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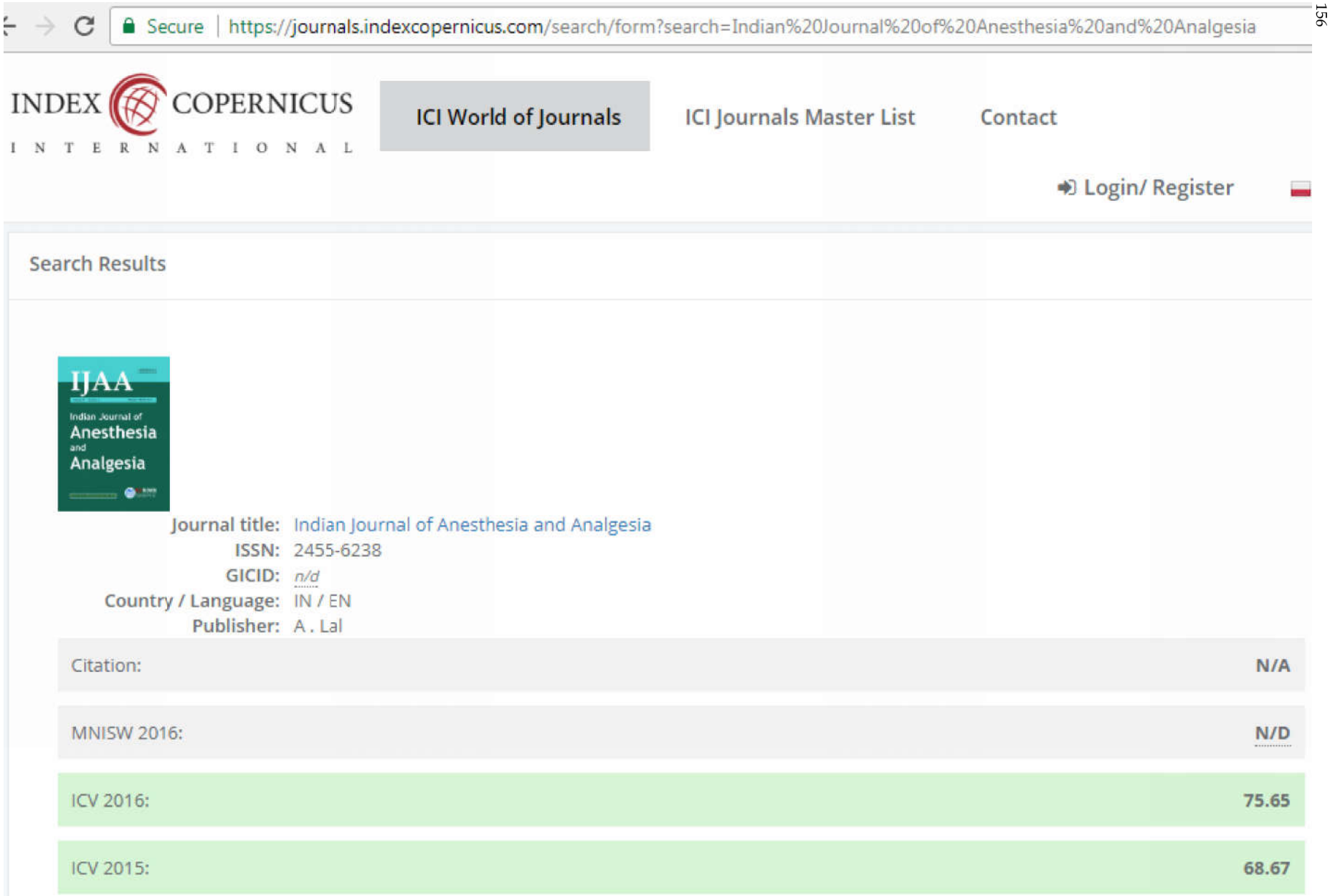
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A Comparison of Dexmedetomidine with Midazolam for Sedation in Elderly Patients Undergoing Regional Anaesthesia

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Abstract

Introduction: Chemically induced tranquillity improves acceptance of Regional Anaesthetic techniques. Intravenous sedative medications are useful for the same as positioning for surgery can be uncomfortable and spontaneous movements by an inadequately sedated patient can cause interference with the surgical procedure. To allay this problem, sedation remains as inevitable modality. *Objectives:* Comparison of the sedation properties and efficacy of Dexmedetomidine with Midazolam when used for intraoperative sedation during Regional Anaesthesia. *Methods:* Prospective, randomized study was carried out in 100 patients of ASA grade 2 & 3, above 60 years of age, weighing 40 to 90 Kg, of both genders, scheduled for elective procedures. In our study, patients were divided into 2 groups of 50 each with the help of a computer generated table of random numbers. They received either Dexmedetomidine or Midazolam intravenously during Sedation for Regional Anesthesia. Accordingly patients receiving dexmedetomidine were classified as group X1 and those receiving Midazolam as group X0. HR, MAP recorded in all patients and compared. *Result:* HR and MAP in Dexmeditomidine group is significantly low than Midazolam group. *Conclusion:* Dexmedetomidine can be considered superior than Midazolam as a sedative agent for sedation under Regional Anaesthesia in Elderly patients.

Keywords: Sedation; Midazolam; Dexmeditomidine; Regional Anaesthesia; Elderly Patients.

Introduction

The operating room is an anxiety provoking environment. The use of regional anaesthesia is often limited by the unwillingness of patients to remain awake during surgery. Though surgeries like Total Knee Replacement, Bipolar Hemiarthroplasty, Total Hip Replacement etc are done under Regional Anaesthesia; patient's anxiety, pain and mobility, and consequent sympathetic responses with hemodynamic instability remain as major problem for surgeon and anaesthetist. Patients usually have three major concerns prior to surgery/procedure - the outcome of the procedure (will I be able to walk again?), complications of the procedure, and most importantly the question "Doctor, how much of the procedure will I feel?" or "Will it hurt?" With modern sedation and careful monitoring the great majority of patients will feel comfortable during the procedure.

Chemically induced tranquillity improves acceptance of Regional Anaesthetic techniques. Intravenous sedative medications are useful for the same as positioning for surgery can be uncomfortable and spontaneous movements by an inadequately sedated patient can cause interference with the surgical procedure. To allay this problem, sedation remains as inevitable modality [1].

An optimal perioperative experience also encompasses effective pain control with minimal side effects from anaesthetic and analgesic drugs. The International Association For The Study of Pain

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(IASP) has aptly defined pain as "*An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*" [1]. As per above definition, anxiety and apprehension of procedure can also affect degree of pain perceived by patient. So it becomes necessary to achieve good anxiety relief, possibly by good sedation.

Sedation *is the reduction of irritability or agitation by administration of drugs, generally to facilitate medical or diagnostic procedure.*

The goal of conscious sedation for surgery is to enhance patient comfort, to include preservation of protective airway reflexes, to avoid painful stimuli and to help maintain hemodynamic stability during the whole surgical procedure[2]. Sedation methods include inhalation sedation (using nitrous oxide), oral sedation, and intravenous (IV) sedation. Oral sedation is generally used in paediatric cases. Inhalation sedation is also sometimes referred to as *Relative Analgesia*. And only inhalational agent used is nitrous oxide, which has its own side effects. Sedation is also used extensively in the intensive care unit so that patients who are being ventilated tolerate presence of an endotracheal tube.

An Ideal supplemental sedative should provide, effective anxiolysis, an easily controllable level of sedation, predictable depth of amnesia, a rapid and clear headed recovery, minimal intraoperative side effects, no evidence of cumulation and minimal postoperative side effects [3]. Numerous agents ranging from Ketamine to Propofol and Midazolam to Dexmedetomidine have been used as sedative adjuvants to regional anaesthesia, with their very own advantages and disadvantages over one another.

Objectives

1. Comparison of the sedation properties of Dexmedetomidine with Midazolam when used for intraoperative sedation during Regional Anaesthesia.
2. Comparison of the efficacy of Midazolam and Dexmedetomidine with respect to the cardio-respiratory parameters as following:-

a. Heart rate
b. Mean arterial pressure
c. Oxygen saturation
d. Respiratory rate

Material and Methods

This prospective, randomized study was carried out following approval from the Institutional ethics committee. Patients included in this study were informed about the procedure in their own language, and a written informed consent was taken from all of them.

100, ASA grade 2&3 patients, above 60 years of age, weighing 40 to 90 Kg, of both genders, scheduled for elective procedures, were included. They were initially assessed in the preoperative check-up room, where along with general and systemic examinations, baseline measurements of heart rate, mean arterial pressure by non-invasive sphygmomanometer, pulse oximetry, respiratory rate was made by a single observer.

Following Patients were Excluded from the Study

- Patients with history of Allergic reaction to the study drugs
- Those with significant cardiac, pulmonary, hepatic or renal dysfunction.
- Patients on Beta Blockers.
- Obese patients (>130% ideal body weight)
- Those with history of chronic use of sedative drugs
- Full stomach patients
- Epileptic patients were excluded from the study.

Sedative premedication was not given to any patient to avoid interference with results.

