. Almost complete block.

3 Unable to move legs or feet: Complete motor blockade.

The side effects such as nausea, vomiting, hypotension, neurological sequelae, delirium reaction, sedation, dizziness, nystagmus were noted down. Hypotension was defined as decrease in systolic blood pressure more than 20% of the baseline value and was treated with injection mephenteramine 6mg intravenous increments and bradycardia as pulse rate<60 / minute and was treated by atropine 0.6 mg intravenous stat.

Results

In the present study, majority of the males (45

Table 1: Weight wise distribution of the patients scheduled for the study.

Weight (KGS)	Male	Female
46-50	4	9
51-55	20	10
56-60	25	9
61-65	14	1
66-70	6	1
71-75	1	0
Total	**70**	**30**

patients) and females (19 patients) were in 51-60 Kgs group.

In the present study, majority of the males (60 patients) were in 5′ 7" – 5′ 9" group, while majority of the female were shorter falling in 5′1" – 5′3" group.

Table 2: Height wise distribution of the patients scheduled for the study

Height (Ft &Inc)	Male	Female
4′10″-5′00″	-	-
5′1″-5′3″	2	20
5′4″-5′6″	8	9
5′7″-5′9″	60	1
Total	**70**	**30**

Table 3: Mean Heart rate in the study group

Time (Minutes)	Mean	± SD.
0	81.89	11.63
5	83.57	10.89
10	84.60	10.47
20	85.06	10.63
30	85.50	10.49
45	85.59	10.09
60	58.53	10.52
90	85.53	10.56
120	85.57	10.29

In the present study there was no much variation in the heart rate.

In the present study there was no much variation in the mean systolic blood pressure.

In the present study there was no much variation in the mean diastolic blood pressure.

In the present study, the most common complication was nystagmus, which was present in all males and females, followed by sedation, which occurred in 45

Table 4: Mean systolic blood pressure in the study group

Time (Minutes)	Mean	± SD.
0	112.26	11.90
5	115.79	11.91
10	118.98	11.79
20	121.62	11.49
30	122.90	11.18
45	123.58	10.74
60	124.20	10.35
90	124.230	9.99
120	124.04	10.07

Table 5: Mean diastolic blood pressure in the study group

Times (Minutes)	Mean	± SD.
0	74.32	7.80
5	76.42	7.63
10	79.00	8.00
20	80.70	7.14
30	81.45	7.16
45	82.10	7.14
60	82.60	6.73
90	82.37	6.49
120	82.14	6.91

Table 6: Complications

Complications	Male	Female
Hypotension	--	--
Nausea	--	--
Vomiting	--	--
Delirium reaction	3	1
Neurological sequelae	--	--
Sedation	45	25
Nystagmus	70	30
Dizziness	--	--

males and 25 females. Only 4 patients had delirium reaction.

Discussion

In the present study, there was increase in the resting blood pressure and pulse rate.In the study conducted by Bansal SK in 1994 [6], they reported that there was a significant increase in the resting blood pressure, pulse rate irrespective of the addition of adrenaline to the injected mixture.The present study is in accordance with their study.

In the present study, the most common complication was nystagmus, which occurred in all the patients. Sedation was seen in 70 patients and delirium reaction was seen in 4 patients. In the study conducted by Chris Hawksworth in 1998 [7], nystagum occurred in six out of ten patients, four patients developed psychomimetic disturbance. One complained of simply feeling strange and three patients had frank hallucination.In the study conducted by Bansal SK in 1994, sedation was observed with all the doses used in the study, which was however of mild or moderate intensity with the patient being easily awakening from the sleep.The present study is in accordance with their studies [8,9].

With all the above observations we can conclude that intrathecal ketamine with adrenaline produces a reliable anesthesia, better operative conditions and patients comfort with minimal side effects.

Conclusion

In addition, unlike other intrathecal local anaesthetics, ketamine stimulated the cardiovascular and respiratory systems, which may be an advantage in emergency operations especially in a shock patient.

References

1. Dowdy EG, Kaya K, Gocho Y. Some pharmacologic similarities of ketamine, lidocaine and procaine. Anaesthesia and Analgesia. 1973 Sep-Oct; 52:839-42.
2. Soliman MG, Bindle F, Kuster G. Response to hypercapnia under ketamine anaesthesia. Canad.Anaesth. Soc. J. 1975 July; 22:486-94.
3. Brock-Utne-JG, Kallichurum S, Mankowitz E, Maharaj RJ, Downing JW. Intrathecal ketamine with preservative – Histological effects on spinal nerve roots of baboons. S. Afr. Med. J. 1982 Mar; 61(12); 440-1.
4. Brock-Utne-JG, Mankowitz E, Kallichurum S, Downing JW. Effects of intrathecal saline and ketamine with and without preservative on the spinal nerve roots of monkeys. S. Afr. Med. J. 1982 Mar; 61(10):360-1.
5. Mankowitz E, Brock-Utne JG, Cosnett JE, Green TR. Epidural ketamine – A preliminary report. S. Afr. Med. J. 1982 Mar; 61(12);441-2.
6. Bansal SK, Bhatia VK, Bhatnagar NS, Bhushan S, Pant KK, Evluation of intrathecal ketamine in emergency surgery. Indian Journal of Anaesthesia 1994; 42:32-36.
7. Hawksworth C, Serpell M. Intrathecalanaesthesia with ketamine Regional Anaesthesia and Pain Medicine 1998; 23(3):283-288.
8. Sonoda H, Omote K. Suppressive effects of ketamine on neuropathic pain. Masui 1998 Feb; 47(2):136-44.
9. Stolz M, Oehen HP, Gerber H. Histological findings after long-term infusion of intrathecal ketamine for chronic pain: A case report. J Pain Symptom Manage 1999 Sept; 18(3):223-8.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.25

A Study on the Efficacy of Ketamine Given Intrathecallyas A Spinal Anesthetic Agent

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Abstract

Introduction: Ketamine a phencyclidine derivative with potent analgesic properties possesses few advantages over the other local anesthetics as it tends to stimulate the cardiovascular system and maintains the respiratory response to carbon dioxide.

Methodology: On the eve of the surgery, all the patients were visited and a detailed examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous system and examination of spine for deformity, infection was carried out.

Results: In the present study, the time taken to achieve maximum sensory blockade ranged from 2-8 minutes. In majority of the males (43 patients) it ranged from 4-6, while in females (26 patients) it ranged from 5.1-7 minutes.

Conclusion: In the present study, the quality of motor blockade assessed by the Bromage scale was grade-III in all the patients

Keywords: Ketamine; Spianal anaesthesia; Efficacy.

Introduction

Spinal anesthesia results from the delivery of the anesthetic agents into the cerebrospinal fluid. It is one of the simplest regional anesthetic techniques to perform.It is chiefly distinguished from its cousin epidural anesthesia by the production of subarachnoid neural blockage covering wide areas of the body with minute quantities of anesthetic agents.Safe practice of spinal anesthesia includes properly selecting and preparing accessing the CSF, administering appropriate anesthetic drugs and adjuvants managing physiologic side effects and overseeing the patient throughout the procedure as well as in the early recovery process [1].

August Bier performed the first spinal anesthetic more than a century ago, by injecting cocaine into the cerebrospinal fluid of a patient. For most of the subsequent hundred years, local anesthetics were the only substances used for neuraxial blockade. This changed with the discovery of opiod receptors in the spinal cord in the 1970s, and epidural and intrathecalopiod administration alone or in combination with local anesthetics became widespread. Since then driven by the ongoing discovery of multiple spinal transmitter and receptors involved in pain transmission many diverse groups of pharmacological agents are being investigated for neuraxial administration [2].

Ketamine a phencyclidine derivative with potent analgesic properties possesses few advantages over the other local anesthetics as it tends to stimulate the cardiovascular system and maintains the respiratory response to carbon dioxide. Thus intrathecally administered ketamine presents certain advantage as it might be possible to combine its beneficial effects on the cardiovascular system and respiratory functions along with the analgesia of spinal anesthesia.

Methodology

100 patients undergoing elective operative procedure under spinal anesthesia for lower abdominal surgeries formed the study subjects

Inclusion Criteria

1. Patients of either sex
2. Patients with ASA grade-I and II.
3. Patients aged between 18-60 years.

Exclusion Criteria

Patients with severe systemic disease metabolic disorders, neurological, congenital or

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Received on 30.12.2016
Accepted on 04.01.2017

cardiovascular disease were excluded from this study.

Perioperative Period

On the eve of the surgery, all the patients were visited and a detailed examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous system and examination of spine for deformity, infection was carried out.

Routine investigations like hemogram, total leucocyte count, differential leucocyte count, ESR, complete urine examination, random blood sugar, electrocardiogram, chest X-ray, blood grouping, blood urea, serum creatinine, etc. were done wherever necessary.

Intraoperative Periods

Once the patient was shifted to the operating room, the patients was connected to the routine monitors, which included electrocardiogram, non-invasive blood pressure and pulse oximeter. All resuscitation equipments like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephentramine was kept ready. The anaesthesia machine was also checked along with oxygen delivery system.

A wide bore intravenous access was obtained and secured. All patients were premediated with injection ranitdine 50mg, injection Odansetron, 4mg, injection diazepam 5mg intravenously. All patients were preloaded with 500ml of ringer lactate prior to spinal anesthesia.Baseline pulse rate, blood pressure, respiratory rate, SPO_2 were noted.

