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To Study the N-Acetylcysteine and Vitamin C Effect on Oxidative Stress in Abdominal Sepsis and Control Patients with Different Weight Range

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Abstract

"Sepsis" was characterized as the foundational reaction to infecdon, showed by at least 2 of the conditions recorded above for SIRS. "Serious sepsis" was characterized as sepsis related with organ dysflmction, hypoperfusion, or hypotension. Hypoperfijsion and perfusion abnomialities may incorporate however are not constrained to lactic acidosis, oliguria, or an intense change in mental status. *Aim:* To Study the N-Acetylcysteine and Vitamin C effect on Oxidative stress in Abdominal sepsis and controle Patients with different weight range. *Material and Methods:* The present Study was conducted in the intensive care Unit of the the Dept of Anesthesiology, Rajiv Gandhi Institute of Medical Sciences, Kadapa. *Conclusion:* Along these lines, the sex, age and weight of the patients can impact the dimension of hematological and biochemical markers in patients with sepsis. In any case, since the statistic profile of the patients in our examination was similar between the nominal control and sepsis patients and furthermore between the gatherings, it didn't impact the in general outcome.

Keywords: SOD; GRx; CRP; Catalase.

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Interduction

"Sepsis" has its inception from a Greek word for disintegration or festering, and has been utilized in that setting since before Hippocrates (Geroulanos and Douka, 2006). In any case, in spite of the fact that the word, sepsis, has been utilized for over 2700 years, it is just moderately as of late that we have started to comprehend the pathophysiology of sepsis in any profundity (Vincent and Abraham, 2006). The rate keeps on expanding, with unsatisfactorily high death rates, not with standing the utilization of particular antibiotics, aggressive agent intercession, healthful help, and calming treatments. Not with standing high mortality, patients with serious sepsis or early septic stun invest drawn out times of energy in the ICU and are altogether more costly to treat than ICU patients without sepsis. It along these lines keeps on having noteworthy clinical and monetary ramifications and remains a zone that pulls in extreme research intrigue.

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E. Wilson, A. David and their group in 1990 compared the sedative effects of Midazolam and Propofol during spinal anesthesia [16]. In their study, 40 patients undergoing orthopedic surgery under spinal anesthesia received an infusion of either 1% Propofol or 0.1% Midazolam was given at a rate adjusted to maintain a similar level of sedation. The mean time to reach this required level was similar in both groups. Quality and ease of control of sedation were good in all patients.

Restoration of higher mental function was significantly faster following Propofol. Amnesia for the immediate postoperative period was significantly greater after Midazolam ($p = 0.0001$).

Hidaka S, Kawamoto M. et al., in 2005 did a comparative study on the effects of Propofol and Midazolam on cardio-vascular autonomic nervous system during spinal and epidural anesthesia [6]. Ninety eight patients were randomly divided into two groups, one group received Midazolam infusion while the other received Propofol infusion until BIS reached 75. The time to reach required sedation was 11 min in Midazolam group (Group I) while it was 6 min in Propofol group (Group II) ($p=0.0$). Fall in MABP was greater with Propofol. Recovery in with Midazolam was slower than with Propofol (18.6 ± 6.5 vs 10.10±3.65 min) ($p=0.00$). They concluded that both Midazolam and Propofol are effective sedatives, but onset and offset was quicker with Propofol, while Midazolam was more cardio stable.

In the present study it was found that both Midazolam and Propofol are effective sedatives in regional anesthesia with Propofol being faster onset and recovery from sedation where as Midazolam causes sedation which is hemodynamically more stable.

Hohener et al showed that Propofol is a substance nearest to an ideal agent for sedation during regional anesthesia because of its favorable pharmacokinetic profile with rapid onset and offset

Conclusion

Current study showed that both Midazolam and Propofol can be used for sedation in regional anesthesia. Propofol has a faster onset of action and recovery from the sedation where as Midazolam found to be more cardio stable.

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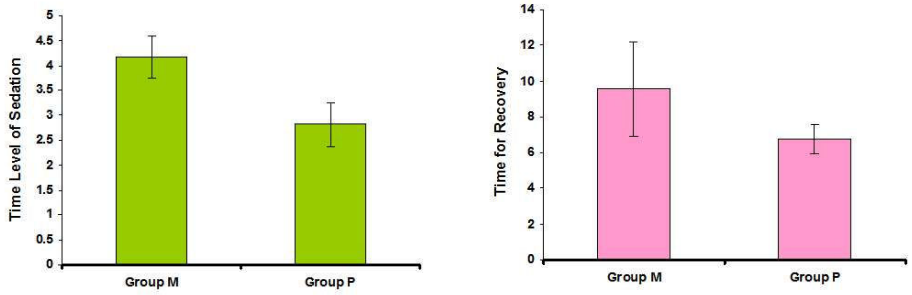
Table 11: Comparison of variables in two groups of patients studied

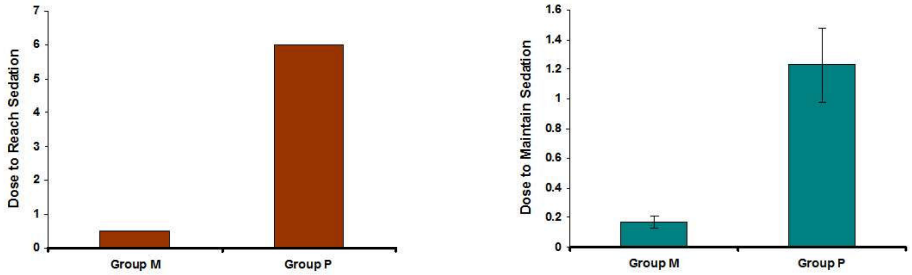
Variables	Group M	Group P	P value
Time Level of Sedation	4.17±0.42	2.81±0.44	<0.001**
Time for Recovery	9.57±2.67	6.76±0.83	<0.001**



Graph 12:

Table 12: Comparison of variables in two groups of patients studied

Variables	Group M	Group P	P value
Dose to Reach Sedation	0.50±0.00	6.00±0.00	-
Dose to Maintain Sedation	0.17±0.04	1.23±0.25	<0.001**



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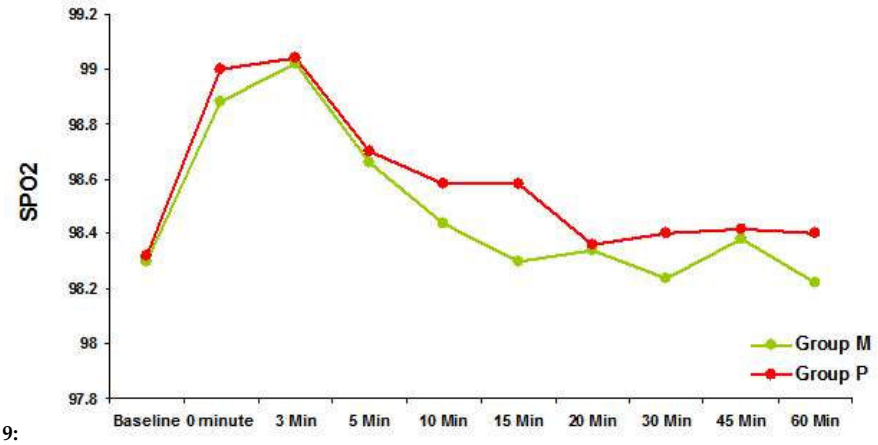
Discussion

Regional anesthesia has become important anesthesia technique which is more popular and emerging as a safe anesthetic procedure. And most of the studies have shown that patients experience anxiety for any type of surgical procedures.

Hohener et al. report an incidence of anxiety of around 50% before receiving a regional block in their study. The study revealed Anxiety was related to higher incidence of nausea and vomiting.

Sedation is a well recognized technique to improve patients' acceptance and comfort during regional anesthesia [4]. The use of this technique is growing exponentially. Many studies have shown that use of different methods of monitoring hypnotic state of the patient is advantageous, as the incidence of side effects is lower and the amount of infused drugs is decreased [2].

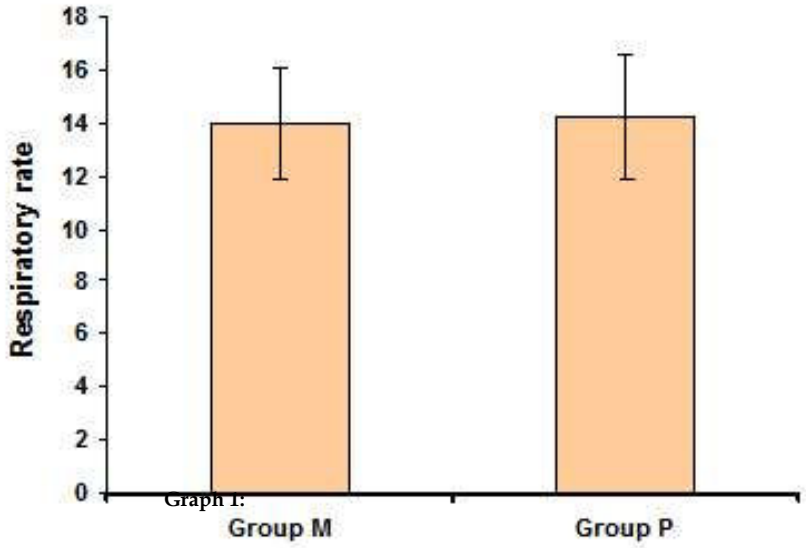
Sedative-hypnotic drugs as well as narcotics are commonly used perioperatively to make regional anesthesia more tolerable for patients by reducing anxiety and providing an appropriate degree of sedation, amnesia and analgesia [3]. Dose required to reach the level of sedation in group M is 0.5 mg/kg/hr and to maintain sedation was 0.17± 0.04 mg/kg/hr and onset of sedation was 4.17±0.42 minutes where as time for recovery from sedation was 9.57±2.67 minutes which was statistically greater than Group P. In Group P, dose to reach the level of sedation was started with 6 mg/kg/ hr to reach required values of Entropy where as to maintain sedation was 1.23±0.25 mg/kg/hr. Onset of sedation in group p was 2.81±0.44 minutes where as time for recovery from sedation was 6.76±0.83 minutes. Hemodynamic changes were significantly higher in Group P than Group M more with DBP. Whereas fall in SpO_2 is more in Group M than Group P but it's not statistically significant.



Graph 9:

Table 9: Comparison of Respiratory rate in two groups of patients studied

Respiratory rate	Group M	Group P	P value
RR	14.00±2.08	14.22±2.34	0.621

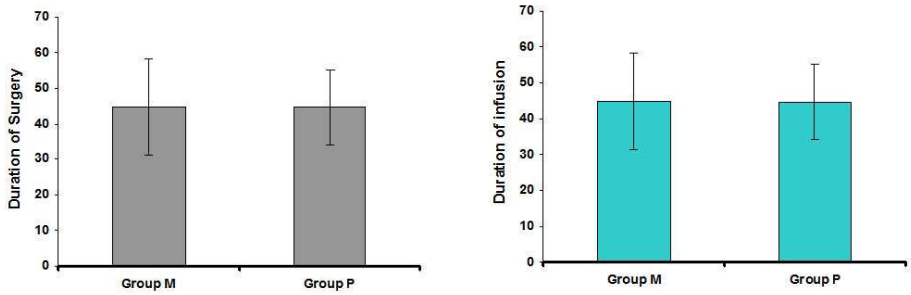


Graph 1:

Graph 10:

Table 10: Comparison of variables in two groups of patients studied

Variables	Group M	Group P	P value
Duration of Surgery	44.70±13.56	44.60±10.49	0.967
Duration of infusion	44.70±13.56	44.60±10.49	0.967



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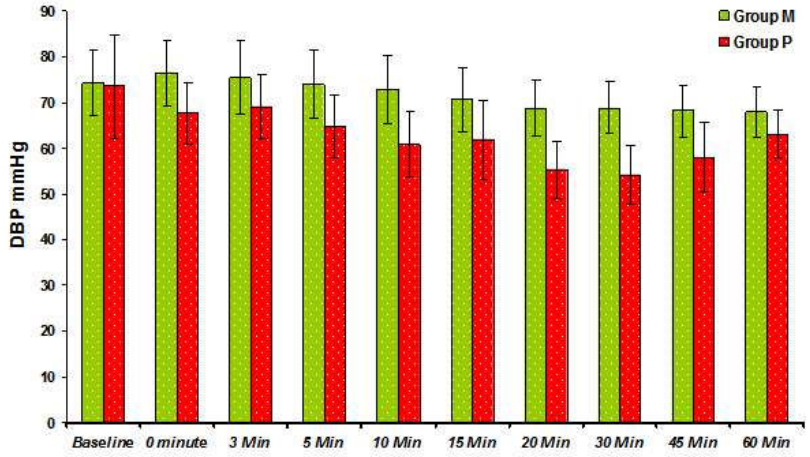

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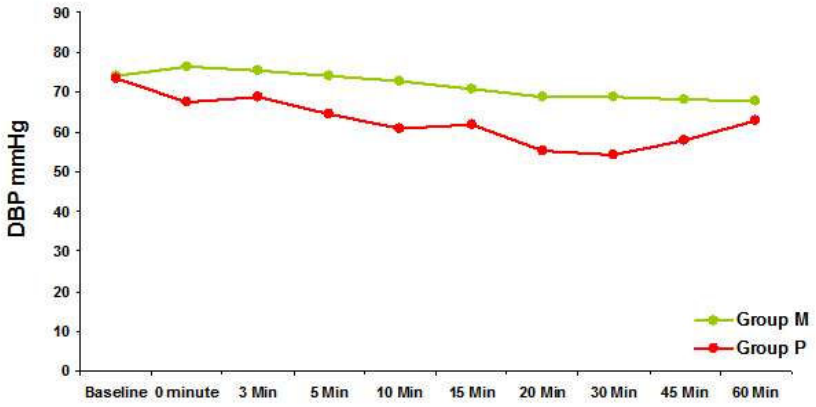
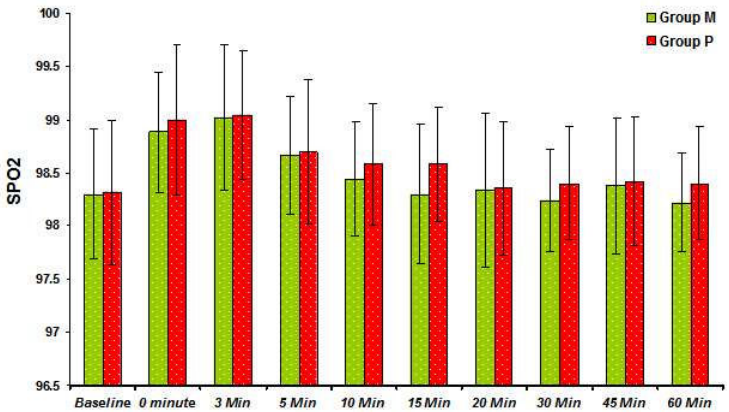


Graph 7:

Table 8: Comparison of SPO2 in two groups of patients studied

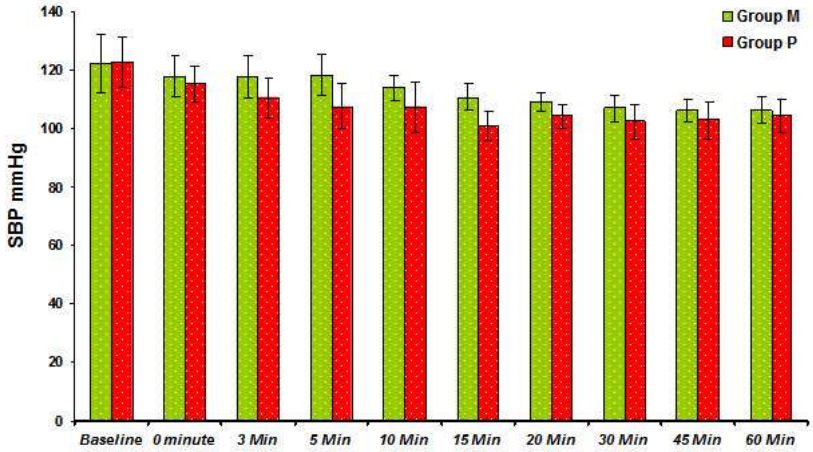
SPO2	Group M	Group P	P value
Baseline	98.3±0.61	98.32±0.68	0.878
0 minute	98.88±0.56	99.00±0.70	0.346
3 minutes	99.02±0.68	99.04±0.60	0.877
5 minutes	98.66±0.56	98.7±0.68	0.748
10 minutes	98.44±0.54	98.58±0.57	0.213
15 minutes	98.3±0.65	98.58±0.54	0.021*
20 minutes	98.34±0.72	98.36±0.63	0.883
30 minutes	98.24±0.48	98.4±0.53	0.117
45 minutes	98.38±0.64	98.42±0.61	0.749
60 minutes	98.22±0.46	98.4±0.53	0.075+



Graph 8:

Table 6: Comparison of SBP mmHg in two groups of patients studied

SBP mmHg	Group M	Group P	P value
Baseline	122.04±9.82	122.56±8.63	0.779
0 minute	117.88±7.00	115.4±6.06	0.061+
3 minutes	117.72±7.02	110.40±6.80	<0.001**
5 minutes	118.36±6.87	107.62±7.87	<0.001**
10 minutes	113.92±4.26	107.32±8.66	<0.001**
15 minutes	110.70±4.79	100.72±4.97	<0.001**
20 minutes	109.06±3.37	104.18±4.23	<0.001**
30 minutes	106.90±4.74	102.34±6.09	<0.001**
45 minutes	106.10±4.19	102.92±6.44	0.004**
60 minutes	106.18±4.71	104.54±5.81	0.124



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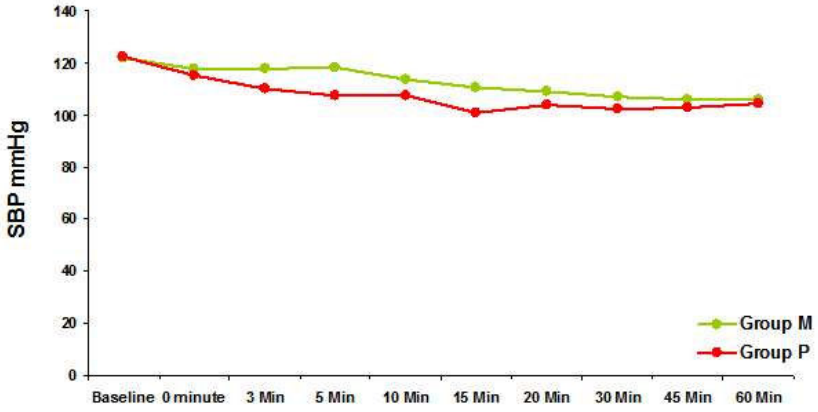


Graph 5:

Table 7: Comparison of DBP mmHg in two groups of patients studied

DBP mmHg	Group M	Group P	P value
Baseline	74.28±7.18	73.6±11.38	0.722
0 minute	76.54±7.17	67.52±6.73	<0.001**
3 minutes	75.34±8.02	68.96±6.90	<0.001**
5 minutes	74.00±7.37	64.66±6.86	<0.001**
10 minutes	72.86±7.40	60.76±7.14	<0.001**
15 minutes	70.68±6.99	61.84±8.79	<0.001**
20 minutes	68.88±6.01	55.38±6.29	<0.001**
30 minutes	68.90±5.67	54.16±6.30	<0.001**
45 minutes	68.08±5.62	57.96±7.60	<0.001**
60 minutes	67.98±5.53	63.00±5.23	<0.001**

maintain entropy of 50 to 60 through syringe pump. Drug infusion was continued till the last suture was completed. Data was collected, Time to reach required level of sedation, Duration of surgery, Duration of infusion, HR, MAP, SpO_2 is recorded every 3 minutes till the required sedation is achieved and then every 10 minutes till the end of surgery, Time of recovery, Side effects: Nausea and vomiting: (1) No vomiting or retching. (2) Retching. (3) Occasional vomiting (1-3 times). (4) Recurrent vomiting (> 3 times). Dose to reach required level of sedation, Dose to maintain required level of sedation. Data was analyze using, Chi-square/ Fisher Exact test, Student t test. Inferential and Descriptive statistical analysis has been carried out in the present study.

Results

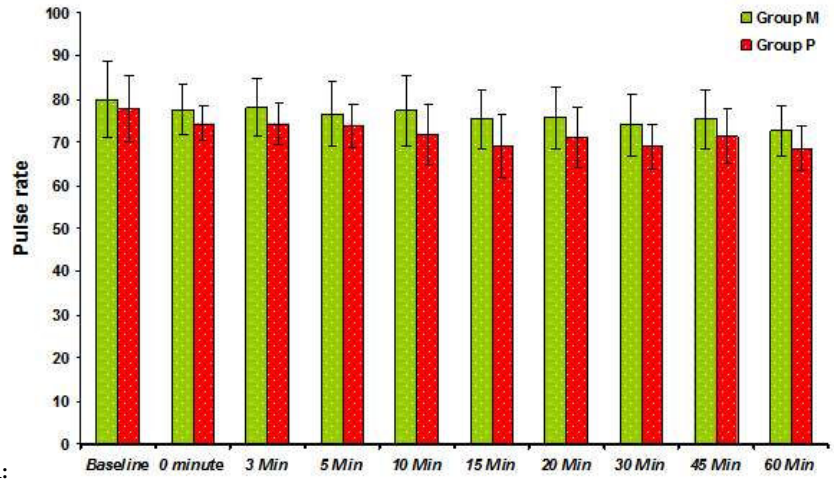
Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

Table 1: Demographic Data

Demographic data	Group M	Group P	p value
Age, years	32.86± 5.44	34.02± 6.58	0.339
ASA Physical Status I/ II	49/1	37/13	0.001
Weight, kg	61.88±6.19	61.04±5.76	0.484

Table 2: Comparison of pulse rate in two groups of patients studied

Pulse rate	Group M	Group P	p value
Baseline	79.98±8.97	77.68±7.65	0.171
0 minute	77.52±5.87	74.30±3.91	0.002**
3 minutes	78.04±6.69	74.34±4.77	0.002**
5 minutes	76.52±7.47	73.74±4.9	0.030*
10 minutes	77.30±8.20	71.70±7.06	<0.001**
15 minutes	75.38±6.94	68.98±7.34	<0.001**
20 minutes	75.66±7.12	71.00±7.10	0.001**
30 minutes	74.06±7.05	69.02±5.32	<0.001**
45 minutes	75.36±6.80	71.36±6.50	0.003**
60 minutes	72.46±5.74	68.56±5.28	0.001**



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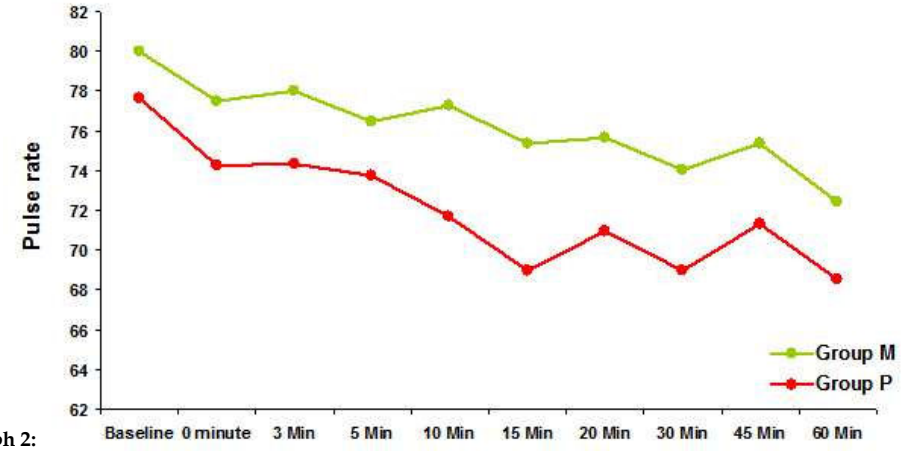

Graph 2:

in the presence of more profound sedation. The long hours of surgery under regional anesthesia in supine or lateral positions can make the patient very uncomfortable. Also during orthopedic procedures, the constant awareness of the noise of instrumentation during surgical procedures creates anxiety in the patients. After sometime because of anxiety, there is persistent tachycardia, rise in blood pressure, which results in increase in blood loss during surgery [4,11].

Anxiety is also associated with significant adverse physiological responses in form of Hypertension, tachycardia, increased myocardial oxygen consumption, Gastric erosion, Intracranial hypertension and Persistent catabolism [11] which may affect the recovery. Therefore anxiolysis is a must.

Primary objectives of conscious sedation include adequate sedation with minimal risk [2,3].

Regional anesthetic techniques can be used for a variety of surgical procedures and may offer certain advantages over general anesthesia. In order to improve patients' acceptability and comfort and to reduce stress it is necessary to provide some form of sedation during the operation.

There are various methods to provide sedation during regional anesthesia, intravenous technique is widely used and suitable agents include the benzodiazepine, opiods and other IV induction agents. Currently midazolam and Propofol are considered to be the most suitable drugs [12-14,19, 22,and 23].

Entropy is an innovative monitoring modality which is designed to provide information on the state of central nervous system during general anesthesia [1,5,7-9]. Entropy monitoring is based on acquisition and processing of EEG and FEMG signals by using Entropy algorithm.

There are two parameters in Entropy

Fast reacting response entropy

More study and robust state entropy

State entropy consists of EEG signals calculated up to 32 Hz

Response entropy includes additional high frequencies up to 47 Hz

Parameters	Measurement Frequency Range	Display Range
Response entropy	0<f<47Hz	0 to 100
State entropy	0<f<32 Hz	0 to 91

Response Entropy

Response entropy is sensitive to the activation of facial muscles i.e. FEMG its response time is very fast and less than two seconds. Activation of response entropy to the painful stimuli may be interpreted as a sign of inadequate analgesia. Facial muscles may also give an early indicator of recovery.

State Entropy

State entropy is always less than or equal to response entropy. Estimation of hypnotic effects of anesthetic drugs in brain during general anesthesia is based on state entropy. State entropy is based on EEG signals. EEG can be considered as a measure for depth of anesthesia due to the following:

Entropy Range Guidelines

100	**Fully awake and responsive.**
60 40	Clinically meaningful anesthesia with low probability of consciousness.
0	Suppression of cortical electric activity.

Methods

A prospective, randomized, single-blind study carried out to evaluate and compare the properties of Propofol and Midazolam in terms of hemodynamic, side effects and dosage requirement as adjuncts to spinal anesthesia. After obtaining approval from institute's Ethical Committee and patients consent, Patients ASA Grade 1 & 2, aged 19-55 years, posted for elective surgeries under regional anesthesia including lower abdominal, perineal and lower limb surgeries were enrolled in study and patients with uncontrolled Hypertension, IHD, stenotic valvular disease, pre-existing neurological deficit, sensitive to used drugs, Obesity (BMI >30) were excluded from the study.

Technique: Under standard monitoring (Pulse oximeter, NIBP and ECG). Entropy sensor was applied to the patient's forehead for Entropy monitoring. The Patients were randomly allocated into 2 groups.

The Midazolam group (Group M): Midazolam 0.1% IV infusion (dilution was done in 5% dextrose in a 50 ml syringe) started with 0.5 mg/kg/hr till entropy value reaches 60 then reduced and titrated to maintain entropy of 50 to 60 through syringe pump.

The Propofol group (Group P): Propofol 1% IV infusion (dilution was done in 5% dextrose in a 50 ml syringe) started with 6 mg/kg/hr till entropy value reaches 60 then reduced and titrated to

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Comparison of Midazolam and Propofol for Entropy - Guided Sedation During Regional Anesthesia

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Abstract

Background and Aims: This study aimed to compare the sedation using Entropy of Midazolam and Propofol in regional anesthesia in terms of Onset, Recovery and Side Effects. *Introduction:* Regional anesthesia is a safe and popular anesthetic technique. Effective sedation is essential for regional anesthetic technique too, to allay anxiety in the patients and improve their comfort, co-operation. Use of entropy will reduce over sedation of the patient and better monitoring of the hypnotic state of the patient. *Methods:* 100 ASA I/II adult patients undergoing elective surgery under regional anesthesia for lower abdominal and lower limb surgeries were enrolled in the study and randomly allocated into two groups. Group M: Midazolam 0.1% IV infusion started with 0.5 mg/kg/hr, Group P: Propofol 1% IV infusion started with 6 mg/kg/hr till entropy value reaches 60 then titrated to maintain entropy of 50 to 60 through syringe pump and was continued till the last suture was completed. *Results:* Dose required to reach the level of sedation was 0.5 mg/kg/hr vs 6mg/kg/hr and to maintain sedation was 0.17±0.04 mg/kg/hr vs 1.23±0.25 mg/kg/hr and onset of sedation was 4.17± 0.42 vs 2.81±0.44 minutes where as time for recovery from sedation was 9.57±2.67 vs 6.76±0.83 minutes in GroupM vs Group P respectively. Hemodynamic changes were significantly higher in Group P than Group M. *Conclusion*: Both Midazolam and Propofol can be used for sedation under regional anesthesia. Onset of action and recovery is faster with Propofol and Midazolam is more cardio stable.

Keywords: Midazolam; Propofol; IV Sedation; BIS (Bispectral Index).

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Introduction

The meaning of sedation is to reduce anxiety that is anxiolysis. Patients undergoing surgery tend to be anxious. What seems like a minor procedure to the anesthesiologist and surgeon may represent a major deal to the patient. Although anxiety usually exists long before the patient is brought to the preoperative room, in some instances, it does not peak until after surgery. So the reduction of anxiety to tolerable levels is a human goal and should be attempted for every patient [4].

Sedation during regional anesthesia is desirable to minimize anxiety in the operating room environment. In addition many patients are concerned about the recall of intra operative events regardless of route of administration, patients satisfaction was reported to be higher

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synergistic interaction between spinal opioids and local anaesthetics. That synergism is characterized by enhanced somatic analgesia without effect on the degree or level of the local anaesthetic-induced sympathetic or motor blockade.

Almost all the previous studies like those of Kararmaz et al. [11], Varrassi et al. [13] and Kuusniemi et al. [14] and Srivastava et al. [15] found an increased incidence of pruritus while in our study the incidence of pruritus was 33.3% (p=0.002) in test group which coincides with above studies. Hypotension was less in Group FB compared to Group B but the difference was found to be statistically non-significant. Similarly bradycardia was seen in two patients in Group FB while four in Group B which required treatment. There was no significant difference between the groups with respect to hypoxia, shivering, post-operative nausea and vomiting. Some studies like those of Singh et al. [9] and Olofsson et al. [16] found no statistically significant differences in perioperative hypotension, bradycardia, desaturation, pruritus, shivering, nausea and vomiting between test and control groups. In study of Kararmaz et al. [11] the incidence of hypotension and shivering was significant between control and test groups.

Conclusion

Addition of fentanyl to hyperbaric bupivacaine increased the duration of analgesia maintaining hemodynamic stability when compared to placebo. Pruritis was the most common side effect observed during the study which is attributed to intrathecal fentanyl.

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Table 2: Sensory and Motor block characteristics

	Group FB	Group B	P value
Onset of sensory block (min)	3.7±1.2 mins	4.0±1.1	0.371
Onset of motor block (min)	4.5±1.2	4.8±0.9	0.277
Median maximum sensory level	T4/T6/T8= 14/12/5	T4/T6/T8= 10/14/6	0.637
Time to reach highest sensory level (min)	12.9±2.8	13.08±2.2	0.789
Time for two segment regression(min)	84.3±16.33	63.3±10.72	<0.0001***
Time for rescue analgesia (min)	180.0±22.2	153.0±13.42	<0.0001***
Time for complete motor recovery (min)	148.66±20.465	142.6±18.06	0.228

Data expressed as Mean ± Standard Deviation

Table 3: Side effects

	Group FB	Group B	P value
Pruritis	10 (33.33%)	0	0.0006*
Hypotension	9 (30.00%)	12 (40.00%)	0.427
Bradycardia	2 (6.66%)	4 (13.33%)	0.393
Hypoxia	0	0	0
PONV	5 (16.66%)	8 (26.66%)	0.351

Results

All the sixty patients enrolled, successfully completed the study. Two groups were comparable with regards to age, gender and ASA grading. (Table 1).

Both the groups were comparable with respect to onset of sensory and motor block. The highest dermatomal level reached and the time taken were comparable in both the groups. (12.9±2.8 vrs 13.08±2.2, p= 0.789).

The time taken for two segment regression was prolonged in Group FB when compared to Group B and the difference was found to be very highly significant (84.3±16.33 vrs 63.3±10.72, p < 0.0001). The time for rescue analgesia and duration of motor block were prolonged in Group FB when compared to Group B which was found to be statistically significant (Table 2).

Both the groups were monitored for side effects both intra and post-operatively. Hypotension was seen more in Group B when compared to Group F which was found to be statistically significant. (13.33% vrs 40.0%, p= 0.02). Six patients in Group FB had pruritis but none of them in Group B. This was found to be statistically significant.

Bradycardia, hypoxia and post operative nausea and vomiting were comparable in both the groups.

Discussion

Subarachnoid block is one of the most popular techniques in our country, which unfortunately has the disadvantages of sympathetic and motor block, resulting in hypotension, bradycardia and immobility [4]. It has been a dream to produce sensory block without its accompanied complications and a major step in this path is the use of intrathecal opioids, [5] but they are not adequate anaesthetics for surgery. So local anaesthetics combined with opioids are the appropriate choice.

Studies using morphine by Semenikhin et al. [6] in 1990 concluded that addition of morphine considerably increased the quality of analgesia produced, but the incidence of late respiratory depression is more with morphine. Fentanyl, a phenyl piperidine derivative [11] and a synthetic opioid, is 100 times more potent then morphine and being more lipophilic, has fewer tendencies to cause late respiratory depression and hence, is more suitable especially in our country which has few monitoring facilities and a greater demand on them.So we decided to use fentanyl as an adjuvant to hyperbaric bupivacaine in our study.

Hunt et al. [7] showed the 6.25 µg fentanyl was capable of producing same analgesia as higher doses, with minimum side effects, after comparing 0, 6.25, 12.5, 37.5 and 50 µg doses (made to 1 ml with normal saline), with bupivacaine 0.75% in 28 parturients for caesarean section. As the dose of fentanyl increases to 0.5 to 0.75 µg/kg post operative pain relief lasts longer, but respiratory changes occur and incidence of adverse effects also increases. Hence, in our study we chose 25 µg fentanyl for non obstetric surgeries.

Hunt et al. [7] and Singh et al. [8] found onset of sensory block and motor block was not affected which was similar to our study. Though onset of sensory and motor block was hastened in our study, the difference was not significant. The time and the highest sensory level achieved were comparable in both the groups which was similar to the studies done in the past. Studies done by Singh et al. [9] and Bruce et al. [10] have shown prolongation of two segment regression which was similar to our present study findings. These findings were contradicted by the findings done by Kararmaz et al. [11].

Duration of sensory blockade was prolonged but no effect on motor block was seen in our study. This is consistent with the studies done by Belzarena et al. [12]. This could be explained by the

anaesthesia [1,2,3]. The discovery of opioid receptors in the spinal cord [4] led to the use of opioids as additives along with the local anaesthetics.

Opioids are being used widely in the world with the advantage of prolonging analgesia, thus providing maximum benefit with low cost and easy techniques. Of the opioids, morphine, pethidine, fentanyl, buprenorphine etc are used. Lipophilic opioids like fentanyl and sufentanilare increasingly being administered intrathecallyas adjuncts to local anaesthetics to overcome the disadvantages of conventional doses of bupivacaine.

In our present study we evaluated the efficacy of intrathecal fentanyl as an adjuvant to 0.5% bupivacaine on sensory and motor block characteristics, hemodynamic stability and side effects due to its intrathecal administration.

Methods

Sixty American Society of Anaesthesiologists physical status I & II, patients of either gender and aged between 18-60 yrs scheduled for lower abdominal surgeries were included for the study. Ethical committee approval was obtained from Institutional Ethical committee, and written informed consent was taken from the patients. Patients with American society of anaesthesiologists physical status III and IV, with history of major cardiac, renal, hepatic, respiratory or neurological disorders and those with spine deformity, psychiatric illness, altered coagulation profile and active infection were excluded from the study.

All patients were evaluated thoroughly on the previous day of surgery and were allowed to fast overnight.Tab. Diazepam 10 mg and Tab. Ranitidine 150mg were prescribed on the night before surgery. On the day of surgery 18 G intravenous cannula was secured in non dominant hand; patients wereco-loaded with ringer lactate intravenous fluid at a rate of 15 ml/kg body weight. Standard monitoring was accomplished using electrocardiogram, non-invasive blood pressure and pulse oximetry.

Patients were randomly allocated into 2 groups by computer generated number and study drugs were prepared by one of our OT technician in colour coded syringes. Group FB (test group, n=30) received 2.5mlof 0.5% Bupivacaine heavy and 25 μg freshly drawn fentanyl citrate (0.5 ml) and Group B(control group, n=30) received 2.5 ml of 0.5% Bupivacaine heavy with0.5ml saline. Anaesthesiologists who administered the drug and patients were blinded for the study.

Subarachnoid block was performed under aseptic precautions with patients in lateral decubitus position using 25G Quincke-Babcock spinal needle at L_2-L_3 or L_3-L_4 interspace. The study solution was injected over 20-30 seconds after confirming free flow of CSF. After the intrathecal injection the patients were immediately made to lie in supine position.