To facilitate blinding, two syringes of "study drug" were prepared for each patient by an anesthesiologist not associated with the study and labeled "Infusion" and "Bolus top-up." One syringe of each pair contained active sedative drug(s), the other contained placebo (saline).

Patients in the X0 Group received a 1mL "Bolus" from 10cc syringe containing 1mg/ml Midazolam and a 50 mL "Infusion" syringe containing placebo that was run via infusion pump.

Patients in the X1 Group received a 50 mL "Infusion" syringe containing Dexmedetomidine 4 μg/mL as well as a 1 mL placebo "Bolus" syringe. Sedation was initiated as follows:

X1 Group

–Initial loading dose of Dexmedetomidine (0.5 μg/kg) over 10 min followed by infusion at 0.2

μgkg^{d1} · h^{d1} from the 50-mL "Infusion" syringe. d1 mL Placebo bolus from the 10-mL "Bolus" syringe followed by 0.5 mL boluses every 30 min after 1st hour of surgery.

X0 Group: d1 mL bolus from the 10 mL "Bolus" syringe (1 mg Midazolam or 0.02mg/kg) followed by 0.5 mL boluses every 30 min after 1st hour of surgery.

–Initial loading dose plus Infusion of Placebo from 50 mL "Infusion" syringe at a corresponding rate to the X1 group.

Result and Statistics

In our study, patients were divided into 2 groups of 50 each with the help of a computer generated table of random numbers. They received either Dexmedetomidine or Midazolam intravenously during Sedation for Regional Anesthesia. Accordingly patients receiving dexmedetomidine were classified as group X1 and those receiving Midazolam as group X0.

During study, 4 patients from X0 group and 2 patients from X1 group required general anesthesia, due to prolonged duration of surgery/ intraoperative surgical complications. These cases are excluded from study, but Sample size in both groups is kept constant.

The data obtained was subjected to statistical analysis using Students Unpaired t- Test and Chi-square test to find out significant difference between the groups and Mann and Whitney non parametric test was used for qualitative data. For statistical comparison, difference was considered significant when the p- value was found to be less than 0.05.

5.82E-05= 0.0000582 (where E stands for 10 raised to)

Where quantitative data failed 'Normality test', non-parametric test has been applied

In group X1 there were 26 female and 24 male patients and in group X0 there were 29 females and 21 male patients. On statistical analysis, the association found was not significant (p value= 0.546) implying that a random distribution of patients was done as concerns the sex of the patient.

Table 1: Association among study group for SEX

St Group		SEX		Total
		Male	Female	
X1 Group	Count	24	26	50
	Percent	48.0%	52.0%	100.0%
X0 Group	Count	21	29	50
	Percent	42.0%	58.0%	100.0%
Total	Count	45	55	100
	Percent	45.0%	55.0%	100.0%
Chi-Square Tests	Value	df	P value	Association is
Pearson Chi-Square	0.364	1	0.546	Not significant
Fisher's Exact Test			0.688	Not significant

Table 2: Comparison among study group for AGE

Age	X1 Group				X0 Group				Mann Whitney Test	P Value
	Mean	Std. Dev.	Median	IQR	Mean	Std. Dev.	Median	IQR		
AGE	70.46	9.29	69.00	16.00	72.04	8.22	72.00	12.00	1.196	0.232

Note: Normality Test (Shapiro-Wilk) Failed (P < 0.050), thus P value calculated for Mann-Whitney Rank Sum Test

Table 3: Comparison among study group for Pulse rate (pre min)

Pulse rate (pre min)	X1 Group				X0 Group				Unpaired T test	P value
	Mean	Std. Dev.	Median	IQR	Mean	Std. Dev.	Median	IQR		
0 min *	86.92	13.39	83.00	24.00	87.08	13.30	89.00	20.00	0.203	0.839
30 min *	66.20	9.99	67.00	17.00	78.94	11.68	80.50	21.00	4.974	0.000
60 min *	63.52	9.34	63.00	15.00	77.26	12.15	79.50	20.00	5.315	0.000
90 min *	62.36	10.35	61.00	17.00	76.54	11.10	76.50	19.00	5.508	0.000
120 min	63.26	9.42	61.00	17.00	78.58	10.36	79.00	15.00	7.734	0.000
150 min	63.48	8.97	63.50	10.00	78.36	10.25	77.50	18.00	7.727	0.000
180 min	80.76	9.76	82.00	16.00	85.34	9.89	84.50	13.00	2.331	0.022

Note: P value calculated for Unpaired T test except at "*". Note:"*" Normality Test (Shapiro-Wilk) Failed (P < 0.050), thus P value calculated for Mann-Whitney Rank Sum Test.

Table 4: Comparison among study group for Mean Arterial Pressure (MAP in mmHg)

MAP (mmHg)	X1 Group				X0 Group				Unpaired T test	P value
	Mean	Std. Dev.	Median	IQR	Mean	Std.Dev.	Median	IQR		
0 min	93.54	7.53	92.50	11.00	92.40	6.50	92.50	9.00	0.810	0.420
30 min	75.64	6.36	74.00	11.00	84.84	8.89	84.50	11.00	5.953	0.000
60 min *	74.38	6.16	73.00	10.00	82.34	9.36	80.50	13.00	4.278	0.000
90 min *	74.56	5.90	73.00	9.00	81.70	9.46	82.00	14.00	3.840	0.000
120 min *	73.78	5.22	73.00	8.00	82.60	13.13	82.50	17.00	4.850	0.000
150 min *	74.26	10.08	76.00	9.00	84.04	9.90	85.00	13.00	4.774	0.000
180 min	89.98	8.01	90.00	11.00	91.42	6.37	91.50	6.00	0.995	0.322

Note: P value calculated for Unpaired T test except at "*". Note: "*" Normality Test (Shapiro-Wilk) Failed (P < 0.050), thus P value calculated for Mann-Whitney Rank Sum Test.

Table 5: Comparison among study group for Ramsay Sedation Score

RSS	X1 Group				X0 Group				Mann Whitney Test	P Value
	Mean	Std. Dev.	Median	IQR	Mean	Std. Dev.	Median	IQR		
0 min	1.68	0.47	2.00	1.00	1.66	0.48	2.00	1.00	0.172	0.863
30 min	3.58	0.88	4.00	1.00	3.42	0.88	4.00	1.00	1.013	0.311
60 min	3.74	0.69	4.00	1.00	3.58	0.73	4.00	1.00	0.841	0.400
90 min	3.58	0.54	4.00	1.00	3.20	1.03	3.00	1.00	1.910	0.056
120 min	3.62	0.57	4.00	1.00	3.44	0.84	4.00	1.00	0.831	0.406
150 min	3.32	0.74	3.00	1.00	3.20	0.86	3.00	1.00	1.006	0.314
180 min	2.28	0.64	2.00	1.00	2.06	1.02	2.00	2.00	1.741	0.082

As depicted in the table, the mean age in Group X1 was 70.46 and the mean age in Group X0 was 72.04 with a p value of 0.232 indicating statistically not significant.

In our study the mean baseline Pulse rate in group X1 was (86.92±13.39) bpm and in group X0 was (87.08±13.30) bpm respectively. Difference between them is not statistically significant as per the p value (0.839). At 30 min Intraoperatively, the mean Pulse rate was decreased to (66.20±9.99) bpm in group X1 and (78.94±11.68) bpm in group X0 respectively. After that the difference in the Pulse rates at all points was analyzed by the unpaired T-Test and P value was less than 0.05 throughout, indicating that there was significant difference in both groups.

The mean baseline mean arterial pressure in group X1 was (93.54±7.53) mmhg and in group X0 was (92.40±6.5) mmhg respectively. Difference between them is not statistically significant as per the p value (0.420). At 30 min intraoperatively, the MAP was (75.64±6.36) mm hg in group X1 and (84.84±8.89) mm hg in group X0 respectively. Both group has shown decrease in MAP than preop MAP, but significantly greater in X1 group than in X0 group.

The difference in the heart rates at all points was analyzed by the unpaired T-Test and P value was less than 0.05 throughout in further study, indicating that there was significant difference in both groups except last reading which shows p value around 0.322.

As sedation score is a qualitative data, we can't apply routine unpaired T test to such data. We have to apply 'Mann- Whitney' test in such case. We don't extract mean but deduce mean rank for such data. In above table we can see there is no significant difference between mean ranks of both groups though value of mean ranks is fluctuating.

As we can see, p value at all readings remained more than 0.05 which denotes that there is no significant difference between sedation achieved in Group X1and Group X0.

Discussion

Sedative-hypnotic drugs are also commonly used to make procedures more tolerable for patients by reducing anxiety and providing an appropriate degree of intraoperative sedation and amnesia. During longer surgical procedures, patients may become restless, bored, or uncomfortable when forced to remain immobile.

Therefore, sedative-hypnotic drugs, as well as non-pharmacologic approaches (e.g., music), may prove beneficial because they allow patients to rest during the operation. Patients' anxiety can be reduced by using benzodiazepines, as well as by good preoperative communication, keeping the patient warm and covered, and allowing the patient to listen to relaxing music during the procedure.