Under strict aseptic precaution lumbar puncture was performed in left lateral position by midline approach by using disposable quince spinal needle (22-25 G) at L3 L4 intervertebral space and injection ketamine 100mg (2ml) + injection adrenaline 0.1 mg (0.1ml of 1:1000) was injected intrathecally after free now of CSF.Patients were monitored continuously using sphygmomanometer, pulse oximeter and electrocardiogram.After spinal anesthesia the patients pulse rate and blood pressure were recorded at 0, 5, 10, 20, 30, 45, 60, 90 and 120 minutes.

Results

In the present study, the male-female ratio was 2.33:1. The majority of males (51 patients) and females (24 patients) were in 26-55 years age group.

Table 1: Age and sex distribution of the patients scheduled for study

Age (Years)	Male	Female
16-25	8	6
26-35	19	7
36-45	15	8
46-55	17	7
55-65	10	2
> 65	1	0
Total	70	30

Table 2: Onset of sensory blockade (minutes)

Time (Min)	Male	Female
1	-	0
2	29	20
3	33	10
4	8	0
> 4	0	0
Total	70	30

Table 3: Onset of motor blockade (minute)

Time (Minutes)	Male	Female
1	-	-
2	-	-
3	7	-
4	40	13
5	23	17
> 5	-	-
Total	70	30

In the present study, the onset of analgesia ranged from 2-4 minutes. Majority of the males (62 patients) had onset of sensory blockade within 2-3 minutes and all the females had sensory blockade between 2-3 minutes.

In the present study, the onset of motor blockade ranged from 2-5 minutes. Majority of the males (63 patients) and all the females had onset of motor blockade between 3-5 minutes.

In the present study, the duration of sensory blockade ranged from 58-108 minutes. In majority of the males (42 patients) and females (19 patients) the duration of sensory blockade ranged from 81-100 minutes.

In the present study, the duration of motor blockade ranged from 80-126 minutes. In the majority of the males (37 patients) and females (19 patients), it ranged from 101-120 minutes.

Table 4: Duration of sensory blockade (minutes)

Time (Minutes)	No. of Cases	
	Male	Female
40-60	3	2
60-80	24	8
81-100	42	19
101-120	1	1
> 120	-	-
Total	70	30

Table 5: Duration of motor blockade (minutes)

Duration (Minutes)	No. of Cases	
	Male	Female
80-90	7	2
91-100	12	3
101-110	20	11
111-120	17	8
121-130	14	6
> 130	-	-
Total	70	30

In the present study the maximum level achieved ranged from T_6-T_{10} and in majority of the males (58 patients) and females (24 patients) the maximum level was T_{10}.

In the present study, the time taken to achieve maximum sensory blockade ranged from 2-8 minutes. In majority of the males (43 patients) it ranged from 4-6, while in females (26 patients) it ranged from 5.1-7 minutes.

Table 6: Maximum level achieved

Level	No. of Cases	
	Male	Female
T_6	1	1
T_8	11	5
T_{10}	58	24
> T_{10}	-	-
Total	70	30

Table 7: Time of Maximum Sensory Blockade

Times (Minutes)	No. of Cases	
	Male	Female
< 4	2	2
4	13	4
5	16	11
6	27	13
7	9	-
> 7	3	-
Total	70	30

Discussion

Spinal anesthesia is a time honoured procedure for producing surgical analgesia and its importance is increasing day by day as it possesses certain advantages over general anesthesia.

Though a number of drugs have been used for inducing spinal anesthesia their use has been usually associated with occurrence of undesirable side effects such as hypotension and bradycardia. Thus, they are not ideal for use in trauma and emergency cases that are susceptible for hypotension and shock.

Therefore, there is a need for find out a safer, effective and reliable spinal anesthetic, which has rapid onset of action, excellent analgesia, satisfactory muscle relaxation with a wide margin of safety.

Ketamine a phencyclidine derivative is a potent analgesic and its sympathomimetic effects may be useful in trauma and emergency cases. The present study is to evaluate the efficacy of ketamine given intrathecally as spinal anesthesia agent and to study its onset of sensory blockade, duration of sensory blockade, motor blockade and the occurrence of delirium reaction and other complications if any and whether ketamine can be safely recommended for lower abdominal surgeries.

Patient Characteristics in the Study Group

In the present study 100 patients satisfied the criteria for the study. Male to female ratio was 2.33:1. Majority of males and female were in 26-55 years of age group.

Sensory Parameters

Onset of Sensory Blockade

In the present study the onset of sensory blockade ranged from (2-4 minutes) mean 2.60±0.64 .

In the study conducted by Dipasri Bhattacharya in 2004 [3], it was reported that onset of sensory blockade ranged from 1-2 minutes with a mean of 1.38±0.05 (SE).

In the present study the onset of sensory blockade was delayed compared to their study, the reason could be the use of hyperbasic solution (5% dextrose was added), which might have enhaced the fixation of the drug and led to faster onset of sensory blockade.

Duration of Sensory Blockade

In the present study duration of sensory blockade ranged from 58-108 minutes with a mean (85.48±11.68). In the study conducted by Dipasri Bhattacharya in 2004 [3], it was reported that duration of sensory blockade ranged from 90-140 minutes with a mean of 122±3.34.

In the present study, duration of sensory blockade was taken as time taken for two segment recession in their study duration of sensory blockade was calculated as the regression time of sensation to return to the L2-3 dermatome.

Maximum Level Achieved

In the present study, the maximum level achieved ranged from T6-T10. In majority of the male and females, the maximum level achieved was T10.

In the study conducted by Bion JF in 1984 [4], they reported that the maximum level achieved ranged from T10-T12 in majority of them maximum level achieved was T10. The present study was in accordance with their study.

Time Taken for Maximum Sensory Blockade

In the present study, the time taken for maximum sensory blockade ranged from 2-8 minutes.

In the study conducted Bion JF [4], the time taken for maximum sensory blockade ranged from5-7 minutes.The present study is in accordance with their study.

Degree of Sensory Blockade

In the present study, the degree of sensory blockade was grade-I in all the 100 patients.

In the study conducted by Dipashri Bhattacharya in 2004 [3], it was reported that 100% of the patients had grade-I sensory blockade. The present study is in accordance with their study.

Motor Blockade

Onset of motor blockade: in the present study, the onset of motor blockade ranged from 2-5 minutes with a mean of 4.33±0.60. In the study conducted by Dipasri Bhattacharya in 2004 the onset of motor from 2-5 minutes with a mean of 2.35±0.07. The present study is in accordance with their study.

Duration of Motor Blockade

In the present study, the duration of motor blockade ranged from 80-126 minutes with a mean of 108.36±11.78. In the study conducted by Dipasri

Bhattacharya in 2004, it was reported that the duration of motor blockade ranged from 90-140 minutes with a mean of 127±1.79.The present study is in accordance with their study.

Degree of Motor Blockade

In the present study, the quality of motor blockade assessed by the Bromage scale was grade-III in all the 100 patients. In the study conducted by Dipashri Bhattacharya in 2004, it was reported that 100% of the patients had grade-III motor blockade.The present study is in accordance with their study.

Conclusion

Ketamine with adrenaline produced a quicker onset of sensory blockade with good muscle relaxation

References

1. Longnecker DE, Tinker JH, Morgan GE Jr. Principles and Practice of Moshy; 1998.
2. Schug et al. New drugs for neuraxila blockade. Anaesthesilogy. 1999 Oct; 12(5):551-55.
3. Bhattacharya D, Banarjee A. A comparative study of clinical effects of intrathecal hyperbaric bupivacaine and ketamine in hyperbaric solution. Indian Journal of Anaesthesia. 2004; 48(2)L:116-120.
4. Bion JF. Intrathecal ketamine for war surgery – A preliminary study under field conditions. Anaesthesia. 1984 Oct; 39(10):1023-28.

STATEMENT ABOUT OWNERSHIP AND OTHER PARTICULARS

"Indian Journal of Anesthesia and Analgesia" (See Rule 8)

1. Place of Publication	:	Delhi
2. Periodicity of Publication	:	Quarterly
3. Printer's Name	:	**Asharfi Lal**
Nationality	:	Indian
Address	:	3/258-259, Trilok Puri, Delhi-91
4. Publisher's Name	:	**Asharfi Lal**
Nationality	:	Indian
Address	:	3/258-259, Trilok Puri, Delhi-91
5. Editor's Name	:	**Asharfi Lal** (Editor-in-Chief)
Nationality	:	Indian
Address	:	3/258-259, Trilok Puri, Delhi-91
6. Name & Address of Individuals who own the newspaper and particulars of shareholders holding more than one per cent of the total capital	:	**Asharfi Lal** 3/258-259, Trilok Puri, Delhi-91

I Asharfi Lal, hereby declare that the particulars given above are true to the best of my knowledge and belief.

Sd/-

(Asharfi Lal)

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.26

Effect of use of oral Pregabalin as an adjunct in Spinal Anaesthesia

Amrita Panda*, Jagadish Chandra Mishra**

Abstract

Background: Pain relief with minimal side effect in post operative surgical patients is essential for early mobility and recovery.

Objective: This study was conducted to find out whether preoperatively oral pregabalin used as an adjunct in spinal anaesthesia has any effect in the prolongation of duration of dose of first rescue analgesic requirements, effect on anxiety, sedation scores and patient satisfaction level in the post operative period.

Patients and Methods: This is a randomized double blind placebo controlled study conducted in 60 ASA 1&2 patients undergoing lower limb orthopaedic surgery under spinal anaesthesia. The patients are divided randomly into two groups. Group -1 patients the control group where placebo drug is given one hour prior to surgery as an adjunct in spinal anaesthesia and Group-2 patients 75mg oral pregabalin is given similarly. VAS Scale was used for anxiety score and Ramsay Sedation Scale was used for sedation score, patient satisfaction level, duration of dose of first rescue analgesic requirements were measured.