Sensory level was assessed by pin prick sensation every minute till adequate sensory level was achieved and thereafter every 5 minutes for the first hour and 20 minutes till 2 segment regression. Onset of sensory block, duration of analgesia, two segment regression, time taken to reach highest dermatomal level and the highest dermatome reached were noted. Motor block was assessed by modified Bromage scale (I - free movement of legs and feet; II - just able to flex knees with free movement of feet; III - unable to flex knees but with free movement of feet; and IV - unable to move legs and feet). Onset of motor block (Bromage II), duration of motor block (regression to Bromage I) were noted.

Intravenous boluses of 6 mg mephenteramine and additional I.V. fluids were given to treat hypotension, which was defined as a systolic blood pressure <20% of preoperative value or <90 mm Hg, atropine 0.6 mg to treat bradycardia (40/min) or 30% of baseline and O_2 via face mask if pulse-oximetry reading decreased below 92%. If respiratory rate decreased to <8/min, patients were gently aroused by tapping.

Presence of side effects like pruritus, nausea, vomiting, respiratory depression and were noted intraoperatively and postoperatively. Results were tabulated and analysed.

Statistical analysis done using software SPSS version 11.5. Continuous variables were summarized as mean and standard deviation. Student unpaired 't' test was applied to onset of sensory and motor block time to highest sensory level, time for 2 segment regression, time for effective analgesia, time to motor activity. Chi-square test was applied to highest sensory level, pruritus and nausea. p value <0.05 is considered as significant (S), <0.01 is considered as highly significant (HS) and <0.001 is considered as very highly significant (VHS)

Table 1: Demographic data

	Group FB	Group B	p Value
Age in years	38.26±13.05	38.76±11.65	0.876
Male/Female	18/12	19/11	0.791
ASA I/II	16/14	17/13	0.795

Data expressed as Mean ± Standard deviation.

Original Research Article

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Intrathecal Fentanyl as an Adjuvant to Hyperbaric Bupivacaine in Lower Abdominal Surgeries: A Placebo Controlled Randomised Study

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Abstract

Aim: The aim of our study was to evaluate the efficacy of intrathecal fentanyl as an adjuvant to bupivacaine on the block characteristics, hemodynamic stability and side effects in patients undergoing lower abdominal surgeries. *Methods:* Sixty patients aged between 18-60 yrs, belonging to ASA I and II posted for elective lower abdominal surgeries under spinal anaesthesiawere recruited for the study. Patients were randomly divided into two groups of thirty each. One group received 2.5 ml of 0.5% Inj. bupivacaine with 0.5 ml of fentanyl (Group FB) and the other group received 2.5 ml of 0.5% Inj. bupivacaine with 0.5 ml of normal saline (Group B). Patients were monitored for onset, duration and quality of sensory and motor block, duration of analgesia, highest dermatomal level, hemodynamic parameters and side effects. *Results:* Onset of sensory block, motor block, time to reach highest dermatomal level duration of motor block was comparable between the groups. Duration of sensory block and two segment regression was prolonged in group FB compared to Group B which was statistically significant ($p < 0.001$). Hemodynamic stability was maintained throughout intra and post-operative period in Group FB compared to Group B. Incidence of pruritis was higher in Group FB compared to Group B which was statistically significant ($p< 0.001$). *Conclusion:* Fentanyl as an adjuvant to bupivacaine provided sufficient post-operative analgesia with hemodynamic stability.

Keywords: Fentanyl; Bupivacaine; Intrathecal; Postoperative analgesia.

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Introduction

Subarachnoid block introduced by Karl August Bier is one of the oldest forms of regional blocks and is still a very commonly used procedure in our country. Subarachnoid block gives a clear advantage which is difficult to duplicate with general anaesthesia for surgical procedures below the level of the umbilicus. Over and above, one of the most useful effects of central neuraxial blockade is postoperative analgesia.

Local anaesthetics used in day to day practice are usually amides like bupivacaine, lignocaine, ropivacaine, levobupivacaine etc. Though bupivacaine has become the mainstay of spinal anaesthesia it has certain disadvantages like late onset of action and prolonged motor blockade which makes it an unsuitable agent for ambulatory

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and C ($p<0.001$)

Duration of analgesia was significantly more in S_2 group than S_1 and C groups. Group C received maximum doses of rescue analgesics followed by group S_1 than S_2.

All patients were hemodynamically stable and no obvious side effects in perioperative period. Patients in group S_2 with $MgSO_4$ 200 mg were more comfortable than S_1 group with $MgSO_4$ 100 mg.

None of the patients experienced any symptoms and signs of Magnesium toxicity.

Discussion

The major results of our study are addition of Magnesium sulphate to local anesthetics prolongs the duration of local analgesia, fastens the onset of sensory and motor block in dose dependent manner. Higher doses have prolonged duration of analgesia without increased incidence of side effects.

There are studies on addition of $MgSO_4$ for peripheral nerve blocks. Gundez et al. [9] found that addition of $MgSO_4$ to 2% prilocaine for axillary block prolonged the duration of sensory and motor block significantly. Hypothesis for analgesic properties of Magnesium on peripheral nerves is surface charge theory. Akutagawa et al. [8] showed that modulation of extracellular magnesium concentration near the nerve bundle speeds the onset of action of local anesthetics. Mert et al. [10] reported that high concentration of divalent ions (Mg^{2+}) attracted by negative charges of surface membrane results in hyperpolarisation of nerve bundles and results in condition block. Hence more the concentration of Mg^{2+} ions, prolonged is the duration of analgesia. It supports our results that higher doses (200 mg) had more prolonged analgesia than lower dose (100 mg).

Another mechanism for analgesic property of $MgSO_4$ is NMDA receptor antagonism, which prevents central sensitisation from peripheral nociceptive stimulation. This is the basis of analgesic effect after intravenous administration and neuraxial route [11].

NMDA receptors are also found in muscles, skin [12], joint and play a role in sensory transmission of noxious signals [13]. In the study by Mukherjee et al. [14] used 150 mg of $MgSO_4$ with Ropivacaine in supraclavicular brachilal plexus block with desirable results. Whereas Bansal et al. [15] used 1.5 gm of $MgSO_4$ in intravenous regional anesthesia with excellent results and less side effects.

A R Lee [16] et al. studied 200 mg of $Mgso_4$ as adjuvant to bupivacaine with adrenaline in interscalene brachial plexus block with prolonged mean duration of analgesia which is consistent with our study.

Regarding total dose of rescue analgesics, control group received maximum doses followed by group S_1 and then S_2, which is correlating with the observation by Mukherjee et al. [14].

Prolonged analgesia with higher doses is consistent with studies by Varsha Verma et al. [17] who compared 250 mg and 125 mg $MgSO_4$ and found that 250 mg provides longer duration of analgesia as compared to 125 mg. Thus it is dose dependent.

Santosh Kumar et al. [18] reported use of $MgSO_4$ 150 mg as an adjuvant in USG guided supraclavicular block is better than Potassium Chloride for post operative analgesia.

Conclusion

After seeing the observations and results we come to conclusion that analgesic action of magnesium sulphate added as additive to bupivacaine for supraclavicular brachial plexus block is dose dependent. It also speeds the sensory and motor blockade and prolongs the duration of blockade.

$MgSO_4$ helps in reducing the rescue analgesic requirement in the post operative period making patient more comfortable.

$MgSO_4$ is economical and easily available.

Higher dose i.e. 200 mg is more effective than 100 mg without any side effects.

$MgSO_4$ can be used as an adjuvant to local anesthetics in regional blocks as it potentiates the action of local anesthetics.

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Table 3: Onset of Sensory Block and Motor Block

Group	Onset of Sensory block(min)	Onset of Motor Block(min)	p Value
S2	6.5±1	9±2	P<0.001
S1	10±2.8	13±2.2	P<0.001
C	15±3	19±2.1	P<0.001

Table 4: Duration of Sensory and Motor Block

Group	Duration of Sensory Block (Min)	Duration of Motor Block (Min)	p Value
S2	550±15	440±30.2	<0.001
S1	440±10	330±15.5	<0.001
C	240±30	200±33.5	<0.001

Table 5: Duration of Analgesia

Group	Duration of Analgesia (min)
S2	540±25 min
S1	440±20 min
C	200±15 min
	p. Value <0.001

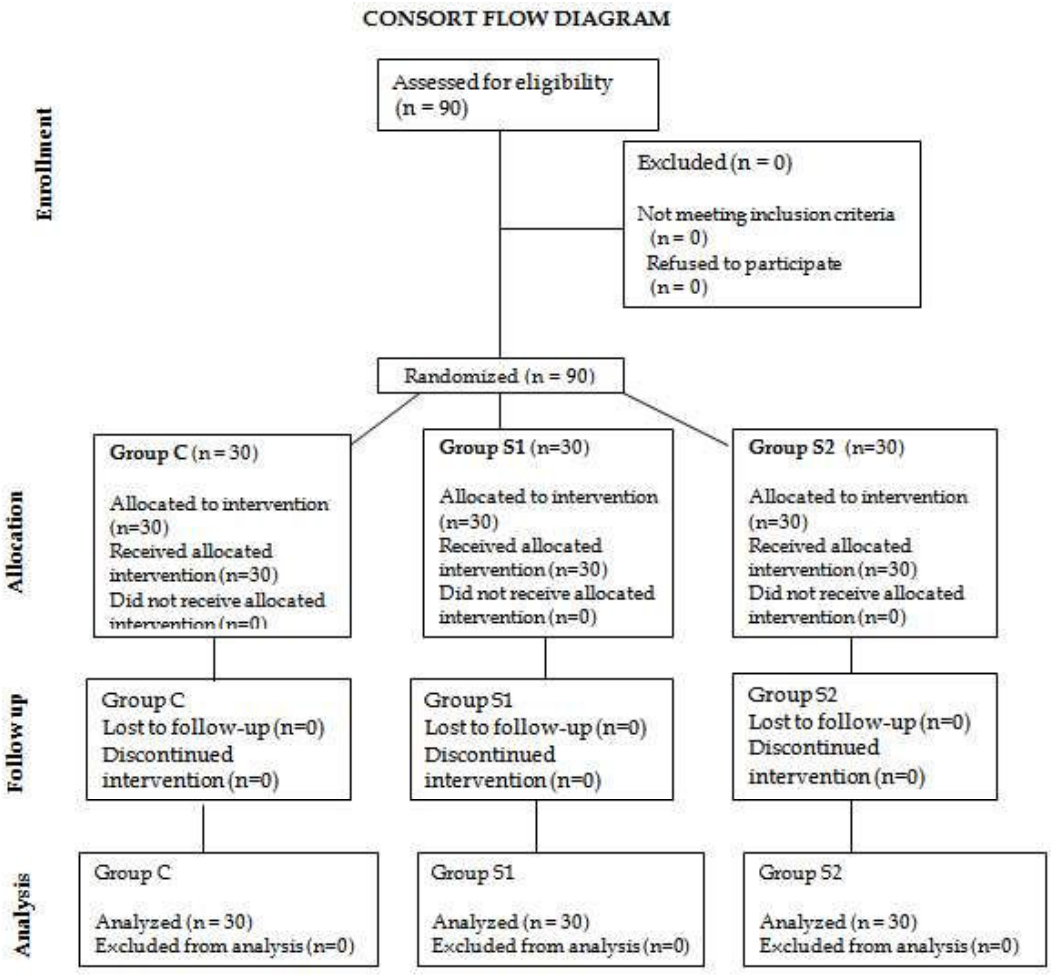

Fig. 1: Consort Flow Diagram

Grade 1 = decreased movements

Grade 2 = complete loss of movements (paralysis)

Assessment of sensory and motor blocks was done every 3 min till 30 min or till complete block is obtained. Assessment was done every hourly in intraoperative period for analgesia and every two hourly in postoperative till the requirement of systemic analgesics.

Onset of sensory block is defined as time interval between administration of drug and complete loss of sensation, and duration is time interval between drug injection and complete recovery of sensation to pin prick. Onset of motor block is defined as time interval between drug injection and complete loss of movement of fingers and duration is time interval between drug injection to complete recovery of finger movements and muscle power. Duration of surgery is time interval between skin incision to skin closure. Duration of analgesia is defined as time interval between drug injection and first injection of systemic analgesics.

Duration of analgesia or duration of sensory block is defined as the time from complete establishment of sensory block to the time of first rescue analgesia.

Analgesia was assessed by using 10 cm Visual Analogue Scale (VAS). Markings of 0 at the extreme left indicates no pain and 10 at the extreme right indicating maximum pain. Patients were asked to mark a point according to intensity of pain. When patient felt pain with VAS > 3, rescue analgesia was provided with either Inj. Diclofenac or Inj. Tramadol.

All patients were monitored in perioperative period for hemodynamic stability, any side effects of the block i.e. arterial puncture, pneumothorax, phrenic nerve palsy, failure of block or inadequate block and the side effects or drugs i.e. nausea, vomiting, respiratory depression, cardiac depression, muscle weakness, neuropathy.

Assessment of sensory, motor blockade and pain score was done at 0 min, 30 min, 1, 2, 3, 4, 6, 9, 12, 15, 18, 21, and 24 (hours).

There was no need of measuring serum Magnesium levels as the dose (100mg and 200mg) used was far less than the therapeutic dose of Magnesium Sulfate which is 300mg to 400mg per day for adults. The study dose will not cause toxic serum levels and clinical parameters were assessed (knee jerk, respiratory rate, muscle power, urine output) for early diagnosis of toxicity.

Statistical analysis was done by using SPSS software. Comparison was done by using Chi Square test. p values considered are $p > 0.05$ (not significant) $p < 0.05$ (significant) and $p < 0.001$ (highly significant)

Observations and Results

All patients completed study successfully. There was no block failure. All patients were comparable in respect to demographic data, duration of surgery, and vital parameters.

Consort Flow Diagram (Fig.1).

Onset of sensory and motor blockade was faster in group S_2 as compared to s1 and c, which is highly significant.

Duration of sensory and motor block was significantly longer in group S_2 as compared to S_1

Table 1: Demographic data of patients in three groups

Parameters	Groups			
	C	S_1	S_2	p
Age (yrs)	35.5±15.4	40.2±12	36.5±13	>0.05
Weight in Kg	60.5±5.5	58±6.6	57.2±5.5	>0.05
Male	12	15	16	>0.05
Female	18	15	14	>0.05
ASA1	20	25	19	>0.05
ASA2	10	5	11	>0.05

Table 2: Vital Parameters and Duration of Surgery

Parameters	Groups			
	C	S_1	S_2	p
Mean Heart Rate (bpm)	78.5±10	84±20	82±14	>0.05
Mean Blood Pressure(mm Hg)	84±8	90±10	88±10	>0.05
Mean Saturation (Sp02%)	99.7±0.5	99.4±0.6	99.2±0.5	>0.05
Duration of Surgery (min)	75.9±10.5	73.8±20	74.5±19.6	>0.05

[4] buprinorphine, [5] tramadol, [6] were used in various studies for early onset and prolonged duration of analgesia providing excellent conditions for surgery. $MgSO_4$ also is an excellent additive to local anesthetics in regional and peripheral nerve blocks [7].

Mechanism of analgesic property of Magnesium on peripheral nerve is explained by surface charge theory [8], high concentration of divalent ions (Mg^{2+}) attracted by negative charges on the outer surface of nerve membrane causes effect on sodium channel gate which results in persistent hyperpolarisation and no conduction of impulse. Another mechanism is voltage dependant. Antagonism of NMDA receptor which prevents central sensitisation from peripheral stimulation and decreases the pain.

Different studies are conducted for $MgSO_4$ as additive to brachial plexus block with fair outcomes. This study was conducted to compare the efficacy of low dose and high dose of $MgSO_4$ for duration of postoperative analgesia and incidence of side effects.

Materials and Methods

Ethical committee approval was obtained and male and female patients of 18 to 50 years age, ASA Grade I or II, undergoing upper limb surgery under USG guided brachial plexus block, were divided into 3 groups of 30 each.

Group C: received 20 ml 0.5% bupivacaine+5 ml of NS

Group S_1: received 20 ml of 0.5% bupivacaine+ 4 ml of NS + 1 ml (100mg) magnesium sulphate.

Group S_2: received 20 ml of 0.5% bupivacaine + 3 ml of NS + 2 ml (200 mg) magnesium sulphate to total volume of 25ml and final concentration of bupivacaine 0.4% in each group.

For calculation of sample size, pilot study was done in 15 patients and randomized in 3 groups of 5 each. The standardized effective size 'cohen's 'd' was calculated, 23 patients per group were required to get stastically significant difference at p=0.05 and 80% power. By taking into consideration, block failure, exclusion, sample size was taken 30 in each group.

One sample Kalmogorov – smirnov test was used to determine differentiation between data sets from normal distribution.

Normally distributed data were analysed using analysis of variance. Catagorical data was analysed by chi square test.

Bonferroni correction was used to correct for multiple testing at different time points.

Study Method

Prospective double blind randomized controlled trial., Randomization done by computer generated random number table.

Exclusion Criteria

Contraindication to block (infection or bleeding disorders), history of cardiac disease, hepatic or renal failure, patients on long term calcium channel blockers, respiratory disorders, neuromuscular disorders, allergy to local anesthetics, mentally retarded patients, pregnant woman, neuropathy, ASA III and IV, failed block.

Thorough pre anesthetic evaluation was done, anesthesia procedure and Visual Analogue Scale (VAS) was explained to patients.

Written and informed consent was obtained. Patients were kept nil orally after 10 pm, oral antacids and anxiolytics were given.

In the operation theatre, monitoring devices were set up, IV line secured, Ringer Lactate infusion was started. Baseline parameters i.e. Heart Rate, Mean arterial pressure, oxygen saturation and respiratory rate were noted.

Procedure explained to patient and placed in supine position with head turned to opposite side. After cleaning and draping, local infiltration was done in supraclavicular area, block was performed by using high frequency linear probe, pulsatile subclavian artery was identified and confirmed with Doppler flow. Plexus located posterolateral to artery with hyper echoic honeycomb appearance. 23 gauge lumbar puncture needle is inserted by using in-plane technique and the drug is injected according to group allocation after negative aspiration for blood. Patient and observer were blind about the study solution. Vital parameters were monitored every 3 min for 30 min, and thereafter every 15 min till the end of surgery.

Sensory block is assessed by three point scale with pin prick method.

Grade 0 = sharp pin prick felt

Grade 1 = loss of pin prick sensation (analgesia) but dull sensation felt.

Grade 2 = loss of sensation (anesthesia)

Motor block is graded as

Grade 0 = normal motor function with full movement of wrist and fingers.

Original Research Article

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Comparative Study of two doses of Magnesium Sulfate as an Adjuvant in Supraclavicular Brachial Plexus block for Post Operative Analgesia

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Abstract

Aims and Objectives: To compare the duration of post operative analgesia with different doses of magnesium sulphate as an adjuvant in USG guided supraclavicular brachial plexus block and its side effects. *Material & methods:* Ninety patients aged 18-50 yr ASA Gr 1-2 divided into 3 groups of 30 each undergoing upper limb surgery under USG guided supraclavicular brachial plexus block. Group C (control group)- (n=30) received 20 ml of 0.5% Bupivacaine + 5 ml of normal saline (NS). Study group 1 (S1) - (n=30) received 20 ml of 0.5% Bupivacaine + 4 ml of NS + 100 mg (1ml) of magnesium sulfate. Study group 2 (S2) - (n=30) received 20 ml of 0.5% + Bupivacaine + 3 ml of NS & 2 ml (200 mg) of magnesium sulphate. *Results:* Onset of sensory block in Group S2 (6.5±1 min), in S1 (10±2.8 min) and in C (15±3 min). Onset of motor block in S2 (9±2 min), in S1 (13±2.2 min) and in C (19±2 min). Duration of post-operative analgesia in S2 (540±25 min), in S1 group, (440±20 min) and in control group C (200±15 min). Addition of $MgSO_4$ as adjuvant hastened the onset of sensory and motor block in study group as compared to control. Duration of sensory and motor block were more in group S2 as compared to S1 and C. Duration of postoperative analgesia was significantly prolonged in group S2 as compared to S1 and C ($p<0.001$) without increased incidence of side effects. *Conclusions:* Addition of magnesium sulphate to local anesthetics in brachial plexus block prolongs the duration of postoperative analgesia. It is dose related, 200mg has greater efficacy than 100mg without increased side effects.

Keywords: Magnesium Sulphate; Postoperative Analgesia; Brachial Plexus Block; Visual Analogue Scale.

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Introduction

Supraclavicular brachial plexus block is widely used for upper limb surgeries (forearm and hand). It is easy, safe with rapid onset and high success rate [1,2]. This block is performed at the level of brachial plexus trunk which blocks the majority of sensory, motor and sympathetic innervations.

USG guided technique allows to see subclavian artery as a prominent marker and neural structures around it above first rib [3] thus increasing success rate and reducing the complications of landmark technique.

Local anesthetics have shorter duration of action and needs additives to increase the duration of postoperative analgesia. Clonidine,

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Conflict of Interest: None

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The incidence of difficult laryngoscopy in their study was 8.2%. Yildiz TS et al. conducted study on 1674 patients of ASA 1-3, whose pre-operative airway assessment was done with Mallampatti and Thyromental distance. They found incidence of difficult intubation was 4.8% and increased with age [13].

Ittichaikuthol W et al. conducted study on 1888 patients undergoing elective surgery under general anesthesia. Airway was evaluated using Mallampatti test and Thyromental distance. They found incidence of difficult intubation to be 3.2% [14].

Khan ZH et al. conducted a prospective study on 380 patients for assessment of airway using various screening tests including Mallampatti test and Thyromental distance. The prevalence of difficult intubation was 5% [15].

Shiga et al. conducted a meta-analysis of bed side screening tests for difficult intubation in apparently normal patients with no airway pathology. Tests included Mallampatti test, Thyromental distance, Sternomental distance and Wilson score. They found an overall incidence of difficult intubation to be 5.8% [16]. The incidence of difficult intubation in our study is 5%, which is comparable to the above mentioned study.

Similar study conducted by Koh et al. on 605 patients, a combined Mallampatti test grade 3 & 4 and thyromental distance < 6 cm was noted during preoperative airway assessment and correlated to Cormack & Lehane laryngoscopic grading during intubation. Grade 3 & 4 were considered difficult intubation [17].

Vani et al. conducted a study on 50 patients whose preoperative airway assessment combined Mallampatti grade 3 & 4 and thyromental distance < 6 cm to Cormack & Lehane grading during intubation. Grade 3 & 4 were considered difficult intubation [18].

Study conducted by Ezri et al. on 1472 patients also used similar parameters for prediction of difficulty during intubation. The results obtained in our study in predicting difficult airway using Mallampatti test alone was found to be having a sensitivity of 67.85% and specificity of 98.89%, the positive predictive value was 86.36%, and a negative predictive value was 96.76% [19].

Iohom et al. conducted a study in predicting difficult airway by using Mallampatti test, thyromental distance and sternomental distance. They found the sensitivity of Mallampatti test to be 43%, specificity 93%, the results of our study are comparable to the values obtained to this study [20].

In our study when thyromental distance was used alone in assessing the difficult airway, the sensitivity was 70.58%, specificity was 96.46%, positive predictive value was 54.4% and the negative predictive value was 98.2%. Frerk conducted a study in predicting difficult airway by using Mallampatti test and thyromental distance. The sensitivity of thyromental distance was found to be 88% and specificity 81% which are comparable to this study [21]. When the combination of Mallampatti test and thyromental distance was used to assess difficult airway and it was used to correlate it with Cormack and Lehanelaryngoscopic grading, the sensitivity was 75%, specificity 98.9%, positive predictive value 80% and negative predictive value 98.6% was obtained. The above result obtained show that, the discriminative power is greater when used in combination rather than alone.

Ulrich B et al. in 1998 conducted a study on 1993 patients surgical patients showed if during the laryngoscopy, a satisfactory laryngeal view is not obtained, the backward – upward-rightward-pressure (BURP) manoeuvre may aid in improving the view. The BURP manoeuvre has shown to improve the laryngeal view, decreasing the difficult intubation in these patients from 4.8% to 1.8% [22].

Benumof et al. described optimal external laryngeal manipulation by pressing posteriorly and cephalad over the thyroid, cricoid, and hyoid improved the laryngeal view by at least one Cormack & Lehane grade [23].

In our study the patients with difficult airway determined by Cormack and Lehane grade 3 & 4 were intubated either by "BURP" manoeuvre or bougie. There were 22 patients belonging to Cormack & Lehane grade 3 and 4 out of which 17 patients were intubated with BURP manoeuvre and 5 patients were intubated with bougie. The airway management was not associated with any patient morbidity or mortality. Further, surgery was never cancelled or postponed secondary to difficulties with airway management.

Conclusion

In our study the incidence of difficult intubation was found to be 5%. No single anatomical factors can be used as a sole predictor of difficult intubation, with few exceptions. Patients with obvious pathological and anatomical deformity of airway have difficult intubations. The present study has shown that the combination of modified Mallampatti test and thyromental distance is better than when used alone in predicting difficult intubation.

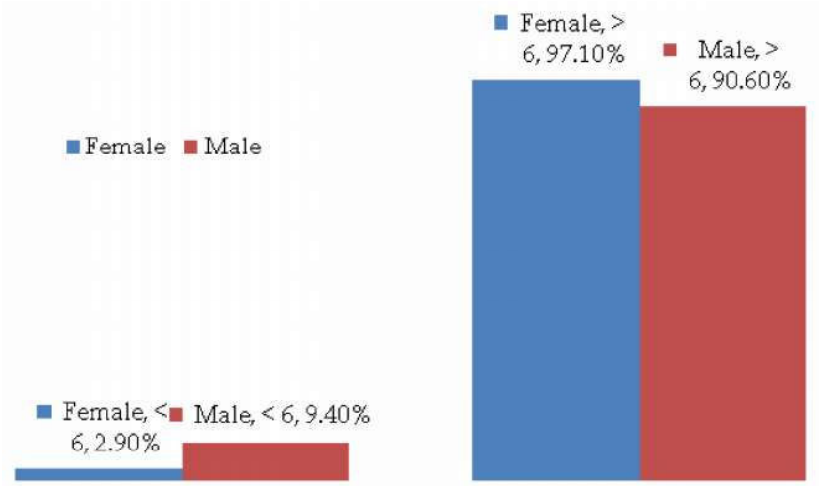

Fig 5: Gender and The Mallampatti Grade and Thyromental distance distribution of study population

Table 5: Distribution of Combination of tests The Mallampatti Grade and Thyromental distance in Male & Female

Gender	Mallampatti Grade + Thyromental distance		Total
	+Ve	-Ve	
Female	5	167	172
	2.9%	97.1%	100.0%
	29.40%	59.01%	57.3%
Male	12	116	128
	9.4%	90.6%	100.0%
	70.60%	40.99%	42.7%
Total	17	283	300
	5.7%	94.3%	100.0%
	100.0%	100.0%	100.0%

Discussion

In earlier days anesthesia was induced by anesthetic vapours given through face mask. Due to inability to maintain a patent airway, adequate depth of anesthesia for surgical procedures and its complication leading to morbidity and mortality led to development of safer anesthetic practice by maintaining anesthesia through endotracheal insufflation.

The endotracheal tube is one of the airway devices which can be introduced into the trachea either orally or nasally, to maintain a patent airway in both unconscious and Anaesthetized patients. The significance of difficult or failed tracheal intubation following induction is a well recognized cause of morbidity and mortality in anesthetic practice. Moreover the need to predict potentially difficult tracheal intubation has received wide attention but withmeagre success.

Many anatomical characteristics and pathological conditions (like Pierre Robin syndrome, Ludwig's angina) have been suggested to be useful in assessing anticipated difficult intubation by altering or distorting the regional anatomy of the airway Unheralded difficult intubation is a risk to the patient's life and a challenge to the skill of the anesthesiologist.

In the absence of pathological conditions, radiographic methods are time consuming and cannot be used routinely for prediction of the difficult intubation. But these factors have limitations because of observer variability, inadequate statistical power and difference in incidence of difficult intubation Based on these observations and studies, our study was conducted to overcome a few of these limitations and hence we have used two simple bed side airway assessment tests i.e., Mallampatti test and measurement of thyromental distance to predict the incidence of difficult intubation.

The study population consisted of 300 ASA grade 1 & 2 patients with apparently normal airway who underwent surgical procedures under general anesthesia. In our study the prediction of difficult intubation was done by combining Mallampatti test grade 3 & 4 and thyromental distance < 6 cm during the preoperative airway assessment and correlating it with the Cormack & Lehane laryngoscopic grading at intubation. Grade 3 & 4 of Cormack & Lehane was considered difficult intubation.

Butler PJ. et al. conducted on 250 patients, who did the pre-operative airway assessment by Mallampatti test and thyromental distance [12].

Table 3: Distribution and Correlation by Combination of Tests: The Mallampatti Grade and Thyromental distance with Cormack & Lehane grade in Prediction of difficult Intubation

Cormack and Lehane Grading	Mallampatti Grade		Total
	+ve(grade 3 &4)	-ve(grade 1 &2)	
+Ve	12	3	15
	80%	20%	100%
	75%	1.1%	5%
-Ve	4	281	285
	1.4%	98.6%	100%
	25%	98.9%	95%
Total	16	284	300
	5.3%	94.7%	100.0%
	100.0%	100.0%	100.0%

Table 4: Distribution of Combination of Tests - The Mallampatti Grade and Thyromental distance in Various Age Groups

Age	Mallampatti+Thyromental distance		Total
	+Ve	-Ve	
21 – 30 Yrs	5	108	113
	4.4%	95.6%	100.0%
31 – 40 Yrs	3	56	59
	5.1%	94.9%	100.0%
41 – 50 Yrs	1	52	53
	1.9%	98.1%	100.0%
51 – 60 Yrs	8	58	66
	12.1%	87.9%	100.0%
Total	17	283	300
	5.7%	94.3%	100.0%

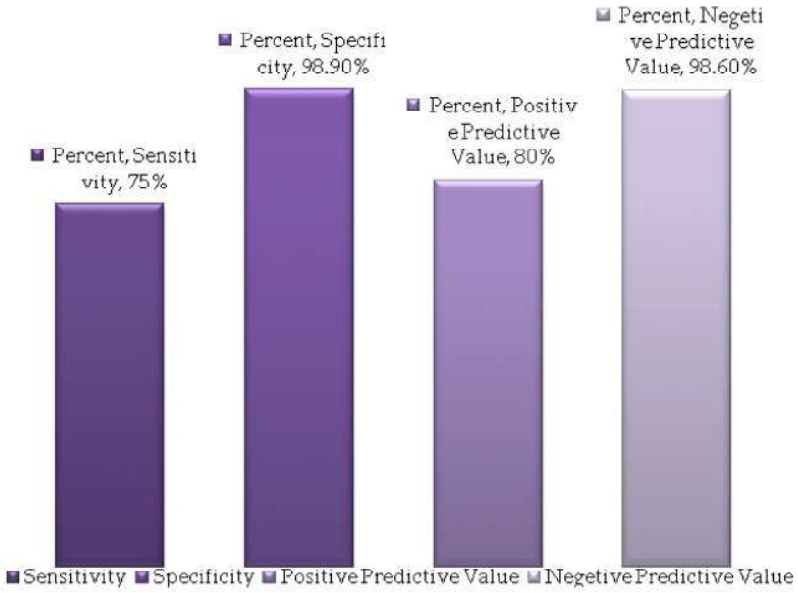

Fig 3: Sensitivity, specificity, PPV and NPV of Cormack and Lehane grading **vs**Mallampatti + Thyromental distance

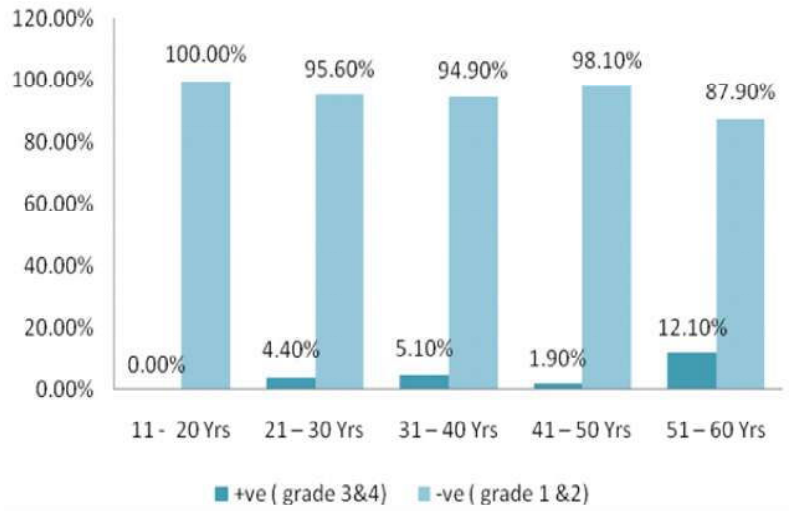

Fig 4: Distribution of combination of tests in various age groups

was found to be less than 6 cm in 17 and more than 6 cm in 283 patients. The Mallampatti Grade and Thyromental Distance in the Study Population as a combination was positive in 16 patients and negative in 284 patients.

Table 1: Distribution and Correlation of Mallampatti Grade with Cormack & Lehane Grade in prediction of difficult Intubation

Cormack and Lehane Grading	Mallampatti Grade predictor +ve (grade 3&4)	-ve(grade 1&2)	Total
+Ve (grade 3&4)	19	3	22
	86.4%	13.6%	100.0%
	67.86%	1.11%	7.33%
-Ve (grade 1&2)	9	269	278
	3.2%	96.8%	100.0%
	32.14%	98.89%	92.67%
Total	28	272	300
	9.3%	90.7%	100.0%
	100.0%	100.0%	100.0%

Table 2: Distribution and Correlation of Thyromental Distance with Cormack & Lehane Grade in prediction of difficult Intubation

Cormack & Lehane Grading	Thyromental Distance < 6 Cm	> 6 Cm	Total
+Ve (grade 3&4)	12	10	22
	54.5%	45.5%	100.0%
	70.59%	5.53%	7.33%
-Ve (grade 1&2)	5	273	278
	1.8%	98.2%	100.0%
	29.41%	96.46%	92.67%
Total	17	283	300
	5.7%	94.3%	100.0%
	100.0%	100.0%	100.0%

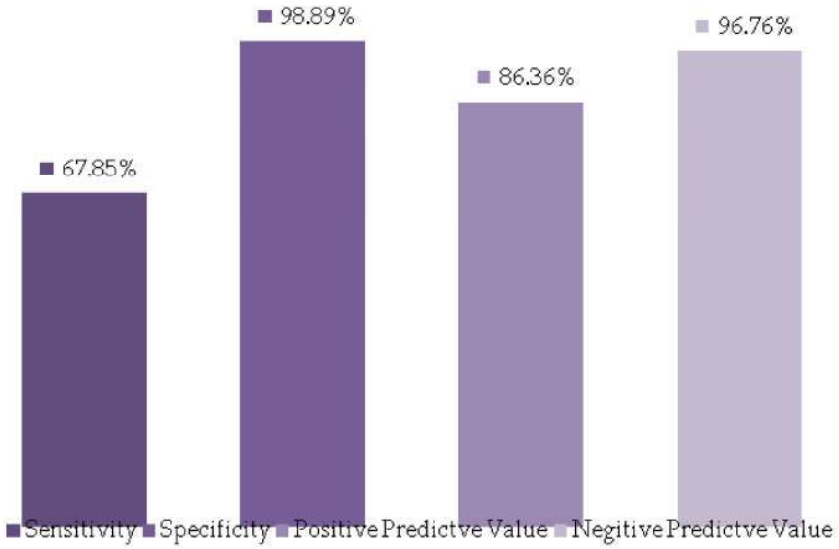

Fig 1: Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Cormack & Lehane Grading Vs Mallampatti Grade Predictor

The incidence of difficult intubation is found to be 5%

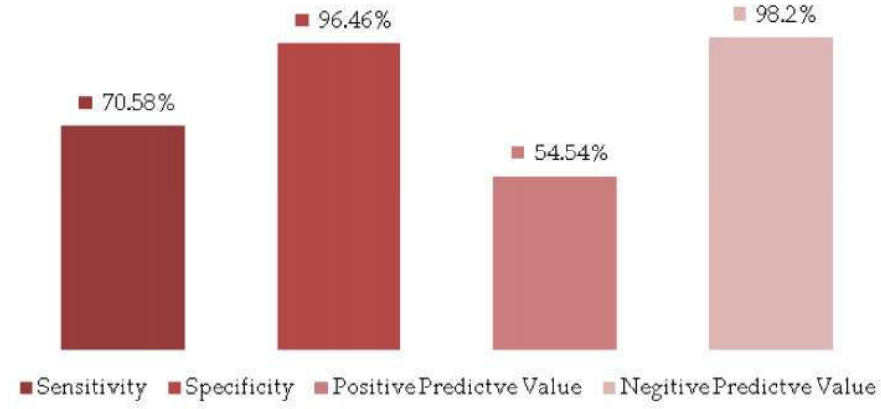

Fig 2: Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Cormack & Lehane Grading Vs Thyromental Distance Predictor

Methodology

Preanesthestic evaluation: The preanesthestic evaluation of patient was done in the ward. The consent was taken for surgical procedure, anesthetic technique and study. Evaluation of the patient was done by history of medical illnesses, surgical procedure, medication, drug allergy and general physical examination. Blood pressure, pulse, hydration were noted, body mass index was calculated, systemic examination was done and American Society of Anesthesiologist (ASA) grading was determined.

Airway Assessment: Airway was assessed by modified Mallampatti test and thyromental distance.