Since the approval of Midazolam by FDA in 1985, practitioners embraced the versatility provided by Midazolam. Opioids also remained as good option/ or supportive drug. The risk of losing airway control, hypoxia and hypotension with higher doses of Midazolam has also been recognized. With the recent development of highly specific α2 agonists clonidine and dexmedetomidine, there has been a renewed interest in this class of drugs for use in perioperative period. as they offer both sedation, analgesia and can provide induced hypotension with a bloodless surgical field [4].

As an ideal sedative agent, it should provide advantages of general anesthesia, viz ; immobility, and controlled hypotension. But simultaneously patient should be cooperative and arousable so that surgeon can interact with patient during surgery. Adequate sedation level must be achieved without losing airway reflexes. In our study we compared two agents for above given parameters. One of them which is classically used, Midazolam, and another is newer drug from alpha 2 agonist group, dexmedetomidine. 100 patients are divided randomly in two groups, each of 50, which received one of the above mentioned drugs and comparison done for parameters such as sedation, analgesia, and cardio respiratory parameters.

In our study the mean age of the patients was comparable between the two groups with mean age in group X1 being (70.46) and that in group X0 being (72.04). The difference was statistically not significant. The proportion of males and females was comparable between the two groups and statistically not significant (p= 0.232).

Thus with respect to demographic variables both the groups were comparable. The importance of the variation being non-significant for age, sex, weight and ASA grading is that a random distribution of patients was confirmed to and there were no confounding factors which would later interfere with the perioperative assessment.

Baseline heart rate at o min, in both X1 & X0 group were 86.92 & 87.08 respectively; the difference between them is not statistically significant (p=0.839). After 30 mins, pulse rate decreased in both groups (X1 group- 66.20 & X0 group-78.94.) It was significantly less in X1 group than X0 group with p=0.000. This trend remained constant according to graph at 60, 90, 120, 150 & 180 minutes. Pulse rate in X1 group was persistently and significantly remained lower than X0 group with p value as respectively. But at end of surgery, at 180 minutes, again there is rise in pulse rate, with (80.76 & 85.34) in group X1 & X0 respectively, approaching to pre op pulse rate.

Dr Indira kumar et al, 2012 [4] observed sixty patients undergoing ENT surgery under MAC. They were divided into two groups of 30 patients each. The patients in Group C received clonidine 2 mcg/kg IV and in Group M received Midazolam 20 mcg/kg IV over 10min. RSS, requirement of intraoperative rescue sedation and analgesic, postoperative VAS & analgesic requirement, adverse effects, recovery profile and satisfaction scores of patients and surgeon were recorded. No significant change was observed in respiratory rate and SpO2 in both the groups (p>0.05).

Results are concordant with study conducted by A. Abdellatif et al, 2012 [5] who compared dexmedetomidine and Midazolam as sedative agents in middle ear surgeries. In group D the HR values started to be lower from the baseline at 10 min from the start of sedation. This significant reduction in heart rate continued till the end of surgery and showed significant difference from those values recorded in group M that showed more stable Hemodynamics. The surgical field bleeding score was superior in group D compared to group M (p <0.001). The surgeon observed grade I surgical field in 18 patients of group D vs only in four cases in group M.

Kenan kaygusuz et al, 2008 [6] studied 40 patients, posted for shockwave lithotripsy which is randomly divided in two groups, one received dexmedetomidine and other got propofol as sedating agent which are compared for Hemodynamics, SpO2, RR and sedation level. In the dexmedetomidine and propofol groups, HR significantly decreased during sedation and recovery, compared with baseline. The Heart rate values during sedation were significantly lower than those in dexmedetomidine group.

Another important haemodynamic parameter we monitored is mean arterial pressure. Mean arterial pressure is directly related to surgical field quality and surgeons satisfaction. Baseline MAP at o min, in both X1 & X0 group were 93.54 & 92.40 respectively; the difference between them is not statistically significant. (p=0.420). After 30 mins, MAP decreased in both groups (X1 group- 75.64 & X0 group- 84.84). When compared to each other, it was significantly less in X1 group than X0 group with p=0.000. This trend remained constant according to graph at 60, 90, 120,150 & 180 mins. MAP in X1 group was persistently and significantly remained lower than X0 group with p value as low as 0.000. But at end of surgery, at 120 mins, again there is rise in MAP, with (89 & 91) in group X1 & X0 respectively, approaching to pre op MAP, though not exactly same as before.

Kamer dere et al, 2010 [7] studied 60 patient with ASA II, to compare the effects of dexmedetomidine versus Midazolam on perioperative Hemodynamics, sedation, pain, satisfaction and recovery scores. In Group D, a significant statistical decrease was found with regard to mean arterial pressure values at the onset of the study and at the 5th minute ($P<0.05$). Changes in MAP were similar between the groups throughout further study.

It can be stated from our result that Dexmedetomidine, showed much better haemodynamic control over Midazolam throughout the procedure. The lower HR and MAP observed in Dexmedetomidine group could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by dexmedetomidine [8,9].

One of the aims of our study is the comparison of effect on respiration by both study drugs. We have monitored Respiratory rate & oxygen saturation. Baseline respiratory rate in both groups are 15.40±0.86& 15.3±1.05 (in group X1 & group X0 respectively). There is no significant difference between both groups according to p value (0.858). After giving drugs, in X0 group, rate decreases and remains lower than X1 group throughout the study. When compared, significant difference is found between two groups according to p values.

Oxygen saturations at baseline in our study are 98.32±1.45 & 98.32±1.74 in group X1 & group X0 respectively. There was no significant difference found in them. ($p = 0.866$.) Values in both groups didn't show clinically significant difference at 30 min, 60 min, 150 min and at 180 min interval in further intraoperative period. P values remained consistently higher than 0.05. But at 90 min & 120 min interval oxygen saturation values in M group were significantly low than those of D group. But it is clear that those values were never low to be called as clinically significant. Active interventions were not required.

The observed lower value of SpO2 in Group X0, at 90 & 120 mins would suggest that breathing was likely low tidal volume at that time. We have seen that Ventilatory frequency found to be consistently lower in X0 group than X1 group. From above results we can conclude that, as compared to Dexmedetomidine; Midazolam shows greater depression in respiratory drive.

Hsu, Yung-Wei; Cortinez, Luis et al, 2004 [10] measured and compared respiratory responses of six healthy male volunteers during (1) a stepwise target-controlled infusion of remifentanil, (2) a stepwise target-controlled infusion of dexmedetomidine, and (3) a pseudo natural sleep session in mechanical controlled ventilation. The respiratory effects of dexmedetomidine markedly contrasted with those of remifentanil. When compared with baseline, during dexmedetomidine infusions, the respiratory rate significantly increased, and the overall apnea/ hypopnea index significantly decreased. The distribution of inspiratory time/ Ventilatory cycle time showed an increased peak. In addition, dexmedetomidine seemed to mimic some aspect of natural sleep.

Main purpose of our study drugs is optimal sedation so as to provide calm & comfortable patient with no intra-op movements. We have used Ramsay sedation scale to assess sedation level. In both groups, after giving sedative RSS score increased from baseline but when compared with each other, according to p value (0.863, 0.311, 0.400, 0.056, 0.406, 0.314 & 0.082) no statistical difference is found at any point in study. Result suggest both drugs achieve same degree of sedation with given doses

Yavuz Demiraran et al [11] investigated and compared the safety and efficacy of dexmedetomidine versus Midazolam in providing sedation for gastroscopy in total of 50 adult patients (25 patients receiving dexmedetomidine and 25 patients receiving Midazolam). Dexmedetomidine performed as effectively and safely as Midazolam when used as a sedative in upper gastroscopy; it was superior to Midazolam with regard to retching, rate of side effects and endoscopist satisfaction.

One of the highest densities of α_2 receptors has been detected in the Locus ceruleus, the predominant noradrenergic nucleus in the brain and an important modulator of vigilance. The hypnotic and sedative effects of α_2-adrenoceptor activation have been attributed to this site in the CNS. The locus ceruleus is also the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. In this region of the brain α_2-adrenergic and opioid systems have common effector mechanisms, indicating that dexmedetomidine has a supraspinal site of action [12,13].

We also studied sedation using Bispectral Index Monitoring. We used BIS scale to assess sedation and used Mann Whitney test to compare mean ranks. In both groups, after giving sedative RSS score decreased from baseline but when compared with each other, according to p value (0.255, 0.341, 0.361, 1.629, 1.771, 1.436, 0.342) no statistical difference is found at any point in study. Result suggest both drugs achieve same degree of sedation with given doses.

Jalowiecki, Przemyslaw et al, 2005 [14] evaluated the ability of dexmedetomidine to provide analgesia and sedation for outpatient colonoscopy. Sixty-four patients were randomly assigned to one of three treatment regimens. In group D, patients received dexmedetomidine, Group P received meperidine with Midazolam, and group F received fentanyl on demand. Supplemental fentanyl was required in 47% of patients receiving dexmedetomidine to achieve a satisfactory level of analgesia (*vs.* 42.8% of patients in group P and 79.2% of patients in group F). That means rescue analgesic requirement was not much reduced by dexmedetomidine.