Results: Demographically there was no significant difference between both the groups. Comparison of time of first rescue analgesia there was statistically significant difference between Group-1 and Group-2 patients(p value >0.95) Sedation scores and anxiety scores are just significant between both the groups. No significant difference was found in the haemodynamic parameters between the groups.Patient satisfaction was better in the treated group as compared to the control group.

Conclusion: From this study we concluded that oral pregabalin reduced the anxiety level and also prolonged the time period for the need of first dose of rescue analgesia. No side-effects of Pregabalin were noted and patient's satisfaction was better in the treated group thanin the control group.

Keywords: Postoperative Pain; Calcium Channel Modulators; Spinal Anaesthesia; Rescue Analgesia; Sedation; Anxiety.

Introduction

Eighty percent of patients undergoing surgical procedures experience postoperative pain and require adequate pain relief for which many drugs are available nowadays [1]. Postoperative pain following orthopaedic surgeries has been shown to be a significant factor that delays patient recovery and contributes to serious complications. It may also result in larger use of healthcare resources and ultimately leads to poor outcomes. Spinal adjuvant drugs have been used in the subarachnoid anaesthesia. Clonidine is the most commonly used as an adjuvant in neuroaxial anaesthesia and analgesia[2].

Also calcium channel modulators like pregabalin and gabapentin are being increasingly used for postoperative pain management effectively. This has the advantage of avoiding the sideeffects of opioids. Pregabalin and Gabapentin are structural analogues of GABA-Gamma-aminobutyric acid. Pregabalin selectively binds to alpha-2 subunit of voltage dependent calcium channels which results in reduction of neurotransmitter release and hence decrease in neuronal hyper excitability [4,5]. Pregabalin is several times more potent than gabapentin. It is rapidly absorbed orally, achieves peak plasma levels within 30 minutes to 2 hours [6]. Pregabalin

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Received on 14.12.2016
Accepted on 28.12.2016

has fewer side-effects with the most common adverse events being dizziness and somnolence.Any visceral irritation causes release of excitatory neurotransmitters which causes pain[7] and spinal anaesthesia is commonly given for orthopaedic procedures. So,the main objective of our study is to find out whether preoperative pregabalin has any effect in the postoperative analgesic requirement, anxiety, sedation scoreand satisfaction in patients undergoing lower limb surgery under spinal anaesthesia.

Patients & Methods

After obtaining clearance from ethics committee of our institution and informed consent from the patients, a randomized double blind placebo controlled study was conducted.60 patients ASA-1and 2 aged 20-60 years undergoing lower limb orthopaedic surgical procedures were chosen.

The exclusion criteria were patient refusal for spinal anaesthesia,local sepsis,spinal deformity, coagulopathy and bleeding disorders and patients on anticoagulant therapy.

Using computer derived random number sequence patients were allocated into two groups by means of sealed opaque envelopes, Group-1(control) and Group-2(study). Group-1 patients received the placebo drug given one hour prior to surgery in patients undergoing spinal anaesthesia. Group-2 patients received preoperative pregabalin 75mg one hour prior to surgery in patients undergoing spinal anaesthesia. All the patients received 0.5% hyperbaric bupivacaine 0.3mg/kg with 30 microgram clonidine intrathecallyusing 25 gauge Quincke needle in sitting posture.Preoperatively patients were nil per orally for 8 hours prior to the procedure.They were shifted to the preoperative room where baseline parameters and scales were assessed before the drug was given and transfer to the operation theatre. The scales of assessment chosen were Visual AnalogueScale(VAS) for anxiety[15].

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VAS score for anxiety

Baseline score was assessed in the preoperative room and one hour after premedication.Scoring of sedation was done using the Ramsay Sedation Score[15].

Score		Response
1	-	Anxious, agitated or restless or both
2	-	Co-operative,oriented,tranquil
3	-	Responding to commands only
4	-	Brisk response to light glabellar tap
5	-	Sluggish response to light glabellar tap
6	-	No response to light glabellar tap

Then the patients were transferred inside the operation theatre room and monitors placed like pulseoximetry,non-invasive blood pressure and electrocardiogram.Infusion was started using 18 gauge intravenous cannula with Ringer's lactate@15ml/kg and subarachnoid block was administered under aseptic measures with 25 gauge Quincke needle at L2-L3 or L3-L4 in sitting posture with 0.5% hyperbaric bupivacaine 0.3mg/kg with 30 microgram clonidine.Baseline parameters noted prior to start of anaesthesia were heart rate and blood pressure.

The following parameters were also measured:-

1-Demographic details like age,weight and height of the patients.

2-Blood pressure,heart rate of patients every 10 minutes intraoperatively and postoperatively every 30 minutes for first 4 hours.

3- The time of requirement of first rescue analgesic drug was noted and rescue analgesia intravenous diclofenac 75mg was administered when patient complained of pain on Visual Analogue Scale>5 in both the groups.Pain was measured using the Visual Analogue Scale 0 ————10(no pain——worst pain)where patients complaining of pain on VAS>5 were treated with first dose rescue analgesia.

4-Sedation and anxiety score,any adverse effect and patient satisfaction level were measured in the postoperative room.The patient's satisfaction for pain relief was recorded as-

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(Not satisfied) (highly satisfied).

Follow up & Results

Table 1:

N	Group 1 30	Group 2 30	P Value	Remark
Age (Years)	41.30+_10.02	40.80+_11.13	0.938	>0.05
Median	45	32		NO SIGNIFICANCE

(Inter Quartile Range)	(32-49)	(28-45)		
Height (cms)	159.5+_7.95	158.10+_8.04	0.891	>0.05
Median	160.4	159.6		NO SIGNIFICANCE
(Inter Quartile Range)	(157-162)	(157-164)		
Body weight (kgs)	52.20+_2.45	51+_2.91	0.861	>0.05
Median	50	48		NO SIGNIFICANCE
(Inter Quartile Range)	(48-54)	(47-55)		
Sex				
Male (%)	16 (53%)	17 (57%)		
Female (%)	14 (47%)	13 (43%)		

Table 2: Comparison of VAS Score for anxiety

	Preoperative [$Mean \pm SD$]	Postoperative [$Mean \pm SD$]
Group I (Control)	70.30 ± 11.96	71.20 ± 8.56
Group II (Treated)	76.30 ± 10.25	58.58 ± 9.87

Table 3: Probability value (Anxiety)

Difference between	Mann Whitney U Value	Standard Error of U	P value	REMARK
Placebo and Pregabalin	18.36	38.632	0.95	SIGNIFICANT

Table 4: Comparison of Sedation Score (Ramsay)

Score	Placebo (Control)	Pregabalin	Total
1	15	5	20
2	8	13	21
3	4	5	9
4	2	3	5
5	1	3	4
6	0	1	1
Total	30	30	60

Table 5: Probability value (Sedation)

Difference between	Mann Whiteny U Value	Standard Error of U	P value	Remark
Placebo and Pregabalin	19.28	43.982	0.95	Significant

Table 6: Time required for first rescue analgesia

	Placebo(Control) [$Mean \pm SD$]	Pregabalin [$Mean \pm SD$]	t-Value (degrees of freedom=58)	P Value	REMARK
N	30	30			
Time (Minutes)	232.45 ± 4.12	360.80 ± 2.58	8.98	> 95%	SIGNIFICANT

Table 7: Comparison of mean Blood Pressure (MBP)

	Placebo(Control) [$Mean \pm SD$]	Pregabalin [$Mean \pm SD$]
N	30	30
Preoperative	96.95 ± 6.92	99.25 ± 9.02
Postoperative	92.39 ± 7.25	88.36 ± 4.85
t-Value (degrees of freedom=29)	0.062	11.235
P Value	< 0.05	> 0.95
Remark	No Significance	Significant

Table 8: Comparison of Patient Satisfaction(VAS)