Modified Mallampatti Test: It is done by examiner sitting in front of the patient, who should be sitting up with head in neutral position and the patient is asked to open their mouth maximally and protrude the tongue without phonating and Mallampatti grading is done accordingly.

Grade 1: Visualization of soft palate, fauces, uvula, anterior and posterior pillars.

Grade 2: Visualization of soft palate, fauces and uvula.

Grade 3: Visualization of soft palate and base of uvula.

Grade 4: Only Hard palate is visible, soft palate is not visible at all.

Grades 3 and 4 are classified as predictor of difficult intubations.

Assessment of airway using Thyromental distance:

Done using a measuring tape from the mentum of the mandible to thyroid notch in the midline with neck in full extension. Measurement of less than 6 cms is considered to be predictor of difficult intubation.

Patient Preparation

All patients were premedicated with Tab. Ranitidine 150 mg and Tab. Diazepam 10 mg given orally night before surgery.

On the morning of surgery patient were shifted to the O.T, Non-Invasive Blood pressure, ECG, SpO2 monitors were connected and basal vitals were recorded. Patients were given Inj Pentazoscine 20-30 mg, Inj Midazolam 25 µg/kg given IV and pre oxygenated for 3 mins with 100% Oxygen.

Induction done with sleep dose of Thiopentone (approx 5 mg/kg) IV and relaxation done with inj Vecuronium 0.1 mg/kg IV. Patients were ventilated with 50% Nitrous oxide and 1% Halothane in oxygen. After 3 mins laryngoscopy was done in sniffing position by using Macintosh blade no 3/4. Cormack & Lehane grading was done accordingly by a senior anesthesiologist with more than two years experience post qualification. Subsequently the patients were intubated.

The following is the Cormack and Lehane grading:

Grade 1: Visualization of entire laryngeal aperture.

Grade 2: Visualization of only posterior commissure of laryngeal aperture.

Grade 3: Visualization of only epiglottis.

Grade 4: Visualization of only soft palate.

Grade 3 and 4 predict difficult intubation. The patients were intubated with appropriate sized endotracheal tube which were secured and anesthesia was maintained.

Results

Three hundred apparently normal ASA grade 1 & 2 adult patients in the age group 18-60 yrs of either sex posted for elective surgical procedures were prospectively studied.

Method of Statistical Analysis

The following methods of statistical analysis have been used in this study. The data were entered into a Microsoft Excel Worksheet and analyzed using SPSS (ver. 18) statistical package.

The results were presented in number and percentage in tables and figures.

The sensitivity and specificity of Mallampatti Grade predictor, Thyromental distance Predictor and Mallampatti + Thyromental distance, compared to the Cormack and Lehane Grading were determined. In addition to sensitivity and specificity, the positive and negative predictive values were calculated.

In our study Average age noted was 37.14±14.14; BMI was 24.04±1.687; female patients were 172 and male 128; Mallampatti grade 3 and 4 were considered as predictors of difficult intubation.28 cases out of 300 patients (9.3%) belonged to Mallampatti grade 3 and 4, remaining 272 were Mallampatti grade 1 & 2. Thyromental Distance

best predicting test in patients who are apparently normal by a combination of Modified Mallampatti test and Thyromental distance and comparing it with Cormack and Lehane Score.

The American society of Anesthesiologists (ASA) has defined endotrachel intubation as when proper placement of endotracheal tube with conventional laryngoscopy requires more than three attempts or more than 10 minutes. Difficult airway is also defined as a clinical situation in which conventionally trained anaethesiologist experiences difficulty with mask ventilation or difficult tracheal intubation or both [1]. Difficult intubation is the second most frequent proclaimed damaging event leading to anesthesia malpractice claims [2].

The ASA database of adverse respiratory events has found that a vast majority (85%) of airway related events involves brain damage or death, and as many as 1/3rd of death is attributed solely to anesthesia due to inability to maintain patent airway [3].

Occasionally with a patient who has difficult airway, the anesthesiologist is faced with a situation where mask ventilation is proved difficult or impossible. This is the most critical emergency that might be faced in the practice of anesthesia [4]. Most catastrophes have occurred when possible difficult airway was not recognized [5].

When anatomical abnormalities are hidden in the air passage, it is likely to be missed. In such patients if difficult intubation is predicted, it may be helpful. During routine anesthesia, the incidence of difficult intubation has been estimated at 5.8% [6].

Although an array of tests are available to predict difficult intubation, it is difficult to for the anesthesiologist as, no single score or combination of scores can be trusted to detect all patients who are difficult to intubate [7]. No system has yet been devised that has 100% positive predictive value or 100% sensitivity and specificity [8]. Hence unidentified difficult intubation can be challenging to the anesthesiologist.

The various bedside screening tests available to predict difficult intubation are the Mallampatti test which was introduced by Mallampatti S Rao and co-workers in 1985, which is classified based on visibility of oropharyngeal structures [9].

The distance from thyroid notch to mentum (thyromental distance), the distance from upper border of manubrium sterni to mentum (sternomental distance) and simple summation of risk factors (Wilson's risk score) are widely recognized as tools for difficult intubation [10,11].

Nevertheless the diagnostic accuracy of these screening tests has varied from trial to trial probably because of difference in the incidence of difficult intubation, inadequate statistical power, different test thresholds, or difference in patient characteristics. Question remains as to whether a combination of tests may improve predictive accuracy.

Therefore there is a need for a test that is quick and easy to perform at the bedside that is sensitive so that majority of difficult cases can be identified and is also highly specific.

Aims and Objectives

To use Mallampatti test during pre–operative assessment to determine incidence of difficult laryngoscopy and intubation; to use Thyromental distance test during pre-operative assessment to determine incidence of difficult laryngoscopy and intubation; to combine sensitivity and specificity of both the tests and determine, if the combination of both the tests increases the predictability of difficult intubations.

Materials and Methods

Source of data

300 consecutive (apparently normal) American Society of Anesthesiologist grade 1 & 2 adult patients undergoing elective surgical procedures under general anesthesia with endotracheal intubation at a tertiary care hospital,were the subjects in this study. Study design was Prospective clinical study.

Inclusion Criteria

All patients aged between 20 to 60 years of either sex; patients belonging to ASA (American Society of Anesthesiologist) Grade 1 and 2 Physical status; patients undergoing elective surgery under general anesthesia with endotracheal intubation.

Exclusion Criteria

Pregnant patients; patients with body mass index more than 30; mouth opening less than 3 cms; mid-line neck swellings; difficult neck movements; ASA (American Society of Anesthesiologists) 3 and 4 patients.

Original Research Article

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Prediction of Difficult Intubation in Apparently Normal Patients by Combining Modified Mallampatti Test and Thyromental Distance

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Abstract

Context: Difficult intubation is associated with serious complications, more so when there is failure of intubation. Inability to secure the airway during general anaesthesia remains one of the leading causes of morbidity and mortality worldwide. The principle goal of this study was to find the best predicting test in patients who are apparently normal by a combination of Modified Mallampatti test and Thyromental distance and comparing it with Cormack and Lehane Score. *Aims:* To use Mallampatti test & Thyromental distance test during pre-operative assessment to determine incidence of difficult laryngoscopy and intubation; To combine sensitivity and specificity of both the tests and determine, if the combination of both the tests increases the predictability of difficult intubation. *Settings and Design:* Prospective clinical study. *Methods and Material:* The preoperative airway assessment of Mallampatti grading & thyromental distance was done on 300 ASA grade 1 & 2 patients, aged between 18-60 yrs presenting for surgeries under general anesthesia. The preoperative Mallampatti test grading and the thyromental distance was compared with Cormack & Lehanelaryngoscopic grade. *Statistical analysis used:* Data was entered in to Microsoft Excel Worksheet and analyzed using SPSS (ver. 18) statistical package. In addition to sensitivity and specificity, the positive and negative predictive values were calculated. *Results:* The Mallampatti grade 3 & 4 were considered as predictors of difficult intubation 28 cases out of 300 patients (9.3%) of the study population belong to this group. Thyromental distance < 6 cm was considered as predictor of difficult intubation There were 17 cases out of 300 patients (5.7%) belonging to this group. When a combination of Mallampatti test and thyromental distance was used as a predictor of difficult intubation, there were 16 patients, which constituted 5.3% of the total cases. The incidence of difficult intubation is found to be 5%. *Conclusions:* The above result shows that the discriminative power is greater in combination of test than when used alone.

Keywords: Difficult Intubation; Mallampatti Test; Thyromental Distance.

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Introduction

An anaesthesiologist's fundamental responsibility is intubation and maintenance of patients airway which is the important step in anaesthesia practice. Difficult intubation is associated with serious complications, more so when there is failure of intubation. Inability to secure the airway during general anaesthesia remains one of the leading causes of morbidity and mortality worldwide. It is the responsibility of the anesthesiologist to perform an evaluation in order to predict potential difficult intubation. The principle goal of this study was to find the

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(lignocaine) both reduced the pain of propofol injection.

In our study we use 2 ml (2%) lignocaine. Our study also showed good results with lignocaine in reducing the pain of propofol injection.

In our study the HR, SBP, DBP were significantly raised in granisetron group as compared to lignocaine group. Moreover in our study we found that average pain score with granisetron was 2.1 while with lignocaine it was 0.8 our results show that pre-treatment with lignocaine is more effective than pre-treatment with granisetron in relieving pain of propofol injection.

Conclusion

Propofol is very commonly used agent for induction of anaesthesia due to its smooth induction and excellent emergence. Pain on propofol injection is very common complaint which can be relieved by number of drugs. We conclude from our study that lignocaine hydrochloride is better than granisetron for alleviating pain of propofol injection.

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treatment with lignocaine in decreasing propofol injection pain. They found significant decrease in pain incidence from 46.7% to 13.5% by mixing lignocaine 10 mg with propofol as compare to pre-treatment with lignocaine 10 mg 30 second before propofol injection (46.7% to 40%) [14].

A 4 point verbal rate scale (VRS) was chosen in this study rather than visual analogue score (VAS). VAS required hand-eye coordination and it's not possible during the rapidly changing state of consciousness. So we used VRS in our study to quantity pain intensity. Dhananjay Kumar Singh et al. [11] and Ahmed et al. [17] also used 4 point verbal rate scale in their study.

Lignocaine is commonly used to decrease the pain on propofol injection [15,16,4]. Ondansteron has long been used for propofol pain by virtue of its mu opioid agonism, 5-HT_3 antagonism and Na^+channel blocking action [9]. We compared a novel drug granisetron which is a 5-HT_3 antagonist like ondansetron and expected to have some effects like it.

King Sy, Davis Fm, Wells JE et al. [2], in 1992 studied various dose of lignocaine and concluded that significant reduction in the pain from 73% with saline to 32% with 20 mg lidocaine 1 ml (1%).

G. Gehan et al. [15], studied optimal dose of lignocaine for preventing pain on propofol injection. They compared the different doses of lignocaine mix with with propofol 0.1 mg/kg, 0.2 mg/kg, 0.4 mg/kg and control group. They concluded that lignocaine 0.1 mg/kg significantly reduced the incidence of pain and there was no improvement as dose was increased. Haemodynamic changes were similar in all four groups and no significant cardiac event present due to lignocaine.

Agarwal et al. [10] in their study compared the efficacy of pre-treatment with thiopental 0.25 mg/ kg and 0.5 mg/kg and lignocaine 40 mg for prevention of propofol induced pain. They found 77% patients complained of pain in the group pre-treated with normal saline as compared with 39%, 37%, 3% in groups pre-treated with lignocaine 40 mg, thiopental 0.25 mg/kg and 0.5 mg/kg respectively. ($p<0.05$)

We also used 40 mg lignocaine and pain relief was in 40% of patients.

Sarita Fernandes et al. [18] also concluded that lidocaine is superior to acetaminophen in reducing the pain on injection of propofol.

Ahmed et al. [17] in 2012 in their study observed that pain reduced from 60% to 15% by pre-treatment with granisetron when the venous drainage was occluded manually at mid arm by assistant for 1 minute after IV injection.

We also used mid arm occlusion technique for our study.

Many other authors have compared lignocaine and granisetron with other drugs to relieving pain of propofol injection.

Ye JH, Mui WC, Ren J et al. [12] in 1997 studied that ondansteron exhibits the properties of a local anaesthetic. It acts as a Na^+ channel blocker, a 5 HT_3 receptor antagonist and mu opioid agonist.

Granisetron is a more 5HT_3 antagonist so relieved pain by a similar mechanism. We used granisetron 2 ml (1 mg/ml) for our study. Ahmed et al. [17], Swati et al. [19] and Dhananjay Kumar Singh [19] also used same dose of granisetron.

Swati et al. [19] also concluded that there was 100% no pain in granisetron group than saline group which was highly significant. While we compared granisetron and lignocaine and observed that lignocaine has good pain relief.

Dhananjay Kumar Singh et al. [11] studied that granisetron reduced the incidence of propofol injection pain most effectively than nitroglycerine followed by magnesium sulphate. They found that granisetron reduced the incidence of propofol injection pain to 40% from 88% in placebo at 15 seconds.

B P Manjula et al. [20] used lignocaine 30 mg and granisetron 2 mg as pre-treatment before propofol injection. They concluded that there was 76% in lignocaine group and 62% in granisetron group did not have pain, 12% and 20% had mild pain, 12% and 18% had moderate pain in lignocaine and granisetron group respectively.

R cork et al., studied in 2008 [21] a comparison of the verbal rating scale and the visual analogue scale for pain assessment. They found an excellent correlation between the two (Pearson coefficient $r = 0.906$ & $p < 0.001$)

The average heart rate (HR), SBP, DBP at 0, 1, 3 min after propofol injection were raised in granisetron group than lignocaine group. Ahmed et al. [17] also noticed that there was transient rise in HR in patients suffering from pain of VRS score 2-3 in both the groups but no changes in blood pressure. The haemodynamic data from this study are difficult to compare because of variation in study.

All studies showed that 5- HT3 antagonists (granisetron, ondansetron etc.) and local anaesthetic

students 'T' test on graph pad software. P value < 0.05 was considered as statistically significant.

Results

All data were recorded and expressed in terms of mean±standard deviation. p value < 0.05 was considered significant. Statistical software from www.Graphpad/instate3 site was used.

Tables 1 shows both groups were comparable with respect to age distribution and gender and statistically not significant (p> 0.05).

Table 2 shows a different trend in both groups. The average HR at 0, 1 & 3 min after propofol injection were 79.6±7.73, 78.16±5. 83 and 76.76±5.88 in the lignocaine group while they were 80.4±9.06, 90.76±9.14 and 92.8±8.18 in the granisetron group was statistically significant (p < 0.0001) and was due to pain induced tachycardia.

Table 3 shows that the systolic blood pressure (SBP) at 0,1 & 3 minute after propofol injection were 122.9±9.88, 118.6±10.01 and 115.0±9.4 mm of Hg in the lignocaine group, while in the granisetron group, it was 126.4±9.87, 132.4±10.9 & 134.2±11.79 mm of Hg. The rise in SBP was more in the granisetron group and the difference in both groups was statistically significant (p < 0.0001).

Table 4 shows the diastolic blood pressure (DBP) in lignocaine group at 0, 1& 3 min were 72.7±7.09, 68.72±6.47 & 66.24±5.54 mm of Hg while DBP in granisetron group were 75.12±6.95, 79.04±8.64 and 82.0±8.92 mm of Hg. The DBP was significantly lower (p< 0.0001) in lignocaine group which shows better control of propofol pain during injection.

Table 5 shows the pain score (VRS) at 15 second. After propofol bolus (2 ml/4s) injection. The pain score in lignocaine group is 0.8±0.81 while in granisetron group it is 2.1±0.68. Now this is statistically significant (p < 0.0001). This means that lignocaine was more effective in blunting pain of propofol injection as compared to granisetron.

Hence the incidence of moderate to severe pain was quite high in granisetron group compared to the lignocaine group (p < 0.0001).

Table 1: Demographic Data

	Age (Yrs.)	p value	Sex (M:F)
Group G	42.5(3.5355)	1.0000	23:02
Group X	40.0(4.2426)	1.0000	18:07

All the data were represented as mean±SD.

Table 2: Changes of heart rate (bpm) at 0, 1, 3 min

Time	Group X	Group G	P value
O Min	79.60(±7.73)	80.40(±9.06)	0.7385
1 Min	78.16(±5.83)	90.76(±9.14)	0.0001(s)
3 Min	76.76(±5.88)	92.80(±8.18)	0.0001(s)

Table 3: Changes of SBP (mmHg) at 0, 1, 3 min

Time	Group X	Group G	P value
0 Min	122.96(±9.88)	126.48(±9.87)	0.2138
1Min	118.64(±10.01)	132.40(±10.96)	0.0001(s)
3 Min	115.04(±9.40)	134.24(±11.7)	0.0001(s)

Table 4: Changes of DBP (mmHg) at 0, 1, 3 min

Time	Group X	Group G	P value
0 Min	72.72(±7.09)	75.12(±6.95)	0.2329
1 Min	68.72(±6.47)	79.04(±8.64)	0.0001(s)
3 Min	66.24(±5.54)	82.00(±8.92)	0.0001(s)

Table 5: Pain score (VRS) at 15 sec

Time	Group X	Group G	P value
15 sec	0.8(0.81)	2.1(0.68)	0.0001(s)

Discussion

Nowadays anaesthesiologists are expected to provide their services with safe and uncomplicated technique to patient. The patient also expects painless, safe and uncomplicated anaesthesia for their operative procedures.

Propofol [13] (2-6-di isopropyl phenol) is one of the most popular anaesthetic induction agent for inducing general anaesthesia for surgery as well as for sedation in various procedures with many advantages and low incidence of side effects. The rapid action, smooth induction as well as quick recovery make it an ideal anaesthetic agent. But pain on injection limits its use, it is a common problem and can be very distressing to the patient.

Propofol preparation we use is a 1% (wt/vol) aqueous emulsion containing 10% w/v soybean oil, 2.25% glycerol and 1.2% purified egg phosphatide lecithin. The pH is 7 and pka of the drug in water is 11.

Scott RP et al. observed that the pain on injection is caused by activation of the Kallikrein-kinin system or by the lipid solvent in propofol by generating kinins, mainly bradykinin, local vasodilation & hyper permeability, increase the contact between the aqueous phase propofol and the free nerve ending. This pain has a delayed onset up to 10-20 seconds. They found that lignocaine mixed propofol was more effective than pre-

pain perception. Moreover, tissue damage causes release of PGs, TX, Serotonin and other chemical mediators which further sensitize the nociceptors and reduce the threshold of pain sensitivity.

Propofol (2, 6, di-isopropyl phenol) is a chemically phenol base anesthetic agent. Pain during injection of propofol is a very unpleasant and irritating event. Incidence of pain during propofol injection varies between less than 10% in large veins at the cubital fossa to 90% in veins at the dorsum of hand [1]. The immediate vascular pain on injecting propofol is attributed to the direct irritant effect of propofol on nociceptors at the intimal layer of vessel.

The delayed pain (after 10-20 sec) is probably due to activation of Kallikrien- Kinin system. Many factors affect the incidence of pain on injection like age of patient, site and size of veins, temperature, PH of the formulation, speed of injection, concentration in the aqueous phase and the buffering effect of blood.

Lignocaine is an amide based local anaesthetic [2] which blocks the Na^+ channel in the nociceptors and prevents the transmission of the noxious stimulus from nociceptor to the pain fibres. Moreover, as it is a weak base, it releases H^+ ion on contact with a lipid like propofol and thus decreases PH. Thereby decreasing concentration of free propofol molecules. These two mechanisms help to decrease pain at propofol injection.

Granisetron is a 5-HT3 receptor antagonist [3]. It blocks the effect of serotonin on the nociceptors and thus reduces the intensity of pain on propofol injection.

Other agents used to reduce pain of propofol includes Opioids [4], Ketamine [5], NSAIDS [6], Nitrous oxide [7], Steroids [8], ondansetron [9], thiopental sodium [10], $MgSO_4$ [11], NTG [11] etc. Ondansetron exhibits property of local anaesthetic. So, granisetron is also 5-HT3 receptor antagonist and may be exhibits local anaesthetic properties [12].

Aim of our study was to evaluate the comparison of granisetron and preservative free lignocaine in alleviating the pain of propofol after intravenous injection.

Material and Methods

After approval from institutional ethical committee, fifty patients aged between 18-50 years of age, of both sexes, belonging to ASA grade I & II, who were scheduled to undergo elective surgeries under general anaesthesia were randomly divided into two groups.

Informed consent from all patients were taken and explained about the procedure. Patients with history of allergy to lignocaine, propofol or granisetron were excluded. Patients belonging to ASA grade III, IV, those undergoing emergency surgery and those who could not communicate properly were also excluded.

Routine preanaesthetic evaluation was performed. All routine investigation was done. On arrival in the operating room, the baseline readings of HR, NIBP, SpO_2 and ECG of all patients were recorded. 20 G IV Cannula was inserted into a vein on the dorsum of patient's non-dominant hand & RL infusion started.

Verbal rating score was recorded during propofol injection.

Patients in Group G received 2 ml of (1 mg/ml) granisetron, while in Group X 2 ml 2% lignocaine were given over 5 seconds. Both drugs were given 5 min after IV cannulation.

At the time of propofol injection, manual occlusion at midarm was applied for 1 min and then released. Next propofol injection of 2 ml bolus was given over 4 second. 15 seconds after this small bolus dose, patients were asked to rate any pain sensation during the injection.

An anesthesiologist blinded to the study recorded the pain using the verbal rate scale:

0 = None (Negative response to questioning)

1 = Mild Pain (Pain reported only on questioning and no behavioural signs)

2 = Moderate Pain (Pain reported on asking with behavioural signs or pain reported spontaneously)

3= Severe Pain (Strong vocal response with facial grimacing, arm withdrawal or tears from eyes.)

After recording this, patients were induced with Glycopyrrolate 4 mcg/kg, Fentanyl 2 mcg/kg, Propofol 2.5 mg/kg and Succinyl choline 2 mg/kg IV. After IPPV with 100% O_2 tracheal intubation was done with appropriate sized portex endotracheal tube.

HR, NIBP, SpO_2 and ECG were recorded before propofol injection and at 0, 1 & 3 min after propofol.

Maintenance was done with N_2O, O_2, and vecuronium bromide 0.1 mg/kg IV and Isoflurane as volatile anaesthetic agent. At the end of surgery patients were reversed with neostigmine bromide 0.05 mg/kg and glycopyrrolate 5 mcg/kg IV and shifted to ICU.

Statistical analysis: Group X and Group G study results were statistically analysed by using unpaired

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Comparative Evaluation of Intravenous Granisetron Hydrochloride and Intravenous Lignocaine Hydrochloride to Alleviate the Pain on Propofol Injection

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Abstract

Propofol is one of the most commonly used induction agent. Pain on injection still remains a considerable concern for anaesthesiologist. The aim of the study was to assess the efficacy of granisetron HCL and ligocaine HCL to alleviate the pain on propofol injection. *Methods:* Fifty patients aged 18-50 years, ASA grade 1-2, posted for elective surgeries under general anaesthesia were randomly divided into two groups. Group G received 2 ml (1 mg/ml) granisetron while group X received 2 ml (2%) ligocaine intravenously before propofol injection. Manual venous occlusion was done for 1 minute after pre-treatment drug. 2 ml of total calculated dose of propofol was given over a period of 4 seconds. Patients were asked about the pain on injection with use of verbal rating score chart after 15 seconds. HR, SBP, DBP, SpO_2 was measured 0, 1, 3 minute after propofol injection. *Results:* HR, SBP and DBP were significantly raised in granisetron group as compared to lidocaine group. Average pain score in group G was 2.1 while in group X it was only 0.8, which was statistically significant. ($p<0.05$). *Conclusion:* We conclude that lignocaine HCL is better than granisetron for alleviating pain after propofol induction.

Keywords: Pain; Propofol; Lignocaine Hcl; Granisetron Hcl.

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Introduction

Pain is a vital function of the nervous system which warns the body of potential or actual tissue damage. The pain pathway begins with the specialized pain receptors (nociceptors) which are spread throughout the body. These nociceptors are stimulated by a number of stimuli like mechanical forces, thermal injuries as well as chemical substances. The noxious stimuli are converted into electrical stimuli and transported to spinal dorsal horn via A and C fibres. In the spinal cord these stimuli are carried via spinothalamic tracts into the thalamus and from there into the cerebral cortex. There are other accessory ascending & descending tracts which modulate the degree of

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paracetamol group to be 4.27 hours and slightly higher 4.86 hours in Tramadol group.

Also, the frequency of rescue analgesic requirement was lower in Group T in the 24 hours study period. The patients in Group T required 1 to 2 times of rescue analgesia with a mean of 1.20 (±0.41), in comparison to the Group P, where patients required 2 to 3 times of rescue analgesia with a mean of 1.67 (±0.71).This was also found to be statistically significant with P-value of 0.001.

In our study, 5 patients complained for PONV in Group P and 16 patients in Group T. Also, 3 patients complained of sedation in Group T. No cases of urinary retention were observed in either group.

Kela et al. [19] compared the efficacy of either drug in the postoperative period in cardiothoracic surgery and found 10.0% of the subjects in paracetamol group and 13.3% of the subjects in tramadol group suffered nausea and vomiting which were comparable and difference was insignificant. Caken T et al. [20], Mohammad Shahid et al. [9], Pratyush Goel [5] et al. and Jeong-Yeon Hong et al. [6] in their study found decreased incidence of nausea and vomiting with the use of IV paracetamol which is similar to our study.

It becomes evident from this study that the paracetamol can be a good alternative to tramadol and thus can avoid the complications associated with non-steroidal anti-inflammatory drugs and opioids.

Potential limitation of the study are that IV paracetamol in head and neck cancer offers central analgesic effects but the anti-inflammatory effects, which is enhances analgesia in the early post-operative period is not possible. So moderate to severe pain and bony pain may not be addressed adequately with paracetamol. Though it is having less incidence of PONV than tramadol, patients with borderline liver dysfunction patients may be at high risk as only repeated administration of paracetamol is effective.

Conclusion

Intravenous paracetamol administration in peri-operative period provided adequate postoperative analgesia in patients undergoing head and neck cancer surgery. In contrast to opioids, paracetamol does not produce sedation, respiratory depression or constipation, nor is it associated with a risk of substance abuse or misuse. Based on these findings, intraoperative IV paracetamol appears to be a reasonable choice for postoperative analgesia in this patient population.

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While comparing the DBP, in both the groups, we have observed that there is no significant variation in both the groups at different intervals, with highest mean value of 86.26 (±2.55) in Group P and 85.66 (±1.72) in Group T, are statistically insignificant on comparison with a p value > 0.05.

Arici et al. [10] studied the pre-emptive analgesic effects of intravenous paracetamol in total abdominal hysterectomy and found a decrease in mean values of heart rate, SBP, DBP intra-operatively after paracetamol administration. They also found decrease consumption of morphine post-operatively.

In this study, the mean VAS was statistically comparable in the immediate postoperative period with a p-value of 0.3953 which is insignificant. At 3 hours, the mean VAS is 3.10 (±0.51) in Group P and it is 2.94 (±0.24) in Group T and they are statistically significant (P=0.0458). But after 6 hours interval, the mean VAS is decreased to 0.88 (±0.59) in Group P and it is increased to 3.84 (±1.47) in Group T, which is statistically significant (p<0.0001). This indicates that after administration of subsequent dose of paracetamol in Group P patients, the mean VAS decreased significantly, whereas it is on higher side in Group T patients in whom next dose was due at that time.

Nikoda et al. [11] in his study of IV infusion of paracetamol in a single dose of 1g (4 g/day) for postoperative analgesia reported a reduction in the intensity and duration of pain and that the IV formulation of paracetamol should be used as multimodal therapy for mild to moderate postoperative pain management.

At 9 hours, the mean VAS is 3.04 (±0.28) in Group P and it is 2.06 (±0.31) in Group T, which is statistically significant (p<0.0001). And at 12 hours, the mean VAS is 1.98 (±0.44) in Group P and it is 3.62 (±0.44) in Group T, which is statistically significant (p < 0.0001). Again at 16 hours, the mean VAS is 3.08 (±0.74) in Group P and it is 1.76 (±0.46) in Group T. There is higher VAS score in Group P as compared to Group T, which is statistically significant (p < 0.0001). This indicates that after administration of subsequent doses of either paracetamol or tramadol, the pain relief is adequate, which is seen in decline in respective mean VAS score in both the groups.

After 20 hours in post-operative period, the mean VAS is 2.12 (±0.38) in Group P and it is 2.10 (±0.51) in Group T, which is statistically insignificant (p=0.8243). And at 24 hours, the mean VAS is 0.88 (±0.59) in Group P and it is 0.76 (±0.48) in Group T, which is also statistically insignificant (p=0.2678).

Sinatra RS et al. [12] in his study found that intravenous acetaminophen was consistently superior to placebo for pain relief and for pain intensity changes from 15 min to 6 h after the first dose and throughout the 24-h evaluation period after repeated dose administration. Jeong-Yeon Hong et al. [6] showed that VAS scores were significantly lower in the paracetamol group at 1, 3, 6 and 24 hours after surgery and significantly fewer patients in the paracetamol group received rescue analgesic than the placebo group.

Aghamir et al. [13] compared propacetamol and tramadol after urologic open surgeries and found propacetamol useful, but inadequate in cases of severe pain, whereas Uysal et al. [14] compared either of the drugs in post-adenotonsillectomy pediatric patients and found iv paracetamol to be superior in terms of early recovery, but associated with similar analgesic properties. Turhan Togrul et al. [15] studied the comparison of intravenous Paracetamol and Tramadol for postoperative analgesia in patients with septo-rhinoplasty and concluded that iv paracetamol administration provided adequate analgesia as opioids especially at early post-operative period for mild to moderate pain therapy in peri-operative period. Howard S. Smith et al. [16] studied the analgesic effects of intravenous paracetamol and NSAIDs and concluded that iv paracetamol represents a safe and effective first-line analgesic agent for the treatment of acute mild-to-moderate pain in the perioperative setting.

Sinatra et al. [12] found that IV paracetamol has rapid onset of analgesia in orthopaedic surgeries and IV paracetamol 1 g administered in patients with moderate to severe pain offered quick and effective analgesia. They found IV paracetamol significantly reduced morphine consumption over the 24 hours period and safe in terms of clinical and laboratory examinations. Cade et al. [17] and Hein et al. [18] in their study did not found postoperative analgesic or opioid sparing effects with paracetamol after minor and major surgery and this might be due to the single injection of paracetamol which would not be expected to provide pain relief even after minor surgery hence in our surgery we used repeated injections of paracetamol to get the desired effect.

We observed that the time to 1st dose of rescue analgesia requirement was lower in Group T in the 24 hours study period, with the mean postoperative rescue analgesic free time interval of 6.23±1.72 hours, as compared to Group P where it is 5.01±1.16 hours. This is found to be statistically significant with P value of 0.0001. Party's et al. [5] in his study found mean duration of analgesia in

Table 7: shows Side Effects

Side Effects	Group P	Group T
Sedation	nil	3
Abdominal pain	nil	nil
LFT complications	nil	nil
Nausea & vomiting	5	16
Respiratory depression	nil	nil
Allergic reaction	nil	nil

Table 7 shows side effects in both the groups. Group P recorded less number of patients (10%) with nausea and vomiting (PONV) as compared to Group T which recorded significantly higher number of patients (32%) in the immediate post-operative period. Also, sedation was seen in 3 patients (6%) in Group T. No alterations were seen in the liver function tests of the patients receiving paracetamol.

Discussion

Pain is a subjective and multidimensional experience that is often inadequately managed in clinical practice. It is a multifaceted and highly personal experience, as McCaffery described "pain is whatever the experiencing person says it is and exists whatever he/she says it does" [7]. It causes significant distress to patients and has adverse effects on the endocrine and immune system function, which can affect wound healing and cardiopulmonary and thromboembolic diseases. Post-operative pain is one of the most frequently reported post-operative symptoms. The post-operative period was defined as the period between arrivals of the patient in recovery to 7 days after surgery, with day 1 being 24 hours after surgery. The incidence of moderate to severe pain with cardiac, abdominal or orthopedic inpatient procedures has been reported to be as high as 25% to 76% [8].

Management of post-operative pain in the initial 24 hours is critical. Inadequate pain management leads to delayed mobilization and longer duration of stay in the hospital. Post-operative pain is an unpleasant sensory, emotional and mental experience which is precipitated as a result of surgery and is often associated with autonomic, endocrine, metabolic, physiological and behavioral response.

With this background, we designed the study to compare the post-operative analgesic effects of intravenous paracetamol and intravenous tramadol in head and neck cancer surgery patients. Analgesic effects were assessed with Visual Analogue Scale (VAS Score) in both the groups.

In our study, we have found that there was no significant variation between the groups when comparing the demographic variables like age, sex, weight, ASA status and the duration of surgeries. Premedication and anaesthetic technique was kept constant in order to avoid variations in our observations.

While comparing the heart rate, we found that there was no statistically significant variation in both the groups. Heart rate was on the higher side just after the recovery from anaesthesia with a mean value of 87.34 (±4.03) in Group P and 86.68 (±3.28) in Group T and their P-value is 0.3713 that is insignificant, but after 3 hours interval, there is mild decrease in the values for heart rate with highest value reaching in Group P is 78.88 (±2.45), and in Group T, it is 78.64 (±2.31), which are statistically insignificant. So, we can correlate the initial increase in heart rate is due to anxiety and not due to pain. Mean changes in heart rate at different intervals are insignificant.

Mohammed Shahid et al. [9] (2015), in their comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies found that nothing statistically significant was observed in terms of hemodynamics including VAS scores between either group. They said that IV paracetamol is a safer alternative to tramadol with lesser PONV in the postoperative period which results into the lesser duration of hospitalization and hence earlier discharge.

Pratyush Goel et al. [5] in their comparative study for pre-emptive analgesia with IV paracetamol and IV diclofenac sodium in patients undergoing various surgical procedures found the comparison of heart rate between paracetamol and diclofenac group was significant. Heart Rate was almost equal to base line value in Diclofenac group patients and it was increased in paracetamol group patients. Mean values of SBP and DBP showed increase in Paracetamol group however it was not significant.

While comparing SBP, we found that changes in SBP in both the groups at different intervals, with highest mean value of 131.74 (±4.47) in Group P and 130.88 (±4.37) in Group T, are statistically insignificant on comparison with a p value > 0.05.

dose of paracetamol in Group P patients, the mean VAS score decreased significantly, whereas it is on higher side in Group T patients in whom next dose was due at that time.

Table 6 shows rescue analgesic requirement in both the groups. Time to 1st dose of rescue analgesia requirement was lower in Group T in the 24 hours study period, with the mean postoperative rescue analgesic free time interval of 6.23±1.72 hours, as compared to Group P where it is 5.01±1.16 hours. This is found to be statistically significant with p-value of 0.0001.

Frequency of rescue analgesic requirement was lower in Group T in the 24 hours study period. Patients in Group T required 1 to 2 times of rescue analgesia with a mean of 1.20 (±0.41), in comparison to the Group P, where patients required 2 to 3 times of rescue analgesia with a mean of 1.67 (±0.71). However, this was also found to be statistically significant with p value of 0.001.

Table 3: Shows SBP changes (mm of Hg) in both groups at different intervals

Time	Group P(Mean±Sd)	Group T(Mean±Sd)	p Value
0 min	131.74±4.47	130.88±4.37	0.3331
3 hrs	128.02±4.11	127.58±3.96	0.5869
6 hrs	125.78±3.09	125.04±2.43	0.1862
9 hrs	123.52±2.13	123.14±1.78	0.3354
12 hrs	121.95±1.93	121.52±1.62	0.2305
16 hrs	120.54±1.82	119.86±1.68	0.0551
20 hrs	119.42±1.57	118.94±1.38	0.1076
24 hrs	117.98±1.67	117.52±1.53	0.1542

Table 4: Shows DBP changes (mm of Hg) in both groups at different intervals

Time	Group P (Mean±Sd)	Group T (Mean±Sd)	p Value
00 min	86.26±2.55	85.66±1.72	0.1709
03 hrs	82.80±2.29	82.36±1.85	0.2932
06 hrs	82.14±2.14	81.68±1.73	0.2401
09 hrs	81.62±1.88	80.96±1.71	0.0693
12 hrs	80.70±1.53	80.02±2.06	0.0639
16 hrs	79.68±1.43	78.98±2.08	0.0527
20 hrs	78.84±1.31	78.48±2.05	0.2980
24 hrs	76.72±1.75	76.10±2.00	0.1022

Table 5: shows Visual Analogue Score (VAS) at different intervals

Time	Group P (Mean±Sd)	Group T (Mean±Sd)	p Value
0 min	2.12±0.39	2.06±0.31	0.3953
3 hrs	3.10±0.51	2.94±0.24	0.0458
6 hrs	0.88±0.59	3.84±1.47	<0.0001
9 hrs	3.04±0.28	2.06±0.31	<0.0001
12 hrs	1.98±0.44	3.62±0.98	<0.0001
16 hrs	3.08±0.74	1.76±0.46	<0.0001
20 hrs	2.12±0.38	2.10±0.51	0.8243
24 hrs	0.88±0.59	0.76±0.48	0.2678

Table 6: shows Rescue analgesic requirement

Rescue analgesia	Group P	Group T	p Value
Time to 1st dose of rescue analgesia (hrs)	5.01±1.16	6.23±1.72	0.0001
Total no of doses of rescue analgesic in 24 hrs	1.67±0.71	1.20±0.41	0.001

the study drug groups. Ondansetron 4 mg IV was administered if patient experienced severe nausea and episode of vomiting.