We didn't find any complication like hypotension, apnea or bradycardia which required active intervention and discontinuation of study drug, throughout the study in any group.

Conclusion

Study shows that Intravenous Dexmedetomidine and Intravenous Midazolam provided similar sedation during Regional Anesthesia.

But considering effect of both drugs on haemodynamic and respiratory parameters, Dexmedetomidine can be considered superior than Midazolam as a sedative agent for sedation under Regional Anaesthesia in Elderly.

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The Effect of Lignocaine versus Ramosetron on Attenuation of Propofol Induced Pain

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Abstract

Background and Aims: Propofol is widely used for induction of anaesthesia, although the pain during its injection remains a concern for all anaesthesiologists. A number of techniques have been adopted to minimise propofol induced pain. Various 5 hydroxytryptamine 3 antagonists have shown to reduce propofol induced pain. Hence, this placebo controlled study was conducted to compare the efficacy of ramosetron and lignocaine in terms of attenuation of propofol induced pain during induction of anaesthesia. *Methods:* Hundred adult patients, aged 18–60 years, posted for various elective surgical procedures under general anaesthesia were randomly assigned to two groups of 50 each. Group R received 0.3 mg of ramosetron, Group L received 0.5 mg/kg of 2% lignocaine. After intravenous (IV) pre treatment of study drug, manual occlusion of venous drainage was done at mid arm with the help of an assistant for 1 min. This was followed by administration of propofol LCT after release of venous occlusion. Pain was assessed with a four point scale. Unpaired Student's *t* test and Chi square test/ Fisher's exact test were used to analyse results. *Results:* In our study out of 50 patients of each study group, 54% in lignocaine group and 60% in ramosetron group did not have pain, 34% in lignocaine group and 24% in ramosetron group had mild pain, 10% in both groups had moderate pain, 2% in lignocaine group and 6% in ramosetron group had severe pain. *Conclusion:* Pre treatment with IV ramosetron 0.3 mg is equally effective as 0.5mg/kg of 2% lignocaine in preventing propofol induced pain.

Keywords: Lignocaine; Pain; Propofol; Ramosetron.

Introduction

Propofol is a common intravenous (IV) anesthetic drug used for induction and maintenance during general anesthesia with rapid onset and short duration of action [1]. However, the incidence of pain following propofol injection varies between 28 and 90% in adults if a vein on dorsum of hand is used [2,3]. The quality of pain was described as extremely sharp, aching, or burning. It has been arranged as the seventh most important problem in current practice of clinical anesthesia by American anesthesiologists [4].

Strategies to reduce the incidence of pain on injection include adding lidocaine to propofol, cooling or warming propofol, diluting the propofol solution, injection of propofol into a large vein, and pretreatment with IV injection of lidocaine, ondansetron, metoclopramide, an opioid, magnesium, or thiopental with or without tourniquet; all have been tried with variable results [5,6,7]. It has been demonstrated that ondansetron, a specific 5-hydroxytryptamine ($5HT_3$) receptor antagonist, provided numbness when injected under the skin and is 15 times more potent than lidocaine. It has been further demonstrated that ondansetron successfully relieved pain following

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propofol injection without any adverse effects in a significant number of patients [8,9]. In our practice, ramosetron is routinely administered as premedication to prevent postoperative nausea and vomiting (PONV) in patients scheduled for general anesthesia.

Ramosetron is a serotonin $5HT_3$ receptor antagonist and demonstrates superior efficacy and longer duration to granisetron [10]. We used ramosetron pretreatment to determine its efficacy to decrease the pain of propofol injection as equivalent to lidocaine.

Materials and Methods

Institutional ethical committee approval was obtained and informed written consent was taken from all patients. Hundred adult patients belonging to American Society of Anesthesiologists (ASA) I and II class, scheduled for elective surgery under general anesthesia were randomly allocated to either of the two groups using computer generated random numbers (50 in each group), for this prospectively randomized, placebo-controlled, single-blinded study. Patients having problems in communication and history of allergic response to either propofol or $5HT_3$ antagonists, pregnant ladies were excluded from this study.

All patients were kept fasting for 6 h for solid food. On arrival to the operation theatre, a 20 G cannula was inserted into a vein on the dorsum of the patient's non dominant hand and lactated Ringer's solution was infused. The pretreatment solutions consisted of 2 ml (0.5 mg/kg, Group L, n = 50) of lidocaine (Loxicard 2%, Neon laboratories ltd, Mumbai, India), and 2 ml (0.3 mg, Group R, n = 50) of ramosetron (Nozia, Cadila Healthcare Ltd, Goa, India).

Pretreatment drug was injected after venous drainage was occluded manually at the mid-forearm for 1 min. Patient's then received one-fourth of the total calculated dose of propofol-LCT (long chain triglycerides) over 5s and 15 s later the patient was assessed for pain during injection of propofol.

The level of pain was assessed by standard questions asked to the patients about the comfort of the injection, verbal response, and behavioral signs (such as facial grimacing, arm withdrawal, or tears). Pain was graded using a four-point scale:0 = no pain, 1= mild pain (pain reported only in response to questioning without any behavioral signs), 2 = moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning), and 3 = severe pain (i.e., strong vocal response or response accompanied by facial grimacing, arm withdrawal, or tears) [11].

Later anesthesia was induced with intravenous propofol-LCT 2 mg/kg. All study drugs were kept at room temperature and used within 30 min of preparation. Tracheal intubation was facilitated with muscle relaxants and anaesthesia was maintained with inhalational drugs and analgesics.

Statistical Analysis

Based on the literature, the incidence of pain on injecting propofol is assumed as 80%, and 50% reduction in pain was considered clinically significant. Fifty patients were calculated as the minimum size for each group assuming a-value of 0.05 and a power value of 80%. All measured values are presented as mean±standard deviation and numbers (%). The results were analyzed statistically using unpaired Student's *t*-test and chi-square test/ Fisher's exact test. Results were considered statistically significant when *P*-value of <0.05 was obtained. Statistical Packages for the Social Sciences (SPSS; Windows ver. 15.0, SPSS Inc., Chicago, IL) was used for statistical analysis.

Results

There was no significant difference in the demographic characteristics among the two groups [Table 1]. No patients in any group experienced pain and discomfort during the injection of pretreatment solution. The incidence and severity of pain during IV injection of propofol in various groups is shown in Table 2.

Table 1: Demographic data

Patients characteristics	Group L (n =50)	Group R (n=50)	P value
Age	31 ± 9.8	32.1 ± 10.1	0.581
Sex (M/F)	19/31	21/29	0.683
Weight	49.7 ± 4.78	48.68 ± 3.68	0.234
ASA 1/2	29/21	31/19	0.683

L = patients who received lignocaine, R= patients who received ramosetron, ASA= American society of Anaesthesiologist, M= Male F= Female

Table 2: Comparison of pain score among the study groups

Pain score	Comparison of Pain score among the study groups				
	Lignocaine group		Ramosetron group		
	Frequency	Percentage	Frequency	Percentage	P value
No Pain (0)	27	54	30	60	0.544
Mild Pain (1)	17	34	12	24	0.271
Moderate Pain (2)	5	10	5	10	>0.99
Severe Pain (3)	1	2	3	6	0.617
Mean ± SD	0.6 ± 0.8		0.62 ± 0.9		0.906

Both ramosetron 0.3mg and lignocaine 0.5mg kg^{-1} significantly reduced pain on propofol injection but there was no statistical significance between the two groups.

Discussion

Considering the extensive use of propofol in clinical practice, the pain frequently reported on induction of anesthesia cannot be neglected. Although it is not a serious complication, efforts are assumed to reduce the severity of the pain or discomfort. Propofol belongs to the group of phenols that can irritate the skin, mucous membranes, and venous intima [9]. Injection pain associated with propofol characteristically occurs immediately or later after the drug injection with a delayed response of 10-20s [12]. The explanation for the pain includes endothelial irritation, osmolality differences, unphysiological pH, and the activation of pain mediators [13].

Many methods have been used to reduce the incidence of pain on propofol injection with variable results. Lignocaine added to or given before injection of propofol is widely employed [6]. Gajraj and Nathanson [11] studied the optimal dose of lidocaine for propofol pain and concluded that 30 mg lidocaine is the optimal dose for attenuation of propofol pain. Cooling the propofol to 4°C reduces its injection pain possibly by delaying the activation of enzyme cascade of pain mediators [14]. Injecting into a large forearm vein also reduces the pain, probably by reducing contact between drug and endothelium [6].

Metoclopramide shares the structural and physiochemical properties with lidocaine and is a weak local anesthetic. It has also shown to be as effective as lidocaine in reducing propofol injection pain [15]. Ye *et al*., [8] found in rats, that ondansetron is approximately 15 times more potent local anesthetic as lidocaine and this property probably contributes to its antiemetic action. Ondansetron had been shown to relieve pain by its multifaceted actions as a Na channel blocker, a $5HT_3$ receptor antagonist, and mu opioid agonist [8,16]. Ondansetron pretreatment may be used to reduce the incidence of pain on injection of propofol with an added advantage of prevention of PONV [9,17].