	Placebo(Control)	Pregabalin
N	30	30
$Mean \pm SD$	36.67 ± 11.52	78.32 ± 9.83

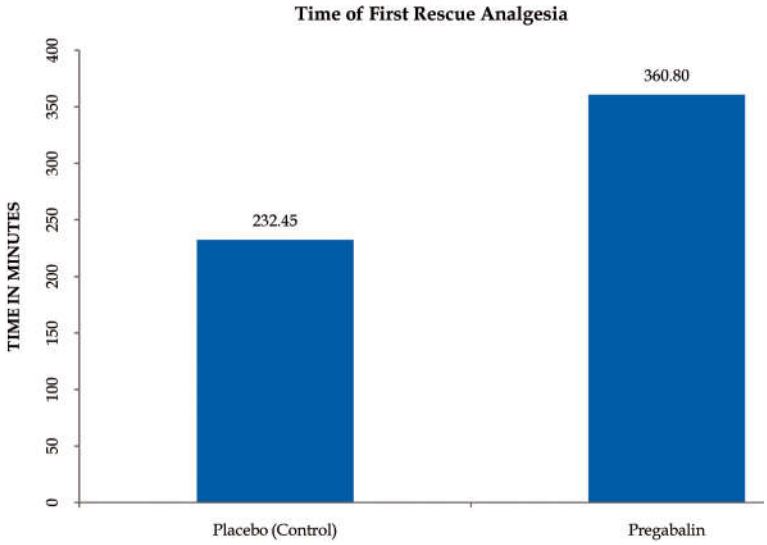

Fig. 1: Time of first rescue analgesia

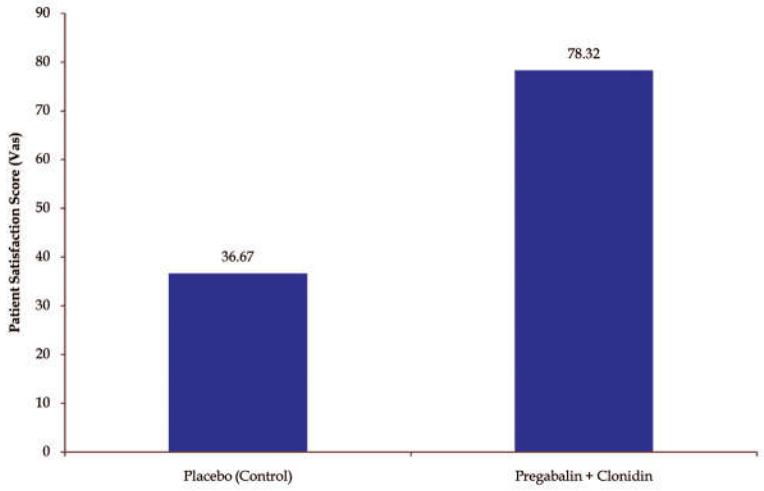

Fig. 2: Patient satisfaction score

Discussion

Postoperative pain is a model of mixed pain with nociceptive as well as neuropathic components. Postoperative pain leads to local inflammatory response, stimulation of nociceptors and nociceptive pain. Surgical stimulus also leads to sensitization of dorsal horn neurons,which is associated with augmentation of pain. This is referred to as central sensitization and represents the neuropathic component. Recent evidence suggests that alpha 2-D subunit calcium channel ligands like gabapentin and pregabalin,may aid in providing effective postsurgical analgesia[12].They mitigate central sensitization by calming down hyper excited dorsal horn neurones. This discovery has opened up the possibilities of using such drugs in the perioperative setting to counter the neuropathic component of postsurgical pain. These drugs were introduced as anticonvulsants presumably due to their ability to reduce neurotransmitter release from activated epileptic neurons[12]. Similarly their ability to reduce

neurotransmitter release from activated neurons in pain pathways and fear circuits may contribute to their role as an adjuvant in pain management and as anxiolytics.

Experimental models of neuropathic pain and inflammatory hyperalgesia have shown that gaba-aminobutyric acid analogues such as gabapentin and pregabalin have antinociceptiveand antihyperalgesic properties[8]. Central neuronal sensitization may result in an amplification of postoperative pain [9]and that preoperative administration of these drugs may reduce the degree of central sensitization[10]. Due to its absence of hepatic metabolism, it has good pharmacokinetic properties and fewer drug interactions which make it a better drug than Gabapentin [11].

Pregabalin targets the alpha2-D subunit of voltage gated channels.The reduction in calcium flow through the channels decreases neuronal transmission in activated neuronal circuits, which may lead to decreased pain perception and analgesia [3].

The use of pregabalin in acute postoperative pain management has been evaluated in recent studies.In the first trial investigating the postoperative analgesic effect of pregabalin, a dose of 300mg pregabalin administered after dental operation was more effective in attenuating acute postoperative pain than placebo. It also had a longer duration of analgesia than ibuprofen [17].

Tippana and co-workers analysed 22 randomized, controlled trials examining the analgesic efficacy, adverse effects and clinical value of gabapentinoids(pregabalin, gabapentin) in postoperative pain. They concluded that gabapentinoids effectively reduce postoperative pain, opiod consumption and opiod related side effects after surgery [13].

In another study, Jokela and colleagues observed that preoperative administration of 300mg pregabalin, followed by the same dose repeated after 12 hours in patients undergoing laproscopic hysterectomy decreases oxycodone consumption. They also noted that the improved analgesia is associated with an increased incidence of adverse effects such as dizziness and blurred vision[14].

In a subsequent study by Jokela and colleagues [14] premedication with pregabalin 150 mg in patients undergoing daycase gynaecological surgery resulted in an improved quality of analgesia, but there was no difference in the amount of postoperative analgesics required or the degree of drowsiness.

In our study (Table 1) there was no significant difference as regards to age,weight and height of patients between the two groups(p-values-0.838 and 0.862 respectively), which is similar to other studies.

Anxiety scores (Table 2 and 3) were appreciably less in the treated group than placebo (Mann Whitney U=18.36, p value>0.95). R. Jokela et al [14] showed no reduction in anxiety scores with 75mg or 150mg Pregabalin. Also in the study by Kohli et al [16] no difference in anxiety scores were noted with higher doses of pregabalin like 150mg or 300mg,but the scores were better than the placebo group.

In our study similarly also the number of patients with various sedation scores (Table 4 and 5) increased in the treated group than the control group for which the Mann Whitney U value=19.28;p>0.95.No sideeffects like nausea, vomiting, dizziness,blurred vision were noted and patients were more satisfied in the treatment group than the control group.

The incidence of sedation is more with higher doses of pregabalin(150mg, 300mg) as in the same study by Kohli et al[15].

In a study conducted by R. Jokela et al[14] they found that 300mg pregabalin was more effective than pregabalin 150mg. The incidence of dizziness, headache, blurred vision were higher in the 300mg pregabalingroup. Also other studies showed that pregabalin has somnolence and dizziness as the most common side effects.

In our study of the time required for the first rescue analgesic drug(Table 6 and Figure 1) is more in the treated group than placebo(for 58 degree of freedom tc=8.98 with p value>0.95)

In the study conducted by Kohli et al[15]pregabalin 300 mg showed more effective prolongation of analgesia than pregabalin 150mg or placebo after spinal anaesthesia and this was correlating with the half life of pregabalin which is 4.6-6.8 hours.The advantage was that along with prolongation of analgesia there was no haemodynamic instability.

Agarwal et al [16] showed that single dose of pregabalin(150mg) was effective in reducing postoperative pain after laparoscopic cholecystectomy.

Hill et al [17] compared pregabalin(50mg, 300mg) to placebo in patients undergoing elective surgery for molar extraction and found that pain relief was better in the 300mg pregabalin group.

In a study conducted by Wichari et al [18] 300 mg pregabalin administered one hour preoperatively before abdominal hysterectomy significantly reduced pain score and improved satisfaction score at 24 hour postoperatively.

In our study conducted in our instituition significant difference in lowest mean blood pressure(Table 7) was observed between preoperative and postoperative periods in the treatment group(calculated value of tc=11.235; p0.95)No sideeffects like nausea, vomiting, dizziness, blurred vision were noted in our study and also patients were more satisfied in the treatment group than the control group(Table 8 and Figure 2). There was reduction in the haemodynamic parameters both blood pressure and heart rate due to the effect of anaesthesia and adjuvants used, but not much significant difference was found between both the treated and the control group.

Similarly in the study conducted by R. Jokela et al[14] they found that 300mg pregabalin was more effective than pregabalin 150mg. The incidence of dizziness, headache and blurred vision were higher in the 300mg pregabalingroup.Also other studies showed that pregabalin has somnolence and dizziness as the most common sideeffects. Also many other studies show reduction in blood pressure and heart rate in all the groups which is significant between pregabalin and placebo group.

Similarly the study by Kohli et al[15]patient satisfaction showed good results with pregabalin 300mg group than 150mg group than placebo. We did not use pregablin at higher doses as mentioned in various literatures, so we do not know whether this is the ideal dose which could be used alone with adjuvants in spinal anaesthesia.The limitation of our study was that the study period was restricted upto the time limit when the first dose of rescue analgesic drug was administered.

Declaration: The authors there is no conflict of interest regarding the publication of the paper.

Conclusion

From this study we conclude that oral pregabalin at the dose of 75mg does reduce the anxiety level and also prolongs the time period for the need of the first dose of rescue analgesic requirement,patients were more satisfied than the placebo group and no sideeffects were noted.

References

1. Apfel baum IL,ChenC,MehtaSS,GanTJ.Postoperative pain experience:results from a national survey suggest postoperative pain continues to be undermanaged.AnesthAnalg 2003; 97:534-40.
2. VictorM, WhizarLugo, JuanC, Flores-Carillo. Intrathecal Clonidine as spinal Anaesthesia Adjuvant-Is there a magical dose?AnestMex 2007; 19:130-134.
3. Miller's Anaesthesia: edited by Ronald D Miller, Elsevier publication: Eighth edition, 2015.
4. Kavoussi R.Pregabalin:From molecule to medicine. Euro Neuropsychopharmacol 2006; 16(Suppl 2):128-33.
5. Shneker BF, McAuley JW. Pregabalin: a new neuromodulator with broad therapeutic indications. Ann Pharmacother2005; 39:2029-37.
6. Frampton JE,ScottLJ.Pregabalin in the treatment of painful diabetic peripheral neuropathy. Drugs 2004; 64:2813-20.
7. Feng Y,CuiM,WillisW.Gabapentin markedly reduces acetic acid induced visceral nociception. Anesthesiology 2003; 98:729-33.
8. Kong VK,IrwinMG.Gabapentin :a multimodal perioperative drug.Br J Anaesth 2007; 99:775-86.
9. Wolf CJ,ChongMS.Preemptive analgesia treating postoperative pain by preventing the establishment of central sensitization.AnesthAnalg 1993; 77:362-79
10. Werner FM, FredrickM, PerkinsK, HolteK, Pederson JL, Kehlet H. Effects of gabapentin in acute inflammatory pain in humans. RegAnesthAnalg 1993; 77:362-79.
11. Shneker BF,McAuley JW .Pregabalin: a new neuromodulator with broad therapeutic indications. Ann Pharmacother 2005; 39:2029-37.
12. Stahl SM.Anticonvulsants and the relief of chronic pain:Pregabalin and gabapentin as alpha 2 delta ligands at voltage gated calcium channels.JClin Psychiatry 2004; 65:596-7.
13. Tippanna EM,HamunenK,KontinenVK,KalsoE.Do surgical patients benefit from perioperative gabapentin/pregabalin?A systematic review of efficacy and safety.AnesthAnalg 2007; 104:1545-56.
14. JokelaR,AhonenJ,TallgrenM,HaanpaaM,KortilaK. Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after daycase gynaecological surgery.Br.J Anaesth 2008; 100:834-40.
15. KohliM, MuraliT, BograJ. Optimization of subarachnoid block by oral pregabalin for hysterectomy. Journal of Anaesthesiology Clinical Pharmacology 2011; 27:101-105.
16. A.Agarwal, S.Gautam, D.Gupta, S.Agarwal, P. K. Singh. Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy.BritishJounal of Anaesthesia 2008; 101(5):700-4.
17. Hill CM, Balkenohl M, Thomas DW, Walker R, MatheH, MurrayG.Pregabalin in patients with postoperative dental pain.Eur J Pain 2001;5:119-24.
18. Wichai Iltichackulthol MD,Tanit VirankabutraMD, MutitaKunopa rtMD, WachirapolKhamhom MD, BN.J Med Assoc Thai 2009; 92(10):1318-23.

Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.27

Reduction in Anaesthetic Requirement and Better Perioperative Hemodynamic by Dexmedetomidine, in Spine Surgery

Mohammed Yahya*, Srinivas Kakhandki, Seema Farhat***, Md Furquan Inamdar*****

Abstract

Aims and Objectives: The present study was conducted to know the efficacy of dexmedetomedine infusion on perioperative hemodynamics and reduction in anesthetic requirement during general anesthesia in spine surgeries.

Materials and Methods: After obtaining institutional ethical committee approval, the study was undertaken at Mahadevappa Rampure Medical College, Gulbarga. After obtaining informed written consent, 60 patients of ASA grade 1 & 2 were randomly allocated into two groups of 30 patients each,as Group C and Group D. The age group was 20-60 years of either sex undergoing elective spine surgery under GA. In group D, patients received dexmedetomidine as 1µg/kg over 10min before induction of anesthesia and maintained with 0.5-0.7µg /kg/hr infusion during anesthesia, and group C was taken as control. Hemodynamic changes and anesthetic requirement were recorded perioperatively.

Results: Dexmedetomedine causes significant reduction in heart rate and mean arterial pressure, blunted tachycardia and hypertensive response to intubation and extubation ($p<0.05$), maintained better hemodynamic intraopertively. Also it reduced the requirement of fentanyl(50%), and inhalational agent isoflurane (29-33%) during general anesthesia.

Conclusion: Dexmedetomedine reduces the requirement of opioids and inhalational agent during general anesthesia and provide stable hemodynamics intraoperatively.

Keywords: Dexmedetomedine; Fentanyl; General Anesthesia; Isoflurane.

Introduction

Dexmedetomidine, a highly selective α_2 agonist, have been used in the perioperative period for better hemodynamic stability. It possess sedative, anxiolytic and analgesic properties withoutcausing respiratory depression [1-4]. Also it reduces anesthetic and opioids analgesic requirementsduring perioperative period [5-7].

The mechanism of action of dexmedetomidine (dexmed) is unique, it causes presynaptic activation of the $\alpha_2$adrenoceptor, inhibits the release of norepinephrine, terminating the propagation of pain signals. Post synaptic activation of $\alpha_2$adrenoceptors in the central nervous system inhibits sympathetic activity and thus can decrease blood pressure(BP) and heart rate(HR). The analgesic effect of dexmed is different from opioids and can be used as an alternative to opioids in general anesthesia [8-10].

We carried out this prospective randomized controlled study to see the reduction in the requirement of isoflurane and fentanyl, and intraoperative hemodynamic stability by dexmedetomidine in lumbar spine surgeries during general anesthesia.

Materials and Methods

After obtaining institutional ethical committee approval, the study was conducted at MahadevappaRampure medical college, Gulbarga. An informed written consent was taken, 60 patients of ASA grade 1 & 2 were randomly allocated in two groups of 30 patients each, as Group C (control) and Group D (dexmed). Following patients were excluded, if patient has basal

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Received on 04.01.2017
Accepted on 09.01.2017

metabolic index more than 30kg/m^2, uncontrolled hypertension, severe respiratory disease such as asthama orischemic heart disease. All patients were premedicated with ondensetron 0.1mg/kg, midazolam 20µg/kg IV, induced with propofol 2mg/kg, vecuronium 0.1mg/kg IV and intubated. Anesthesia was maintained with O_2 and N_2O 50:50 in closed circuit system. In group D, patients received initial dose of dexmedetomedine as 1µg/kg over 10min before induction of anesthesia and then maintained with 0.5-0.7µg/kg/hras infusion during anesthesia. Group C patients received fentanyl 2µg/kg before induction, and Group D patients received 1µg/kg of fentanyl. Heart rate, blood pressure, inspired concentration of isoflurane were recorded before induction, intraoperatively at every 5, 10, 15, 20, 30, 40, 50, 60, 70, 80 and 90 min, and at extubation. Monitoring was done with ECG, NIBP, SPO_2, $EtCO_2$.

Heart rate and blood pressure were not allowed to increase more than 15% of the baseline values. If heart rate(HR) or mean arterial pressure(MAP) increases more than 15% of baseline values, Dexmed infusion titrated or fentanyl 1µg/kg was added or isoflurane concentration used to be increased by 0.1% in step wise manner. If HR and MAP still persists high, than other measures were taken to control it, and that case was excluded from the study. Heart rate of less than 50 beats/min was treated with ephedrine. MAP below 60mm of Hg was considered as hypotension and infusion dose of dexmed was reduced accordingly.

Dexmedinfusion andisoflurane was continued until the skin suture were initiated. Reversal was done with 0.01mg/kg glycopyrrolate and 0.05mg/kg of neostigmine IV, and patient extubated. Injparacetamol 1gm IV was given to all patients before extubation.

Statistical analysis was done with unpaired t-test and Kruskal-Wallis test. Chi-square test was used for categorical variables. Values were expressed as mean±SD, and a value <0.05 was considered as statistically significant.

Results

Both the groups were similar in terms of age, gender, weight and duration of surgery (around 80 mins). Before induction of anesthesia, HR and MAP were similar between the two groups. Intra operatively there was significant decrease in the HR and MAP in group D at all given time points compared to group C. Maximum average fall in MAP (6.8%) and HR (22.2%) was seen at 50min and 60 min, compared to baseline value, respectively, in group D, whereas there was average increase in HR (8.1%) and MAP (7.7%) at 5min after induction, compared to baseline value, in group C,.(P<0.05) Figure 1 and 2.

There was significant decrease in inspired isoflurane concentration, between 29-33%, at all time points, in group D as compared to group C (P<0.05) Figure 3. Also fentanyl requirement was less in group D, 1µg/kg, as compared to group C, 2µg/kg, (50% reduction) to maintain the HR and BP within the 15% of baseline values at all the time. In group D 5 patients developed bradycardia, and were treated with ephedrine, and 3 patients required supplemental analgesia.

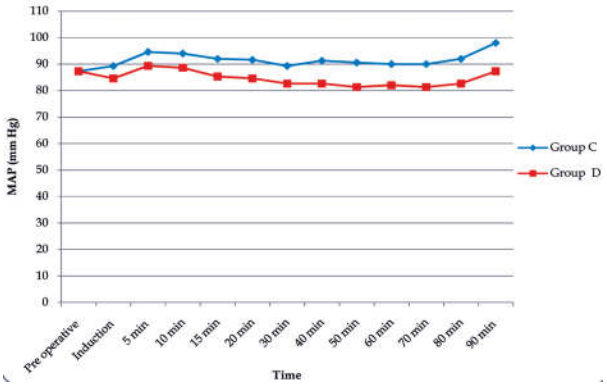

Fig. 1: Graph showing mean arterial pressure at different time points

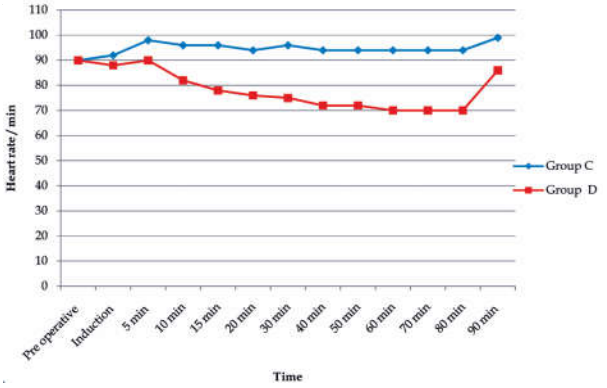

Fig. 2: Graph showing heart rate at different time points

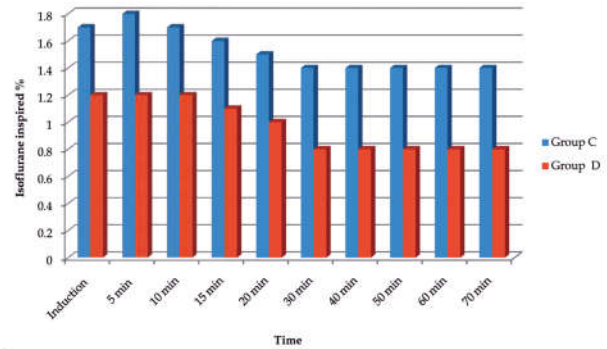

Fig. 3: Graph showing inspired concentration of Isoflurane at different time points

Discussion

The initial dose of dexmed blunts the pressor response to laryngoscopy and endotracheal intubation [11]. In our study also Dexmed reduced HR and MAP by an average of 8.1% and 5.6% respectively, following laryngoscopy, compared to control group. Dexmed also maintained better intraoperative hemodynamic compared to control group. In a study done byAhoM, et al [11] it showed that the increase in blood pressure or heart rate did not differ from that of the saline group. In our study HR and MAP were less at all time points compared to control group. It may be because we used 1μg/kg of fentanyl and dexmed dose was 0.5-0.7μg/kg compared to Aho et al study, where they did not use fentanyl and dexmed dose was 0.3 μg/kg.