Results

This study was a prospective, randomized one. The total number of 100 patients, who were posted for head and neck cancer surgeries, were enrolled in the study. The data was recorded in Excel panel and statistical analysis was done after completion of the study. Data was analyzed by standard statistical unpaired t-test using Graph pad software and for significant difference between the groups, p-value of < 0.05 was taken as a reference of significance.

Table 1 shows demographic details. Mean age (yr) and wt (kg) in both the groups are comparable and statistically not significant ($p > 0.05$). Mean surgical duration in both groups is statistically not significant ($p > 0.05$).

Table 2 shows heart rate changes in both groups at different intervals**.** Changes in heart rate between the two groups at different intervals were not significant and were statistically comparable in both the groups. Heart rate was on the higher side just after the recovery from anesthesia with a mean value of 87.34 (±4.03) in Group P and 86.68 (±3.28) in Group T and their P value is 0.3713 that is insignificant, but after 3 hours interval, there is mild decrease in the values for heart rate with highest value reaching in Group P is 78.88 (±2.45), and in Group T, it is 78.64 (±2.31), which are statistically insignificant.

Table 3 shows systolic blood pressure changes in both groups at different intervals. Changes in systolic blood pressure at different intervals between the two groups were not significant and were statistically comparable in both the groups. Highest mean value of SBP was 131.74 (±4.47) mm of Hg in Group P and 130.88 (±4.37) mm of Hg in Group T, are statistically insignificant on comparison with a p value > 0.05.

Table 4 shows diastolic blood pressure changes in both groups at different intervals. Changes in diastolic blood pressure at different intervals between the two groups were not significant and were statistically comparable in both the groups. There is no significant variation in both the groups at different intervals, with highest mean value of 86.26 (±2.55) mm of Hg in Group P and 85.66 (±1.72) mm of Hg in Group T, are statistically insignificant on comparison with a P value > 0.05.

Table 5 shows visual analogue score (VAS) at different intervals. VAS was significantly lower at certain time intervals in both the groups. First analgesic time was longer in the Tramadol group as compared to Paracetamol group. Mean VAS was statistically comparable in the immediate postoperative period with a p-value of 0.3953 which is insignificant. At an interval of 3 hours, the mean VAS is 3.10 (±0.51) in Group P and it is 2.94 (±0.24) in Group T and they are statistically significant (P=0.0458). But after 6 hours interval, the mean VAS decreased to 0.88 (±0.59) in Group P and it is increased to 3.84 (±1.47) in Group T, which is statistically significant (p<0.0001). This indicates that after administration of subsequent

Table 1: shows Demographic Data

Variables	Group P	Group T	p value	Significance
Age (Years)	48.40±12.18	48.04±10.70	0.8756	NS
Weight(kgs)	60.18±6.48	58.96±5.37	0.3079	NS
Sex (M/F)	39/11	40/10	-	-
ASA status(I/II)	24/6	25/5	-	-
Duration of surgery(mins)	210.83±41.83	219.33±47.32	0.7434	NS

Table 2: shows Heart rate changes (BPM) in both groups at different intervals

Time	Group P (Mean±Sd)	Group T (Mean±Sd)	p Value
00 min	87.34±4.03	86.68±3.28	0.3713
03 hrs	81.94±2.66	81.80±2.64	0.7922
06 hrs	78.88±2.45	78.64±2.31	0.6154
09 hrs	75.50±2.45	75.52±2.20	0.9658
12 hrs	73.84±1.87	73.90±1.64	0.8649
16 hrs	73.22±1.45	73.10±1.39	0.6736
20 hrs	72.74±1.06	72.60±1.07	0.5125
24 hrs	72.54±0.91	72.48±0.84	0.7326

actual or impending tissue damage. Acute pain in perioperative setting is defined as pain that is present in a surgical patient because of pre-existing disease, surgical procedure or a combination of these. It is an unpleasant and inevitable component of the postsurgical experience. It also exerts deleterious effects on systems like respiratory, cardiovascular, neuroendocrine, gastrointestinal and other systems of the body [4].

Inadequately controlled postoperative pain causes discomfort, increased use of medications, slower recovery, longer hospital stay and increased risk of pulmonary complications [5]. Postoperative analgesia with safer drugs and minimal side effects is the first choice.

NSAIDs, opioids and acetaminophens are used to alleviate postoperative pain. NSAIDs are associated with risk of bleeding and renal dysfunction while opioids are associated with potentially harmful effects like respiratory depression, post operative nausea and vomiting (PONV), sedation etc [6]. Acetaminophens are nowadays used for postoperative analgesia because of its well established safety and analgesic profile without significant drug interaction. Hepatic toxicity is rare but can occur with its overdose.

Paracetamol is commonly used drug for the treatment of pain and fever. Intravenous paracetamol crosses blood brain barrier easily and its analgesic action starts within 15-20 min. Maximal analgesic activity occurs 1-2 hours after peak plasma levels and peak plasma concentration is achieved approximately 25 min after 1 gm of IV infusion of paracetamol. Adverse reactions occurring from the use of IV paracetamol are extremely rare (1/1000).

Tramadol is a centrally acting analgesic. It has effect on norepinephrine and 5- hydroxytryptamine neurotransmitters. It has weak opioid agonist properties. Onset of IV formulation is within 5 min, analgesic effect peaks within 15 min and last for 4-6 hours.

This study was undertaken to evaluate the effect of two different drugs Inj. Paracetamol vs. Inj. Tramadol in terms of post-operative pain relief, hemodynamic stability and side effects after head and neck cancer surgeries.

Material and Methods

After institutional review board approval and informed consent, the study was conducted in 100 patients belonging to both sexes in the age group of 18-60 years with ASA physical status I & II, undergoing elective head and neck cancer surgery. Patients excluded were those with known allergy or hypersensitivity to paracetamol or tramadol, patients with history of alcohol, coagulopathy, and impaired liver and renal function. Patients were assessed in the preoperative visit and routine general and systemic examination was done. Preoperative vital parameters were noted. Patients were kept nil by mouth after 10 PM on the previous night before operation.

Patients were divided into two groups: Group P (Paracetamol): Inj Paracetamol 15 mg/kg IV over 15 minutes and 30 minutes prior to the end of surgery and subsequent doses at 6 hours intervals for 24 hours. Group T (Tramadol): Inj Tramadol 1 mg/kg diluted in 10 ml saline IV slowly over 10 minutes and 30 minutes prior to the end of surgery and subsequent doses at 8 hours interval for 24 hours.

After taking patient on the OT table, IV line was established and monitoring in the form of ECG, HR, NIBP, SpO_2 and $EtCO_2$ was done. Patients were pre-oxygenated with 100% O_2 for 3 minutes and general anaesthesia was administered with Inj Glycopyrolate 0.04 mg/kg + Inj Fentanyl 2 µg/kg + Inj Thiopentone Sodium (2.5%) 5 mg/kg and intubation was facilitated using Inj Succinylcholine HCL 2 mg/kg IV. Patients were intubated with appropriate size portex cuffed endotracheal tube. Bilateral air entry was checked and tube was fixed. Anesthesia maintained with O_2, N_2O, Isoflurane with controlled ventilation using Inj Vecuronium bromide 0.08 mg/kg IV. Intraoperative HR, BP, SpO_2, ECG and $EtCO_2$ were monitored. All the study drugs namely Paracetamol and Tramadol were given as described above to two groups of 50 patients each. After completion of surgery, neuromuscular blockade was reversed with Inj Glycopyrrolate 0.08 mg/kg and Inj Neostigmine 0.05 mg/kg IV. Extubation was done after adequate oropharyngeal and endotracheal suctioning when they were fully conscious.

In the postoperative period vital parameters heart rate (HR), systolic & diastolic blood pressure (SBP) (DBP) and pain score (VAS) (0-10) were assessed and documented at 0 min, 3, 6, 9, 12, 16, 20 and 24 hours intervals.

If VAS > 4, rescue analgesic Inj. Tramadol 1 mg/kg IV was given. Need of rescue analgesia in 24 hours was assessed and documented.

Adverse effects like nausea, vomiting, respiratory depression, abdominal pain, allergic reactions, alteration in liver function tests within 24 hours of surgery were assessed and documented in both

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Role of Intravenous Paracetamol for Peri-Operative Pain Management in Head and Neck Cancer Surgeries

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Abstract

Background: Inadequately controlled postoperative pain causes discomfort, increased use of medications, slower recovery, longer hospital stay and increased risk of pulmonary complications [5]. Postoperative analgesia with safer drugs and minimal side effects is the first choice. This study was undertaken to evaluate the role of Inj. Paracetamol vs. Inj. Tramadol in post-operative pain relief after head and neck cancer surgeries. *Material & Method:* After IRB approval and informed consent, this prospective, randomized study was conducted in 100 patients (ASA I & II) with age group of 18-60 years undergoing elective head and neck cancer surgery. Patients were divided into two groups. A) Group P: Inj. Paracetamol 15 mg/kg IV over 15 min, 30 min prior to the end of surgery and subsequent doses at 6 hours interval 24 hours. B) Group T: Inj. Tramadol 1 mg/kg diluted in 10 ml saline IV slowly over 10 min, 30 min prior to end of surgery and subsequent doses at 8 hours interval for 24 hours. *Results:* Postoperative VAS decreased at various time intervals in both groups. Time to 1st dose of rescue analgesia requirement was lower in Group T, with mean postoperative rescue analgesic free time interval of 6.23±1.72 hours as compared to Group P where it is 5.01±1.16 hours. Frequency of rescue analgesic requirement was lower in Group T, with mean of 1.20 (±0.41), in comparison to Group P 1.67 (±0.71). Postoperative nausea, vomiting is more in group Tas compared to group P. *Conclusion:* Intravenous paracetamol administration in peri-operative period provided adequate postoperative analgesia with fewer side effects in patients undergoing head and neck cancer surgery. Intraoperative IV paracetamol appears to be a reasonable choice for postoperative analgesia in this patient population.

Keywords: Pain; Paracetamol; Tramadol.

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Introduction

The word "pain'' has been derived from the Latin word "poena'' for punishment [1]. The International Association for the Study of Pain defines pain as an "unpleasant sensory and emotional experience associated with actual damage or potential tissue damage or described in terms of such damage" [2]. The Joint Commission on Accreditation of Healthcare Organizations has coined the phrase "Pain: The 5th Vital Sign" to elevate awareness of pain treatment among health care professionals [3].

Pain, a common presenting feature of many disease processes, is usually associated with

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of cardiac toxicity, without compromising on time of onset or duration of motor and sensory blocks

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±1.81 minutes in group-R. The results were similar to published literature (Table 8).

Time to highest level of sensory block was 22.07 ±1.93 minutes in group-L and 20.5±1.81 minutes in group-R. The results were similar to published literature (Table 9).

Time to two segment regression of sensory block was 69±8.5 minutes in group-L and 61.83±6.31 minutes in group-R. The results were similar to published literature (Table 10).

Average duration of sensory block was 188.73 ± 29.94 minutes in group-L and 192.2±36.01 minutes in group-R. The results were similar to published literature (Table 11).

In the current study he mean duration of post-operative analgesia was 137.70±28.01 minutes in Group L and 131.2±38.97 minutes in Group R. The results were similar to published literature (Table 12).

Conclusion

From the present prospective, interventional, double blind study of intrathecal equipotent doses of Ropivacaine and Levobupivacaine, it can be concluded that Ropivacaine is reliable and safe alternative to Levobupivacaine and can be used interchangeably. Hyperbaric Ropivacaine can be specifically used for population that is at higher risk

Table 7: Comparison of average duration of motor block of current study with literature

	Average duration of motor block (Minutes)				
Literature	**Current study**	**Suri A et al. [26]**	**Gautier P et al. [17]**	**Luck JF et al. [22]**	**Mantouvalou M et al. [24]**
Group-L	116.73±29.95	118.53±18.14	121±25	180 (90–210)	273±80
Group-R	112.93±15.40	111.42±16.70	116±19	90 (60–120)	269±20

Table 8: Comparison of time of onset of sensory block of current study with literature

	Mean time of onset of sensory block (Minutes)			
Literature	**Current study**	**Suri A et al. [26]**	**Luck JF et al. [22]**	**Khan A et al. [19]**
Group-L	17.07±1.93	18.62±3.09	5 (2–15)	9.66±1.99
Group-R	15.5±1.81	17.93±2.98	5 (2–15)	9.48±1.92

Table 9: Comparison of time to highest level of sensory block of current study with literature

	Mean time to highest level of sensory block (Minutes)			
Literature	**Current study**	**Gautier P et al. [17]**	**Luck JF et al. [22]**	**Mantouvalou M et al. [24]**
Group-L	22.07±1.93	17±9	25 (10–30)	11±6
Group-R	20.5±1.81	15±9	20 (2–30)	12±7

Table 10: Comparison to two segment regression of sensory block of current study with literature

	Time to two segment regression of sensory block (Minutes)			
Literature	**Current study**	**Mantouvalou M et al. [24]**	**Gautier P et al. [17]**	**Luck JF et al. [22]**
Group-L	69±8.5	65±11	69±14	131 (50–205)
Group-R	61.83±6.31	60±9	60±21	84 (45–145)

Table 11: Comparison average duration of sensory block of current study with literature

	Average duration of sensory block (Minutes)				
Literature	**Current study**	**Suri A et al. [26]**	**Gautier P et al. [17]**	**Khan A et al. [19]**	**Luck JF et al. [22]**
Group-L	188.73±29.94	189.0±19.53	124±24	175.38±13.60	255 (180–360)
Group-R	192.2±36.01	196.78±20.31	120±27	170.80±19.81	210 (180–330)

Table 12: Comparison mean duration of post-operative analgesia of current study with literature

	Mean duration of post-operative analgesia (Minutes)			
Literature	**Current study**	**Suri A et al. [26]**	**Gautier P et al. [17]**	**Khan A et al. [19]**
Group-L	188.73±29.94	253.78±24.43	140 (110-270)	190.27±18.61
Group-R	192.2 ± 36.01	263.0 ± 22.77	135 (95-175)	187.67±23.92

Table 5: Time to two segment regression of sensory level (Minutes) in both the groups

Study group		Time to two segment regression of sensory level (minutes)	P-value	Remarks
Group-L	Mean	69	<0.05	S
	SD	8.5		
Group-R	Mean	61.83		
	SD	6.31		

Time to two segment regression of sensory block was compared in both the groups. It was seen that mean time to two segment regression of sensory block was 69±8.5 minutes in group-L and 61.83±6.31 minutes in group-R. The difference was clinically significant (Table 5).

Table 6: Duration of sensory block (Minutes) in both the groups

Study group		Duration of sensory block (minutes)	P-value	Remarks
Group-L	Mean	188.73	>0.05	NS
	SD	29.94		
Group-R	Mean	192.2		
	SD	36.01		

Average duration of sensory block was compared in both the groups. It was seen that average duration of sensory block was 188.73±29.94 minutes in group-L and 192.2± 36.01 minutes in group-R. The difference was not clinically significant (Table 6).

Discussion

Literature, suggest that ropivacaine on a molar to molar basis is considered to be less potent than levobupivacaine due to lower lipid solubility, and thereby using an equipotency ratio of 1.5:1 between ropivacaine and levobupivacaine provides nearly similar efficacy outcome [9]. etron. This study was conducted to compare the efficacy and safety profile of equipotent doses of levobupicaine and ropivacaine in patients undergoing lower limb and lower abdominal surgeries. Current study was conducted in 60 patients aged between 20 and 60 years having ASA grade I or II and scheduled for elective lower abdominal surgeries under spinal anaesthesia. Group L (Levobupivacaine group) – received hyperbaric levobupivacaine [0.5% Levobupivacaine (3 ml) + 25% dextrose (1ml) (Total 4 ml)].

Group R (Ropivacaine group) – received hyperbaric ropivacaine [0.75% Ropivacaine (3 ml) + 25% dextrose (1 ml) (Total 4 ml)] the following parameters were observed:

1. Time of onset (time of intrathecal injection of drug to achieve T10 segment level block)
2. Time to highest level of sensory blockade,
3. Time for two segment regression of sensory level
4. Duration of sensory block (time period from onset of block to the time of two segment regression from T10)
5. Time of onset (when Bromage scale 3 ie. patient is unable to move the hip, knee and ankle joint is achieved)
6. Duration of motor blockade were recorded (time period from onset to Bromage scale 0 ie. patient is able to move the hip, knee and ankle joint)

In our study the mean time of onset of motor block was 25.07±1.97 minutes in group-L and 24.37 ±1.70 minutes in group-R and the difference was not clinically significant. This was similar to the findings by Suri A et al., where in the mean onset of time of motor block was 24.09±3.07 vs 25.47±4.13 minutes in group L and group R and the difference was not clinically significant (p = 0.076) [26]. However, the mean time of onset of motor block in study by Mantouvalou M et al. was 12±5 min in the ropivacaine group (group B) and 11±7 min in the levobupivacaine group, the early onset in this study as compared to our study may be due to the fact that, Mantouvalou M et al. used isobaric preparation in their study which may have resulted in rapid intrathecal spread [24]. Additionally, the mean age of the patients in the study by Mantouvalou M et al. was higher compared to our study and as per literature at the extremes of age there are small but significant increases in maximum spread, rate of onset of motor block and cardiovascular instability, regardless of the solution used [3]. Luck JF in their study observed that mean time to maximum motor block was 5 (2–20) and 10 (5–20) (min) in levobupivacaine and ropivacaine group respectively [22]. The early onset seen in Luck JF study may have been due to the fact that the mean age of the patients enrolled in the study was 57 (26–73) and 59 (37–75) in group L and R respectively which was higher compared to our study.

The average duration of motor block in the current study was 116.73±29.95 minutes in group-L and 112.93±15.40 minutes in group-R. Similar findings were seen in the published literature, although Mantoualou M et al. have observed significantly higher duration of motor block, authors have offered no explanation for the same (Table 7).

In the current study time of onset of sensory block was 17.07±1.93 minutes in group-L and 15.5

period from onset to Bromage scale 0 ie. patient is able to move the hip, knee and ankle joint).

Intra-Operative Patient Monitoring: All patients of both groups were monitored for: Systolic and Diastolic blood pressure & Pulse rate (Haemodynamic parameters) Arterial oxygen saturation (SpO2) and Respiratory rate Side effects and complications (if any). Decrease in systolic arterial pressure (SAP) by more than 20% from the pre-anaesthetic value or decrease of patients' mean arterial pressure (MAP)to below 60 mmHg were considered to be suggestive of significant hypotension and were managed using injection Mephentermine 6 mg in increments intravenously along intravenous fluid replacement. Significant bradycardia (HR <60 beats/min) was treated with inj. atropine sulphate 0.6 mg intravenously.

Results

The data were analyzed using SPSS software version 18.0. Statistical analysis of data among groups was done, performed by

- Nominal data (such as Age groups) were presented as number and Percents.
- Continuous data (such as age, lab values) were expressed as mean, standard deviation and range.
- *'f' test and 't' test* was applied as appropriate for comparison of continuous data.
- *'Chi' test* was applied as appropriate for comparison of nominal data.
- '*p*' value of 0.05 was considered as statistically significant. (Confidence interval of 95% was taken into account).

In the present study, a total of 60 patients with ASA grading II and III undergoing lower abdominal surgery were enrolled. Equal number of patients were randomized in group- L (those who received levobupivacaine as spinal anesthesia) (n=30) and group – R(those who received ropivacaine as spinal anesthesia) (n=30).

Table 1: Comparison of time of onset of motor block in both the groups

Study groups		Time of onset of motor block (minutes)	P-value	Remarks
Group-L	Mean	25.07	>0.05	NS
	SD	1.97		
Group-R	Mean	24.37		
	SD	1.70		

Time of onset of motor block was compared in both the groups. It was seen that mean time to onset of motor block was 25.07±1.97minutes in group-L and 24.37±1.70 minutes in group-R. The difference was not clinically significant (Table 1).

Table 2: Comparison of average duration of motor blockade in both the groups

Study groups		Duration of motor blockade (Minutes)	P-value	Remarks
Group-L	Mean	116.73	>0.05	NS
	SD	29.95		
Group-R	Mean	112.93		
	SD	15.40		

Average duration of motor block was compared in both the groups. It was seen that average duration of motor block was 116.73±29.95 minutes in group-L and 112.93±15.40 minutes in group-R. The difference was not clinically significant (Table 2).

Table 3: Time of onset of Sensory block (Minutes)

Study Groups		Time of onset of Sensory block (Minutes)		
Group-L	Mean	17.07	>0.05	NS
	SD	1.93		
Group-R	Mean	15.5		
	SD	1.81		

Time of onset of sensory block was compared in both the groups. It was seen that mean time to onset of sensory block was 17.07±1.93 minutes in group-L and 15.5±1.81 minutes in group-R. The difference was not clinically significant (Table 3).

Table 4: Time to highest level of Sensory block (Minutes) in both the groups

Study Group		Time to highest level of sensory blockade minutes	P value	Remarks
Group-L	Mean	22.07	<0.05	S
	SD	1.93		
Group-R	Mean	20.5		
	SD	1.81		

Time to highest level of sensory block was compared in both the groups. It was seen that mean time to attain highest level of sensory block was 22.07±1.93 minutes in group-L and 20.5±1.81 minutes in group-R. The difference was clinically significant (Table 4).

It provides sensory as well as motor blockade. Levobupivacaine, an amide local anesthetic, is an S-enantiomers of racemic bupivacaine. On a per-milligram basis, it is less cardio toxic than bupivacaine, as it has decreased potency at the sodium channel. Studies have suggested that it has equivalent clinical efficacy to bupivacaine [6]. Ropivacaine is another amino-amide local anesthetic (LA) agent that is similar in chemical structure to bupivacaine, but it is 30-40% less potent than bupivacaine. Intrathecal Ropivacaine is safe, has shorter duration of action than bupivacaine and lesser incidence of transient neurological symptoms (TNS) as compared with intrathecal lignocaine.

In this study, we evaluated and compared the influence of hyperbaric Levobupivacaine and hyperbaric Ropivacaine on onset, duration of motor and sensory blockade, the incidence of side effects and complications particularly bradycardia, hypotension, fall of mean arterial pressure etc for spinal anaesthesia in patients undergoing lower abdominal and lower limb Surgeries.

Materials and Methods

This prospective, interventional, double blind study included sixty patients who were scheduled for lower abdomen and lower limb surgery under spinal anesthesia whose consents were taken. A detailed pre-anaesthetic check-up was done a day prior to surgery. In pre-induction phase details like temperature, pulse, blood pressure, respiratory rate, oxygen saturation (SpO_2), intravenous line, details of pre medication and pre-loading were captured.

Inclusion criteria: Patients of either gender aged between 20-60 years, Scheduled for surgery to be performed under spinal anaesthesia, Patient with American Society of anaesthesiologists grade-I and II (ASA I & II), Weight: 40-80 kg, No known history of drug allergy, sensitivity or history of other form of reaction.

Exclusion criteria: Patient with ASA III or IV, Patients with history of coagulopathy. Patients with spine deformity. Patients with local skin infections at the site of injection. Patient having fever, history of drug allergy. Patients who had shivering even before administering spinal anaesthesia Patients requiring supplementation with general anaesthesia Patients who were not willing to participate in the study.

Investigational medicinal product details

Study drug 1: Hyperbaric Ropivacaine

Study drug 2: Hyperbaric Levobupivacaine

Preparation of equipotent doses of hyperbaric Levobupivacaine and Ropivacaine: Various studies suggest that Ropivacaine is less potent than Levobupivacaine because of its lower lipid solubility, however using an equipotency ratio 1.5:1 between Ropivacaine and Levobupivacaine results in substantially similar in clinical profile. On the day of the surgery, patients were randomly assigned by computer generated randomisation table to either of the two arms mentioned below:

Group – R–Hyperbaric Ropivacaine [0.75% Ropivacaine (3 ml) + 25% dextrose(1 ml) (Total 4 ml)]

Group–L –Hyperbaric Levobupivacaine [0.5% Levobupivacaine (3 ml) + 25% dextrose (1 ml) (Total 4 ml)]

Dosage: 3.5 ml of the prepared solution was injected in each of the groups.

Procedure for study drug administration

All the patients were kept nil by mouth for more than 6 hours, i.e. were fasted preoperatively since 10 pm, night before surgery. All the patients were pre medicated with Inj. Ondansetron 4 mg and Inj. Ranitidine 50 mg and inj. Glycopyrrolate 0.2 mg intravenously. On the day of surgery the patients were brought to the operation theatre (OT), standard monitors (that measure pulse, blood pressure, Respiratory rate, Oxygen saturation) were attached and baseline parameters recorded. Patients were pre-loaded with ringer lactate 10 ml/kg and spinal anaesthesia performed. Efficacy / safety assessment was performed by investigator, who was blinded to study treatment allocation.

Efficacy (Onset of the Sensory and Motor Block) / Safety Assessment

Sensory block assessment - It was tested by pin prick using hypodermic needle.

Following parameters were recorded: Time of onset (time of intrathecal injection of drug to achieve T10 segment level block) Highest level of sensory blockade, Time for two segment regression of sensory level, Duration of sensory block (time period from onset of block to the time of two segment regression from T10).

Motor block assessment- It was tested using Bromage scale.

Following parameters were recorded: Time of onset (when Bromage scale 3 ie. patient is unable to move the hip, knee and ankle joint is achieved), Degree of motor blockade

Duration of motor blockade were recorded (time

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Comparison of Equipotent Doses of Hyperbaric Ropivacaine and Hyperbaric Levobupivacaine in Spinal Anaesthesia for Patients Undergoing Lower Abdominal and Lower Limb Surgeries

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Abstract

Background: Spinal anaesthesia provides sensory as well as motor blockade. Levobupivacaine is less cardio toxic than bupivacaine, as it has decreased potency at the sodium channel. Ropivacaine is similar in chemical structure to bupivacaine, but it is less potent than bupivacaine. Intrathecal Ropivacaine is safe, has shorter duration of action than bupivacaine and lesser incidence of neurological symptoms as compared with intrathecal lignocaine. Literature suggest that potency of Ropivacaine is less when compared with levobupivacaine since it has lower lipid solubility, and thereby using an equipotency ratio of 1.5:1 between Ropivacaine and Levobupivacaine provides nearly similar efficacy outcome. *Method*: The study was carried out as prospective, interventional, double blind in 60 patients divided in two equal groups using equipotent doses of intrathecal hyperbaric Ropivacaine and hyperbaric Levobupivacaine (with ASA grading I and II). *Results:* The distribution of patients with respect to age, height, weight was statistically not significant in both the groups. (p value > 0.05). Mean time to onset of motor block was 25.07±1.97 minutes in group-L and 24.37±1.70 minutes in group-R. Average duration of motor block was 116.73±29.95 minutes in group-L and 112.93±15.40 minutes in group-R. Mean time to onset of sensory block was 17.07±1.93 minutes in group-L and 15.5 ± 1.81 minutes in group-R. Mean time to attain highest level of sensory block was 22.07±1.93 minutes in group-L and 20.5±1.81 minutes in group-R. Mean time to two segment regression of sensory block was 69±8.5 minutes in group-L and 61.83±6.31 minutes in group-R. Average duration of sensory block was 188.73±29.94 minutes in group-L and 192.2±36.01 minutes in group-R. There were no changes in vital parameters and oxygen saturation in the intra-operative and post-operative period. Mean duration of post-operative analgesia was 137.70±28.01 minutes in Group L and 131.2±38.97 minutes in Group R. Analgesic consumption for 24 hours postoperatively was similar in both the groups. It was observed that both the molecules showed similar time of onset of motor and sensory block and also nearly similar duration of motor and sensory blocks. Both the drugs were also found to be safe in terms of impact on hemodynamic parameters and no complications observed. *Conclusion:* Both drugs are reliable in terms of efficacy and safety and can be used interchangeably. Ropivacaine can be specifically used for population that is at higher risk of cardiac toxicity, without compromising on time of onset or duration of motor and sensory blocks.

Keywords: Spinal Anesthesia; pain; Ropivacaine; Levobupivacaine; bupivacaine.

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Introduction

Spinal anaesthesia was introduced in clinical practice by Karl August Bier, in 1898 [1]. it is obtained by administering local anaesthetic agents in the subarachnoid space and thereby blocking nerves. Subarachnoid block is usually performed for lower abdominal and lower limb surgeries.

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anaesthesia in infraumblical surgeries. With the adjuvants adequate level can be attained for lower abdomen and lower limb surgeries. Adding 25 µg fentanyl causes early onset of action whereas 30 µg clonidine to 15 mg isobaric levobupivacaine has more prolonged action. But isobaric levobupivacaine with clonidine is better than levobupivacaine with fentanyl because with clonidine there is longer duration of sensory blockade and postoperative analgesia. But there were more chances of hypotension and bradycardia with clonidine than fentanyl as well as prolonged effect can delay ambulation which can be easily managed. The hemodynamic parameters should be vigilantly monitored with these adjuvants and should be more meticulous when clonidine used.

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was 6.86±3.73 minutes with fentanyl and 8.61±7.18 minutes with clonidine [18]. Sharan Radhe et al. compared the effect of 30 μg of clonidine verses 25 μg of fentanyl with 2.5 ml of 0.75% ropivacaine in lower abdomen surgeries. Here time to attend peak sensory level was 9.64±1.67 minutes with fentanyl and 9.68±1.78 minutes with clonidine [19]. Bajwa et al. compared 50 μg clonidine verses 25 μg fentanyl with 2.5 ml 0.5% hyperbaric bupivacaine in lower abdomen surgeries. Time for peak sensory onset was 7.34±0.96 minutes with fentanyl and 7.56±1.78 with clonidine [6]. The alteration in the values is because of different doses of adjuvants and the difference in local anaesthetic agents used.

In Nesrin Bozdogan et al. study where isobaric levobupivacaine was given with fentanyl the TSSR was 96.48±24.46 minutes and in Kuikarni J et al. study with isobaric levobupivacaine combined with clonidine the TSSR was 157.83±3.49 minutes [15,20]. Both the above mentioned study were done on patients undergoing lower segment caesarean section. This shows the faster regression action of fentanyl than clonidine. The observation in these two studies is in accordance to our study where we noticed TSSR of 94.75±11.23 minutes in fentanyl whereas it was 107.00±11.39 minutes with clonidine as additive to isobaric levobupivacaine. The difference was highly significant statistically.

In our study total duration of sensory blockade was 303.25±31.91 minutes and motor blockade was 287.12±20.7 minutes in fentanyl group. Total duration of sensory blockade was 324.12±25.84 minutes and motor blockade was 298.25±21.03 minutes in clonidine group. In Agarwal et al. study total duration of sensory blockade was 241.57±1.87 minutes and motor blockade was 187.48±12.12 minutes with 15 mg isobaric levobupivacaine and 25 μg fentanyl [12]. In Bhavani V et al. study total duration of sensory blockade was 288.87±18.651 minutes and motor blockade was 190.97±17.38 minutes with 15 mg isobaric levobupivacaine and 30 μg clonidine [13]. This is in accordance to our study as the drug volume and quantity in the above two studies is resembling our study. This suggests that clonidine has longer sensory and motor blockade effect compared to fentanyl as an adjuvant to isobaric levobupivacaine.

Duration of postoperative analgesia was 249.59±10.40 minutes in Agarwal A P et al. study and 288±18.6 minutes in Bhavani V et al. study with fentanyl and clonidine respectively [12,13]. Clonidine have more tendency to prolong the analgesia. This is also in accordance with Singh Baljit Bajwa et al. and Chabbra Anita et al. study who used both these adjuvants with bupivacaine and ropivacaine respectively [6,18]. Even in Agarwal Archana et al. study where both these adjuvants were used with isobaric levobupivacaine there was prolonged postoperative analgesia with clonidine than fentanyl in lower limb surgeries. Likewise in our study postoperative analgesia duration was highly statistically significantly prolonged with clonidine. It was 318.00±78.21 minutes with fentanyl and 393.37±81.91 minutes with clonidine as adjuvant to isobaric levobupivacaine. From the above mentioned studies it can be derived that clonidine hashigher potency than fentanyl to prolong the analgesic duration.

There was fall in BP in both the groups; more in the group LC from baseline immediately after intrathecal drug administration. This is similar to Glaser et al. study, which used volume of 3.5 ml of levobupivacaine for hip surgeries [11]. Around 5% patients in group LF and 12.5% patients in group LC had hypotension and around 7.5% of patients in group LF and 12.5% of patients in group LC bradycardia which was managed. Though not statistically significant these haemodynamic changes were, more with clonidine may be because of presynaptic noradrenaline inhibition and its action on atrioventricular node after systemic absorption [21].

Patra et al. reported 46% of patients had pruritus with fentanyl [22]. Similarly other investigators have also reported pruritis with fentanyl. Erkan et al. reported pruritus in around 25% of transurethral resection of prostate patients anaesthesised with intrathecal levobupivacaine and clonidine [23]. Liu S et al. also noticed pruritus with intrathecal fentanyl in his study [24]. In our study 5% of patients developed pruritus. The effect of pruritus was transient and hardly needed treatment. In our study 20% of patients had sedation with clonidine and 5% of patients in fentanyl. None had respiratory depression or fall in saturation. This is due to the action at nucleus cerueleus where hyperpolarisation of excitatory neurons takes place [25]. In Kothari et al. study, where 45 μg clonidine was added to bupivacaine in ceasserean patients there was sedation in 35% to 45% patients [26]. One patient in the fentanyl group had nausea and two patients had vomiting. Incidence of nausea and vomiting were noticed with intrathecal fentanyl in the literature [27].

Conclusion

There are many studies stating that levobupivacaine can be safely used for spinal

taken for maximum motor blockade were earlier with fentanyl than clonidine. Average maximum motor blockade was around B3 in both the groups. Duration of motor blockade was lower in both the groups than sensory blockade (which is SRL1) but it was prolonged with clonidine than fentanyl as shown in Table 3.

There was fall in HR and MAP in both the groups after spinal anaesthesia. But there was statistically significant fall in HR and MAP with LC group than LF group during the first 15-30 minutes which was eventually managed as shown in figure-1. Bradycardia and hypotension was more with clonidine than fentanyl. One patient had nausea, two patients had vomiting and three patients had pruritus with fentanyl. Patients in clonidine group were more sedated than fentanyl after about 90 minutes after intrathecal drug injection administration.

Postoperative analgesia was statistically significantly longer with clonidine than fentanyl as shown in Table 4.

Discussion

There are many adjuvants available along with levobupivacaine agents to increase its potency. Fentanyl used in our study facilitates the afferent sensory blockade by stimulating μ1 and μ2 receptors in the spinal cord [9]. On the other hand clonidine prolongs the blockade by activation of post-synaptic α2 receptor in substantia gelatinosa of spinal cord [10].

In Glaser et al. study, who compared isobaric levobpivacaine 3.5 ml with isobaric bupivacaine 3.5 ml in hip replacement surgeries, onset of sensory blockade, was 11±6 minutes [11]. Compared to this the onset time of sensory blockade was shorter in our study. Though the volume of the intrathecal drug was similar as in our study, the adjuvants we used caused the shorter onset time of sensory blockade in our study. In Agarwal A P et al. sensory onset time was 2.62±0.95 minutes and motor onset time was 3.53±0.17 with intrathecal 3 ml levobupivacaine and 25 μg fentanyl in lower abdomen and lower limb surgeries [12]. In Bhavani V et al. sensory onset time was 6.03±1.923 minutes and motor onset time was 7.48±2.2 minutes with intrathecal 3 ml levobupivacaine and 30 μg clonidine in vaginal hysterectomy patients [13]. In our study sensory onset time was 155.62 seconds (2.59 minutes) and the motor onset time was 198.62 seconds (3.31 minutes) with isobaric levobupivacaine 3.5 ml combined with 25 μg fentanyl whereas sensory onset time was 184.75 seconds (3.07 minutes) and the motor onset time was 245.00 seconds (4.08 minutes)with isobaric levobupivacaine 3.5 ml combined with 30 μg clonidine in our study The dosage of intrathecal drug used in Agarwal AP et al. and Bhavani V et al. study were similar to our study and the sensory onset and motor onset time in both these studies are consistent to our study. In our study sensory onset and motor onset were statistically significantly faster with the adjuvant fentanyl than clonidine.

Glaser et al. also had highest sensory level at T8 level [11]. In our study the maximum sensory level attained with isobaric levobupivacaine was at an average of 6.3 when combined with fentanyl and 5.35 when combined with clonidine. In Filiz Karaca et al. and Nesrin Bozdogan et al. study the effect of isobaric levobupivacaine with fentanyl was observed in patients undergoing caesarean section [14,15]. Both the studies had highest sensory level of T4 level with levobupivacaine. The gravid uterus and raised abdominal pressure might have caused higher sensory level in the above studies. Camorcia M et al. who compared relative potencies for motor block after intrathecal ropivacaine, levobupivacaine, and bupivacaine reported intermediate motor blocking effects of levobupivacaine in his study [16]. In our study the average maximum motor block was MBS-B3 which correlates with the above study asthe complete motor blockade of MBS-B4 was hardly achieved with either of the group which signifies that adjuvant might have no much effect on levobupivacaine to enhance the motor blockade.