In a study by Ahmed *et al*. [18] the incidence of propofol injection pain was reduced from 60 to 15% after granisetron pretreatment. Pretreatment with granisetron/lidocaine may be effective not only in attenuating pains during IV injection of propofol, but also in preventing postoperative nausea, vomiting, and shivering [19,20]. In a study by Piper *et al*. [21] severity but not the incidence of pain on injection was significantly reduced by dolasetron (50%) compared with placebo and there was no significant difference between dolasetron and lidocaine. Ramosetron is a recently developed $5HT_3$ receptor antagonist. Lee *et al* [22] reported the incidence of pain in the groups pretreated with ramosetron 0.3 mg or combination with ramosetron and lidocaine 20 mg were 60 and 38%, respectively. These results show effective reduction in propofol injection pain. Pretreatment with ramosetron alone or with combined pretreatment of ramosetron and lidocaine also prevented pain effectively for moderate to severe pain.

In our study out of 50 patients of each study group, 54% in lignocaine group and 60% in ramosetron group did not have pain, 34% in lignocaine group and 24% in ramosetron group had mild pain, 10% in both groups had moderate pain, 2% in lignocaine group and 6% in ramosetron group had severe pain. Thus both ramosetron 0.3mg and lignocaine 0.5mg kg^{-1} significantly reduced pain on propofol injection but there was no statistical significance between the two groups.

Our study had few limitations. Occlusion at mid forearm was done manually, which will vary from person to person, this could have been overcome by using tourniquet with constant pressure. Also drug could have been injected using syringe pump instead of injecting manually.

Conclusion

We concluded that IV ramosetron when given as pretreatment is as effective as lidocaine on propofol associated pain with an added advantage of preventing PONV.

Source of Support

Nil

Conflict of Interest

None declared.

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Comparative Evaluation of Nerve Stimulation and Ultrasound Guidance for Popliteal Block: A Randomized Double Blinded Study

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Abstract

Introduction: Popliteal block is one of the rarely performed regional anaesthetic techniques because it requires great expertise in anatomical land marks and is often very technically challenging. Recent introduction of ultrasound technique for nerve blocks has gained popularity when comparing to the standard nerve stimulation technique. In this study, we have compared the success rate, duration of block procedureand complications between nerve stimulation and ultra sound guidance of popliteal block. *Methods*: 120 patients undergoing foot and ankle surgery were randomized to receive the block using either the nerve stimulation (n = 60) or the ultra sound technique (n = 60). Ropivacaine 0.25% (30 mL)was injected for both the groups. *Results*: Duration of the block procedure and block failure rate were significantly higher in nerve stimulation technique than the ultra sound technique (P value < 0.05). There were no differences in onset and duration of block between two techniques. The nerve stimulation guidance was associated with significant incidence of vascular puncture (13.3%) but ultrasound technique was safer with nil incidence of vascular puncture. *Conclusions*: Ultrasound guidance technique was better in lesser block procedure time and a good success rate (P value < 0.05) and was safer, with no incidence of vascular puncture.

Keywords: Nerve Stimulation; Popliteal Block; Ropivacaine; Ultra Sound.

Introduction

Sciatic nerve block in the popliteal fossa (Popliteal block) is one of the regional anesthetic techniques used for ankle and foot surgeries. Compared to spinal anesthesia it is safe because it is devoid of adverse effects such as hemodynamic changes, post dural puncture headache and also provides good postoperative analgesia. Despite these advantages, popliteal block is not often performed because of inadequate technical experience and a highly unpredictable success rate of the block. The most routinely used guidance for popliteal block is the nerve stimulation which can cause significant discomfort to the patient due to the electric stimulation of the nerves. The introduction of ultrasound guidance for nerve blocks has made a new mile stone in regional anaesthesia which is less discomfort to the patient. In this study we are comparing the two approaches in respect to duration of block procedure, success rate, onset and duration of block and complications.

Material and Methods

This study was performed between january 2016 to march 2017 in a 1500 bedded super-specialty teaching hospital. A total of 120 patients were involved in this single-center, double-blinded,

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parallel-group randomized clinical trial. Patients posted for elective surgery in foot or ankle, planned for regional anaesthesia were enrolled in this study. Criteria for inclusion were, American Society of Anesthesiologists status I and II, age more 18 and less than 65 years. The exclusion criteria include: patient refusal, allergy to local anesthetics, pregnancy, emergency surgery, injection site deformities, infection at the injection site, peripheral neuropathy, coagulopathies and other contraindications to peripheral nerve blockade. During the pre-anaesthetic checkup, patients were explained about the procedure and written informed consent was obtained. The anesthesiologist performing the procedure was blinded to the patient allocation until he or she was ready to commence with the block. At that point, a lot system was used to select the technique by categorizing them into either of the two groups namely N for nerve stimulation and U for ultrasound techniques and the anesthesiologist performed the block accordingly. Another anaesthesiologist who was blinded to the group allocation assessed the block progress and monitored the patient till the end of surgery. The anaesthesiologist who took care of the patient in the post-operative care unit was also blinded of this study.

Popliteal blocks were performed by qualified anesthesiologists who were trained in peripheral nerve blockade using nerve stimulation as well as ultrasound techniques. After shifting into the operating room, intravenous line was started using a 20 G cannula and the patients were put on prone position and monitors like pulse-oximeter, noninvasive blood pressure, and electro-cardiogram were connected. The injection site was prepared with povidone iodine 5% solution and draped with sterile linen. A local anesthetic solution (3mL of lidocaine, 1%) was infiltrated subcutaneously at the site of planned needle insertion. Patients were sedated with 10 - 30 microgram/kg midazolam to relieve anxiety while maintaining verbal interaction. According to group allotment, patients received their popliteal nerve blocks under one of the following two techniques.

Nerve stimulation technique:This technique was performed with patient in prone position with leg fully extended and ankle projecting slightly beyond the end of the table. The nerve stimulator was turned on, and a grounding lead was placed on the lateral aspect of the leg being blocked. The popliteal fossa was identified by the popliteal crease inferiorly, the semimembranosus and semitendinosus muscles medially and the biceps femoris muscle laterally. The needle insertion site was 7cm above the popliteal crease and 1cm lateral to the midline of the popliteal fossa triangle. After local anaesthetic infiltration 22-gauge, 90-mm insulated needle (Inmed) was inserted with the nerve stimulator (Inmed) set at 1.0mA (0.1 milliseconds) at 2Hz. The needle was inserted perpendicular to the skin and advanced from posterior to anterior until the sciatic nerve was identified by twitch response. If motor response at the ankle was elicited, the nerve stimulator intensity was reduced while maintaining this response at 0.4 mA or less. If the evoked response persists at 0.2mA, the needle was withdrawn until the response was maintained between 0.2 and 0.4 mA. If no motor response was achieved, the needle was withdrawn until the skin, redirected in 5° laterally and advanced. When the correct needle position was achieved, 30mL of 0.25% ropivacaine was injected slowly after negative aspiration for blood. The injection was stopped if there was a blood aspirate, pain or paresthesia reported during the injection and the needle was then repositioned to achieve a satisfactory response [1,2].

Ultrasonography technique: Ultrasound machine with linear transducer (8-12 MHz), sterile sleeve, and gel (in a very obese patient, a curved transducer might be needed). Patient was put in prone or oblique position with the legs slightly abducted. A small footrest may be used to relax the hamstring tendons, making transducer placement and manipulation easier. Ultrasound probe was placed in the popliteal fossa just above the popliteal crease and pulsation of the popliteal artery was identified. The tibial nerve would lie superficial and lateral to the artery. Changing the angle of the probe in different directions might help with getting the ideal view of the nerve. Once the tibial nerve was identified, the probe moved proximally with the same rotation and to identify the common peroneal nerve and the bifurcation of the sciatic nerve [3]. Once identified, a skin wheal was made immediately lateral or medial to the transducer. Once the needle tip was confirmed to be adjacent to the nerve, the syringe was gently aspirated and the local anesthetic was injected. Such injection should result in distribution of the local anesthetic within the epineural sheath, and often, separation of the tibial and common peroneal nerves. The injection was stopped if blood aspirated or if pain or paresthesia was reported; the needle was repositioned or the block abandoned.

Duration of the block procedure (from positioning of the patient till the end of the drug

injection) was noted. After the procedure, the tibial and common peroneal nerve distribution area was assessed for sensory loss every 5 minutes until complete sensory block was achieved. Block was assessed every 5 minutes; hence, the onset time was recorded in 5-minute intervals.

Sensory block was evaluated with cotton wool with spirit: full sensation (2); decreased sensation (1); and no sensation (0). Patients without complete sensory loss in both distributions within 30 minutes of the end of injection were considered failed blocks. Postoperatively, duration of block was assessed by onset of pain and recorded. The block duration was defined as the elapsed time between block completion and first demand of analgesics, as reported by the patient in the postoperative care ward [4]. Routine follow-up was performed in the post anesthesia care unit until 72 hours after the procedure.

The primary outcome was the failed block even after 30 minutes of the procedure. The following secondary outcomes were also measured:duration of block procedure, sensory block onset time, duration of analgesia and complications if any.