Dexmed has been shown to reduce perioperative dose requirements for fentanyl [12] and isoflurane [13,14]. In our study there was reduction in the fentanyl requirement by 50% and isoflurane requirement by 33% throughout the intraoperative period. In a study conducted by Khan zp et al [15], showed 35 -50% reduction of maintainance concentration of isoflurane with low to high dose of dexmedetomidineon healthy human volunteers. This larger reduction in isoflurane requirement seen when compared to our study might be due to the higher doses of dexmed used in that study,(up to 2.85μg/kg/hr) and type of study group(volunteers).

In another study done by Chirag RP, et al [16], there was reduction in the fraction of inspired sevoflurane by 13%. This may be due to not using fentanyl in that study as compared to our study where we used 1μg/kg of fentanyl in dexmed group, further they have used entropy as assessment method, which may be better than hemodynamic monitoring.

Reduction in isoflurane requirement of our study, by 30%, is consistant with the study done by AhoM et al [11], done on patients undergoing abdominal hysterectomy. In this study they used hemodynamic monitoring for assessing depth of anaesthesia, similar to our study.

In our study there was reduction in fentanyl requirement by 50% in Dexmed group, because of opioid sparing effect. Aho MS et al [17], showed 33% decrease in morphine requirement with 0.4μg/kg dose of dexmed on patients undergoing tubal ligation. Cortinez et al [18], showed Dexmed when administered as infusion at a dose of 0.5μg/kg/hr has specific analgesic effect and provides visceral pain relief. Salman et al [19], showed Dexmed, when used as sole substitute for remifentanil in ambulatory gynecologic laparoscopic surgery, provides better peri-operative hemodynamic stability. Our study also showed better hemodynamic stability in the perioperative period by dexmed.

Our study has certain limitations like, we used hemodynamic monitoring as assessment tool for monitoring depth of anaesthesia, which is less reliable compared to BIS, EEG or entropy, or measuremenr of dexmed plasma concentration. These facilities are not available at our institute, and they are costly.

Conclusion

Dexmedetomidine provide better perioperative hemodynamic stability, blunts the pressor response to laryngoscopy and intubation. It also reduces opioid and inhalational agent requirement upto some extent during general anesthesia. For the better assessment of depth of anesthesia, BIS, entropy or plasma dexmed concentration to be used.

References

1. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose Dex infusions. AnesthAnalg. 2000; 90:699–705.
2. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperativepharmacokinetics and sympatholytic effects of dexmedetomidine.AnesthAnalg. 1997; 85:1136–42.
3. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. CurrOpinAnaesthesiol. 2005; 18:412–8.
4. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology. 2000; 93:382–94.
5. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration ofisoflurane by dexmedetomidine. Anesthesiology. 1997; 86: 1055–60.
6. Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Dexmedetomidineinfusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. AnesthAnalg. 1992; 75:940 – 6.
7. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth. 2006; 53:646 –52.
8. Cortinez LI, Hsu YW, Sum-Ping ST, Young C, Keifer JC, Macleod D, et al. Dexmedetomidine

pharmacodynamics: Part II: Crossover comparison of the analgesic effect of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology. 2004; 101:1077–83.

9. Salman N, Uzun S, Coskun F, Salman MA, Salman AE, Aypar U. Dexmedetomidine as a substitute for remifentanil in ambulatory gynecologic laparoscopic surgery. Saudi Med J. 2009; 30:77–81.
10. Techanivate A, Dusitkasem S, Anuwattanavit C. Dexmedetomidine compare with fentanyl for postoperative analgesia in outpatient gynecologic laparoscopy: A randomized controlled trial. J Med Assoc Thai. 2012; 95:383–90.
11. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology. 1991; 74:997–1002.
12. Scheinin H, Jaakola M-L, Sjovall S, Ali-Melkkila T, Kaukinen S, Turunen J, Kanto J: Intramuscular dexmedetomidine as premedication for general anesthesia. Anesthesiology 1993; 78:1065-75.
13. Erkola O, Korttila K, Aho M, Haasio J, Aantaa R, Kallio A: A comparison of IM dexmedetomidine and midazolam premedication for elective abdominal hysterectomy. AnesthAnalg 1994; 79:646-53.
14. Aho MS, Erkola OA, Scheinin H, Lehtinen A-M, Korttila KT: Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. AnesthAnalg. 1991; 73:112-18.
15. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers.1: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth. 1999; 83:372–80.
16. Chirag Ramanlal Patel, Smita R Engineer, Bharat J Shah, and S Madhu. The effect of dexmedetomidine continuous infusion as an adjuvant to general anesthesia on sevoflurane requirements: A study based on entropy analysis. J Anaesthesiol Clin Pharmacol. 2013 Jul-Sep; 29(3):318–322.
17. Aho MS, Erkola OA, Scheinn H, Lehtinen AM, Korttila KT. Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. AnesthAnalg. 1991; 73:112–8.
18. Cortinez LI, Hsu YW, Sum-Ping ST, Young C, Keifer JC, Macleod D, et al. Dexmedetomidine pharmacodynamics: Part II: Crossover comparison of the analgesic effect of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology. 2004; 101:1077–83.
19. Salman N, Uzun S, Coskun F, Salman MA, Salman AE, Aypar U. Dexmedetomidine as a substitute for remifentanil in ambulatory gynecologic laparoscopic surgery. Saudi Med J. 2009; 30:77–81.

Case Report

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.28

Bilateral Pleural Effusion: An Unexpected Complication after Right Subclavian Venous Catheterization for Total Parenteral Nutrition

Rayees Najib*, Suhail Sidiq, Iram Ali***, Mohammad Akbar Shah**, Abdul Waheed Mir****

Abstract

Bilateral pleural effusion occurred after total parenteral nutrition was administered via a right subclavian venous line. The most likely explanation for the fluid passage into both pleural cavities was migration of the tip of the catheter from within the vein into the mediastinum. Fluid can pass into both pleural cavities via anatomical communications, yet to be described, which exist between the two pleural cavities1 Central venous catheterization can cause various complications, which are on the whole simple to explain with our current knowledge of anatomy. This case report, however, describes a complication occurring after subclavian venous catheterization, which is difficult to explain with our current knowledge of anatomy. Reports of ipsilateral pleural effusion following misplacement of a central venous catheter are not unusual. However, communications between the two pleural cavities are not known. A similar case of bilateral pleural effusion following a left internal jugular venous cannulation has been reported [1]. A second case of bilateral pleural effusions following an attempted right subclavian venous cannulation has also been reported [2]. No explanation was provided for the complication in either paper.

Keywords: Pleural Effusion; Subclavian Vein; Total Parentral Nutrition.

Case Report

A 55 yr old man an operated case of Ca Colon with a 2 day history of severe abdominal pain associated with vomiting was admitted to hospital as an emergency case of acute abdomen. He underwent an uneventful redo laparotomy on the same day. The operative findings were a 50 cm section of infarcted terminal ileum and 10 cm of ischaemic terminal ileum in continuity with the caecum. A small bowel resection and ileostomy were done. The patient was shifted intubated from the emergency OT to SICU for further management and electively put on ventilator in view of severe metabolic acidosis and haemodynamic instability. The patient had already been put with a triple lumen central venous catheter into the right subclavian catheter in the emergency OT. A portable anteroposterior chest X-ray confirmed the position of the line to be satisfactory and a good central venous pressure (CVP) trace was measured with a transducer. Because this patient had a complex surgical history of multiple laprotomies for intestinal obstruction and severe metabolic acidosis and a high ionotropic requirement, he was admitted to surgical ICU after the surgery.

On the third day of his hospital admission, a decision was made to start parenteral feeding as he was not expected to absorb enteral feed and total parenteral nutrition (TPN) was started through the already placed right subclavian vein. There was no reason to doubt the position of the catheter in the vein as it was already confirmed

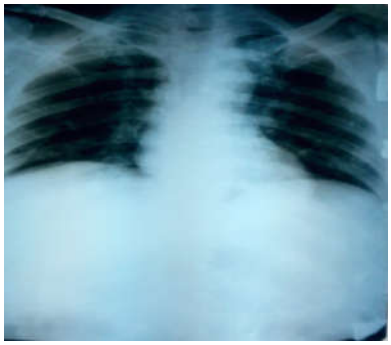

Fig. 1: Chest x ray AP view showing tip of the right subclavian line in a position consistent with placement within the superior vena cava on the ist day of admission to SICU

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Received on 10.11.2016
Accepted on 26.11.2016

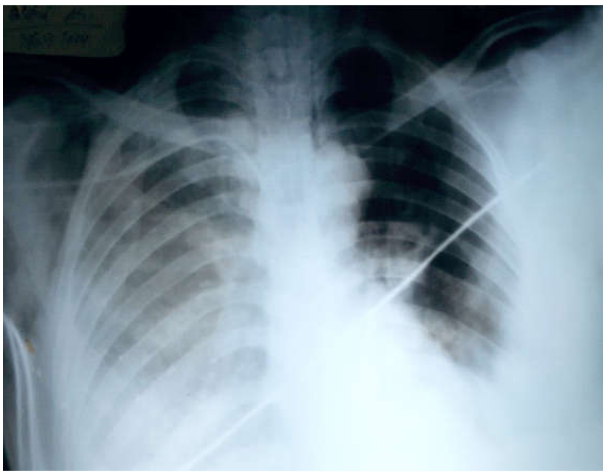

Fig. 2: Chest x ray AP view showing bilateral pleural effusion, more on the right side two days after commencement of the TPN.

from the chest x ray findings and the cvp tracing. The patient continued to be sick and could not be weaned from the ventilator in view of his haemodynamic instability and was treated as per our ICU guidelines for abdominal sepsis.