Agarwal archana et al. compared the effect of intrathecal fentanyl 15 μg with clonidine 30 μg on 2.5 ml of 0.5% isobaric levobupivacaine in the patients undergoing lower limb surgery [17]. Time to attend the peak sensory effect was 9.67±1.18 minutes with fentanyl and it was 9.70±1.32 minutes with clonidine. Though not statistically significant it was relatively lower with fentanyl. In our study, the time to attend maximum sensory blockade was 4.73 minutes with fentanyl and 6.96 minutes with clonidine. It was statistically significantly lower with fentanyl might be because of higher dose of fentanyl of 25 μg which we used. The delayed onset of maximum sensory effect with clonidine than fentanyl is also consistent with other studies where these two adjuvants were compared with different local anaesthetic agents like: Chabbra Anita R et al. assessed the effect of 60 μg clonidine verses 25 μg fentanylcombined with intrathecal 3 ml of isobaric 0.5% ropivacaine in lower limb surgeries. Here time to attend peak sensory level

Table 3: Sensory and motor characteristics in both the groups.

Sl. No	Characters	Group LF	Group LC	P Value
1.	Time of onset of sensory blockade -TOSB in seconds (minutes)	155.62 ±18.26 (2.59 min)	184.75±21.89 (3.07 min)	<0.005
2.	Maximum level of sensory blockade – MLSB	6.3±1.62	5.35±1.51	0.1662
3.	Time taken for maximum level of sensory blockade - TMLSB(min)	4.73±1.09	6.96±1.15	<0.005
4.	Two segment sensory regression-TSSR(min)	94.75±11.23	107.00±11.39	<0.005
5.	Sensory regression to L1-SRL1(min)	303.25±31.91	324.12±25.84	0.002
6.	Time of onset of motor blockade-TOMB(seconds)	198.62±23.12 (3.31 min)	245.00±36.37 (4.08)	<0.005
7.	Maximum level of motor blockade –MLMB	3.17	3.25	0.598
8.	Time taken for maximum level of motor blockade -TMLMB(min)	6.66±1.21	7.62±1.43	0.0354
9.	Total duration of motor blockade - TDMB(min)	287.12±20.7	298.25±21.03	<0.005

Table 4: Complications and postoperative analgesia in both groups.

Sl. No	Complications	Group LF	Group LC	P- Value
1.	Bradycardia	2 (5%)	5 (12.5%)	0.235
2.	Hypotension	3 (7.5%)	5 (12.5%)	0.456
3.	Nausea	1 (2.5%)	0	0.314
4.	Vomiting	2 (5%)	0	0.152
5.	Pruritis	3 (7.5%)	0	0.077
6.	Shivering	0	0	-
7.	No of Patients with Ramsay Sedation Score >2 at 90 Minutes	2 (5%)	8 (20%)	<0.005
8.	Postoperative Analgesia Duration (Minutes)	318.00±78.21	393.37±81.91	<0.005

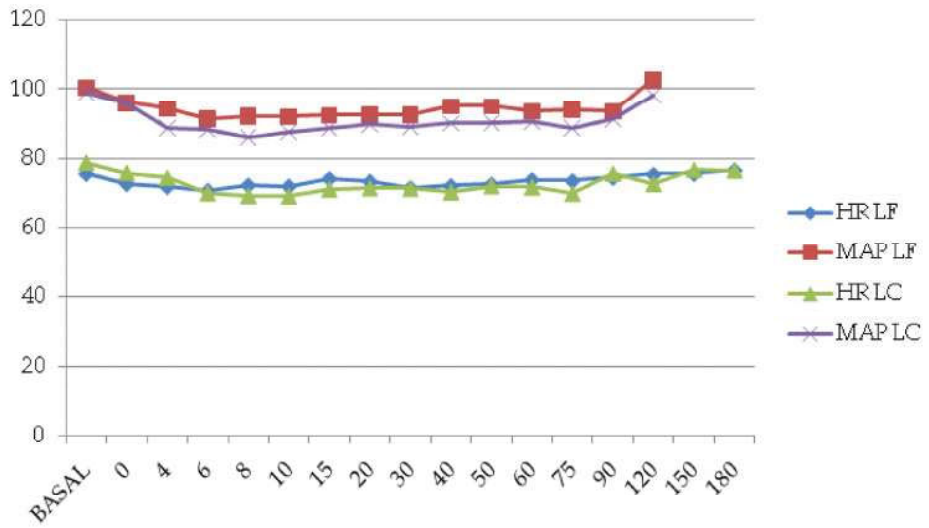


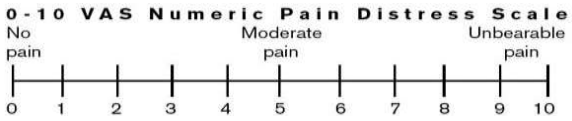
Fig. 1: Variation in HR and MAP after intrathecal block in both the groups.

duration of motor blockade which was the time taken for MBS to be 1.

4. Two segments sensory regression time which is the duration between highest sensory level attained to two segment regression.
5. Total duration of analgesia was upto the period where patient had VAS of 4. Haemodynamics were monitored via PR, SBP, DBP, MAP, ECG and oxygenation monitored via SpO_2. If MAP decreases more than 30% of basal it was considered hypotension managed with IV ephedrine 6 mg bolus doseand fluid bolus at the rate of 2-3 ml/kg/hour. Heart rate decreasing to less than 50 was considered as bradycardia and it was treated with IV atropine 0.6 mg. If patient complained of pain regional was converted to general anaesthesia and they were excluded from the study. Total duration of surgery and side effects like nausea and vomiting, shivering, pruritus were also noted. Sedation was assessed using Ramsay's sedation score (RSS) every half an hourly after spinal anaesthesia. RSS is as follows: 1) anxious, agitated or restless; 2) co-operative, oriented and tranquil; 3) responds to commands; 4) asleep but has a brisk response to light glabellar tap or loud auditory stimulus; 5) asleep but has a sluggish response to light glabellar tap or loud auditory stimulus; 6) asleep no response.

Post operatively patient shifted to post anaesthesia care unit (PACU). Here hemodynamic, sensory and motor level and pain assessment via VAS (0-10) was done. Rescue analgesic IV diclofenac 75 mg was given if VAS score was 4 or above.

Statistical analysis was done using SPSS 19 version. Data are presented as mean and standard deviation. p value of < 0.05 was considered as significant and < 0.001 highly significant. Paired and unpaired t-test and analysis of variance was used for statistical calculations. Numerical variables were compared using chi-square test for nonparametric data and Student-t test for parametric data.



Results

Both LF and LC groups were comparable with respect to their demographic characteristics; duration of surgery and mean of baseline HR and BP as shown in Table 1 and type of surgeries as shown in Table 2.

Sensory onset time was significantly faster with fentanyl than clonidine. Average maximum sensory level attained in both the groups was 6.3 in group LF and 5.35 in group LC. Time to attend this level was statistically significantly shorter with fentanyl than clonidine. TSSR and SRL1 were also statistically significantly faster with fentanyl. This means the regression of spinal effect with fentanyl as additive was faster than clonidine as additive. Onset of motor blockade and time

Table 1: Demographic; surgical characteristics and mean of baseline heart rate and mean arterial pressure

Sl. No	Characters	Group LF	Group LC	p Value
1.	Age	37.37±10.65	36.15±10.8	0.611
2.	Sex (M:f)	31:9 (77.5% : 22.5%)	34:6 (85% :15%)	0.390
3.	American Society of Anesthesia Grade (I:ii)	22:18 (55% : 45%)	25:15 (62.5% : 37.5%)	0.496
4.	Body Mass I Ndex	22.66±1.53	22.91±1.22	0,423
5.	Duration of Surgery (Min)	134.37±33.28	126.05±28.88	0.236
6.	Mean Baseline Heart Rate	75.67±12.71	78.72±10.51	0.2
7.	Mean Baseline Of Mean Arterial Pressure	100.58±10.02	99.15±8.66	0.5

Table 2: Type of surgeries

Sl. No	Type of Surgeries	Group LF	Group LC	p Value
1.	Lower Abdomen	13	15	0.639
2.	Orthopedic Surgery	17	14	0.491
3.	Genital Surgeries	7	6	0.761
4.	Varicose Veins	3	5	0.711

adjuvants commonly used are opiods. Fentanyl has low risk of respiratory depression with rapid onset of action [7]. Intrathecal clonidine with alpha-2 agonistic activity is also an adjuvant potentiating the action of intrathecal drugs [8]. It reduces shivering and devoid of side effects associated with opiods like pruritis, nausea and vomiting, respiratory depression and urinary retention.

There are limited studies showing the difference in the effects of adjuvants like fentanyl verses clonidine with isobaric levobupivacaine for infraumblical surgeries. This triggered us to do the study to compare the potency of anaesthesia, hemodynamics and side effects between these two adjuvants in addition to isobaric levobupivacaine.

The primary objective of the study was to compare onset of sensory and motor blockade; maximum level attained and time required for the same; total duration of sensory and motor blockade and two segment sensory regressions time; postoperative analgesic requirement and hemodynamic effects. The secondary objective was to assess for any side effects like shivering, pruritus, nausea and vomiting, respiratory depression and sedation.

Materials and Methods

It is a prospective, randomised and double blinded study. After institutional ethical and scientific committee approval, 80 patients scheduled for the elective infra umbilical surgeries at our hospital were selected. Informed written consent was taken from the patients after the procedure was explained to them. Inclusion criteria were adult patients of either sex, aged between 18-55 years belonging to ASA class I or II with height between 154 to 174 centimetres. Exclusion criteria were patients belonging to ASA class III, IV, V and with Body Mass Index > 30 kg/m^2; or with absolute contraindications for spinal anaesthesia like raised intracranial pressure, severe hypovolumia, bleeding diathesis, local infection and history of allergy to any of the drugs.

The data were collected in a presetperforma meeting the objectives of this study. They were made aware of visual analogue score (VAS) scoring system required post operatively for pain assessment. They were randomly divided using sealed opaque envelope technique into 2 groups of 40 patients each. Group LF and Group LC. Group LF received 15 mg of 0.5% isobaric levobupivacaine with 25 µg of fentanyl whereas group LC received 15 mg of 0.5% isobaric levobupivacaine with 30 µg clonidine.

After preoperative assessment patients were kept fasting overnight. Patients were premedicated on the night before surgery with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg. On morning of surgery intravenous (IV) line obtained with 18 guage cannula and preloaded with ringer lactate 10 ml/kg half an hour before anaesthesia. The monitoring was done using multiparameter monitor having pulse oximetry, electrocardiograph (ECG) and non invasive blood pressure (NIBP). Baseline pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), electrocardiography (ECG) and arterial oxygen saturation (SpO_2) were noted. Patients were placed in lateral decubitus position with operative side downwards. Under aseptic precautions subarachnoid block was performed at level of L3-L4 through a midline approach using 25G Quincke's spinal needle. In both the groups the volume was kept constant up to 3.5ml by adding saline. Study drug was loaded by the senior anaesthesiologist who was not involved in the study. All spinal blockades was performed by the another anaesthesiologist, who was also the observer. Thus both patient and observer were blinded for the study. During injection operating table was kept flat. Patient was turned to supine posture immediately. Sensory blockade was tested using pinprick method with a blunt tipped 27G hypodermic needle at midclavicular line every 30 seconds for first 2 minutes, every minute for next 5 minutes and every 5 minutes for next 15 minutes and every 10 minutes for next 30 minutes and every 15 minutes till the end of surgery and there after every 30 minutes until sensory block is resolved. Quality of motor blockade was assessed by modified Bromage scale (MBS): 0 – patient is able to move the hip, knee and ankle; 1- patient is unable to move the hip but is able to move the knee and ankle; 2 – patient is unable to move the hip and knee but is able to move the ankle; 3- patient is unable to move the hip, knee and ankle and 4- patient is unable to move toes.

The following time were noted from the point of drug injection:

1. Onset of sensory blockade when the sensory loss was up to the T8 dermatome. Surgery was allowed to start when this level was attained. Onset of motor blockade which was the time taken for MBS to be one.
2. Maximum level of sensory and motor blockade attained and time taken for it.
3. Duration of sensory blockade which was time taken for sensory regression to L1 and

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A Randomised Prospective Double Blinded Study of Intrathecal Levobupivacaine with Fentanyl Verses Clonidine for Infraumblical Surgeries

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Abstract

Background and aims: Subarachnoid block can be performed with many local anaesthetic agents. Besides hyperbaric bupivacaine even isobaric levobupivacaine and ropivacaine can also be used with minimal cardiotoxicity. Adjuvants like opiods and alpha-2 agonist prolongs the duration of levobupivacaine action. The aim of the present study is to compare fentanyl and clonidine effect used as adjuvants to levobupivacaine with respect to onset of sensory and motor blockade; maximum level attained and the required for the same; duration of blockade and post operative analgesia. *Materials and Methods:* After ethical committee approval, 80 patients posted for infraumblical surgeries divided into two groups. Group LF received 15 mg of levobpivacaine with 25µg fentanyl whereas group LC received 15 mg of levobupivacaine with 30µg clonidine. The volume of solution was 3.5 ml in both groups. Hemodynamic, sensory and motor characteristics were monitored. *Results:* Onset of sensory and motor blockade as well as regression of both was faster with fentanyl than clonidine. There was slight fall in heart rate and mean arterial pressure in both the groups after intrathecal drugs but it was more with clonidine. Bradycardia and hypotension was noted more with clonidine than fentanyl which was easily manageable. Though the onset was delayed, sensory, motor and analgesic effect was prolonged with clonidine. *Conclusion*: Levobpiacaine can be safely used for spinal anaesthesia in infraumblical surgeries. Adding fentanyl causes early onset of action whereas clonidine has more prolonged action.

Keywords: Levobupivacaine; fentanyl; clonidine; spinal anaesthesia.

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Introduction

Spinal anaesthesia is the choice for infraumblical surgeries which includes lower abdominal, perineal and lower limb surgeries. It is a simple, cost effective technique having rapid onset of action with reliable sensory and motor blockade [1].

Levobupivacaine is a pure S-enantiomer of racemic bupivacaine (S-1nbutyl-2 piperidyl formo 2′6′ xylidide hydrochloride). It is a newer long acting local anaesthetic agent with minimal cardiovascular and central nervous system toxicity [2,3]. It is widely used in recent days for spinal anaesthesia and isobaric levobupivacaine alone has short lasting effect [4,5]. Addition of low dose adjuvants with local anaesthetic agents intrathecally improves the block quality and its duration [6]. The

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There was good intra operative protection against cardiovascular responses to surgical stimulation. There was good response to the pressor effects during extubating in most of the cases because of its long half-life. The during is easily available, easy to administer, cost is reasonable and needs to be administered only one a day. It has minimal side effects. No side effects were observed during the study.

It is concluded that enhanced sympathetic drive which results in hypertension and increased heart rate, associated with laryngoscopy and endotracheal intubation was attenuated with use of long acting beta-1 selective blocker tab. Nebivolol. The rate pressure product which is a major determinant of myocardial oxygen demand was also decreased because of the nebivolol.

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in myocardial oxygen demand Attempts to attenuate have responses by various drugs and techniques have met with varied success [5].

Various B. blockers have been used to attenuate the cardiovascular response to laryngoscopy and intubation with variable to reasonable amount of success [6]. In the present study oral nebovol a long acting beta-1 blockers (B1) 5 mg once daily started 3-4 days prior to surgery orally was usedto study its efficacy in the attenuation of pressor response to laryngoscopy and intubation. This study was conducted in normotensive, ASA grade -1 patents belonging to the age group 25-60 yrs, undergoing elective surgery.

The study consisted of 25 patients taken as control group and 25 patients taken as study group, who received tablet nebivolol 5 mg once orally and started 3-4 days prior to surgery. Both groups were pre-medicated with injection hetorlac 1 mg/kg weight I.M and glycopyrolate 0.2 mg IM 60-90 minutes before surgery. Blood pressure and heart rate response to laryngoscopy and intubation was studied in both groups who received the same drugs for induction and intubation. There was statistically no significant difference between the pre-inductionvalues of systolic diastolic arterial pressure sin both groups, but there is significant difference in mean arterial pressure and heart, rate statistically ($p<0.001$). mean arterial pressure, heart rate and rate pressure product ratios are lower in the study group who received tablet nebivolol.

After induction with thiopentone and vecuronium bromide difference in hemodynamic value b/w two groups was significant statistically in all the parameters, there was much fall in systolic arterial pressure and increase in heart rate to pre-induction values. One minute after laryngoscopy and intubation there was significant difference statistically in the hemodynamic values b/w the two groups ($p<0.001$). The increase in hemodynamic values till the 5th minute after intubation to pre-induction values in control group was significant statistically ($p<0.001$). so, this study confirms the potential hypertensive and tachycardia effects of laryngoscopy and intubation.

In the study group increase inhemodynamic values occurred till 2 minutes after intubation and almost touched the preinduction values (basal values) by 3rd minute change of hemodynamic values statistically only 1st one mte after intubation ($p<0.001$). In hemodynamic value the increase in study group compared to prelinduction values in two or 3 minutes intubation was not significant statistically. In the study group the difference observed at 3 minutes after laryngoscopy and endotracheal intubation to prenduction values as Heart rate 3.48 beats/minutes, Systolic arterial pressure as 0.32 mm Hg, Diastolic arterial pressure as 1.96 mm Hg, Mean arterial pressure as 69 mm Hg and Rate pressure product is also within the critical level (< 12,000). The changes in study group when compares to the changes in control group were statistically significant ($p<0.001$). this shows that oral nebivolol effectively attenuates the hemodynamic response to laryngoscopy and endotracheal intubation [7].

In the study groups the systolic, diastolic, mean arterial and heart rate have returned to the basal values, whereas in the control group the hemodynamic values are still above their basal values, whereas in the control group the hemodynamic values are still above their basal values and arte statistically significant ($p<0.001$) rate pressure product which denotes myocardial oxygen consumption was increased very much above the critical level 12,00 in the control groups after laryngoscopy and intubation but not in the study groups. The hemodynamic values in control group did not touch the basal values till 5 minutes after laryngoscopy and intubation the values are significant statistically ($p<0.001$). In the study group the hemodynamic values are similar to their values respectively which is not significant statistically at 5 mats after laryngoscopy and intubation.

There are not many studies on the effects of nebivolol a long acting B1 blocker on the attenuation of hemodynamic presser responses 6to laryngoscopy and intubation. Studies have been done on other B blockers i.e., atenolol, practolol, metoprolol, pindolol, esmolol, labettclol etc., The present study with nebivolol a new long acting beta blocker has given a positive result i.e., a good response of attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation [8].

Study group patients were given Nebivolol (nubeta) orally 5 mg/day three (3) days before the surgery and on the day of surgery morning fourth day (4) at 5 AM with a sip of water and the patients were premediated with inj. Glycopyrrolate) 0.2 mg+inj. Ketorlac 1 mg/kg body weight IM and the hemodynamic value recorded. Significant changes of hemodynamic values were in study group.

Conclusion

The principal advantages observed with nebivolol during the study are Good attenuation of heart rate response, Good attenuation of blood response.

Table 4: Hemodynamic responses to laryngo scopy and endotracheal intubation

Cardio Vascular parameters	1 minutes after laryngoscopy and intubation	2 minutes after laryngoscopy	3 minutes after laryngoscopy	4 minutes after laryngoscopy	5 minutes after laryngoscopy	10 minutes after laryngoscopy	15 minutes after laryngoscopy
SAP in mmHgs	152.4 (12.34) 129.6 (15.67)	150.96 (13.57) 115.8 (15.52)	149.56 (13.25) 111.52 (14.93)	147.04 (15.13) 110 (16.33)	146.4 (15.53) 109.6 (16.20)	142.72 (10.70) 109.2 (14.70)	139.68 (19.34) 106.80 (14.06)
DAP in mmHgs	88.88 (7.21) 81.48 (9.67)	86.64 (7.20) 78.80 (9.19)	85.60 (7.37) 74.16 (10.13)	83.60 (7.37) 72.96 (10)	81.44 (7.06) 72.96 (10)	81.84 (6.40) 71.36 (7.83)	81.44 (6.15) 70.64 (8.85)
MAP in mmHgs	110.00 (7.05) 98.16 (8.90)	106.08 (8.62) 91.03 (6.92)	104.29 (6.97) 84.51 (8.35)	102.75 (5.80) 86.33 (8.92)	105.33 (8.67) 85.17 (5.08)	115.26 (10.40) 95.36 (6.82)	100.58 (12.23) 86.93 (7.96)
Heart rate beat/minutes	121.92 (6.28) 99.8 (5.92)	121.6 (5.26) 86.88 (5.39)	120.36 (4.54) 79.6 (8.30)	119.2 (5.42) 76.64 (5.71)	118.52 (4.20) 76.32 (5.82)	118.04 (4.42) 75.4 (4.55)	117.36 (4.35) 73.84 (4.2)
Rate pressure product	18492.00 11990.82	18356.73 11896.63	17920.64 887640	17467.67 8754.00	17128.00 8236.27	16893.67 8233.68	16382.84 7896.11

SAP- Systolic arterial pressure, DAP-Diastolic arterial pressure, MAP-Mean arterial pressure

HR- Heart rate, RPP=Rate pressure product

after induction this also significant ($p<0.001$) statistically.

In the control group the hemodynamic values increased very much above the basal values.

Systolic arterial pressure -30.72

Diastolic arterial pressure -10.96 mmHg

Mean arterial pressure -17.49 mmHg

Heart rate -30.64/beat/min

In the study group the difference is as follows:

Systolic arterial pressure -18.4 mmHg

Diastolic arterial pressure -9.28 mm Hg

Mean arterial pressure -12.96 mmHg

Heart rate -23.68 beats/minutes

This comparison gross increase in the hemodynamic responses to pre-induction readings (basal values) they are significant statistically.

Difference b/w the two groups (control and study) i.e., systolic arterial blood pressure ($p<0.001$), diastolic arterial pressure ($p<0.001$), mean arterial blood pressure ($p<0.001$) and heart rate ($p<0.001$) are statistically significant. There is also profound difference in rate pressure product values b/w control and study group.

There is not much difference b/w pre-induction value and 3 minutes after intubation. It shows attenuation response was achieved by 3rd minutes in study group, whereas in control group there is significant difference seen b/w pre-induction and there minutes and three after intubation values statistically.

The values 4 mints after intubation shows there is not much difference b/w control and study group compare three minutes after intubation values. Surgical incision was given five minutes after post intubation reading was recorded. All the patients were stable hemodynamically during the intra operative period and post-operative period; there was no incidence of bradycardia or hypertension during the study.

The values taken 10 min, 15 min, after intubation in respective tables both in control and study group without supplementing any drug. In control group the values did not touch the base line even by fifteenth minute after intubation. Whereas in study the values touched to base line by the 15th minute. This study shows nebivol was useful in attenuating the introduction response. At the end of surgery all the patients were reversed with neostigmine methyl sulphate and atropine sulphate. All the patients were followed in the post-operative period. There were no incidence of nauseas, vomiting, bradycardia, hypotension or any other untoward side effects.

Discussion

Reflex cardiovascular effects of laryngoscopy and endotracheal intubation in anaesthetized patients have been described previously and included a pressor response and tachycardia which occur at their peak approximately 30 minutes 45 seconds and the peak sustained till 1 minute after laryngoscopy and intubation [4].

There have been many studies which demonstrated increased sympathetic response to laryngoscopy and endotracheal intubations there changes during laryngoscopy and endotracheal intubation can lead to major complication like left ventricular failure, acute myocardial infarction, intracerebral hemorrhage In hypertensive patients this hyper dynamic response causes large increase

pulse rate, blood pressure and ECG monitoring started. This was done by monitoring with ECG in the standard limb leads along with SP02 maintaining. An adult sphynomanometer cuff tied to the left arm and attached to non-invasions blood pressure monitor.

Premedication: premedication was given with glycopyrrolate 0.2 mg and ketocele 1 mg/kg body weight intramuscularly 60 minutes before induction.

Induction: induction was done with thropentone sodium, dose of 5 mg/kg.

Intubation: intubation was performed with vecornium bromide with a dose of 0.1 mg/kg muscle relaxant used was vecuronium bromide for maintenance of anesthesia.

Patients requiring intubation time more than 40 seconds were excluded from the study. Halothane was used in maintenance of anesthesia only 15 minutes after induction prevent wrong interpretation. at the end of surgery, the residual neuromuscular was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg.

Systolic blood pressure, diastolic blood pressure and heart rate were recorded at regular intervals in both control and study group as follows.

Just before induction, after induction at 1st, 2nd, 3rd, 4th, 5th, 10th and 15th minutes.

Results

The characteristics of patients are shown in the following anthropometric

Table 1: Demographic details in both groups.

Demographic details	Control(n=25) Mean(SD)	Study(n=25) Mean(SD)
Age in Yrs	36.68(8.09)	40(10.35)
Range	28-44	30-40
Weight(kgs)	50.00(11.31)	51.56(5.59)
Range	43-60	40-58
Male/female(nos)	14/11	16/9
Range	26-56	25-60

There is no significant difference of demographic parameters in both groups.

Table 2: Hemodynamic reading recorded at the time of pre-anesthetic checkup.

Pre-anesthetic checkup	Control group n=25 Mean(SD)	Study group n=25 Mean(SD)	P-Value
SPD (mm Hg)	119.6(12.74)	127.44(15.88)	p>0.05
DAP (mm Hg)	76(7.64)	78.8(11.58)	p>0.05
MAP (mm hg)	99.23(6.31)	100.2(7.01)	p>0.05
heart rate (beat / minute)	88.32(9.86)	91.6(9.02)	p>0.05

Hemodynamic reading recorded at the time of pre-anesthetic checkup are shown above in the table are heart rate, systolic arterial pressure (SAP) diastolic arterial pressure (DAP) are almost similar in both control and study groups and there are no significant differences at the time of pre-anesthetic checkup.

In control group also standardized with same pre-medication the value taken as pre-induction values (basalvalues) in study and control group. Hemodynamic readings heart rate, systolic arterial pressure (sap), diastolic arterial pressure (DAP) are amount similar in both (control with study) group and there is insignificant difference at the time of pre-anestheticcheckup.

Following induction, there is fall in systolic, diastolic and mean arterial pressures in both groups compared to theirpre-inductionvalue (basal values) respectively the fall is significantly statistically in the same group and between the two groups ($p<0.05$). more significant in MAP and heart rate (HR). There is rise in the heart rate in both groups

Table 3: Hemodynamic values recorded at the time of induction (pre-induction)

Pre-induction	Control group n=25 Mean(SD)	Study group n=25 Mean(SD)	P-Value
SPD (mm Hg)	121.68(11.44)	113.2(16.66)	P<0.005 significant
DAP (mm Hg)	77.92(6.56)	70.2(11)	p>0.10
MAP (mm hg)	92.51(7.26)	85.2(8.86)	P<0.001 significant
heart rate (beat / minute)	91.28(9.79)	78.12(7.79)	P<0.001 significant
Rate pressure product (RPP)	11048.64	10900.40	p>0.10
After induction			
SAP (mm hg)	119.52(20.53)	101.16(14.40)	P<0.005 significant
DAP (mm hg)	79.72(8.6)	68.12(11.95)	P<0.05 significant
MAP (mm hg)	90.70(6.00)	80.00(9.40)	P<0.001 significant
Heart rate (beat/mt)	105.08(11.88)	86.96(8.62)	P<0.001 significant
Rate pressure product	12670.12	9267.60	P<0.001 significant

catecholamine has demonstrated increase in noradrenaline following laryngoscopy.

Attempts were made to differentiate between the effects of laryngoscopy and those of tracheal intubation and their individual contribution to hemodynamic changes. Prys Roberts et al. [1] observed that a majority of patients had reflex tachycardia and hypertension well before the act of intubation and this was often enhanced by intubation. So, it is laryngoscopy rather than endotracheal intubation, which generates the stimulus.Increase in heart rate and blood pressure is transitory, variable and unpredictable. the CVS response to intubation is exaggerated in hypertensive patients.

Cardiovascular response to intubation is of a serious concern in patients with hypertension, raised intracranial pressure, diseased cerebral vasculature or with ischemic heart disease where increase in myocardial oxygen consumption can lead to myocardial infraction [2,3]. Cardiovascular effects are observed during induction, during and after intubation during recovery of the patient. The various complications observed during endotracheal intubation are arrhythmias, myocardial ischemia, acute left ventricular failure, intracranial hemorrhage and pulmonary edema. Convulsions may be precipitated in eclamptic patients. Almost all types of dysrhythmias have been reported in addition to sinus tachycardia. The common abnormalities are nodal rhythm, atrial and ventricular extra systoles and pulses alternans. Less commonly, multifocal extrasystoles, pulsus bigeminus and atrial fibrillation have been reported. Heart block, ventricular tachycardia and fibrillation are fortunately rare. Radionuclide studies have shown that stress response to laryngoscopy and endotracheal intubation produce a rapid decline in global left ventricular function (ejection fraction) within seconds, often exercise in patients with symptomatic artery disease. Therefore, various techniques have been used to attenuate these responses. there are local, central and peripheral methods to achieve this purpose.Theseinclude topical and intravenous lignocaine, deep inhalational anesthetics, ganglion blockers, precurarization, narcotics (morphine, buprenorphine fentanyl, alfentanyl) adrenoceptor blocking drugs, vasodilators, nitroglycerin ointment, intranasal nitroglycerin, calcium channel blockers, reducing the duration of direct laryngoscopy to less than 15 seconds and avoiding laryngoscopy and resorting to blind nasal intubation.

Present study is undertaken to evaluate the efficacy of a new beta blocker viz., oral Nebivolol, a novel long acting beta blocker with endothelial protection activity, to attenuate cardiovascular Reponses to laryngoscopy and endotracheal intubation in health, ASA grade I normotensive patients.

Material and Methods

Fifty healthy ASA grades 1 patients scheduled for elective general surgery were selected forth present study Patients in group of 25 yrs. to 60 yrs. of either sex were selected and their weight, age and sex were comparable in both the groups. These fifty patients divided into two groups, control group consisting of 25 patients and study group consisting of 25 patients.

Complete paranesthesia checkup was done 3-4 days prior to surgery, detailed history taken and complete physical examination performed and presence of any organic medical disorder and history of other drug intake was excluded. Patients with history of angina, asthma, other respiratory disorders like COPD, atelectasis, pneumothorax, tuberculosis, haemothorax, pneumothorax were excluded from the study. patients with raised intracranial pressure were also excluded.

Patients with ECG changes of coronary artery disease, cardiac conducting defects, left ventricular hypertrophy, bradycardia (HR<60) congestive cardiac failure, cardiac valvular abnormalities myocardial disease another congenital cardiac defect were also excluded.

Laboratory Investigations: the laboratory investigation performed included a haemogram, serum creatinine, blood sugar, ECG and chest X-ray. Patients in study group were started 3-4 days prior to surgery with tab. nebivolol (nubeta) 5 mg/day orally for those weight was below fifty kilograms (50 kgs). Those patients, whose weight was greater than fifty kilograms (>50 kgs) were given tab nebivol (nublet) 10 mg/day. The drug was allowed to be taken at 8:00 AM every morning beginning 3-4 days prior to surgery. The last dose of nebivolol was given to the patients 4-6 hrs prior to induction of anesthesia with sip of water (upto ½ glass of water).

The drugs used to premedication and muscle relaxation to facilitate intubation were standardized for two groups (study and control). Boyled machine and circuits were thoroughly checked and required size endotracheal tubes and a Macintosh curved blade laryngoscope with required sized blades was kept. Before induction of anesthesia, patients

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Study on Oral Nebivolol in Attenuating the Cardio Vascular Responses to Laryngoscopy and Endotracheal Intubation

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Abstract

Introduction: Laryngoscopy and intubation are almost always associated with hemodynamic changes due to sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. *Aim:* To study the efficacy of oral Nebivolol in attenuating the cardio vascular reflex responses to laryngoscopy and endotracheal intubation. *Materials and methods:* The attenuation of cardiovascular reflex responses to laryngoscopy and endotracheal intubation has been done with oral nebivolol, a long acting beta-1 blocker in 25 healthy ASA grades 1 patients of both sexes b/w age groups 25-60 yrs. and compares with 25 others in the same age group, termed as control. The study group receives oral nebivolol 5 mg once daily for those below 50 kgs. In the premedication inj. Glycopyrolate 0.2 mg IM and inj. Ketorolac 1 mg/kg IM was given in both groups, inj. Glycopylate was preffered over injection atropine as it has better antisecretory properties with minimal cardiac effects, which would change basic monitoring values. *Results:* Laryngoscopy and endotracheal intubation there was significant increase in blood pressure (SAP, DAP and MPA) and heart rate in the control group, but was significantly less in the study who received the beta blocker nebivolol. In control group rate pressure product, a measure of myocardial oxygen demand was increased significant after laryngoscopy and endotracheal intubation. *Conclusion:* Hence, because of long duration of action and being beta, selective agent, oral nebivolol agent when used prior to surgery ensures a stable normotensive or a mild hypotensive field during surgery.

Keywords: Nebivolol; Laryngoscopy; Endotracheal Intubation.

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Introduction

Endotracheal intubation is translaryngeal placement of endotracheal tube into trachea via, the nose or mouth. It was during the world war-I that blind naos-tracheal intubation was popularized by rowbotham and Magill. Continued improvement in equipment and use of neuromuscular blockers combined with technical skills of anesthesiologist have made endotracheal intubation safe in common practice in modern day anesthesia. Commonly observed cardiovascular effects seen during intubation arehypertension and tachycardia which have been recognized since.

Direct recording of sympathetic nervous activity is difficult in man, but measurement of plasma

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Conclusion

Clonidine (1 mcg/kg) when added to levobupivacaine 0.25% and ropivacaine 0.25% in paediatric caudal block had similar post operative analgesia with fewer side effects and either combination can be used safely in children undergoing sub umbilical surgery.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Appendix

University of Michigan Sedation Scale (UMSS).

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score were comparable between the groups throughout the study period [Fig. 3]. Both the group required only one dose of rescue analgesic in the first 24 hours.

As evident from the Table 3, Sedation scores were lower as well as similar in both the groups and difference was not statistically significant. There were no complications in the 60 study patients, like nausea, vomiting, bradycardia, hypotension and respiratory depression in the post operative period.

Discussion

Ropivacaine and levobupivacaine are the newer local anaesthetic agents, which are associated with reduced systemic toxicity and hence has greater margin of safety [13]. Clonidine an alpha 2 adrenoreceptor antagonist is one of the widely used adjuvant in caudal block to prolong the duration of analgesia. Clonidine when given neuraxially, its analgesic effect was more pronounced, suggesting spinal mode of action. Sharp and colleagues, in their study found that, a lesser volume of bupivacaine (0.5 ml/kg) after caudal injection may not deliver the clonidine up to the spinal cord, there by leaving only direct action on nerve roots in the caudal area [19]. Further studies on ropivacaine showed that 1 ml/kg 0.25% ropivacaine when administered caudally, produces a maximal plasma concentration of 0.72±0.24 mg/lit(litre), which is way much lower than the maximal plasma concentration of ropivacaine (2.2±0.8 mg/lit) tolerated in adult volunteers [7]. Ingelmo P and colleagues in their study about relative analgesic potencies of levobupivacaine and ropivacaine for caudal anaesthesia in children found that the potency ratio at Effective Dose(ED)50 was 0.92 and at ED95 was 0.89, suggesting similar potency between the two anaesthestic agent in caudal block [8]. Therefore, we chose 1 ml/kg of 0.25% ropivacaine and levobupivacaine. Various doses of clonidine have been used caudally (1–5 mcg/kg), we selected a dose of 1 mcg/kg as it produces similar effect and fewer adverse effects when compared to 2 mcg/kg of clonidine [5].

In the present study, the primary outcome was the duration of analgesia (time duration from administration of caudal block to first requirement of rescue analgesia) which was comparable between the groups (around 11 hours). The duration of analgesia in other studies varied between 5.8 hours to 16.5 hours. This wide range of variation might be due to the difference in the dosage of clonidine, dosage and concentration of local anaesthetics agents, use of various premedication, different scales of pain assessment, indication for rescue analgesia and drugs used for rescue analgesia. Non standardised surgeries and anaesthetic techniques might be the other major factors. [1,2,9,15,16] [Table 4].

Sedation after clonidine is due to alpha 2 adrenoreceptor activation in locus ceruleus, an important modulator of vigilance, resulting in increased activity of inhibitory interneurons to produce central nervous system depression. It is dose-dependent as demonstrated by Lee and colleagues in their study on adding 2 mcg/kg of clonidine [12]. As we used lower dose of clonidine in our study, we had lower sedation scores in both the groups score and all the patients were easily arousable, which are consistent with the findings of previous studies [9,15,16]. Hypotension and bradycardia are the two haemodynamic side effects of clonidine in neuaxial blocks. This is due to stimulation of alpha 2 inhibitory neurons in the medullary vasomotor centre of the brainstem causing a decrease in sympathetic outflow. These are more pronounced in adults and with higher dose of clonidine. Because of lower dose of clonidine (1 mcg/kg) in our study, heart rate and mean arterial pressure were maintained within 20% of the baseline value and were comparable between the groups, which were similar to the previous study [29]. There have been documentation of respiratory depression with the use of caudal clonidine, which were more pronounced in neonates; 20 None of the patients in our study suffered this side effect [9,15,16]. A systematic review and meta-analysis by Yang Y and colleagues on Clonidine as additive to local anaesthetics for paediatric neuraxial blocks, demonstrated the increase in the duration of post operative analgesia, lesser number of rescue analgesic requirement and fewer side effects when lower doses were used. We found similar results in our study [20].