Statistical Analysis

Data are given as percentages for nominal data and means±SD for continuous variables. Differences in proportions of patients in nominal data among two groups (Sex) were tested using Fishers exact test or chi-square test. Differences in continuous variables (Age, weight, onset of block, duration of block) were tested using student t test. Differences were considered significant at 0.05 level.

Results

A total of 120 patients were assessed for eligibility and offered enrollment in this study. There were no significant differences in ASA status, demographics (Age, weight, sex) and in onset and duration of anaesthesia between the groups. Block failure was significant in nerve stimulation technique than that of USG ($P<0.05$) (Table 1). For the comparison of block procedure time, onset and duration of the block, a sample size of 100 patients were selected, 50 in each group who had successful block was taken. In our study the block procedure time was significantly lesser in U group than in the N group but regarding the onset and duration of analgesia there were no statistically significant difference between the two groups (Table 2). In the N group was 10% (6) of patients had vascular puncture as a complication but the U group is free of complications as far as this study is concerned.

Table 1: Demographic characteristic of the study groups (mean±SD) and success rate

Variable	Group N (n=60)	Group U (n=60)	P
Asa I	35	34	
AsaII	25	26	0.2490
Age	32±12.5	34±11.6	0.3655
Sex Male	41	40	
Sex Female	19	20	0.3412
Successful Blocks	50 (83.33%)	57 (95%)	0.0406

Table 2: Time for first demand analgesia (mean±SD) in the study groups

Variable	Group N (n=50)	Group U (n=50)	P
Duration of block procedure (min)	25±7	10±8	0.0001
Onset of block (min)	17±4	15±5	0.0295
Duration of analgesia (min)	365±45	376±50	0.2504

Discussion

Peripheral nerve block in general is safer than general anesthesia as it has lesser incidence of complications such as nausea and vomiting or cardiovascular adverse reactions. Also, it is known to reduce several side effects caused by central neuraxial anesthesia like hypotension, bradycardia, shivering, postoperative urinary retention, and post dural puncture head ache which are commonly associated to spinal anesthesia [5]. In addition, surgery could be carried out in hemodynamically unstable patients and who were on anticoagulation therapy with less risk [6]. Even with the above advantages, peripheral nerve block done by traditional anatomical land mark and paresthesia technique has an unpredictable success rate and has

its own demerits which may often limit the usefulness of the procedure. The common side effects are: direct nerve damage, hematoma and consequent ischemic nerve damage, intravenous administration of local anesthetic and infection [7]. Hajek et al. reported superficial peroneal nerve and sural nerve damage in 3 patients (1.91%) out of 157 patients who were treated with continuous popliteal block. Possible causes were exposed nerve damage, neural toxicity of the local anesthetics, direct nerve damage and ischemia, and usage of tourniquet [8]. Usage of nerve stimulation guidance reduced most of the complications but still needle skin punctures for initial localization of the nerve often may cause problems like multiple needle prick and vascular puncture as we blindly approach the nerve. Moreover pain associated with the electrical stimulus may often be very troublesome to the patients [9].

We performed the classical posterior approach for both the groups than the newer lateral approach because posterior approach is technically easy to perform as the anatomical land marks are easily identifiable [10]. An advantage of ultrasound guidance is that peripheral nerves can be identified precisely and the median number of needle skin punctures can be reduced there by reducing the block procedure time [11]. In addition the spread of the local anaesthetic can be directly visualized and the needle direction may be altered to have an adequate spread of the drug in all directions ensuing a high success rate of the block [12]. Anahi Perlas et al. demonstrated that injection through a common paraneural sheath at the site of sciatic nerve bifurcation is simple and highly effective than injecting the individual nerves and it resulted in a faster onset of sensory and motor blockade than previously reported approaches without an increase in the incidence of intraneural injection [3]. Since ultrasound guidance is a real time procedure, the course and direction of the needle and the adjacent structures can be appreciated very well and complication such as vascular puncture could be avoided [13]. Various studies were performed for block procedure time with different techniques. Dufour et al. reported that combined ultrasound and nerve stimulation guidance does not reduce block time of posterior popliteal sciatic block versus nerve stimulation alone [14]. Perlas et al. demonstrated that block procedure time was similar between ultrasound and nerve stimulator-guided blocks [15]. In our study we observed that ultrasound guidance resulted in shorter procedure times and almost no incidence of vascular puncture than that of nerve stimulator-guidance. In future, this study gives the scope for further researches in this field such as continuous block technique and use of three dimensional ultrasound technologies for nerve blocks. Limitations of the present study include the fact that, like most procedure-related studies, it is not possible to blind the anaesthesiologist to group allocation. To minimize bias, 15 different anaesthesiologists, who were unrelated to the study performed the block procedures. In addition, assessment of sensory block and documentation of study outcomes were carried out by an independent investigator blinded to group allocation whenever feasible as described. Despite these measures, performance bias may not be completely ruled out.

Conclusion

We conclude that ultrasound guidance technique was better in less block procedure time and a good success rate (P value < 0.05) and was safer, with no incidence of vascular puncture than the traditional nerve stimulation guidance for popliteal block.

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Original Research Article

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A Comparative Study to Evaluate Efficacy of Two Doses of Intrathecal Clonidine (15mcg Versus 30mcg) as an Adjuvant to Bupivacaine for Prolongation of Spinal Anaesthesia

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Abstract

Background: Clonidine, an α2-agonist, has been used intrathecally as an adjuvant to bupivacaine in spinal anaesthesia, for prolonging anaesthesia and postoperative analgesia. This study was designed to compare efficacy of two doses of intrathecal clonidine (15μg versus 30μg) for prolongation of anaesthesia, with maintainance of heamodynamic parameters, to find out lowest possible effective dose. *Methods:* Sixty patients, scheduled to undergo lower abdominal surgery, were enrolled. They were randomly divided into two groups, of 30patients in each group. Group BC_{15} received 15mg (3ml) of hyperbaric bupivacaine plus 15μg clonidine plus 0.1ml of normal saline and Group BC_{30} received 15 mg hyperbaric bupivacaine plus 30 μg (0.2ml) clonidine, thus keeping volume of injectable solution constant to 3.2 ml, in both groups. *Results:* Highest level of sensory block achieved, was recorded which was almost similar in both groups. Time taken to achieve highest level of sensory block , time to achieve two segment regression, time to achieve regression to L_1 dermatome , time to first analgesic request , time to achieve maximum Bromage scale 4, time to achieve regression back to minimum Bromage scale 1 and haemodynamic changes, showed no stastically significant difference amongst both groups (P value >0.05). *Conclusion:* Both doses of intrathecal clonidine i.e.15μg and 30μg with bupivacaine, produce equal prolongation of sensory and motor block alongwith time to first analgesic request.So, clonidine15μg intrathecally with bupivacaine is preferred over 30μg or higher dose to achieve prolongation of desired sensory and motor block alongwith postoperative analgesia with clinically insignificant haemodynamic effects.

Keywords: Intrathecal; Clonidine; Adjuvant; Postoperative Pain; Haemodynamics.

Introduction

Spinal anaesthesia is immensely popular for lower abdominal and lower extremity surgeries. However, it has some limitations. For example, it has fixed duration of action, which, sometimes falls short of and general anaesthesia has to be supplemented.

To overcome this and for post-operative analgesia, some adjuvants have been tried intrathecally along with local anaesthetics like bupivacaine, to prolong their effect e.g. midazolam [1], α-2 agonists like clonidine [2], neostigmine [3,4], fentanyl [5], ketamine. But some side effects of these adjuvants were reported e.g. opiods cause nausea, vomiting and respiratory depression. Parenteral alpha-2 agonists have also been tried for the same purpose, but since they have to be given in higher doses, they cause significant side effects in the form of hypotension and bradycardia, because of systemic actions.

So intrathecal (IT) alpha-2 agonists have been studied by different researchers in varying doses, with variable efficacy and side effects.

Thus, aim of this comparative study, was to evaluate efficacy of two doses of IT clonidine (15μg versus 30 μg) in prolongation of spinal anaesthesia with maintainance of haemodynamic parameter.

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Material and Methods

Patients

After approval by institutional ethical committee, the study was conducted at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana Distt Ambala (Haryana). A total of 60 patients undergoing elective lower abdomen surgeries, under spinal anaesthesia were enrolled for the study. It was designed in the form of a prospective, randomized and double blinded study. All patients were allocated randomly by a computer generated number, in two groups, of 30 patients in each group. GROUP BC_{15} received 15 mg (3 ml) of 0.5% hyperbaric bupivacaine plus 15 µg (0.1 ml) of clonidine,with addition of 0.1 ml of normal saline to make total 3.2 ml solution and Group BC_{30} received 15 mg (3 ml) of 0.5% of hyperbaric bupivacaine plus 30µg (0.2 ml) of clonidine. So, in both groups, the volume of solution to be injected intrathecally was kept constant i.e. 3.2 ml.

Inclusion Criteria

All patients between 18 to 60 years of age ,of either gender with ASA grade I and II, undergoing elective surgical procedures in lower abdomen , under spinal anaesthesia were considered for study. Written informed consent was obtained in all cases for inclusion in study population and undergoing surgery.