Two days after the commencement of TPN, the patient was noted to be worsening from the ventilation point of view. Both the Fio 2 requirement and the PEEP were increasing so as to maintain oxygen saturation above 90%. Arterial blood gas analysis showed a mixed pattern of worsening respiratory and metabolic acidosis. A repeat chest x ray showed b/l infiltrates and b/l pleural effusion with more effusion on the right side. Ultrasonography of the thorax confirmed large bilateral pleural effusions. The clinical picture was correlating with features of mild to moderate ARDS with unexplained pleural effusion. A 20 F chest drain was placed into each side of the chest. Over 500 ml of white, milky fluid was drained from the right hand side and another 300 ml of a similar milky coloured fluid was drained from the left hand side. As the fluid was suspected to contain TPN, the infusion was immediately stopped. It was not possible to aspirate blood, air or fluid from the venous cannula. Biochemical analysis of the drained fluid from both sides suggested that it was TPN. The two samples of drained fluid had glucose concentrations of 180mg/dl and 200mg/dl. The patient's blood glucose was 150mg/dl at the time. The glucose concentration of the TPN was 300mg/dl. The drained fluid was presumably a mixture of TPN and pleural fluid.

After placing the chest tubes the chest radiograph showed resolution of both pleural effusions and re expansion of both lungs. Antibiotic treatment with Ceftriaxone, Amikacin and metronidazole was continued, which had been started empirically after surgery. Over the next 3 days, further drainage from both chest drains was minimal. The ventilator parameters got improved with reduction in the Fio2 requirement and improvement in the Pao2 and PCO2, but the patient continued to be in severe abdominal septic shock. The antibiotics were changed as per the blood and peritoneal culture reports and the antibiotic sensitivity. But the patient succumbed to the severe sepsis and was declared dead after 8 days of ICU admission.

Discussion

This is a case of bilateral pleural effusions after attempted right subclavian venous cannulation. The most likely explanation of the bilateral effusions is the passage of TPN from the displaced catheter into the mediastinum and then into both pleural cavities via anatomical communications between them.

Reports of ipsilateral pleural effusion following misplaced central venous catheters are not unusual [3,4]. Possible channels communicating between the peritoneal cavity and the pleural cavity have also been reported [5]. However, no communications are known between the two pleural cavities. Hence, this case is unusual. Two similar cases of bilateral pleural effusions following attempted central venous catheter placement have been reported [1,2] although no explanations were suggested for the complication.

I.V. nutrition in patients who are unable to start enteral nutrition is a well established clinical technique. Because of their hypertonicity, these solutions must be given into a vessel with rapid blood flow and adequate mixing. This usually involves using a central venous catheter. Usual complications of central venous catheter placement include pneumothorax, pleural effusion, thrombophlebitis, brachial plexus injury, mediastinal haematoma and arterial cannulation [6].

Percutaneous insertion of central venous catheters are usually done by using surface anatomical landmarks (palpable or visible structures) with known relationships to the desired vein. The infraclavicular approach to the subclavian vein requires finding the correct location of the clavicle, suprasternal notch and sternocleidomastoid–clavicular triangle landmarks, proper positioning of the patient and operator and correct venepuncture point depth, direction and insertion angle. Similarly,

the various approaches to the internal jugular vein require thorough knowledge of this vein's course in relation to the sternocleidomastoid muscle and carotid artery.

Newer techniques, such as portable ultrasound devices, provide bedside imaging of the central veins during catheter placement [7,8]. The advantages of ultrasound guided central venous catheter placement include detection of anatomical variations, exact vessel location, avoidance of central veins with pre existing thrombosis that may prevent successful catheter placement and guidance of both guidewire and catheter placement after initial needle insertion. Although there is no doubt that these devices improve the safety of central venous catheter insertion, they may not prevent subsequent malposition or vascular perforation. Free aspiration of blood from the catheter, an appropriate pressure trace and the chest X- ray remain the routine methods of confirming the position of a catheter. Contrast studies are a gold standard for catheter position assessment.

Catheterization via the internal jugular vein may result in fewer malpositions than catheterization via the subclavian vein [6]. Generally, catheterization via the left internal jugular vein results in more malposition and vascular perforation than a catheter placed from the right internal jugular vein. This is because the right internal jugular vein runs into the right brachiocephalic vein in a fairly straight course whereas the left internal jugular vein forms a greater bend when it becomes the left brachiocephalic vein.

Catheter tip migration is a recognized phenomenon following central venous catheterization, occurring to some degree in approximately 17% of all percutaneously introduced catheters [9]. Poor position or aberrant location from catheter tip migration has been shown to occur in up to 6% of catheters [10]. However, only two similar cases of bilateral pleural effusions following central venous catheterization were found in the literature. This is a rare complication that is yet to be satisfactorily explained.

Refrences

1. Campagnutta E, Segatto A, Maesano A, Sopracordevole F, Viscentin MC, Scarabelli C. Bilateral hydrothorax and hydromediastinum after cannulation of the left internal jugular vein. Minerva Ginecol 1989; 41:479–83.
2. Simmons TC, Henderson DR. Bilateral pleural and pericardial effusions because of mediastinal placement of a central venous catheter. J Parenteral Enteral Nutr1991; 15:676–9.
3. Rudge CJ, Bewick M, McColl I. Hydrothorax after central venous catheterization.Br Med J 1973; 3:23–5.
4. Thomas CJ, Butler CS. Delayed pneumothorax and hydrothorax with central venous catheter migration. Anaesthesia 1999; 54:987–90.
5. Kanno T, Yoshikawa D, Tomioka A, Kamijyo T, Yamada K, Goto F. Hydrothorax: an unexpected complication after laparoscopic myomectomy. Anaesthesia 2001; 87:507–9.
6. Dunbar RD, Mitchell R, Lavine M. Aberrant locations of central venous catheters.Lancet 1981; 1:711–5.
7. Denys BG, Uretsky BF, Reddy PS. Ultrasound assisted cannulation of the internal jugular vein. A prospective comparison to the external landmark guided technique.Circulation 1993; 87:1557–62.
8. Gualtieri E, Deppe SA, Sipperly ME, Thompson DR. Subclavian venous catheterization: greater success rate for less experienced operators using ultrasound guidance. Crit Care Med 1995; 23:692–7.
9. Lang Jensen T, Nielsen R, Sorensen MB, Jacobsen E. Primary and secondary displacement of central venous catheters. Acta Anaesthesiol Scand 1980; 24: 216–8.
10. Vazquez RM, Brodski EG. Primary and secondary malposition of silicone central venous catheters. Acta Anaesthesiol Scand Suppl 1985; 81:22–6.

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Case Report

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4117.30

A Case Report of Ca. Breast Patient with Metastasis, DVT and Hypoalbuminemia Posted for Modified Radical Mastectomy Under Thoracic Epidural Anaesthesia: A Challenge for Anaesthesiologist

Kandarp G. Vyas*, Malini K. Mehta, Mukul V. Sharma*****

Abstract

Modified Radical Mastectomy, the surgical procedure for carcinoma of breast is routinely performed under general anaesthesia. Patient with lung metastasis and low serum albumin are at increased risk of perioperative morbidity and mortality. We report a case of carcinoma of breast with lung metastasis, right axillary vein thrombosis and low serum albumin (1.7 gm% with A/G ratio 0.61) managed successfully under sole thoracic epidural anaesthesia.

Keywords: Thoracic Epidural Anaesthesia; Modified Radical Mastectomy; Low Serum Albumin; DVT.

Introduction

Breast cancer is the commonest cancer in women and its incidence is increasing at an alarming rate. Modified radical mastectomy (MRM) is the standard surgical procedure for these patients, in which the entire breast is removed including the skin, areola, nipple and most axillary lymph nodes. MRM is usually performed under general anaesthesia. There may be delayed recovery and patient may require ventilatory support postoperatively in patients with lung metastasis and low serum albumin. There were studies reporting the use of thoracic and cervical epidural anaesthesia for MRM in patients of carcinoma of breast [1,2,3]. But these techniques are not practiced routinely. We report a case of carcinoma of breast with lung metastasis, right axillary vein thrombosis, low serum albumin, minimum ascites and mild bilateral pleural effusion managed successfully under sole thoracic epidural anaesthesia.

Case Report

35 years old female weighing 50 kg was admitted at Dhiraj hospital in the month of September with a complaint of lump in right side breast with pus discharge from it. Lump grew slowly and gradually over a period of 1 year and was painful. She also complained of weakness and dizziness. She had undergone a surgery for excision of small cyst in axilla 1 year back which was uneventful. There was history of deep vein thrombosis in right upper and lower limbs for last 3 months and was on heparin 500 units which were discontinued on the next day of admission. She had received transfusion of 8 PCV during the last 3 months. She had taken 6 cycles of chemotherapy, last was 10 days before the hospital admission.