The standardised method of premedication, anaesthesia and analgesia are strengths of our study. Further we used CHIPPS score for pain assessment, which is a simple, objective and validated scale for assessing post-operative pain in children aged 1-6 years [3]. The pain was assessed for 24 hours postoperatively by anaesthesiologists and didn't involve parents. This was to prevent any bias or inconsistency in treating pain among kids. Ours was a single centric study with a small sample size. We didn't measure the motor blockage characteristics. We included children undergoing both inguinal hernia and orchidopexy, thus surgeries were non standardised. These were the limitations of our study.

Table 3: The comparison of sedation scores of patients in both the groups

UMSS score	Group L	Group R
0	8	10
1	20	18
2	2	2
3	0	0
4	0	0

UMSS=University of Michigan Sedation Scale

Group L= Levobupivacaine - Clonidine, Group R= Ropivacaine - Clonidine

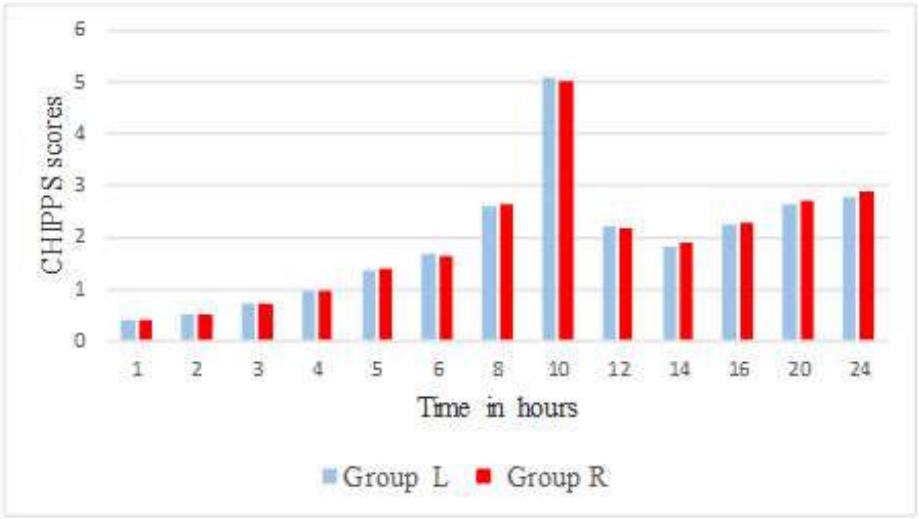

Fig. 3: The comparison of mean Children and Infants Postoperative Pain Scale (CHIPPS) scores in Group L and Group R.

Group L= Levobupivacaine - Clonidine, Group R= Ropivacaine – Clonidine.

Table 4: Duration of analgesia in the published literature

References	Authors	Surgery	Clonidine (mcg/kg)	Local anaesthetic agent	Duration of analgesia (in hours)	Pain Scale used
9	Kanaujia S K and colleagues	Lower abdominal surgeries	1 mcg/kg	Levobupivacaine 0.25% (1 ml/kg)	10.39±0.38	FLACC
16	Potti R L and colleagues	Hypospadiasis repair,inguinal herniotomy	1 mcg/kg	Levobupivacaine 0.25%(1 ml/kg)	16.68±4.7	CHIPPS
15	Manickam A and colleagues	Subumbilical and urological surgeries	1 mcg/kg	Ropivacaine 0.1% (1 ml/kg)	9.8	FLACC
2	Bajwa SJS and colleagues	Inguinal Hernia repair	2 mcg/kg	Ropivacaine 0.25% (0.5 ml/kg)	13.4±3.4	OPS

FLACC: Face, Legs, Activity, Cry, Consolability OPS: Objective Pain Score CHIPPS: Children and Infants Postoperative Pain Scale.

Results

Figure 1 shows the flow of patients through the trial. The groups were comparable with respect to age, weight, gender, ASA physical status, type of surgery and mean duration of surgery as conveyed by Table 2. All the caudal blocks were regarded successful as none required additional doses of intravenous fentanyl. Intraoperative haemodynamic parameters were within 20% of baseline value in both the groups.

The mean duration of analgesia (primary outcome) in group L was 11.05±0.26 and in group R was 10.86±0.22 hours respectively, implying no much difference in duration of analgesia (p value =0.84) between the groups [Fig. 2]. CHIPPS

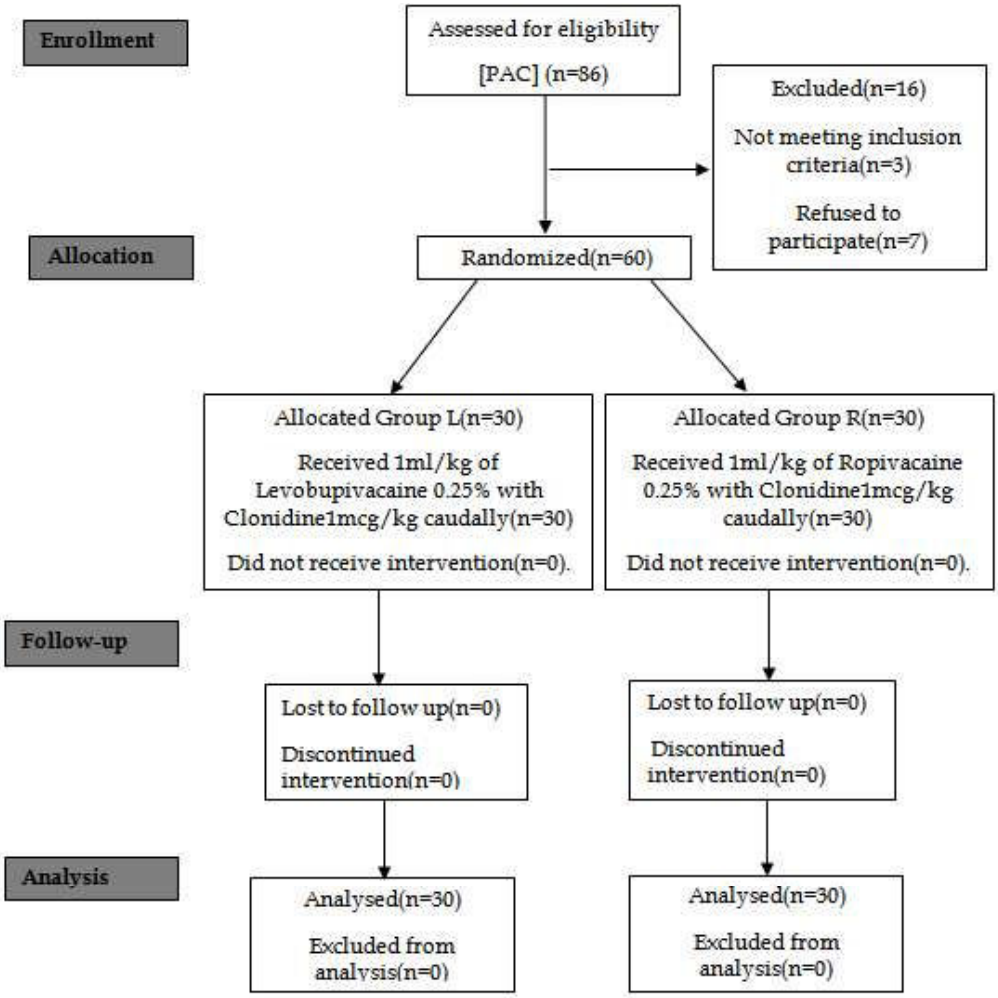

Fig. 1: Consolidated Standards of Reporting Trials flow diagram showing patient progress through the study phases

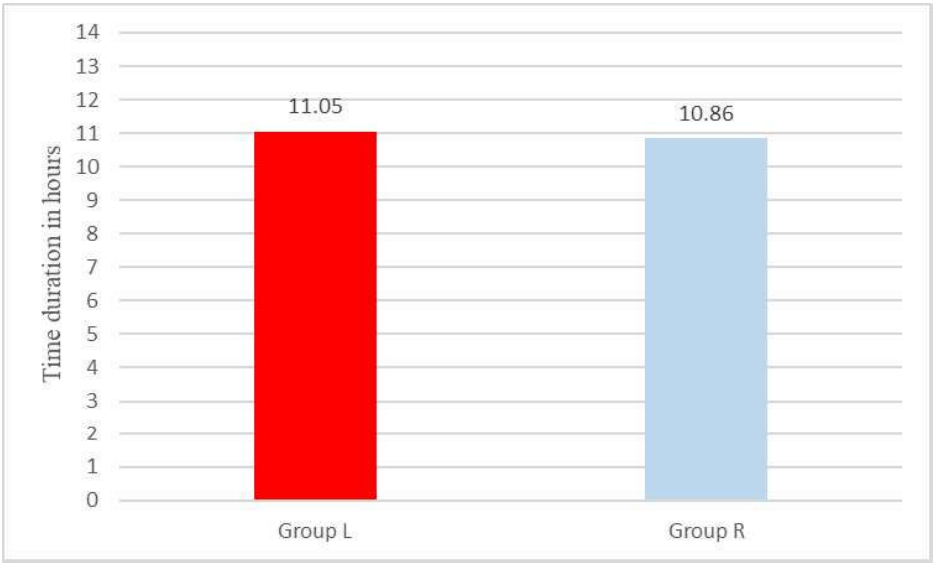

Fig. 2: Comparison of mean duration of analgesia (in hours)

saturation), post operative pain status and side effects were recorded by blinded observer (Senior Resident) every 15 minutes for first two hours, every 30 minutes for next four hours and thereafter hourly till 24 hours. Post operative pain status was assessed using Child and Infant post-operative Pain scale (CHIPPS) Score 3 [Table 1]. The degree of sedation was graded using University of Michigan Sedation scale (UMSS) 14 and was assessed every 15 minutes for first 2 hours only.

The primary outcome of the study i.e. the duration of analgesia (the time duration from caudal placement of drug until the requirement of first rescue analgesia) was recorded. Rescue analgesia was given with intravenous paracetamol 15 mg/kg, when CHIPPS score was ≥ 4. Secondary outcome such as the number of rescue analgesic doses required for first 24 hours, adverse effects like post operative nausea and vomiting, respiratory depression (a decrease in SpO_2 to < 92% requiring supplemental oxygen), hypotension (fall in mean arterial blood pressure > 20% of the baseline value) and bradycardia (fall in heart rate > 20% of the baseline value) were recorded. Next day the patients were discharged and the parents were given phone numbers to inform any untoward incidents.

Based on the pilot study, sample size was determined using Open EPI software. The mean duration of analgesia expected for levobupivacaine – clonidine and ropivacaine – clonidine group were 11.05±0.26 and 10.86±0.22 hours respectively. This indicated a sample size of 26 subjects would be required in each group at an alpha error of 0.05 and power of 80%. We, therefore recruited 30 patients in each group. Statistical analysis was performed using the statistical package SPSSv19.0 [IBM India Pvt Ltd, Bangalore, India]. The categorical data were represented as numbers and percentages and numerical data were represented as mean and standard deviation. The data collected were analysed for normal distribution by one-way analysis (and were normally distributed). Student's t-test was used for Numerical data and Chi-square test for categorical data. Significance was defined as p value<0.05.

Table 1: Children and Infants Post-operative Pain Scale (CHIPPS)

	CHIPPS score	
Item	**Response**	**Score**
Crying	None	0
	Moaning	1
	Screaming	2
Facial expression	Relaxed/smiling	0
	Wry mouth	1
	Grimace (mouth and eyes)	2
Posture of the trunk	Neutral	0
	Variable	1
	Rear up	2
Posture of the legs	Neutral/released	0
	Kicking about	1
	Tightened	2
Motor restlessness	None	0
	Moderate	1
	Restless	2

Table 2: Patient characteristics, type and duration of surgery

Variables	Group L	Group R
Age in years Mean±SD	4.23±1.3	4.47±1.46
Weight (in kilograms) Mean±SD	13.70±2.32	13.73±2.48
Sex ratio Male: Female	24:6	22:8
ASA physical status(I/II)	26/4	25/5
Type of surgery		
Inguinal hernia repair	27	28
Orchidopexy	3	2
Duration of surgery (in minutes) Mean±SD	51.5±5.59	49.83±5.65

SD = Standard Deviation

Group L= Levobupivacaine - Clonidine, Group R= Ropivacaine - Clonidine

ropivacaine are S-enantiomers, which provide wider margin of safety by reducing the occurrence of cardiotoxicity and neurotoxicity [4].

Usage of local anaesthetic agent alone in caudal block provides shorter duration of analgesia. Prolongation of analgesia can be achieved by the addition of various adjutants and amongst them opioids are most widely used. Strict regulations on opioid use (in India) [17] and unpleasant side effects (respiratory depression) [10] has compelled the clinician to use non opioid drugs. Clonidine, an alpha 2 adrenergic agonist produces analgesia without significant respiratory depression [20]. Previous studies have demonstrated that when clonidine was used as an additive to levobupivacaine and ropivacaine in paediatric patients, resulted in prolongation of duration of analgesia significantly [11,16].

To the best of our knowledge, there have been no studies published, comparing levobupivacaine with clonidine and ropivacaine with clonidine for caudal analgesia in paediatric population. The primary aim of this prospective, randomized, double blinded study was to compare the duration of analgesia and secondary aim to measure the number of rescue analgesic doses and any side effects.

Materials and Methods

Following due permission from the Hospital Ethics Committee and written informed consent from parents, this, randomized, double-blinded clinical study was conducted on 60 paediatric patients, aged 2-6 years, of either sex and American Society of Anesthesiologists (ASA) physical status I or II, undergoing subumbilical surgeries (inguinal hernia repair or orchidopexy). Children with history of developmental delay or mental retardation, neurological disorders, pre-existing bleeding disorders, cardiac diseases, sacral abnormalities, infection at caudal injection site and hypersensitivity to local anaesthetic (amide) drugs were excluded from the study.

A pre-anaesthesia evaluation was done day before the surgery, anaesthetic technique and perioperative course were explained to the parents. Patients were randomly allocated to one of the two groups (30 in each) by computer-generated random list which were delivered in sequentially numbered opaque sealed envelopes.

Group L: Received caudal mixture of 1 ml/kg Levobupivacaine 0.25% with preservative free Clonidine 1 mcg/kg.

Group R: Received caudal mixture of 1 ml/kg Ropivacaine 0.25% with preservative free Clonidine 1 mcg/kg.

The investigator who open the sealed envelope, prepared the solutions for caudal administration as per the group mentioned and labelled it as caudal solution without revealing the group or drug. Further he was not involved in the follow-up of the study. Another investigator, who is not aware of the composition of the caudal solution, performed the caudal block and recorded the observations intra operatively.

In our institute, all paediatric patients had intravenous access secured on the previous day of surgery. On the day of surgery, in the preoperative room, patients were re-examined, nil per oral status was confirmed and baseline vitals were recorded. An infusion of Ringer Lactate was started, midazolam (50 mcg/kg) and glycopyrrolate (5 mcg/kg) were given intravenously. Patients were then shifted to operating room, multiparameter monitor were attached and induction of general anaesthesia was done with fentanyl (1 mcg/kg intravenous), propofol (2.5 mg/kg intravenous) and an appropriate size I gel was inserted. Anaesthesia was maintained with mixture of oxygen and air (50:50) and sevoflurane was adjusted to maintain an end-tidal concentration of 1.5–2%, based on intraoperative haemodynamics. Patients were then placed in the lateral position and under all aseptic precautions caudal block was performed using a short bevelled 23G needle. Needle position was confirmed by the characteristic 'pop' sensed during penetration of sacrococcygeal ligament, followed by "whoosh" test (using 0.5 ml of air) as per our institutional practice. After negative aspiration for blood and cerebrospinal fluid, the study drug prepared was injected caudally and the time was noted. All the blocks were performed by same anaesthesiologist throughout the study. The surgical incision was made 15 minutes after caudal placement of the drug. Gross movements or any intraoperative increase in heart rate or mean arterial pressure by more than 15% after 15 minutes of caudal block was defined as inadequate analgesia and additional dose of intravenous fentanyl 1 mcg/kg was given. The intraoperative hemodynamic and respiratory parameters were monitored and documented every 5 min till awakening. The duration of surgery and anaesthesia were noted. At the end of the surgery, inhalation agent was discontinued. I gel was removed, once the children were sufficiently awake. They were then shifted to post- anaesthesia care unit (PACU) for continuous monitoring. Heart rate, mean arterial pressure, SpO_2 (oxygen

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A Clinical Comparative Study between Caudal Levobupivacaine-Clonidine and Ropivacaine- Clonidine for Postoperative Analgesia in Paediatric Subumbilical Surgeries

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Abstract

Context: The use of clonidine as adjuvant to newer anaesthetic agents like levobupivacaine or ropivacaine in caudal block enhance postoperative analgesia. *Aims:* the purpose of the study was to compare the efficacy of levobupivacaine 0.25% with clonidine 1 mcg/kg to that of ropivacaine 0.25% with clonidine 1 mcg/kg with respect to post-operative analgesia following caudal administration in children. *Settings and Design:* Prospective, double blinded, randomized controlled trial. *Materials and Methods:* sixty children aged 2-6 years, of American Society of Anesthesiologists (ASA) physical status I or II, undergoing subumbilical surgeries were randomly allocated to two groups. After induction with general anaesthesia, Group L received 1 ml/kg of 0.25% levobupivacaine with clonidine 1 mcg/kg and Group R received 1 ml/kg of 0.25% ropivacaine with clonidine 1 mcg/kg caudally. Duration of analgesia (primary outcome), pain scores, number of rescue analgesic doses and side effects if any were recorded. *Statistical analysis used:* All the results were tabulated and analysed statistically. After checking for normality assumption, Student's t test was used for numerical data and Chi-square test for categorical data. p values<0.05 were considered significant. *Results:* Groups were comparable with respect to age, weight, sex, type and duration of surgery. Mean duration of analgesia in Group L was 11.05±0.26 versus 10.86±0.22 hours in Group R, hence comparable between the two groups. None of the groups had nausea, vomiting, bradycardia or hypotension and no significant sedation was noted. *Conclusion:* Clonidine(1 mcg/kg) when used as an adjuvant in caudal block along with either levobupivacaine 0.25% or ropivacaine 0.25% produces similar post-operative analgesia with fewer side effects.

Keywords: Levobupivacaine; Ropivacaine; Clonidine; Caudal block; CHIPPS score.

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Introduction

Caudal block is one of the simplest and safe technique used for surgical anaesthesia in children undergoing subumbilical surgery. It provides excellent pain relief with minimum side effects. As children are not cooperative, caudal block is usually administered in combination with general anaesthesia. This makes detection of early symptoms of systemic toxicity due to accidental intravascular injection of local anaesthetics extremely difficult [6].

Bupivacaine is the most commonly used local anaesthetic agent. It is a racemic mixture of R and S enantiomers, of which R enantiomer is cardiotoxic. Newer local anaesthetics like levobupivacaine and

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formic acid and formimino glutamicacid urinary excretion after 3 hour of Nitrous oxide exposure during hip replacement inelderly patients. Formic acid and formimino glutamic acid urinary excretion are markers of Methionine synthase function. In younger patients undergoing longer surgery a minorincrease in these markers was found. Whether the elderly represent a vulnerable population to Nitrous oxide induced Methionine synthase inhibition needs further investigation. Care should be taken with folate or cobalamin deficient patients [60]. In 1990 another study by Waldman et al. [16]. on Hematologic effects of Nitrous oxide in surgical patients did not find hematologic abnormalities in orthopedic and neurosurgical patients exposed to Nitrous oxide, apart from a smaller perioperative increase in Leukocyte count [61].

Conclusion

Based on the present study, we conclude that there are Health Effects on OT personnel on Chronic Exposure to Trace Anaesthetic Gases. Our sample size was comparable in terms of age, sex, BMI. Subjects in the exposed group are distributed in the Homocysteine values of > 12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of < 12 µmol/L. Statistical analysis showed significant difference in Homocysteine levels between OT exposed and non exposed groups. So we conclude that long term exposure to trace Anaesthetic gases like Nitrous oxide can lead to elevated Homocysteine levels in health care workers.

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exposure to Nitrous oxide on Methionine synthase activity. A 24 hour exposure to concentrations of ≤ 860 parts per million (ppm) N_2O showed no change in Methionine synthase function in Sprague-Dawley rats. However, at anesthetic concentrations, Methionine synthase activity is inhibited rapidly in rats. In Koblin study on Inactivation of Methionine synthase by Nitrous oxide in mice demonstrated that N_2O (70%) inhibited Methionine synthase activity in Liver biopsies with a 50% reduction in activity predicted after approximately 1.5 hour. Consistent with this effect, the duration of N_2O exposure is correlated with increased Homocysteine levels. 5,10-Methylenetetrahydrofolate reductase (MTHFR), also plays an important role in the conversion of Homocysteine to Methionine by generating 5-methyltetrahydrofolate [11]. Waclawik AJ et al. [7] described a case of Myeloneuropathy from Nitrous oxide abuse. A Nitrous oxide abuse patient developed diffuse paresthesias and sensory loss and mildly reduced serum vitamin B12 concentration with high levels of Methylmalonic acid (MMA) and Homocysteine. There was no evidence of B12 malabsorption in this patient. Following parenteral B12 administration, his neurological deficit resolved and B12 and MMA levels normalized, but Homocysteine level is elevated. After halting N_2O exposure patients Homocysteine level normalized. This demonstrates the importance of serum Homocysteine level measurements in cases of suspected N_2O toxicity.

In Doran et al. [12] study on Toxicity after intermittent inhalation of Nitrous oxide for analgesia noted Nitrous oxide abusers present with altered mental status, paresthesias, ataxia, and weakness and spasticity of the legs. Tsung-Ta Chiang et al. [13] described a case of Recreational Nitrous Oxide Abuse Induced Vitamin B12 Deficiency. This patient presented with skin pigmentation over the dorsum of fingers, toes, and trunk, and Myeloneuropathy of the posterior and lateral columns. Low serum vitamin B12 level and an elevated serum Homocysteine level were present. Patients history revealed N_2O exposure. Only Symptoms improved significantly with vitamin B12 treatment. Methyl group from N5-methyltetrahydrofolate is transferred to Homocysteine by Methionine synthase producing Tetrahydrofolate and Methionine. In humans, inhibition of Methionine synthase results in the development of Megaloblastic anemia, and eventually Subacute combined degeneration of the spinal cord.

Repeated occupational exposure to N_2O may disturb vitamin B12 metabolic status. N_2O preferentially targets metabolically active cobalamin (I). So decreased levels of vitamin B12 were reported in N_2O abusers and sporadically during N2O anaesthesia. Several studies demonstrated that intraoperative exposure to N_2O is associated with postoperative increases in plasma tHcy [1-3]. In the present study, we extend these observations to operating theatre personnel under repeated occupational exposure to N_2O. Theoretically, in healthcare workers active under excessive occupational exposure to N_2O, disturbances of vitamin B12 metabolism were evident. They might be more susceptible to development of vitamin B12 deficiency symptoms under certain conditions such as dietary vitamin B12 restriction. Moreover, they are likely to develop Hyperhomocysteinaemia, and it is a well-recognized independent risk factor for Arterial and Venous thrombosis and Coronary heart disease. Our study was in contrast with following Literature. Gudrun Abascall et al. [14] studied whether routine blood test is of value, for evaluating effects among midwives working with Nitrous oxide for pain relief in delivery unit. The study was done to determine if work place ambient air Nitrous oxide exposure resultsin detectable Hyperhomocysteinemia or signs of Macrocytocis in midwives. One of 3 delivery units ambient air quality measures exceeded recommended ranges. There were no signs of routine blood test pathology in the personnel studied.

All the personnel in the present study are exposed continuously to trace gases in OTs unlike the midwives.

M Salo et al. [15] study on signs of vitamin B12 - Nitrous oxide interaction in operating theatre personnel showed no changes in the peripheral blood samples. Peripheral blood counts and films, serum vitamin B12 and plasma and erythrocyte folate concentrations were studied in eight anaesthetists and seven internists to find if the interaction is an occupational health hazard to operating theatre personnel chronically exposed to trace concentrations of Nitrous oxide. In addition, blood counts were studied in two retrospective materials of 118 operating theatre nurses working in scavenged operating theatres and in ten subjects working in unscavenged theatres. No definite signs of B12- nitrous oxide interaction could be observed in the peripheral blood samples from these persons. Number of subjects in the exposed group in the present study are 30 compared to the above study and even in this present study 12 out of 30 subjects in the exposed group showed elevated Homocysteine levels. Koblin et al. [11]. study on the of Effect of Nitrous oxide on Folate and vitamin B12 metabolism in patients did not find any changes in

to Anaesthetic gases in one group. The subjects in exposed group are fulltime doctors and nurses working in OTs. The mean duration of exposure in OT exposed group is 14.5 years and it is zero in thecontrol group as it is not exposed to any Anaesthetic gases. There is a difference in theduration of exposure which resulted in a statistical difference in the Homocysteinelevels. Nitrous oxide reacts with the cobalamin corrin nucleus oxidizing the cobalt atom. So themolecule loses its power to form a carbon-cobalt bond with the methyl ligand [6]. Thus, Nitrous oxide prevents the formation of Methylcobalamin and inactivates circulating Methionine synthase. Nitrous oxide induced inactivation of Methylcobalamin isirreversible in animal and human tissues since only bacteria possess the enzymes torevert the oxidative damage to cobalamin. Therefore, recovery of Methionine synthaseactivity requires replenishment of cobalamin (I). Waclawik AJ et al. [7] described a case of Myeloneuropathy from Nitrous oxide abuse.

Following parenteral B12 administration, his neurological deficit resolved and B12 and MMA levels normalized, but Homocysteine level is elevated. After halting N_2O exposure patients Homocysteine level normalized [12] Because of interassay variability leading to method dependent normal ranges, tHcyconcentration of 12 µmol/litre reflecting 95th percentile value in the control group wastaken in this study as a cut-off value discriminating between elevated and normal tHcylevels.

In our study the mean value of Homocysteine is 13.285 µmol/L and 10.546 µmol/L in the exposed and control group respectively. The statistical analysis resulted in a P-Value of 0.0135 (confidence interval of 95%). This implies that the difference is statistically significant. In W. Krajewski, M. Kucharska et al. [5] study, subjects exposed to N2O presented with lower Vitamin B12 [372.8 (12.1) vs 436.8 (13.2) pmol litre, p = 0.001] and higher tHcy. [11.2 (0.5) vs 8.9 (0.5) mmol litre, p¼=0.006]. The changes in Vitamin B12 status were aggravated in subjects exposed to N_2O in concentrations substantially exceeding occupational exposure limit. Observations in present study are in accordance with the W. Krajewski et al. study [5]. The reason for increase in Homocysteine levels is, Nitrous oxide by oxidizing vitamin B12 and inactivating Methionine synthase. In patients exposed to Nitrous oxide there is inactivation of Vitamin B12 leading to increased circulating levels of Folates and Homocysteine.

Subjects in the exposed group are distributed in the Homocysteine values of >12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of <12 µmol/L. Mean Homocysteine value in Females in OT exposed group is 12.029 µmol/L and in controls is 9.51 µmol/L, which are not equal. Mean Homocysteine value in Males in OT exposed group is 17.408 µmol/L and in controls is 13.392 µmol/L, which are not equal. There is a difference in the Homocysteine levels between the two groups. Chronic Hyperhomocysteinemia is concurrent with ischemic heart disease (coronary heart disease, myocardial infarction), and cerebrovascular disease, (fatal and hemorrhagic stroke) [8]. Whether this assosciation is due to pathogenic effect of Homocysteine (causational) or increased levels is an assosciated marker, remains controversial.

ENIGMA (Evaluation of Nitrous oxide In the Gas Mixture for Anesthesia) trial showed there is a pathophysiologic rationale for increased long-term cardiovascular morbidity and mortality in patients receiving Nitrous oxide. Post surgery Homocysteine concentrations were ≥13.5 µmol/L in these adults and these were also associated with an increased risk of major complications and cardiovascular events [9].

There is generation of reactive oxygen species like Superoxide anions (O^{2-}) and Hydrogen peroxide (H_2O_2), with high Homocyteine levels, since these originate from the auto-oxidation of Homocysteine. Reactive oxygen species promote loss of membrane function and increased membrane permeability (lipid peroxidation). Either the decreased production of Nitric oxide, or the increased formation of superoxide, or both may result in endothelial cell dysfunction. These observations are in accordance with the following Literature. W. Krajewski, M. Kucharska, et al. [5] study on Impaired vitamin B12 metabolic status in healthcare workers exposed to Nitrous oxide showed no significant differences in Haematological parameters and folic acid between both the groups. However, subjects exposed to N_2O presented with lower vitamin B12. The changes in vitamin B12 status was aggravated in subjects exposed to N_2O in concentrations exceeding occupational exposure limit. N_2O exposure level and vitamin B12 concentration showed significant negative correlation and N_2O exposure level and tHcy concentration showed a significant positive correlation. N_2O exposed subjects with various vitamin B12 concentrations have Abnormal tHcy concentrations.

Sharer et al. [10] studied the Effects of chronic

the Homocysteine value of >12 µmol/L (Graph 3).

Mean Homocysteine value in females OT exposed group is 12.029 µmol/L and in controls is 9.51 µmol/L. The p-Value of 0.0281 is "statistically significant" ($p < 0.05$) and hence concluding that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure (Table 2).

Mean Homocysteine value in males OT exposed group is 17.408 µmol/L and in controls is 13.392 µmol/L which are not equal. The p-Value of 0.00502 is "statistically significant" and hence we conclude that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure.

Mean homocysteine value inover all analysis OT exposed group is 13.285 µmol/L and in controls is 10.545 µmol/L which are not equal. The P-Value of 0.00135 is "statistically significant", and hence concluding that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure.

Discussion

There are many trails indicating that exposure to Nitrous oxide during surgery in adults causes raise in Homocysteine levels during post operative period 1-3. The first clear association of N2O and hematologic disease was reported by Lassen et al in the Lancet in 1956. They found that Granulocytopenia was developed on the fourth day (with 50% N_2O) and Bonemarrow biopsy was consistent with Pernicious anaemia with Megaloblastic changes. Homocysteine is produced by demethylation of Methionine [3]. Under normal conditions, Homocysteine is remethylated to Methionine by the enzyme Methionine synthase and this requires the reduced form of vitamin B12 as a coenzyme and 5-methyltetrahydrofolate as the methyl donor 36. Nitrous oxide irreversibly oxidizes the Cobalt atom of vitamin B12. This leads to inactivation of vitamin B12, which is a co-factor for Methionine synthase. Whether this acute effect has relevant clinical outcome, has been the research objective of two recent prospective trials in adults [1,2]. In these studies, there is Nitrous oxide induced acute Hyperhomocysteinemia (>13.4 µmol/L) and this was associated with increased risk of major post-surgical complications. Paul S. Myles, Chan MT et al. [4] study showed there is significant increase in postoperative Homocysteine in N_2O exposed group. There was also decrease in flow-mediated dilatation in N_2O exposed group. Endothelial function in patients undergoing noncardiac surgery was significantly impaired. N_2O exposure could be a risk factor for postoperative cardiovascular morbidity [1]. Badner NH et al. [1] study found a significant increase in Homocysteine levels with N_2O administration in patients undergoing Carotid endarterectomy and these patients were associated with increased postoperative myocardial ischemia. There is an assosciation between exposure to N_2O and alteration of vitamin B12 metabolic status in healthcare workers and the extent of alteration depends on the level of exposure. Some of these studies have demonstrated a relationship between N_2O exposure and altered vitamin B12 metabolism and plasma Homocysteine levels.

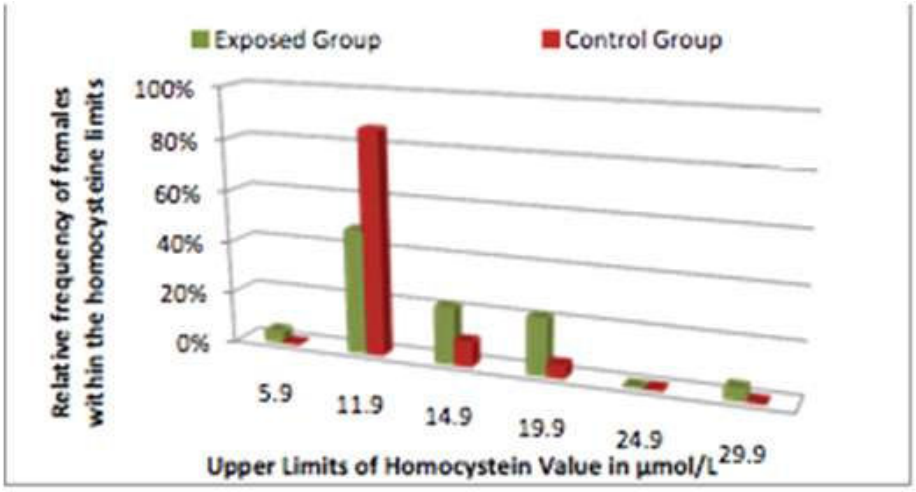
The aim of our study is to find the effect of chronic exposure to trace anaesthetic gases on plasma Homocysteine levels in operating room personnel.

Subjects

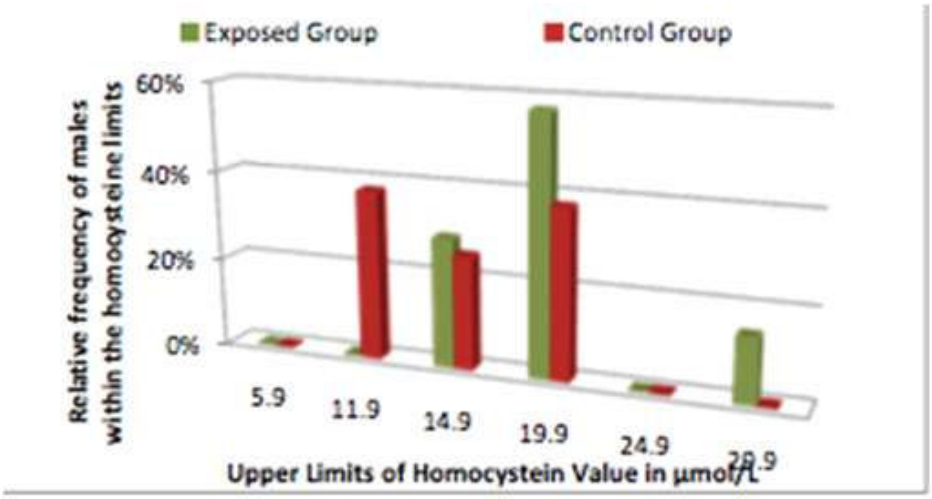
Our study design included 30 subjects who are exposed to gases and 30 controls who are not exposed. In the present study subjects in the 2 groups did not vary much with respect to age, sex and BMI. In terms of sex distribution of the sample, 23% (7) of the subjects were male and 77% (23) were female in the exposed group and 27% (8) of the subjects were male and 73% (22) were female in the control group. In our study a balanced sample was selected to ensure that there was no statistical difference in Homocysteine levels based on the sex. Comparing the current study with that of W. Krajewski, M. Kucharska, et al. study which included only females (95) in study group and only females (90) in control group [5].

In the present study all the subjects were aged between 28 to 58 years in both the exposed group and control group with a mean age of 41.9 years and 42.8 years respectively. The similarity ensures that there is no statistical difference in the Homocysteine levels based on the age. W. Krajewski, M. Kucharska, et al. [5] study included subjects aged between 25 and 56 years. 5 Mean BMI Value in our study is 24.4 and 24.7 respectively in exposed group and control group. BMI values of both the groups is equivalent.

To compare the difference between the Homocysteine values in the exposed and control groups, the subjects were exposed to > 5 years



Graph 2: Distribution of Homocysteine values in female subjects



Graph 3: Distribution of Homocysteine values in male subjects

Table 2: Female and male observation of the mean values of homocysteine

Female Analysis	Homocysteine value (in umol/L)	Age in years	Duration of exposure in years	BMI
Mean values of Exposed Group	12.02956	39.260	12.6956	24.53957
Mean values of Control Group	9.510454545	40.090	0	24.09227
p Value	0.028131938	0.68656	5.46E-11	0.574845
Male analysis				
Mean values of Exposed Group	17.40714286	50.57143	20.42857143	24.35714
Mean values Control Group	13.39125	50.25	0	26.37875
p Value	0.050269817	0.946344	9.94E-05	
Over analysis				
Mean values of Exposed Group	13.28433333	41.9	14.5	24.497
Mean values of Control Group	10.54533333	42.8	0	24.702
p Value	0.01353611	0.6897	1.95E-13	0.7651

Results

The sample considered for the study included 60 subjects of which 30 subjects were in the exposed group who are exposed to waste Anaesthetic gases in unscavenged OT and 30 subjects were in the control group.

Table 1: Demographic distribution of the exposed group as well as control group

Demogrphic details	Exposed Group: With Gas Exposure	Control Group: Without Gas Exposure	p-Value
Age(in years)	41.9	42.8	0.68966
Males	7(23%)	23(77%)	0.78
Females	8(27%)	22(73%)	
BMI	24.497(6.629)	24.702(7.359)	0.7651
Average duration of exposure in years	14.5 0	0 0	1.95

All the subjects were aged between 28 to 58 years in both the exposed group and control group with a mean age of 41.9 years and 42.8 years respectively. The statistical analysis with a confidence interval of 95% resulted in a p-Value of 0.68 which is considered to be "statistically not significant" as it is greater than the ideal value of 0.05 (A p-value of 0.05 or less rejects the null hypothesis). In terms of the sex distribution of the sample, 23% (7) of the subjects were male and 77% (23) were female in the exposed group and 27% (8) of the subjects were male and 73% (22) were female in the control group. A balanced sample was selected to ensure that there were no statistical differences in the Homocysteine levels based on the sex (Table 1).