Exclusion Criteria

1. History of hypersensitivity to bupivacaine or clonidine,
2. History of taking β-blockers, α2-agonists including methyldopa,
3. Patients who will not give consent for spinal anaesthesia,
4. All contraindications to spinal anaesthesia e.g. sepsis of back, spine deformity, coagulation disorders etc and
5. Any cardiovascular disease like ischaemic heart disease, congenital heart disease, arrhythmias, bradycardia etc.

Study Procedure

All patients were given alprazolam 0.25 mg and ranitidine 150 mg orally on night prior to surgery. A fasting period of eight hours was ensured. In operation theatre, a multipara monitor was applied to patient to record electro cardiogram (ECG), oxygen saturation (SpO_2) and non- invasive blood pressure (NIBP). Intravenous line was secured with 18G cannula. Preloading was done with 12 ml/kg of ringer lactate 15-20 minutes before start of subarachnoid block. Basal blood pressure, pulse and SpO2 was recorded. Under all aseptic conditions, lumbar puncture was done in lateral decubitus position at L_{3-4} position and drug injected as per group, mentioned above. Sensory block was judged by pin prick method using short bevelled 25G needle. It was checked at regular interval of two minutes to see highest level of block. Time taken to achieve highest level was recorded. Recovery from sensory blockade was recorded for two segment regression. Further, it was recorded upto L_1 dermatomal level and duration of sensory block was considered as time from intrathecal injection to regression till L_1. Similarly, duration if motor block was considered as the time from intrathecal (IT) injection of drug to the time till regeression to Bromage scale 1. Total duration of analgesia was assessed by the timing of first rescue analgesic administered. During and after surgery, time to rescue analgesia was recorded and treated with injection diclofenac sodium 75mg intravenously, whenever VAS was >4.

Motor block was assessed at the same time intervals as for sensory block, with modified Bromage scale as under:

1. Grade1. Free movement of legs and feet.
2. Grade 2. Just able to flex knees with free movement of feet.
3. Grade 3. Unable to flex knees with free movement of feet.
4. Grade 4. Unable to move legs or feet.

Time to have maximum degree of block as per above scale and its regression to Bromage scale 1 was recorded. Haemodynamic parameters were recorded, after subarachnoid block: (a) Every 2 minutes up to 10 minutes (b) Every 5 minutes upto 30 minutes (c) Every 15 minutes upto 2 hours and (d) every 30 minutes for 5 hours after subarachnoid block.

The level of sedation was observed intraoperatively. Any episode of hypotension (i.e. 20% or more reduction of blood pressure from baseline) was recorded and treated with increments of intravenous mephenteramine 6mg and intravenous fluids. And any episode of bradycardia (i.e. heart rate of 50/minute or below this) was also recorded and treated with injection atropine in required dose.

The results were evaluated, compiled and appropriate statistical analysis was done, using unpaired Student T-test.

Outcome

The primary outcome was to compare efficacy of two doses of intrathecal clonidine (15µg versus 30µg) as an adjuvant to bupivacaine for prolonging sensory and motor block of spinal anaesthesia and post-operative analgesia. Secondary outcome was to compare side effects like hypotension, bradycardia, sedation , nausea and vomiting etc.

Results

Observations of all 60 patients enrolled in the study were included for analysis. Their age, sex, weight, height and ASA status were comparable amongst both groups (Table 1). All patient underwent Gynaecology and Obstetrical surgery. Highest level of sensory block achieved, was recorded which was almost similar in both groups. Time taken to achieve highest level of sensory block, time to achieve two segment regression, time to achieve regression to L_1 dermatome, time to first analgesic request, time to achieve maximum

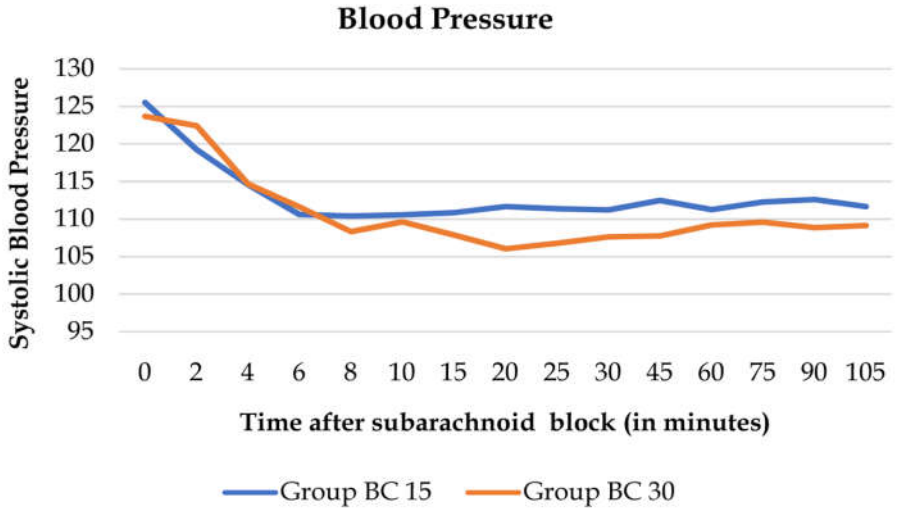

Fig. 1: Comparison of Systolic Blood Pressure of mean±standard deviation between groups BC_{15}& BC_{30}, at different time intervals after subarachnoid block

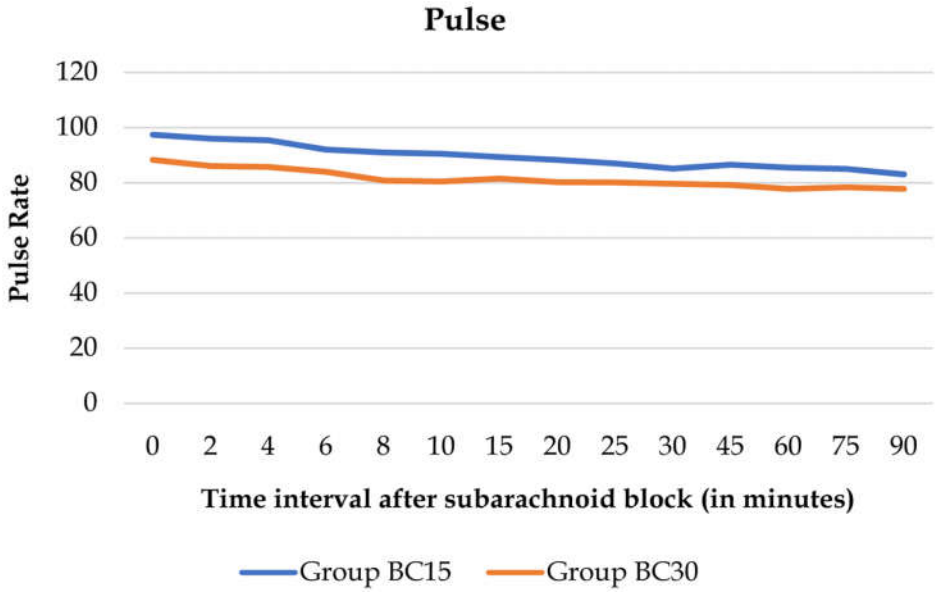

Fig. 2: Comparison of Pulse Rate of mean±standard deviation between groups BC_{15}& BC_{30}, at different time intervals after subarachnoid block

Table 1: Patient characteristics

Age (years)	35.33 ± 11.80	41.33 ± 11.95
Weight (kgs)	61.47 ± 8.32	61.33 ± 12.37
Height (cms)	151.33 ± 4.79	152 ± 4.78
ASA I:II	22:8	23:7

Table 2: Comparison of characteristics of Analgesia, Sensory Block and Motor Block (P-value <0.05 was considered statistically significant)

	Group BC_{15}	**Group BC_{30}**	**p-value**
Highest level of sensory block:			
T_4	14 patients	16 patients	
T_6	14 patients	12 patients	
T_8	2 patients	2 patients	
Time (in minutes) to achieve highest level of sensory block	6.033 ± 1.35	5.73 ± 1.48	0.23
Time (in minutes) to achieve two segment regression	154.2 ± 14.54	157 ± 14.12	0.26
Time (in minutes) to achieve regression to L_1 dermatome	209.93 ± 16.26	217.13 ± 15.57	0.09
Time (in minutes) for first analgesic request	234.3 ± 18.43	243.9 ± 20.19	0.06
Time (in minutes) to achieve highest Bromage Scale 4	6.033 ± 1.35	5.73 ± 1.484	0.23
Time (in minutes) to achieve regression back to lowest Bromage Scale1	246.2 ± 18.56	252.87 ± 15.45	0.08

Table 3: Incidence of side effects

	Group BC_{15}	**Group BC_{30}**
Bradycardia	2 (7%)	2 (7%)
Hypotension	6 (20%)	9 (30%)
Sedation	0	4 (13%)
Nausea	0	1 (3%)
Vomiting	0	1 (3%)

Bromage scale 4 and time to achieve regression back to minimum Bromage scale 1, were recorded and analysed (Table 2). These parameters showed no statistically significant difference amongst both groups (P value >0.05) as shown in Table 2.