On clinical examination patient was pale, oedema present on right upper and lower limbs. She was afebrile, pulse 108/minute and BP 90/60mm Hg. The size of the axillary lump was about 12 × 5 cms, which was necrosed with slough and bleeding. On examination of respiratory system air entry was reduced in right upper lobe. Rests of the systemic examinations were normal.

Laboratory investigations carried out were; Hb estimation 10.6 gm% on the day of operation. Total protein 4.5 gm%, Albumin 1.7 gm%, globulin 2.8 gm%, A/G ratio 0.61. INR on the day of admission was 4.9; it came to 1.25 on the day of operation. Blood urea, Serum creatinine, serum electrolytes, ECG and 2D echo were normal. X-ray chest showed ill defined soft tissue opacity in right axillary region suggestive of? metastasis. CECT showed ill defined heterogeneously enhancing soft tissue density mass lesion measuring approximately 12 × 5.4 cm involving right axillary region of breast, possibility of malignant mass lesion. There were multiple enhancing metastatic nodes

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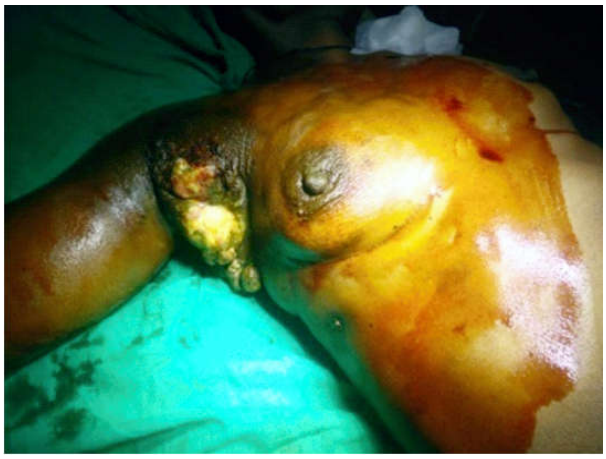
Received on 18.11.2016
Accepted on 26.11.2016

in right lateral aspect of chest wall. Partial thrombosis involving IVC. Minimal ascites and mild bilateral pleural effusion (Rt > Lt). Pet CT showed hypertrophic large nodal mass in the Rt. axilla with multiple discrete axillary and subpectoral nodes. Multiple lung nodules noted suggestive of likely metastasis. Right upper limb doppler showed right axillary vein thrombosis and right lower limb doppler showed DVT in right superficial femoral vein, profunda femoral and popliteal vein.

Patient was explained about the procedure of anaesthesia and informed written consent was obtained under ASA IV.



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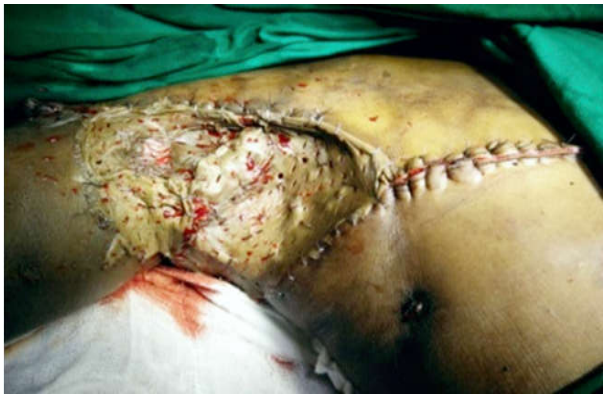

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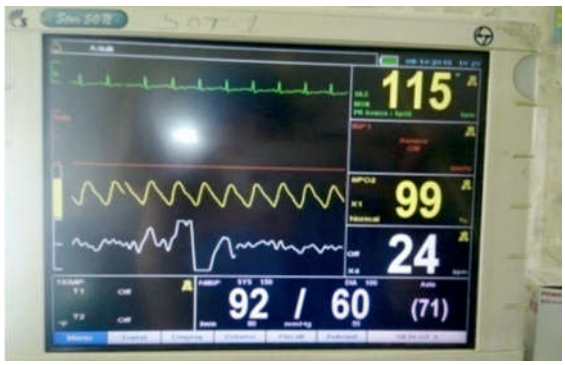

Fig. 3:

Anaesthesia Technique

On the day of surgery in the operation theatre femoral venous line was taken as peripheral line was not accessible and RL infusion started. L & T multipara monitor attached. Pulse - 150/ minute, BP - 110/70 mmHg and SpO_2 100%. Surgery planned under thoracic epidural anaesthesia. Patient was premedicated with 0.2 mg inj. glycopyrrolate and inj. ondansetron 4 mg intravenously. Patient was kept in sitting position. After aseptic and antiseptic precautions 18 no. tuohy needle was introduced at T_{6-7} level, after local anesthesia. Epidural space was identified by using loss of resistance with saline technique. 20 G epidural catheter was inserted 4 cm. into the epidural space through the needle in cephalad direction. The catheter was fixed and patient was made to supine. 9 ml of 0.75% inj. Ropivacaine and 50 µg of inj. Clonidine injected through the catheter(5cc+5cc). Anaesthesia was achieved in the area from C_7 to T_7 level in 15 minutes. After adequate sensory block patient was handed over to surgeon. At the time of axillary node dissection Inj. Ketamine 20 mg was given twice. Under local infiltration thin thickness skin graft taken and put over wound area. Duration of Surgery lasted for 2 hours. One PCV was given intra-operatively. Patient was hemody-namically stable. Because of the DVT of right upper limb, surgeon gave bandage encircling the chest wall and was to keep it for 6 -7 days and also if the surgeon wants to start heparin, at the end of surgery inj. Ropivacine 0.1% 10 cc was given by epidural catheter and catheter was removed .

Discussion

Thoracic epidural anaesthesia has been practiced in the perioperative management for thoracic, abdominal surgeries with advantage of rapid recovery, adequate analgesia and improved outcome [1]. However, it is not used frequently. We planned anaesthetic technique of sole thoracic epidural anaesthesia as there was lung metastasis, serum albumin only 1.7 gm%, minimal ascites and mild bilateral pleural effusion. The analgesia was adequate and surgical field was relatively blood less. O' Connor et al gave thoracic epidural anaesthesia for bilateral mammoplasty in a patient with Klippel-Feil syndrome with difficult airway and found to be successful [2]. Ashok Jadon highlighted the usefulness of cervical epidural analgesia in managing a complex situation of carcinoma breast

with associated periarthritis of shoulder joint and chronic regional pain syndrome of right upper limb [3]. Some retrospective studies reported improved survival with reduced prevalence of tumour recurrence after thoracic epidural anaesthesia or paravertebral block in cancer patients [4,5]. Snyder et al (2010) commented that anaesthetic technique and other perioperative factors had the potential to effect long term outcome after cancer surgery. Anaesthetic technique and drug choice can interact with the cellular immune system and effect long term outcome. The potential effect of intravenous anaesthetics, volatile agents, local anaesthetic agents, opiates and NSAID were reviewed and found that regional anaesthesia appeared to be beneficial.[5]

Successful use of high thoracic epidural anaesthesia avoids tracheal intubation hence also minimizes postoperative pulmonary complications [6]. The level should not exceed beyond C_5 as blockade of phrenic nerve might lead to horner's syndrome and stoppage of respiration might require ventilator support.

The only problem in our patient is hypotension and that was treated by 6 mg ephedrine and IV fluids.

While using thoracic epidural anaesthesia one has to assess risk and benefit ratio. Common complications are dural puncture, epidural haematoma and neurological injury. But these complications are rare with experienced anaesthetists.

Conclusion

Thoracic epidural anaesthesia is safe and better technique in patients of carcinoma of breast with lung metastasis, low serum albumin, minimal ascites and mild pleural effusion undergoing Modified Radical Mastectomy.

References

1. Freise H. Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. Br. J Anaesth. 2011; 107(6):859 -68 (cross ref.).
2. O'Connor PJ, Moysa GL, Finucane BT. Thoracic epidural anaesthesia for bilateral reduction mammoplasty in a patient with Klippel-Feil Syndrome. Anesth Analg. 2001; 92(2):514-6.
3. Ashok Jadon, Prashant S. Agarwal. Cervical epidural anaesthesia for radical mastectomy and chronic regional pain syndrome of upper limb-A case report. Indian J of Anesthesia. 2009; 53(6):696-9.
4. Exadaktylos AK, Buggy DJ, Moriarty DC, Mascha E, Sessler DI. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? Anesthesiology. 2006; 105(4):660-4 (cross ref.).
5. Snyder GL. Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. Br. J Anaesth. 2010 ;105(2):106-15 (cross ref.).
6. Groeben H. Effects of high thoracic epidural anaesthesia and local anaesthetic on bronchial hyperactivity. J. Clin. Monit Comput. 2000; 16(5-6):457-63.

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The second page should carry the full title of the manuscript and an abstract (of no more than 150 words for case reports, brief reports and 250 words for original articles). The abstract should be structured and state the Context (Background), Aims, Settings and Design, Methods and Materials, Statistical analysis used, Results and Conclusions. Below the abstract should provide 3 to 10 keywords.

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Standard journal article

[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540-7.

[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347-55.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3-9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792-801.

Unpublished article

[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

Personal author(s)

[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O, Kidd EAM,

editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. p. 7-27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

Reference from electronic media

[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/theme_health/HSQ 20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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