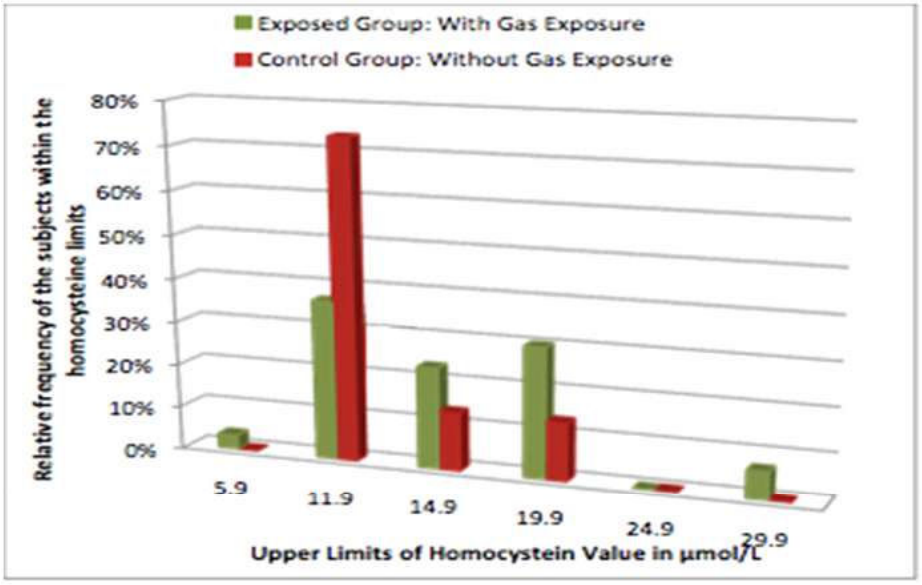
BMI Value resulted in a p Value of 0.76 which is considered to be "statistically not significant". Hence the BMI values of both the groups is equivalent.

To compare the difference between the Homocysteine values in the exposed and control groups, the subjects in the exposed group were exposed to > 5 years of Anaesthetic gas. The mean duration of exposure in OT exposed group is 14.5 years and is observed to be zero in the control group as it is not exposed to any gases. The statistical analysis resulted in a very low p-Value of 1.95E-13 which is considered to be "statistically highly significant". Hence we conclude that there is a difference in the duration of exposure which resulted in a statistical difference in the Homocysteine levels.

The graph 1 we can observe that the maximum number of subjects in the control group are distributed within the ideal Homocysteine value of < 12 µmol/L while the subjects in the exposed group are distributed in the Homocysteine values of > 12 µmol/L as well (Graph 1).

From the graph 2 we can observe that the number of females in the control group are distributed within the ideal Homocysteine value of < 12 µmol/L while the females in the exposed group are distributed in the Homocysteine values of > 12 µmol/L as well (Graph 2).

From the graph 3 we can observe that the number of males in the exposed group are distributed within



Graph 1: Distribution of Homocysteine values in the subjects

developed polyneuropathy and it was linked to the deficiency of Vitamin B12. A growing body of evidence indicates that Homocysteine acutely rises as a side effect of exposure to Nitrous oxide during surgery in adults [1]. Homocysteine is an intermediary metabolite in the metabolism of the sulfur-containing amino acids. It is produced by de-methylation of Methionine and is a substrate for synthesis of Cystathionine and then Cysteine. Under normal conditions, Homocysteine is remethylated back to Methionine by the enzyme Methionine synthase which requires the reduced form of Vitamin B12 as a coenzyme and 5-Methyltetrahydrofolate as the methyl donor.

Nitrous oxide irreversibly oxidizes the Cobalt atom of Vitamin B12, inactivating it which is a co-factor for Methionine synthase. Whether this acute effect translates into clinical outcomes of relevance has been the research objective of two recent prospective randomized control trials in adults1-3. In these trials, Nitrous oxide induced acute Hyperhomocysteinemia (>13.4 µmol/L) was associated with increased risk of Myocardial ischemia, and other major post-surgical complications1. Exposure to N_2O inhealthcare workers is associated with alterations of Vitamin B12 metabolic status, theextent of which depends on the level of exposure [4,5]. Some of these studies havedemonstrated a relationship between N_2O exposure and altered Vitamin B12 metabolismand plasma Homocysteine levels. Here, we evaluated the level of serum Homocysteinein personnel exposed to ot atmosphere in Gandhi hospital Secunderabad, and compared with non OT healthy controls by using ADVIA Centaur and ADVIACentaur XP systems.

Materials and Methods

Blood samples are collected according to National Committee for Clinical Laboratory Standards. 5 ml of blood collected in EDTA vaccutainers from an antecubital vein after 6-8 hours of fasting and should not have a high protein meal 6-8 hours before collection from all the subjects who gave their consent to participate in the study after explaining to them the purpose of study. Samples are centrifuged and red blood cells are separated. Speciemens are capped tightly and refrigerated at 2-8^{0}C until testing.

A total of 30 subjects exposed to waste Anaesthetic gases for a minimum of 5 years who routinely provide full-time assistance during operations on a day-to-day basis in operation theatres, who gave their consent to participate in the study are registered to study various epidemiological parameters and to screen for the plasma Homocysteine levels. Obtained the permission from institutional Ethical committee.

Inclusion Criteria

OT Personnel, who are exposed to Anaesthetic gases for >5 years in operation theatres. Also 30 controls who are not exposed to Anaesthetic gases are selected at random to compare with the data generated on the subjects exposed to these gases.

Exclusion Criteria

Age < 20 years and > 65 years, Recent use of vitamins, Pregnancy, Bleeding tendencies, Systemic diseases like liver and renal failure, Clinical signs and symptoms of cobalamine or folate deficiency . Medications known to effect plasma Homocysteine.

From all the cases and controls detailed information pertaining to various epidemiological parameters such as age, sex, history of exposure, other comorbidities are collected using a specific proforma.

Homocysteine testingdone by ADVIA Centaur XP assays use Acridinium ester (AE) as the chemiluminescent label, because AE does not require the addition of a catalyst or substrate. It is easy to automate direct Chemiluminescence using AE and provides many benefits, such as long reagent shelf life, fast reaction time, and assay sensitivity. The ADVIA Centaur XP assays use the dimethyl form of AE because its stability allows long reagent shelf life.

Statistical Analysis

The results are expressed as frequencies or mean values (SD). Differences in demographic characteristics between groups were analysed. Since we are studying the effectiveness of a single variable (Homocysteine Value) on two control groups (With Gas Exposure and Without Gas Exposure) a One-Way ANOVA with a Confidence Interval of 95% (Alpha = 0.05) is used between the subjects. To identify whether our null hypothesis (H0) that the means of the groups are equal or the alternative hypothesis (H1) that the means are not equal we shall look at the results. A p-value of 0.05 or less rejects the null hypothesis that is; the statistical assumptions used imply that only 5% of the time would the supposed statistical process produce a finding this extreme if the null hypothesis were true.

Original Research Article

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Effect of Chronic Exposure to Trace Anaesthetic Gases on Plasma Homocysteine levels in Operating Room Personnel

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Abstract

Introduction: A growing body of evidence indicates that Homocysteine acutely rises as a side effect of exposure to Nitrous oxide during surgery in adults. Under normal conditions, Homocysteine is remethylated back to Methionine by the enzyme Methionine synthase which requires the reduced form of Vitamin B12 as a coenzyme and 5-Methyltetrahydrofolate as the methyl donor. Exposure to N_2O inhealthcare workers is associated with alterations of Vitamin B12 metabolic status. *Aim:* To find the Effect of Chronic Exposure to Trace Anaesthetic Gases on Plasma Homocysteine levels in Operating Room Personnel. Objective of my study is to find plasma Homocysteine levels in operating room personnel compared to non exposed. *Materials and Methods:* This study is conducted on 60 personnel. A total of 30 subjects exposed to waste Anaesthetic gases for a minimum of 5 years in unscavenged operation theatres and also 30 controls who were not exposed to Anaesthetic gases were selected at random to compare. From all the cases and controls detailed information pertaining to various epidemiological parameters and evaluated the level of serum Homocysteine by using ADVIA Centaur and ADVIA Centaur XP systems. *Results:* Mean Homocysteine value in over all analysis OT exposed group is 13.285 µmol/L and in controls is 10.545 µmol/L which are not equal. The p-Value of 0.00135 is "statistically significant", there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure. *Conclusion:* Subjects in the exposed group are distributed in the Homocysteine values of >12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of <12 µmol/L. Statistical analysis showed significant difference in Homocysteine levels between OT exposed and non exposed groups. So we conclude that long term exposure to trace Anaesthetic gases like Nitrous oxide can lead to elevated Homocysteine levels in health care workers.

Keywords: Homocysteine levels; 5-Methyltetrahydrofolate; Nitrous oxide.

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Introduction

Nitrous Oxide was first Synthesized by Joseph Priestly in 1722. Its Psychotropic effects were first appreciated by Humphrey Davy. The first clear association of N_2O and hematologic disease was reported by Lassen et al. in the Lancet in 1956. They studied it prospectively and found that Granulocytopenia developed on the fourth day (with 50% N_2O). A Bonemarrow biopsy was consistent with Pernicious anaemia with Megaloblastic changes. In 1978, Sahenk reported a case of polyneuropathy from recreational Nitrous oxide use and Layzer reported on dentists who

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Sd/-
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ug/Kg/min) was started after induction-intubation.

In the present study, infusion rate was based on the patient's body weight and hemodynamic response and blood pressure was maintained within the range of 60-70 mmHg. Nitroglycerin acts predominantly on venous capacitance vessels, primarily decreases preload to the heart, in addition, it also decreases systemic vascular resistance and afterload. The production of controlled hypotension using this drug depends more on intravascular fluid volume. Excessive decreases in diastolic blood pressure may decrease coronary blood flow. These decreases in diastolic blood pressures may also evoke baroreceptor-mediated reflex increases in sympathetic nervous system activity manifesting as tachycardia and increased myocardial contractility. Nitroglycerin produces a dose-related prolongation of bleeding time that parallels the decrease in blood pressure. It inhibits platelet aggregation. Increased bleeding time could also be the result of vasodilation secondary to a direct effect of Nitroglycerin on vascular tone.

Karl-Erik Karlberg and associates [13] assessed the influence of intravenous Nitroglycerin on platelet aggregation. It was concluded that increasing doses ofintravenous Nitroglycerin profoundly and dose-dependently inhibit platelet aggregation. This inhibitory effect correlates with glyceryl dinitrate formation.

In this study, the mean heart rates in Group-D and Group-N for the entire duration of surgery were 60.61±4.49 & 95.58±9.41 respectively. There was statistically significant difference between the two groups regarding pulse rates. The mean systolic blood pressures in Group-D and Group-N for the entire duration of surgery were 92.73±8.58 & 91.86±8.77 respectively. There was no statistically significant difference between the two groups regarding systolic blood pressures. The mean diastolic blood pressures in Group-D and Group-N for the entire duration of surgery were 58.40±7.03 & 58.33±7.48 respectively. There was no statistically significant difference between the two groups regarding diastolic blood pressures. The mean arterial pressures in Group-D and Group-N for the entire duration of surgery were 69.85±7.47 & 69.54±7.91 respectively. There was no statistically significant difference between the two groups regarding mean arterial pressures. This suggests that both the drug groups are good for achieving controlled hypotensive anaesthesia in endoscopic resection of nasopharyngeal fibroangioma. The mean blood loss in Group-D & Group-N for the entire duration of surgery was 310.71±140.58 ml & 482±141.42 ml respectively.The mean blood loss in Group D was less than the average blood loss in Group N. The difference in blood loss between both the groups was considered to be statistically significant. Infusion of the hypotensive agent was stopped 10 minutes before the anticipated end of surgery. The average blood loss was more with Nitroglycerin when compared to dexmedetomidine. This can be due to increased heart rate caused by Nitroglycerin that is partially offsetting the beneficial effects of hypotension & prolongation of bleeding time by NTG due to inhibition of platelet aggregation because similar decrease in mean arterial pressure was achieved by both the drugs. Dexmedetomidine, on the other hand is an alpha-2 receptor agonist with central sympatholytic action similar to clonidine. This results in decreased in both systemic blood pressure and heart rate.

Conclusion

- Endoscopic removal of Nasopharyngeal Fibroangioma under controlled hypotension technique- Provided a clear field of vision for endoscopic surgery.
- There was no statistically significant difference between the two groups regarding mean arterial pressures.
- Both Nitroglycerine and Dexmedetomidine can be used safely for maintaining hypotensive anaesthesia to achieve a target mean arterial pressure around 60-70 mm/Hg.
- There was statistically significant difference between the two drug groups regarding variations in pulse rate.
- The average blood loss was more with Nitroglycerin when compared to dexmedetomidine.
- Dexmedetomidine is superior to Nitroglycerin in relation to reduction in blood loss during the resection. Dexmedetomidine improved the perioperative hemodynamic stability & causeed controlled hypotension by its central & peripheral sympatholytic action and has got inherent analgesic, sedative and anaesthetic sparing properties which avoids administration of multiple drugs and there side effects.

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the V5 lead with ST segment analysis was done to detect cardiac ischemia. Prevention of hypercarbia and hypocapnia are essential in hypotensive anaesthesia. Hypothermia was avoided because it decreases the effectiveness of vasodilators and increases the dose requirements if compensatory vasoconstriction occurs. Proper fluid therapy is essential during hypotensive anaesthesia. The aim of induced hypotension is to lower MAP while maintaining adequate perfusion to all vital organs. Thus, preoperative fluid status was assessed and corrected.

Hypotension was only carried out to that level needed to reduce bleeding and only for that time of the surgery where it is of benefit in reducing significant blood loss. Head end was slightly elevated. Position of the patient is critical to ensure success of the controlled hypotensive technique. Elevation of the site of operation allows easy venous drainage from the site of surgery. This is critical to ensure a bloodless field. But exaggerated head end elevation compromises blood supply to brain during hypotensive anaesthesia, so head end elevation was only limited to 15 degrees.

In this prospective randomized study comparing Dexmedetomidine and Nitroglycerin groups, efforts were made to provide this optimal surgical field. Both the drugs were equally effective in achieving MAP (Mean Arterial Pressure) of 60-70 mm/Hg. The average blood loss was more with Nitroglycerin when compared to Dexmedetomidine. This can be due to increased heart rate & prolongation of bleeding time by NTG due to inhibition of platelet aggregation because similardecrease in mean arterial pressure is achieved by both the drugs. Dexmedetomidine ensured good surgical conditions during endoscopic resection of NPF.

Dexmedetomidine loading dose (1 µg/kg) was given in 15 min before induction of anaesthesia and infusion started after the loading dose. There was significant decrease in MAP and HR. This Dexmedetomidine induced hemodynamic profile can be attributed to the known sympatholytic effect of α2 agonists. The α2-receptors are involved in regulating the autonomic and cardiovascular systems. Alpha 2 receptors are located on blood vessels, where they mediate vasoconstriction on stimulation, and in the brain on sympathetic terminals, where they inhibit, norepinephrine release. At lower doses, the dominant action of α2 agonists is sympatholysis by their central action inhibiting norepinephrine release [23]. Higher doses may cause transient increase in blood pressure due to predominant action on peripheral α2-receptors causing vasoconstriction The efficacy of Dexmedetomidine in providing better surgical field and less blood loss during controlled hypotension was previously reported during tympanoplasty, septoplasty and maxillofacial surgeries as well [24].

Basar et al., [6] investigated the effect of single dose of Dexmedetomidine 0.5 µg/kg administration 10 min before induction of anaesthesia and reported significant reduction in MAP and HR. No other analgesic was used in the Group-D (Dexmedetomidine group); because Dexmedetomidine has inherently got analgesic property due to its action in the locus ceruleus of the brain stem [7,8]. It has been shown to stimulate α2 receptors directly in the spinal cord, thus inhibiting the firing of nociceptive neurons. Even peripheral α2 adrenoceptors may mediate antinociception. No other agent for anxiolysis was also used because Dexmedetomidine has anxiolytic property as well. The efficacy of Dexmedetomidine, in terms of providing an ideal surgical field during control hypotension, was previously reported during middle ear surgery and maxillofacial surgery with predictable hemodynamic effects. The results of the present study showed the same results. The optimal anaesthetic technique to reduce blood loss at the surgical field seems to cause relative bradycardia and associated hypotension.

Ulger et al., [9] compared Dexmedetomidine with Nitroglycerine to achieve controlled hypotension in patients scheduled for middle ear surgery. The infusion rate of drugs was titrated to maintain a mean arterial pressure between 65 and 75 mmHg. They concluded that Dexmedetomidine was better for maintaining hemodynamic stability and a drier surgical field, and was devoid of reflex tachycardia and rebound hypertension. The results of the present study are in accordance with these data.

In the current study, the induction dose of Thiopentone sodium was significantly lower in the Group- D (Dexmedetomidine group) in most of the patients. This effect coinciding with the result of Peden et al., [10] who reported that Dexmedetomidine caused a reduction in the overall dose of induction agent required to produce loss of consciousness. This is because of the sedative and hypnotic properties of Dexmedetomidine.

Guven et al., and Goksu et al., [11,12] reported better hemodynamic stability and visual analog scale pain scores; as well as a clear surgical field and few side effects, with dexmedetomidine infusion in functional endoscopic sinus surgery. In Group-2, Fentanyl 2 ug/Kg was given 3 minutes before induction. Nitroglycerin infusion (0.5-5

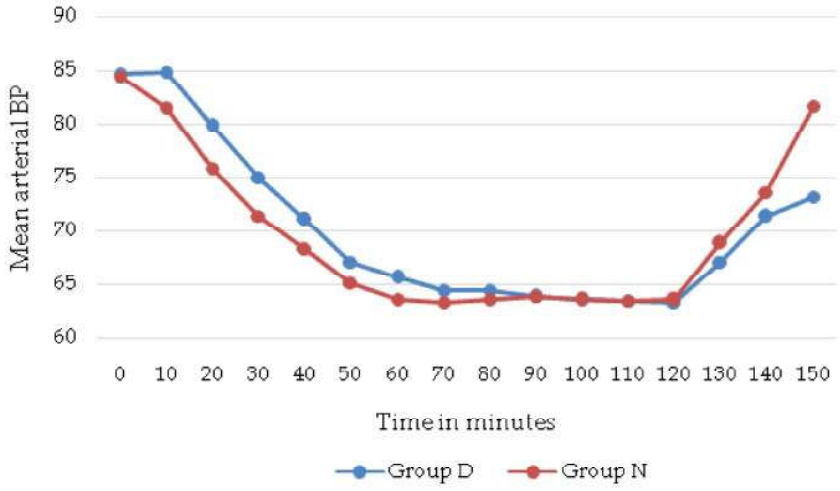

Fig. 4: Mean Arterial Pressure Between Study Groups

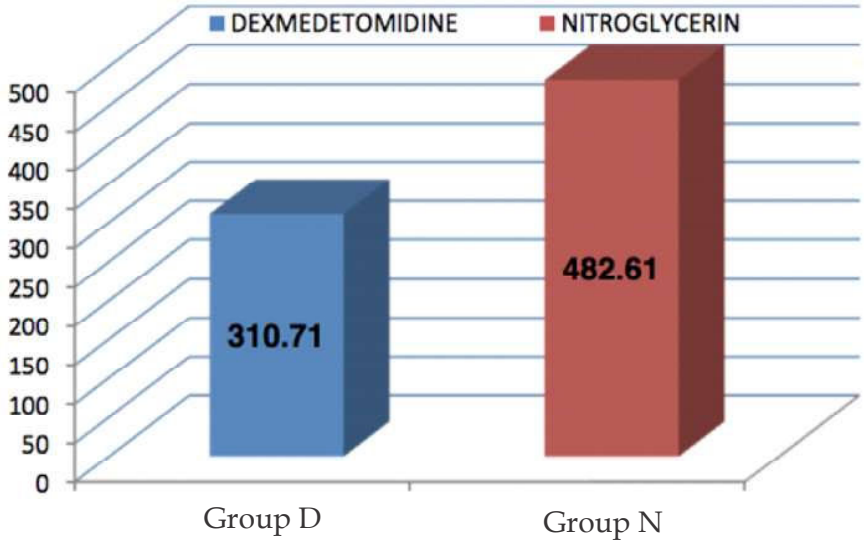

Fig. 5: Mean Blood Loss Between Study Groups

average blood loss in Group N. The difference in blood loss between both the groups was considered to be statistically significant (Fig. 5).

Discussion

Nasopharyngeal Fibroangioma is the most common benign neoplasm of the nasopharynx. It is almost exclusively encountered in adolescent males. They are enormously vascular tumors and open surgical resection is associated with significant blood loss and postoperative morbidity. Recently, endoscopic excision has been widely employed for the excision of angiofibromas. The major problem with endoscopic surgery is that even minimal bleeding can interfere with endoscopic vision. Thus hypotensive anaesthesia is required to assist in decreasing blood loss and providing a bloodless, clear field to facilitate surgery.

Induced or controlled hypotension is a method by which the arterial blood pressure is decreased in a predictable and deliberate manner. The intent of deliberate hypotension is to reduce bleeding and thus facilitate surgery and to decrease the amount of blood transfused.

Care was taken to protect the pressure points by padding. A hypotensive technique reduces the peripheral circulation. This is especially important in areas overlying weight-bearing and bony prominences. Hence, additional supportive pads were placed beneath the patient with special attention paid to the occiput, scapulae, sacrum, elbows and heels. Monitoring of ECG, especially

10 minutes before the end of surgery. Any residual neuromuscular block was antagonized with Inj. Neostigmine 50 µg/kg & Glycopyrrolate 10 µg/kg. Continuous monitoring was carried out throughout the procedure for heart rate, cardiac rhythm, urine output, MAP, oxygen saturation& $EtCO_2$. The urine output was maintained between 0.5 ml/kg/hr and 1 ml/kg/hr in patients.

Observations

The hemodynamic variables were recorded as pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, preoperatively (baseline parameters & intra-operatively at an interval of every 10 mins until the completion of surgery). After the extubation and full recovery, patients were transferred to the post anaesthesia care unit (PACU). The surgery lasted for 150 mins in almost all the patients, so pulse rate and blood pressures and mean arterial pressures were recorded for this duration.

The Statistical analysis was done using Mean, Standard deviation and Independent t- test (for hemodynamic parameters). All recorded data were entered using MS Excel software and analysed using SPSS 16 version software for determining the statistical significance. p values < 0.05 were considered to be statistically significant.

Results

Table 1: Distribution Patient Characteristics in Study Groups

Groups	N	Mean	Standard Deviation	p Value
Age Distribution				
Group- D	20	15.94	±2.26	0.4373
Group- N	20	15.33	±2.64	
Weight Distribution				
Group D	20	45.29	±9.75	0.8192
Group N	20	45.96	±8.63	

The range of ages was between 10–20 years in both the study groups.

The range of weight was 28–60 Kg in both the study groups.

There was no statistically significant difference (p>0.05) between the two groups in age and weight distributions (Table 1).

There is statistically significant difference between the two groups (p <0.05), when the pulse rates were compared (Fig. 1).

Intraoperatively, there is no statistically significant difference between the two groups (p>0.05), when systolic blood pressures were compared (Fig. 2).

Intraoperatively, there was no statistically significant difference between the two groups (p >0.05), when the diastolic blood pressures were compared (Fig. 3).

Intraoperatively, there was no statistically significant difference between the two groups (p>0.05), when the Mean Arterial Pressures were compared (Fig. 4).

The blood loss was measured as blood volume in suction bottle and amount soaked in swabs. The mean blood loss in Group D was less than the

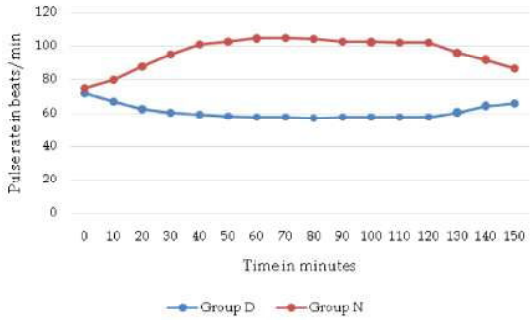

Fig. 1: Hemodynamic Variables Mean Pulse Rates Between Study Groups

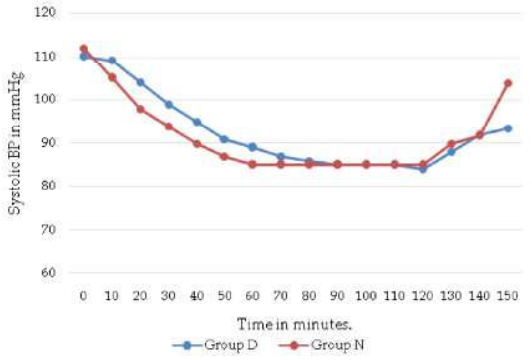

Fig. 2: Mean Systolic Blood Pressure Between Study Groups

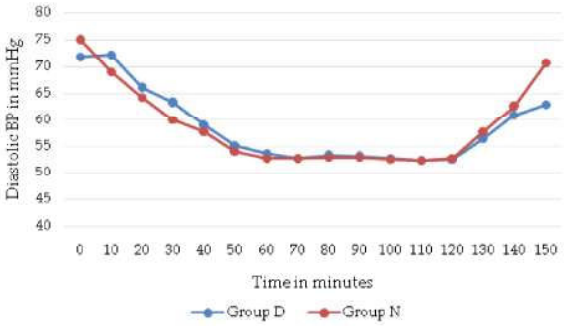

Fig. 3: Mean Diastolic Blood Pressure Between Study Groups

vision. Thus, hypotensive anaesthesia is required to assist in decreasing blood loss and providing a bloodless clear field to facilitate surgery. Controlled (deliberate/induced) hypotension is a technique wherein the arterial blood pressure is lowered in a deliberate but controllable mannerto minimize surgical blood loss and enhance the operative fieldvisibility [3]. There are several pharmacological and non-pharmacological techniques for inducing hypotension. The various pharmacological interventions include volatile anaesthetics, direct-acting vasodilator drugs, ganglion blocking drugs, alpha blockers, beta blockers, combined alpha and beta blockers, calcium channel blockers, propofol, magnesium sulphate, alpha-2 agonists, prostaglandins, tranexamic acid etc. [4]. Nitroglycerin is a direct acting peripheral vasodilator, which primarily dilates capacitance vessels, reducing venous return with concomitant reduction in stroke volume and cardiac output. Dexmedetomidine is an α2 adrenergic receptor agonist causes controlled hypotension by its centraland peripheral sympatholytic action, results in decrease in blood pressure [5]. Hence the present study is undertaken to compare Nitroglycerinvs. Dexmedetomidine infusion for hypotensive anaesthesia in endoscopic resection of Nasopharyngeal Fibroangioma.

Materials and Methods

This is a prospective, randomized, single blinded study conducted on 40 patients between the age group of 10-20 years undergoing endoscopic resection of Nasopharyngeal Fibroangioma in Government ENT Hospital, Osmania Medical College, Hyderabad. After approval by the institutional ethical committee, written informed consent was obtained from the patients during the pre-anaesthetic evaluation. Result values were recorded using a presetproforma.

Inclusion Criteria: ASA Grade I or II, Aged between 10–20 years

Exclusion Criteria: ASA Grade III and IV, Coagulopathy or on Anti-coagulation, with known End – Organ damage, History of known drug allergy to any of the drugs used in this study.

Investigations done: CBC, BT, CT, Blood grouping and typing, Random Blood sugar, Serum Urea and Serum Creatinine, Chest X-Ray, ECG, HIV, HBsAg. Patients included in this study were randomly assigned to receive either Dexmedetomidine (Group D, n=20) or Nitroglycerin (Group N, n=20). In the operating room, following monitors were used as Pulse Oximetry, Blood Pressure cuff for non-invasive blood pressure monitoring, 5 lead ECG, $EtCO_2$ (after intubation). Two cannulas were inserted, one for infusion of Dexmedetomidine or Nitroglycerin infusion and the other for administration of fluids and other drugs. A urinary catheter was inserted.

All the patients were premedicated with Inj. Glycopyrrolate 0.04 mg/Kg, Inj. Ondansetron 0.08 mg/ Kg. In Group- D an infusion of Dexmedetomidine was made by adding 200 µg (2 ml) of Dexmedetomidine to 100 ml of normal saline, administered in paediatric volumetric IV burette set, making it to a final concentration of 2 µg/ml. The infusion was then started; with a loading dose of 1 µg/kg over 15 min followed by a maintenance infusion at 0.5 µg/kg/hr titrated according to the patients desired target blood pressure (21). In Group- N, patients received fentanyl (2 ug/Kg) before induction followed by an infusion of NTG, made by adding 25 mg (5 ml) of NTG to 100 ml of normal saline, administered in paediatric volumetric IV burette set, making it to final concentration of 250 µg/ml. The infusion was then started at the rate of 0.5 µg/kg/min and titrated in between 0.5-5 µg/kg/min according to the target blood pressure.

Both the study groups received standard anaesthetic technique with Inj. Thiopentone sodium 3-5 mg/ kg titrated to loss of eyelash reflex. Endotracheal intubation was facilitated with Inj. Suxamethonium (1.5 mg/kg) and intubation was done with suitable sized cuffed tube. All the patients were mechanically ventilated with 33:66 O_2/N_2O mixtures and Desflurane 4-6% to maintain $EtCO_2$ within normal range of 30-35 mm/ Hg. Muscle relaxation was continued by Inj. Vecuronium. Respiratory rate (RR) and Tidal Volume (TV) were adjusted according to body weight to maintain normocapnia. Patients received normal saline and dextrose; were placed in a 15^0 Reverse trendelenburg position to improve venous drainage and oro-pharyngeal pack was placed. The MAP was then gradually reduced in both the groups to achieve and maintain the target MAP of 60-70 mm/Hg. Patients who developed severe hypotension (MAP < 55 mmHg) were observed by discontinuation of the hypotensive agents and reducing the concentration of Desflurane. If the MAP did not improve 6mg bolus of mephentermine was given intravenously. If any patients developed bradycardia (<50 bpm) then they received Inj. Atropine 0.6 mg I.V.

Infusion of the hypotensive agent was stopped

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Comparative Study of Nitroglycerin and Dexmedetomidine in Patients Undergoing Endoscopic Resection of Nasopharyngeal Fibroangioma

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Abstract

Introduction: Nasopharyngeal Fibroangioma (NPF) is a rare, benign, but locally invasive tumor removed with nasal endoscopy which is minimally invasive and provides a magnified view of the tumor. Hypotensive anaesthesia technique is required to assist in decreasing blood loss and providing bloodless clear field to facilitate surgery. *Aim:* To compare Nitroglycerin and Dexmedetomidine groups for hypotensive anaesthesia in patients undergoing endoscopic resection of Nasopharyngeal Fibroangioma. *Materials and Methods:* This is a prospective, randomized, single blinded study conducted on 40 patients between the age group of 10-20 years undergoing endoscopic resection of Nasopharyngeal Fibroangioma. The patients were randomly divided into two groups of 20 patients each. Group D – Patients who received 'Dexmedetomidine' Group N – Patients who received 'Nitroglycerin'. *Results:* There was no statistically significant difference between the two groups regarding mean arterial pressures. There was statistically significant difference between the two drug groups regarding pulse rate. The mean pulse rate in Dexmedetomidine group was significantly less than in Nitroglycerin group. The average blood loss was more with Nitroglycerin when compared to Dexmedetomidine. *Conclusion:* Nitroglycerine and Dexmedetomidine can be used safely for maintaining hypotensive anaesthesia to achieve the target mean arterial pressure around 60-70 mm/Hg. The blood loss was significantly less in Dexmedetomidine group. Dexmedetomidine was superior to Nitroglycerin in reducing blood loss during the resection.

Keywords: Dexmedetomidine; Nitroglycerin; Nasopharyngeal Fibroangioma.

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Introduction

Nasopharyngeal Fibroangioma (NPF) is a rare, benign, but locally invasive tumor, with an incidence of 1:150000, almost exclusively encountered in the adolescent males [1]. Surgery is considered to be the gold standard treatment. These are enormously vascular tumors and open surgical resection is associated with significant blood loss and postoperative morbidity. Recently, endoscopic excision has been widely employed for the excision of small and medium sized angiofibromas. Nasal endoscopy is minimally invasive and provides a magnified view of the tumor. It is also associated with less postoperative morbidity and low recurrence rate [2]. The major problem with endoscopic surgery is that even minimal bleeding can interfere with endoscopic

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Table 1: Time of onset of sensory block and time of onset, degree, duration of motor block

Grade	Group X	Group XM_1	Group XM_2
Sensory block			
onset time (min)	2.05 +0.58	2.016 + 0.46	2.0 +0.70
Motor block			
onset time (min)	4.8+0.89	4.266+0.79*	4.233+0.40*
Degree of motor blockade	2.03 + 0.40	2.13+0.33	2.23+0.42
Duration of motor blockade (min)	92.16 + 6.53	94.06 + 10.46	92.36+9.4

*p value <0.05 (statistical significant); Group X = 5% Xylocaine hydrochloride; Group XM_1 = 5% Xylocaine hydrochloride ±1 mg midazolam; Group XM_2 = 5% Xylocaine hydrochloride ±2 mg midazolam

Table 2: Intergroup comparison of post operative pain relief

Parameters	Grade X	Grade XM_1	Grade XM_2
Time of first pain medication in hours	2.9+0.63	3.99+0.62**	4.37+5.09**
VAS at first pain medication	35+4.3	36+5.76	34+5.2

**p value <0.001 (statistically highly significant)

There was no incidence of bradycardia, sedation, dizziness, pruritis, respiratory depression neurological deficit. Thus addition of intrathecal midazolam is devoid of any side effects.

Discussion

The present study entitled "Evaluation of intrathecal midazolam (preservative free) for postoperative pain relief in lower segment caseraean" section was carried out to assess the effects of Intrathecal midazolam and to study the sideeffects and complication related to the use of this drug in different dosage during spinal anaethesia.

The onset of analgesia (mean±SD) recorded in the present study was 2.05±0.58 minutes, 2.016±0.46 and 2.0±0.7 minute in group X, XM_1, and XM_2 respectively and in the intergroup comparison the differences were found to be statistically insignificant (p>0.05). No local anaesthetic effect of midazaolm on afferent nerve going into spinal cord has been reported [4,5]. The onset and duration of motor block (mean±SD) in group X was 4.8±0.79 and 94.06±10.46 minutes and in group XM_2 was 4.23±0.40 and 92.36±9.4 minutes. The differences were found to be statistically significant (p<0.05).

Thus it is reasonable to assume that the midazolam acting at the spinal cord level caused synergistic effect in muscle relaxation produced by local anaesthetic action [6-8].

In this study the time to first pain medication in hours (mean±SD) was 2.9±0.63 minutes, 3.99±0.62 minutes and 4.37±5.09 minutes in group X, group XM_1 and group XM_2 respectively. The differences were statistically highly significant (p<0.001). Our results were similar to various authors who have found midazolam as an effective analgesic by intrathecal route [3,4,9]. The mean±SD of VAS at first pain medication in three groups are 35±4.3, 36±5.76 and 34±5.2 in the control group X, Group XM_1 and Group XM_2 respectively. The intergroup comparison is insignificant (p>0.05).

Interaction of intrathecal midazolam with non opiod GABA receptor complex in dorsal horn have been attributed to anti-nociceptive effect [10-12]. There were no significant changes in hemodynamic parameters in any of the 3 groups. Hypotension is a normalsequelae of centro-neuraxial blockade and it is quite clear that addition of midazolam has not increased the severity of hypotension. Majority of workers who evaluated the hemodynamic effects of epidural/intrathecal midazolam have found it safe [4,13].

Conclusion

From this study it can be concluded that both of intrathecal midazolam 1 mg and 2 mg are effective in increasing the analgesic effects of spinal blockade with xylocaine. Both the doses were able to significantly prolong the time to first pain medication and it was found to be better with increasing dose. Addition of midazolam with xylocaine intrathecally did not have any deleterious effects on the hemodynamic stability. No side effects attributed to midazolam were identified. Thus intrathecal midazolam at these dosages appears safe and has clinically detectable analgesic properties.

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water-soluble benzodiazepine [2]. It is also the first benzodiazepine that was produced primarily for use in anaesthesia.

Midazolam has marked analgesic properties with minimal adverse effect. It can be used either epidurally or intrathecally [3]. Hence, it was planned to do a comparative evaluation of inrathecal preservative free midazolam and 5% lignocaine in patients undergoing lower segment caesarean section for its analgesic properties.

Material and Methods

The study was conducted at tertiary care health institute of northern India. Patients between age groups of 20-35 years who underwent lower section cesarean section were divided into three groups of 30 each to receive either 1.2 ml of 5% heavy Xylocaine Hcl for group X, one mg of midazolam in 0.2 ml along with 1.2 ml of 5% heavy Xylocaine Hcl for group XM_1 and 2 mg of midazolam in 0.4 ml along with 1.2 ml of 5% heavy XylocaineHcl for group XM_2. All patients received an uniform premedication of injection Glycopyrrolate bromide 0.2 mg I.M. Injection Ondeansetron 4 mg I/V, injection Metoclopromide 10 mg I/V were given 30 minutes prior to operative procedure upon arrival into the operation theater. Ringer Lactate solution 500 ml was infused as a preload, followed by dextrose 5%. Under all aseptic conditions lumber puncture was performed at l2-L3 space and following drugs were injected.

Group X: 1.2 ml of 5% heavy Xylocaine Hcl

Group XM_1: 1 mg of midazolam in 0.2 ml along with 1.2 ml of 5% heavy Xylocaine Hcl

Group XM_2: 2 mg of midazolam in 0.4 ml along with 1.2 ml of 5% heavy Xylocaine Hcl.

The onset, intensity and duration of analgesia and motor loss, sedationscore, time of first pain medication, duration of surgery were recorded. Changes in pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate were recorded every minute till 5 minutes, then every 5 minutes till 15 minutes, then every 10 minutes until completion of surgery.

Measurement of analgesia

Analgesia was assessed by pinprick method. Onset time was taken as time from injection of drug into subarachnoid space and complete sensory loss. From this point to the time when sensation recorded to segments as noted as duration of Analgesia.

Measurement of motor loss

Motor loss was assessed by straight leg raising test. Time interval between injection of drug into subarachnoid space to patient's inability to lift the leg was taken as onset time. From this point to the time when patient was able to lift leg was recorded as duration of motor loss.

Time to first medication

This was the time taken from the onset of analgesia to the time at first pain medication. Assessment of Pain was done by patients themselves and for this assessment visual analogue scale (VAS) was used (Pilowsky and Bond 1956). During the pre-operative interview subjects were familiarized with the recording of scale. VAS rating was done as follows; 0 as No pain, 1-25 as mild pain, 26-50 as moderate pain, 51-75 as severe pain and 76-100 as very severe pain.

All the recorded variables were recorded in predesigned proforma. The variables were checked for normal distribution. The continuous variables were presented as mean±SD. The continuous variable related to time of sensory and motor blockade and the post operative pain relief were analysed using Annova test. p value <0.05 was considered as statistically significant.

Results

There were total of 90 patients involved in the present study with 30 patients in each group. All the three groups were demographically comparable with respect to age, sex and type of surgery performed. In all three groups there was statically insignificant alteration in pulse rate, systolic and diastolic blood pressure and respiratory rate.

Sensory and motor block

All the ninety patients had intense grade three analgesia after the intrathecal administration of drugs in Group X, 10 patients each (33%) had analgesia upto T7-T8 and T10. In group XM_1, 17 patients (56.66%) had highest level upto T7, where as in Group XM_2 19 patients (63.33%) had level upto T6.

There was no significant difference in onset time intensity and duration of sensory and motor block, central side effect in intergroup statistical comparison (Table 1). The time of first pain medication was significantly delayed in group XM_1 & XM_2 as compared to X ($p<0.001$) (Table 2)

Original Research Article

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Intrathecal Midazolam for Post Operative Pain Relief in Lower Segment Caesarean Section

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Abstract

Background: Postoperative pain relief is one of the important component which needs to be managed in patients undergoing lower segment cesarean section. Midazolam is a drug which can be used for postoperative pain relief as an adjunct to anaesthetic medication. *Methods:* The study was conducted at tertiary care health institute. Total of 90 patients, 30 patients in each group were included in the study. Each group was evaluated for onset, intensity and duration of sensory and motor block, central side effects, time to first pain medication. Visual analog scale was used to assess the postoperative pain. *Result:* Time to first pain medication was significantly prolonged in group XM_1 (n=30 with 2 mg midazolam) as compared to group X (n=30, 5% xylocaine hydrochloride). Nevertheless VAS at first pain medication was comparable in all the three groups. The side effects were no different in three groups. *Conclusion:* Addition of intrathecal midazolam at these dosages appears safe and has clinically proven analgesic properties with no major side effects.

Keywords: Intrathecal Midazolam; Post-Operative; Pain Relief; Xylocaine.

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Introduction

Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage or described in term of such damage. The distress and pain which a patient often experiences in immediate post-operative period is beyond description. Post-operative pain relief can improve functionality, reduce physiological and emotional morbidity and improve quality of life of the patients. As an anaesthetist it is our duty as well as priviledge to use all legitimate means to bring down the physical sufferings of patient in terms of pain not only during operation itself but also during post-operative period. Various modalities available for pain relief include intra muscular injection of strong analgesics, nerve block using local anaesthetic, intrathecal injection of certain drugs like opiods, ketamine, benzodiazepine either via subarachnoid or epidural route. They have advantages, as they reduce the dose of local anaesthetic medications; provide long lasting post-operative analgesia with reduced incidence of central nervous system depression, motor effects or hypotension [1]. Midazolam, synthesized by Walsar and colleagues in 1976, was the first clinically used

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Journal of Orthopedic Education	Triannual	5500	5000	430	391
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Comparison of side effects-

In group A, side effects are seen in 5 out of 30 patients. In group B, side effects are seen in 5 out of 30 patients p value is 1 and the difference is statistically not significant. This finding correlated well with the study performed by Conceicao et al., (1998) [6].

Conclusion

Caudal block with 0.2% Ropivacaine resulted in equal duration of analgesia with less duration of motor block as compared with 0.25% caudal Bupivacaine, without an increase in incidence of side effects when administered pre-operatively in a volume of 0.5 ml/kg to children undergoing lower abdominal and urogenital surgeries.

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Discussion

Post-operative pain is an acute pain, which starts with surgical trauma and usually ends with tissue healing. Post-operative analgesia has been neglected for a long time whereas post-operative pain has been considered an inevitable cost of operations. Post-operative pain, apart from causing discomfort and distress, has got deleterious effects on body mechanisms.

The caudal block is most accepted method of analgesia in children undergoing inguino-genital operations, used for providing both surgical and postoperative analgesia. Caudal epidural block, advocated by Kay B (1974) [5] using 0.5% bupivacaine with 1 : 200000 Adrenaline at dose rate of 0.5 ml/year of age is an effective and simple method. They proposed that the identification of the landmarks of the blocks i.e. sacrococcygeal hiatus is extremely easy in children and block application is rapid and easy with minimal failure. It requires lateral or prone positioning. This block has produced satisfactory operative anaesthesia and post-operative analgesia.

Trend of changes in the pulse rate-

In this study group the mean pulse rate in group A is 107.77±13.942 /min, in group Bis 112.67±16.647/min. the pulse rate remained stable throughout intraoperative period in both the groups. In post-operative period pulse rate remained stable up to 2 hours in both groups. There is slight increase in pulse rate seen after 3 hours post operative in group A while in group B it is stable. This time correlate with the time when mean pain score in group A is more than that in group B, leading to increase in the pulse rate and group B did not have pain at this time leading to stable pulse rate. This finding correlated well with the study performed by Conceicao et al., (1998) [6]. Similarly in the study conducted by Rosemary Hickey et al (1991) [7] did not observe at significant variation in the mean pulse rate and systolic blood pressure between 0.5% ropivacaine and 0.5% bupivacaine at different time intervals.

Trend of changes in the blood pressure-

In this study mean preoperative blood pressure both systolic and diastolic is comparable and the difference is not statistically significant. Blood pressure remained stable and comparable in both the groups throughout the intraoperative period .But in the postoperative period the BP showed slight increase in group A with statistically significant difference. Similarly as the patient had tachycardia they also showed increase in the blood pressure due to pain. This finding correlated well with the study performed by Conceicao et al., (1998) [6]. Similarly in the study conducted by Rosemary Hickey et al. (1991)[7] did not observe at significant variation in the mean systolic blood pressure between 0.5% ropivacaine and 0.5% bupivacaine at different time intervals.

Trend of changes in pain score-

In this study mean pain score in both groups are more or less similar up to 2 hours post operative. The difference is statistically not significant. After this in 3rd & 4th post operative period mean pain score in group A is 2.670.479 and 3.170.379, while in group B is 2.130.346 and 2.80.551 respectively. The difference is statistically significant. In 5th post operative hour, most of the patients in both groups required rescue analgesia. This finding correlated well with the study performed by Conceicao et al., (1998) [6].

Comparison of duration of analgesia-

The duration of adequate post-operative analgesia or pain free period was taken as time from caudal analgesic till the pain score ≥ 4 was observed at which time rescue analgesic was given. In group A the mean duration of analgesia is 344.5 ±29.37 min while that in group B is 346.3±10.66 min. (paired) two tailed p value 0.749 which is statistically not significant. The mean duration of post-operative pain relief (or pair free period) between the two groups is not significant. This finding correlated well with the study performed by Conceicao et al., (1998) [6]. Studied done by Hickey R, Candido (1990) [7], Casati A, Fanelli G (1999) [8] also showed duration of analgesia with ropivacaine was 11-14 hrs while with bupivacaine it was 10-12 hrs which was not statistically significant.

Comparison of duration of motor block-

Mean duration of motor block in group A is 176.6 ±21.02 min and in group B is 103.8±11.79 min with P value of 0.000 which is statistically significant. This finding correlated well with the study performed by Conceicao et al., (1998) [6]. Similarly in the study conducted by Surendra Raikwar et al., Onset of sensory & motor blockade was 12.9±2.8 minutes and 13.2±1.99 minutes in Ropivacaine and for bupivacaine it was 15.9±2.8 minutes and 20.2± 3.22 minutes which was found to be significant for group R ($p<0.05$) [9].

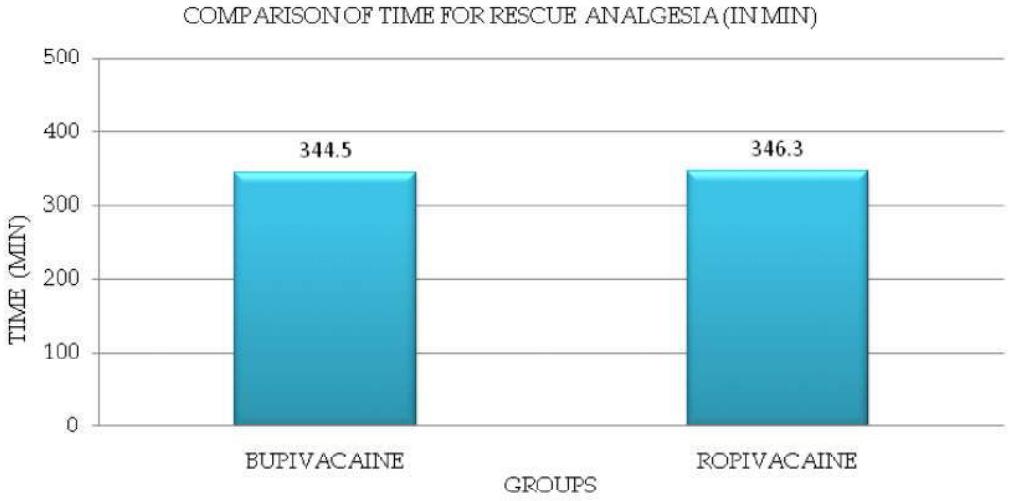
Mean time for rescue analgesia between two groups is statistically not significant (Table 5).

Mean duration of motor block in group A is 176.6 ±21.02 min and in group B is 103.8±11.79 min with p value of 0.000 which is statistically significant.

In group A, side effects are seen in 5 out of 30 patients (Flushing =2, Nausea vomiting= 3) In group B, side effects are seen in 5 out of 30 patients (Flushing = 3, Nausea vomiting= 2). p value is 1 and the difference is statistically not significant (Table 6).

Table 5: Comparison of Time for Rescue Analgesia

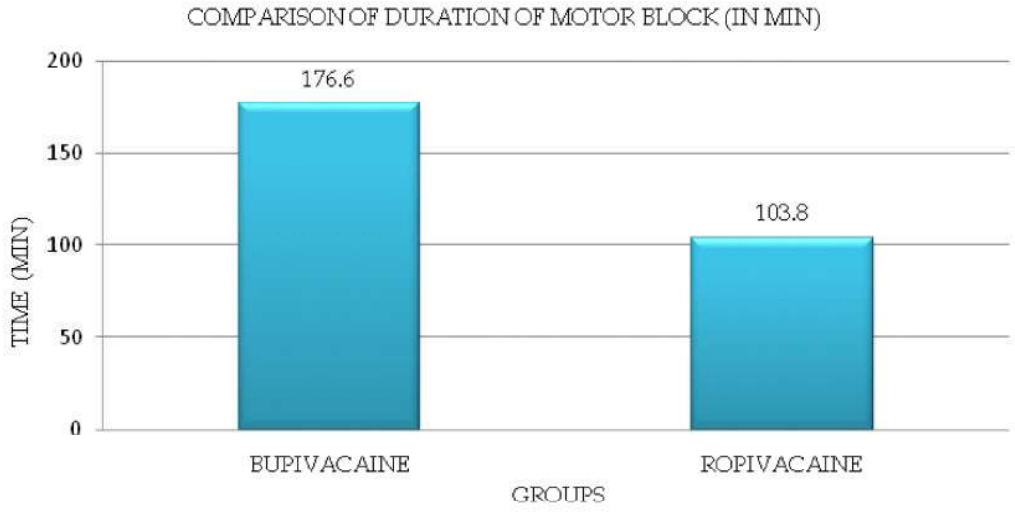
	Group	N	Mean	Std. Deviation	Std. Error Mean	P value	Significance
DOA	Bupivacaine A	30	344.5	29.37	5.36	0.749	Not Significant
	Ropivacaine B	30	346.3	10.66	1.94		



Graph 5:

Table 6: Comparison of Duration of Motor Block

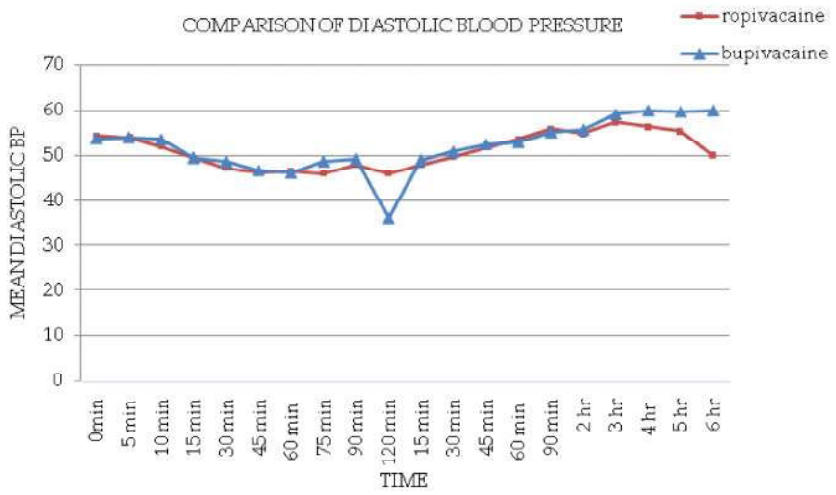
	Group	N	Mean	Std. Deviation	Std. Error Mean	P value	Significance
DOMB	Bupivacaine A	30	176.6	21.02	3.83	0.000	Significant
	Ropivacaine B	30	103.8	11.79	2.15		



Graph 5:

The diastolic blood pressure remained stable and comparable in both the groups throughout the intra operative period. In post operative period, diastolic blood pressure remained stable up to 3 hours in both group A and group B. There is slight increase in diastolic blood pressure seen after 4 hours post operative in group A, while in group B it is stable (Table 3).

Mean pain score in both groups are more or less same up to 2 hours, and the difference is statistically not significant. After this, in 3rd and 4th post operative period mean pain score in group A ismore than mean pain score in group B, and the difference is statistically significant. In 5 thpost operative hour, most of the patients in both groups required rescue analgesia (Table 4).



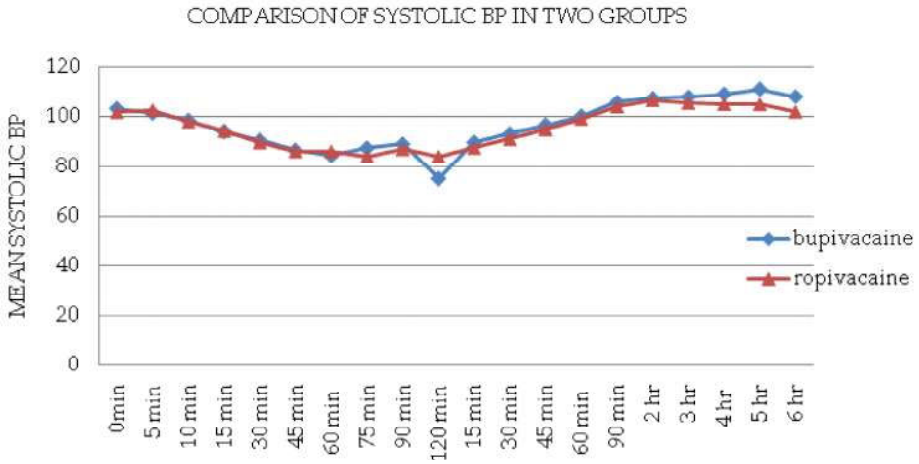
Graph 3:

Table 4: Comparision of Changes in Pain Score

Mean		Bupivacaine A		Ropivacaine B		P value	Significance
		Std. Deviation	Mean	Std. Deviation	Mean		
Post-op	15 min	0	0	0.03	0.183	0.321	Not Significant
	30 min	0.2	0.407	0.17	0.461	0.768	Not Significant
	45 min	0.93	0.254	1.03	0.32	0.185	Not Significant
	60 min	1.13	0.346	1.17	0.379	0.723	Not Significant
	90 min	1.73	0.45	1.63	0.49	0.414	Not Significant
	2 hour	2.07	0.254	2.1	0.305	0.647	Not Significant
	3 hour	2.67	0.479	2.13	0.346	0	Significant
	4 hour	3.17	0.379	2.8	0.551	0.004	Significant
	5 hour	3.96	0.2	3.96	0.189	0.936	Not Significant

Graph 4:

Post-op	15 min	89.53	6.383	87.53	7.838	0.283	Not Significant
	30 min	92.87	5.649	91	7.423	0.278	Not Significant
	45 min	96.41	5.11	95.07	6.028	0.359	Not Significant
	60 min	100.07	4.441	99.13	4.918	0.444	Not Significant
	90 min	105.73	3.269	104.2	3.295	0.076	Not Significant
	2 hour	107.33	2.591	106.73	2.377	0.354	Not Significant
	3 hour	107.93	3.503	105.67	5.228	0.053	Significant
	4 hour	109.13	5.002	105.2	4.221	0.002	Significant
	5 hour	111.12	4.729	105.14	3.979	0.001	Significant



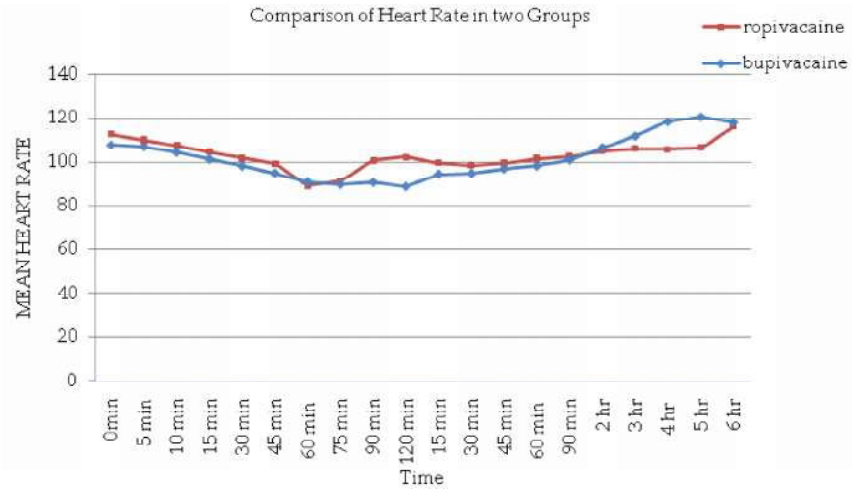
Graph 2:

Table 3: Comparison of Changes in the Diastolic B.P.

Mean		Bupivacaine A		Ropivacaine B		P value	Significance
		Std. Deviation	Mean	Std. Deviation	Mean		
Pre-op	0 min	53.8	4.881	54.4	6.134	0.677	Not Significant
Intra-op	5 min	54.07	3.463	54.07	5.078	1	Not Significant
	10 min	53.6	4.994	52.07	4.712	0.226	Not Significant
	15 min	49.53	5.164	49.4	5.308	0.922	Not Significant
	30 min	48.6	6.871	47.2	5.671	0.393	Not Significant
	45 min	46.69	6.217	46.2	6.088	0.761	Not Significant
	60 min	46.12	4.029	46.63	5.965	0.775	Not Significant
	75 min	48.75	5.849	45	5.774	0.318	Not Significant
	90 min	49.2	9.121	48	2.828	0.869	Not Significant
	120 min	36	5.657	46	2.57	0.386	Not Significant
Post-op	15 min	49.07	5.552	47.93	6.528	0.472	Not Significant
	30 min	50.87	5.77	49.87	6.516	0.532	Not Significant
	45 min	52.53	4.953	51.87	6.642	0.661	Not Significant
	60 min	53	5.401	53.6	4.082	0.629	Not Significant
	90 min	55.33	4.678	55.87	5.198	0.678	Not Significant
	2 hour	55.87	4.297	54.93	5.959	0.489	Not Significant
	3 hour	59.2	4.597	57.47	4.783	0.158	Not Significant
	4 hour	60.07	6.443	56.47	5.244	0.021	Significant
	5 hour	59.84	6.656	55.36	4.961	0.007	Significant

Table 1: Comparison of Changes in the Pulse Rate in two Groups

Mean		Bupivacaine A		Ropivacaine B		P value	Significance
		Std. Deviation	Mean	Std. Deviation	Mean		
Pre-op	0 min	107.77	13.942	112.67	16.647	0.221	Not significant
Intra-op	5 min	106.93	13.196	109.77	16.644	0.468	Not significant
	10 min	104.33	12.704	107.23	15.456	0.43	Not significant
	15 min	101.27	12.889	104.47	15.793	0.393	Not significant
	30 min	98.07	14.263	101.57	15.776	0.371	Not significant
	45 min	94.76	13.185	99.17	16	0.254	Not significant
	60 min	90.65	12	88.88	11.057	0.663	Not significant
	75 min	89.63	10.849	90.75	11.354	0.871	Not significant
	90 min	90.4	12.522	100.5	2.121	0.332	Not significant
	120 min	88.5	14.849	102	2.3	0.593	Not significant
Post-op	15 min	94.27	11.753	99.2	15.314	0.167	Not significant
	30 min	94.67	10.466	98.23	13.733	0.263	Not significant
	45 min	96.83	9.502	99.37	14.308	0.422	Not significant
	60 min	98	8.781	101.27	13.235	0.265	Not significant
	90 min	100.97	7.289	102.4	13.014	0.601	Not significant
	2 hour	106.5	7.291	104.87	13.994	0.573	Not significant
	3 hour	111.83	6.783	105.93	14.125	0.044	Significant
	4 hour	118.4	7.546	105.6	14.265	0.01	Significant
	5 hour	120.68	8.41	106.32	13.94	0.01	Significant



Graph 1:

Table 2: Comparison of Changes in the Systolic B.P.

Mean		Bupivacaine A		Ropivacaine B		P value	Significance
		Std. Deviation	Mean	Std. Deviation	Mean		
Pre-op	0 min	103.13	6.532	101.87	6.033	0.438	Not Significant
Intra-op	5 min	101.2	5.448	102.73	6.528	0.327	Not Significant
	10 min	98.33	6.83	97.8	7.034	0.767	Not Significant
	15 min	93.87	8.565	94.33	7.862	0.827	Not Significant
	30 min	90.33	7.915	89.87	8.959	0.831	Not Significant
	45 min	86.48	7.609	86.27	9.032	0.921	Not Significant
	60 min	84.35	6.901	86.13	8.747	0.522	Not Significant
	75 min	87.25	9.794	84	4.899	0.552	Not Significant
	90 min	88.8	13.084	87	4.243	0.863	Not Significant
	120 min	75	4.243	84	.4.63	0.333	Not Significant

All the parents were informed regarding the procedures of anaesthesia and surgery and a written consent of the parents was obtained.

The children were kept nil by mouth for atleast 4 hours before surgery and mothers were informed to give glucose water in the morning 4 hours before the scheduled time of surgery. Oral Midazolam 0.5 mg/kg 30 minutes before scheduled time of surgery was given.

After taking patient on operating table, the standard intra operative monitors i.e. ECG, NIBP, pulse oximeter & temperature probe were applied. Intravenous cannulation was done with 22G or 24G cannula and crystalloid (ringer lactate)infusion was started according to Holiday Segar formula.

Preoxygenation with 100% oxygen by mask was done for 3 minutes. Premedication was done with iv inj. Glycopyrrolate (0.004 mg/kg), inj. Ondensetron (0.08 mg/kg) excluding opioid analgesics. Anaesthesia was induced with injpropofol (2 mg/kg) iv & inj atracurium (0.5 mg/kg) iv was given after checking mask ventilation. Endo tracheal intubation was performed after 3 minutes. Anaesthesia was maintained with O_2 + N_2O + isoflurane through Jackson-Rees paediatric circuit with controlled ventilation.

Then the child was placed in the lateral position with the hips and knees flexed and caudal block was performed. The sacral region was prepared with betadine and spirit solution and following identification of sacral cornua, a 23G needle was inserted into the skin overlying the sacral hiatus. The epidural space was identified by the loss of resistance when the needle pierced the sacrococcygeal ligament. The needle was made parallel to the back and inserted into the canal 2-3 mm more. After the negative aspiration for blood or CSF, the drug was injected.

Group A – 0.5 ml/kg of 0.25% Bupivacaine

Group B – 0.5 ml/kg of 0.2% Ropivacaine

Continuous ECG, B.P, heart rate, pulseoximetric measurements were recorded. After the block (any of the two), patients were placed in supine position and Surgery was carried out. anaesthesia was maintained with oxygen (40%), nitrous oxide (60%), Isoflurane (1-1.5%) and top ups of muscle relaxant. Heart rate (ECG), NIBP & oxygen saturation (SpO_2) was monitored intraoperatively for every 5 mins for first 15 minutes & thereafter every 15 mins till the end of surgery. At the end of surgery, residual neuromuscular blockade was reversed with iv inj. Neostigmine (0.05 mg/kg) & Glycopyrrolate (0.008 mg /kg) & Thorough oropharyngeal and endotracheal suction was done and patient was extubated after return of reflexes.

Post operatively Heart rate, NIBP & oxygen saturation (SpO_2), pain score & motor blockade was monitored at 15 min, 30 min, 60 min, 90 min, 120 min, 3 hr, 4 hr, 5 hr, 6 hr after surgery. Pain was assessed by mCHEOPS score. Inj paracetamol 20 mg/kg wasgiven iv when mCHEOPS score was greater than 4. The time from caudal block to first post op rescue analgesic administration was the end point of study. Finally assessment of the duration of effective analgesia was done by comparing time from caudal block to administration of first analgesic. Degree of motor blockade was assessed by motor power scale. Other adverse effects like nausea, vomiting, facial flushing, fever were noted. Both groups were comparable in respect to mean age, sex, weight and duration of surgery.

Results

Both groups were comparable in respect to mean age, sex, weight and duration of surgery. The mean duration of surgery in group Ais 58±21.51 min. and of group (B) is 53.33±16.78 min. The difference is not statistically significant. Mean total duration of surgery is more or less same in both the groups.

In this study group the mean pulse rate in group A is 107.77±13.942 /min, in group B is 112.67±16.647/min in preoperative period, this is comparable. The difference is not statistically significant. The pulse rate remained stable throughout intra operative period in both the groups. In post operative period, pulse rate remained stable up to 2 hours in both group A and group B. There is slight increase in pulse rate seen after 3 hours post operativein group A, while in group B it is stable (Table 1).

In this the mean preoperative systolic blood pressureis 103.13±6.532 mm of Hg ingroup A and in group B is 101.87±6.033 mm of Hg which is comparable and the difference is not statistically significant. The systolic blood pressure remained stable and comparable in both the groups throughout the intra operative period. In post operative period, systolic blood pressure remained stable up to 2 hours in both group A and group B. There is slight increase in systolic blood pressure seen after 3 hours post operative in group A, while in group B it is stable (Table 2).

In this the mean preoperative diastolic blood pressure is 53.8±4.881 mm of Hg ingroup A and in group B is 54.4±6.134 mm of Hg which is comparable and the difference is not statistically significant.

tolerate the discomfort well, they don't respond to the pain as adult do. Therefore paediatric pain management is challenging and one of the frontiers of modern anaesthesiology.

The post-operative pain has equal importance as that of operative analgesia, Relief of post-operative pain is a challenge for all anaesthesiologists. Expressions of gratitude from patients, free of pain can contribute to feelings of self-esteem and job satisfaction.

In the last 15 years, the use of innovative techniques for the management pain, the awareness of severe complications connected with insufficient pain relief, the neurohormonalsequelae connected with pain, created new philosophy due to which at present there is no reason why neonates, infants and children should be denied of adequate analgesia.

There are many reasons for surgical encounter of the little-angels in the early childhood, lower abdominal surgeries being the most common. They are associated with considerable post operative pain which results in restlessness, agitation, bleeding and psychological stress in children. Insufficient pain relief in early post-operative period also leads to delay in full recovery, prolonged hospital stay, discouraged ambulation, behavioural and psychological problems and parental agony. Caudal epidural block being prescribed by many as the "Wonder Technique" for analgesia has a definitive place in the post-operative pain relief protocols in many hospitals. Caudal epidural block is the most commonly used regional technique for post-operative analgesia in children.

In order to maximize post-operative analgesia, a number of agents been tried by epidural and spinal route. Epidural and spinal opioids have been used but the associated major side effects like sedation; itching, urinary retention, nausea, and vomiting, respiratory depression have limited widespread use. Ropivacaine which is newer and long-acting amide local anaesthetic with a potentially improved safety profile when compared to bupivacaine [1,2]. Ropivacaine being less lipophilic, it is less likely to penetrate in large myelinated motor fibres as compared to bupivacaine, resulting in a relatively earlier recovery from motor blockade without compromising duration of sensory blockade. This property of ropivacaine is helpful in earlier diagnosis of nerve injury which can occur during reduction and fixation of upper limb fractures. Ropivacaine has selective action on the pain-transmitting Aδ and C nerves rather than Aβ fibres, which are involved in motor function. Many comparative studies between ropivacaine and bupivacaine proved that ropivacaine produces less cardiac as well as central nervous system toxic effects, less motor block and a similar duration of action of sensory analgesia as bupivacaine [3,4].

Because of the side effects of bupivacaine which include motor weakness, cardiovascular and central nervous system toxicity, this study was conducted to compare duration of analgesia, motor block, incidence of side effects with single shot caudal block with either 0.2% Ropivacaine or 0.25% Bupivacaine.

Aims and Objectives

1. To compare quality and duration of intra and post operative analgesia and need of rescue analgesia
2. To compare quality and duration of motor block
3. As an adjunct to general anaesthesia
4. To compare margin of safety of ropivacaine over Bupivacaine.

Material and Methods

The present randomized prospective study titled "To study and compare efficacy of Ropivacaine and Bupivacaine for caudal analgesia in paediatric patients." was carried out; after obtaining the local ethical committee approval. 60 patients of either sex requiring GA with Caudal block for lower abdominal surgeries and genitourinary surgeries were selected after fulfilling following inclusion and exclusion criteria. Patient of ASA class I between 1 year to 10 years of age Patient of both sexes undergoing only elective lower abdominal surgery, genitourinary surgeries were included in the study.

Patients with neurological diseases, bleeding disorders, local infection at the site and patients with obvious skeletal deformities were excluded from the study and patients with upper respiratory tract infections, cardiorespiratory diseases, systemic Problems, meningocele and myelocelewere excluded.

Each patient was examined and interviewed (parents also) on the evening prior to operation. Detailed history about previous illness and treatment was elicited. Thorough physical examination was carried out and patients weight was recorded. Investigations like haemoglobin estimation, urine analysis for albumin and sugar, TLC and DLC were done.

Original Research Article

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To Study and Compare Efficacy of Ropivacaine and Bupivacaine for Caudal Analgesia in Paediatric Patients

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Abstract

Aims and objectives: The aim of the study was to compare quality and duration of intra and post operative analgesia and need of rescue analgesia of 0.5 ml/kg of 0.25% Bupivacaine. and 0.5 ml/kg of 0.2% Ropivacaine. *Methodology:* We conducted a prospective, randomized, double blind study, in which 60 paediatric patients undergoing lower abdominal and genitourinary surgeries. Group A received 0.5 ml/kg of 0.25% Bupivacaine and Group B received 0.5 ml/kg of 0.2% Ropivacaine. Quality and duration of motor block, Adjunct to general anaesthesia, Margin of safety of ropivacaine over Bupivacaine was assessed. *Results:* Both the drugs provided post-operative analgesiaMean duration of post-operative analgesia is 344.5±29.37 min in group A & that In group B is 346.3±10.66 min (paired) two tailed p value is 0.749 which is comparable & statistically not significant. Mean duration of motor block in group A is 176.6±21.02 min and in group B was 103.8±11.79 min with P value of 0.0001 which is statistically significant. The incidence of the side effect between the two groups is not statistically significant. *Conclusion:* Caudal block with 0.2% Ropivacaine resulted in equal duration of analgesia with less duration of motor block as compared with 0.25% caudal Bupivacaine, without an increase in incidence of side effects when administered pre-operatively in a volume of 0.5 ml/kg to children undergoing lower abdominal and urogenital surgeries.

Keywords: Ropivacaine; Bupivacaine; Abdominal and urogenital surgeries.

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Introduction

Pain is by far one of the most common and distressing effects of disease and all medical persons regard its relief as one of their main duties. An acute pain service must act as a research vehicle while anaesthesiologists remain crucial contributors in the fascinating field of pain management. If pain is agony, relieving pain is ecstasy. "Failure to relieve pain is morally and ethically unacceptable". Adequate pain relief is considered as basic human right. Whether it is by drug, nerve injection, surgery or any other means, every patient want desperately to be relieved by pain. The history of pain management in children is rather described as under diagnosis, misinterpretated. It was misbelieved that children do not suffer from the pain they don't feel it, they

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by the supraglottic airway devices, controlled ventilation may not be always possible and there is a risk of pulmonary aspiration of regurgitant matter. Aspiration requires regurgitant fluid to reach the laryngeal inlet and it depends on the seal the SAD makes with oesophagus (oesophageal seal) combined with seal with pharynx (pharyngeal seal), which will determine the likelihood of spill into the larynx [14].

In our study we measured OLP in cm of H_2O at 1 min, 15 min and 30 min time interval in both groups LMA-S and LMA-P it was 25.27±1.20, 22.83±1.34, 21.17±0.95 and 27.50±1.28 25.67±1.58, 23.23±1.13 respectively it is seen that all time intervals group LMA-P had high OLP compared to the group LMA-S ($p<0.05$).

Similar result was found in study done by Balena JM et al. [12] where they compared LMA Proseal and LMA Supreme among 120 adult patients. They observed mean oropharyngeal leak pressure in the LMA Proseal group was significantly higher than that in the LMA Supreme group (30.7±6.2 versus 26.2±4.1 cm H_2O; $P<0.01$). Lee et al. [15] observed The mean oropharyngeal leak pressure in the LMAS was significantly lower than in the PLMA (27.9±4.7 vs 31.7±6.3 cm H_2O, $P = 0.007$).

Hosten T et al. [11] conducted similar study in 60 adult patients they observed Oropharyngeal leak pressures were similar (LMA Proseal: 26.9±6.6 cm of H_2O; LMA Supreme: 26.1±5.2 cm of H_2O). This study showed no differences in OLP between devices, although it only included female patients with a size 4 LMA.

Verghese C et al. [16] comparing LMA-P and LMA-S in 36 patients showed no difference in the OLP. In only 22 were given muscle relaxant so this might have had an effect on OLP.

The higher OLP for the LMA-P is mainly related to the dorsal cuff and the silicone rubber double cuff design compared to the polyvinyl chloride single cuff of the LMA-S. Lower OLP observed in LMA-S may be due to the movement of the semi-rigid curved airway tube, something which doesnot seem to happen with the elastic tube of the LMA-P.

In our study no patient had serious complication, 5 patients in both the group had post Extubation cough and 2 patients in LMA-S group and 3 patients LMA-P group had blood tinged LMA after removal.

Study conducted by Balena JM et al. [12] observed sore throat in both groups 17 and 21 had in group LMA-S and LMA-P respectively and no patients suffered from any serious complication.

Hosten T et al. [11] also showed no difference between two groups in intraoperative and post operative complication rate.

There are limitations to our study. First, insertions were done in patients with normal airway (MPC grade I, II) and normotensive patients. Present results may not apply to patients with difficult airways and hypertensive patients. Second, present results are specific to the anesthetic administered and might not apply for other anesthesia regimes. there was no blinding in the data collection, which is a possible source of bias.

Thus, the results of these various studies comparing the efficacy of the LMA-S and LMA -P shows both devices are similar in terms of insertion attempts, ease of passing ryles tube and complication rate. Insertion time required to insert LMA-S is less compared to LMA-P. Intracuff pressure increased more quickly in LMA-P compared to LMA-S. Oropharngeal leak pressure was better in LMA-P group compared to LMA-S group.

Conclusion

Both LMA Supreme and LMA Proseal can be used safely and effectively in selected patients undergoing general anaesthesia. LMA supreme is easy to insert compared to LMA Proseal but LMA Proseal had better oropharyngeal seal compared to LMA Supremeinspite of increased intracuff pressure. Ease of passing ryles tube was similar in both groups, complication of usage of LMA are minimal and similar in both the devices.

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