Mean systolic blood pressure (SBP) varied from baseline of 126±SD12 mmHg to minimum reading of 110±SD13 in group BC_{15} and from baseline of 124±SD14 mmHg to minimum reading of 106±SD8.9 mmHg in group BC_{30}, during surgery Comparison of difference of SBP±SD from baseline to SBP±SD after an hour of surgery (i.e. till the time, data of maximum number of patients is available, in both groups), amongst both groups is not statistically significant (P-value 0.34). As shown graphically (Figure 1), both groups show steady and almost equal trend of fall in blood pressure. Most frequently, fall in blood pressure occurred around 8-10 minutes after intrathecal injection, in both groups and in some patients, episode of fall in blood pressure occurred upto 30 minutes. Six patients in group BC_{15} and nine patients in group BC_{30} had single episode of hypotension which got treated with single dose of 6mg mephenteramine, given once only in every such case.

Mean pulse rate (PR) varied from baseline of 97±SD15 to minimum of 83±SD8.8 beats/minute in group BC_{15} and from 88±SD10 to 78±SD8.4 beats/minute, respectively in group BC_{30}. Comparison of difference of pulse rate±SD from baseline to pulse rate after an hour of surgery , amongst both groups is not statistically significant (P-value 0.82). Whereas, in Group BC_{15}, baseline pulse rate was 97±SD15 and after an hour, it was 86±SD9.6, in group $BC_{30,}$ at similar timings the values were 88±SD10 to 78±SD8.4 beats/minute respectively. As shown graphically, (Figure 2) both groups showed steady downward trend of pulse rate after injection of drug to end of surgery. Both groups showed equal incidence of bradycardia i.e. two cases in each group (Table 3). All such cases had single episode of bradycardia and required one injection of atropine (0.6mg)for correcting the same.

Incidence of sedation, nausea and vomiting was more in group BC_{30} and there was no case with these side effects in group BC_{15}(Table 3).

Discussion

Clonidine is a partially selective agonist for α2 adrenoreceptors. Being lipophilic, like opiods, its intrathecal (IT) administration with local anaesthetic like bupivacaine, can prolong analgesia, post

operative period [6]. It has been used intrathecally as a sole analgesic for pain relief after caesarean delivery , in doses of 150 to 450 μg [7,8]. Its analgesic effect occurs by activating post synaptic α2 receptors in substantia gelatinosa of spinal cord. The rationale behind ITadministration of clonidine is to provide high concentration near these α2 receptors and then by blocking conductance of C and A-delta fibres, by increasing potassium conductance, thereby inducing hyperpolarization and hence, intensifying conduction block of local anaesthetics. The mechanism of clonidine-induced potentiation of spinal anaesthesia is reported to be mediated by presynaptic (inhibition of transmitter release) and postsynaptic (enhancing hyperpolarization) effects. Race et al [9]and Bonnet F et al [10] demonstrated potentiation of intensity and duration of motor blockade with in IT clonidine combined with local anaesthetics.The explanation of this could be again induction motor neurone hyperpolarization in ventral horn of spinal cord by α2 –adrenoreceptor agonist, to facilitate the local anaesthetic action.

Our results regarding duration of sensory block, motor block and post operative analgesia showed that there was statistically no significant difference in these parameters, between groups BC_{15} and BC_{30}. Prolongation of duration of these sensory, motor blocks and post operative analgesia is similar to the study done by Anil Thakur et al [11]. These researchers also used similar dosage of IT clonidine. They observed duration of sensory block as 270±39.69 and 276±40.62 minutes, motor block as 223.2±46 and 230.4±55 minutes and time to first analgesic request as 223,17±37 and 214.6±46 minutes, for groups BC_{15} and BC_{30} respectively versus control group which showed sensory block as 178.8±33, motor block as154.2±35 and time to first analgesic request as 140.4±37 minutes. With the same dosage of clonidine intrathecally, H Saxena et al [12] observed motor block time as 206.75±20 and 220.47±47 minutes and time to first analgesic request as 164.5±24 and 264.75±44 minutes, for groups BC_{15} and BC_{30} respectively. Dobrydnjov et al [13] suggested, after their study, suggested that analgesia significantly increases by 15mcg of intrathecal clonidine but increasing dose to 30mcg, does not increase duration of analgesia further.

In contrast tour study, Shah Bhavini et al [14], who used similar doses of IT clonidine, showed significantly more duration oftime to first analgesic request and that too was different in two groups. They observed these durations as 387.1±97 and 436.65±149 minutes respectively for groups BC_{15} and $BC_{30.}$. But, in their study, time to achieve two segment regession was 127.85±13 and 137±11 minutes and duration of motor block was 186.5±15 and 186.2±11 minutes, which were similar in both groups but were less than in our study. Also, S Vardhan etal [15], who used 30mcg IT clonidine with local anaesthetic, observed time to two segment regression was very less (i.e. 62.2 minutes) than in our study.

Various studies with different higher doses than our study have been done, doses varying from 50 mcg to 300 mcg IT clonidine. The results had been variable, regarding sensory and motor parameters. For example, Ranju Singh et al [16], OlfaKaabachi et al [17] and S Strebel et al [18] used 75mcg of clonidine intrathecally .The studies done by these researchers independently drew different results. They showed duration of sensory block as 199.26±17, 136±56 and 325±69 minutes respectively, with time to first analgesic request as 760.50±284, 461±147 and 381±117 minutes and by B S Sethi et al [19] as 614 minutes. But with the same dose of clonidine, Dan Benhamou et al [20] and I.vanTuiji [21] et al observed time to first analgesic request as only 183±80 and 129 minutes respectively. Duration of motor block with 75 mcg IT clonidine,by these researchers, has been recorded as 230±33 min by Ranju Singh et al [16], 205 minutes by B S Sethi et al [19], 198±50 min by Ajay Wahi et al [22], 252±79 min by OlfaKaabachi et al [17] and 172±62 minutes by Dan Benhamou et al [20].

Despite beneficial effect of intrathecal clonidine in enhancing sensory block, motor block and post operative analgesia , it is presumed to be associated with side effects of clonidine on perioperative *haemodynamics* (hypotension and bradycardia), sedation etc. Normally, after spinal anaesthesia with only local anaesthetic, hypotension and bradycardia can occur because of sympathetic blockade, leading to vasodilation with subsequent decrease in venous return and thereby decreasing intrathoracic blood volume (approximately 300 ml). Consequently central venous pressure, cardiac output, blood pressure and heart rate are reduced,depending upon height of sympathetic blockade .Bradycardia , and even asystole can occur due to blockade of cardioaccelerator sympathetic fibres,if level of anaesthesia involves T1-4 level and also due to BezoldJarisch reflex. Various strategies have been proposed to prevent these cardiovascular side effects e.g. prophylactic use of vasopressors like mephenteramine and vagolytics like atropine, volume preload or coload with crystalloids or colloids [23,24]. Addition of intrathecal clonidine to local anaesthetic, affects haemodynamics in a

complex manner because of opposing action at multiple sites. Clonidine, an α-2 adrenergic agonists produces sympatholysis and reduces blood pressure by its effects at specific brainstem nuclei and on sympathetic preganglionic neurons in spinal cord. These sympatholytic effects are counteracted by direct vasoconstriction, resulting from α-2 adrenergic agonists on peripheral vasculture [18]. These rather complex action of intrathecally injected α-2 adrenergic receptor agonists on haemodynamic variable, are further dependent on segmental site of injection, patient position, type of surgery e.g. caesarean section which has its own haemodynamics etc. In our study, haemodynamic changes were not clinically significant, as one dose of mephenteramine (6mg) was needed for treating hypotension which occurred in few cases in either group. Similarly, only one dose of atropine (0.6mg) was required for treating bradycardia which occurred invery few cases and that too equally in each group. Further, these incidence of haemodynamic changes are routinely observed in patients where spinal anaesthesia is given, with only local anaesthetic without addition of clonidine.

Dan Benhamou et al [20], in their study, on caesarean delivery patients, using IT75µg clonidine with local anaesthetic, achieving level upto T4 in all patients, observed that maximum haemodynamic changes occurred during 0-30 minutes in form of hypotension and bradycardia. These changes settled at slightly lower level than baseline after 80-120 minutes. They, alongwith studies by Alahuhuta et al [25] and Pederson H et al [26] (using very small amount of IT clonidine i.e.25-75 µg with local anaesthetic), showed increased duration of pain free interval compared from only spinal local anaesthetics, and without causing any significant side effect. Their study is in consonance with our study regarding timing of hypotension and bradycardia which, in our study, occurred from 0-30 minutes irrespective of whether patient was undergoing caesarean section or any other gynaecological or obstetrical surgery, as per scrutiny of our master chart. Ranju Singh et al [16] also observed fall in SBP occurred most frequently at either 3-6 min after SA or 5-10 min after delivery. The fall in SBP 3-6 min after SA is most likely due to sympatholysis by IT bupivacaine and not due to to IT clonidine because haemodynamic changes of clonidine after IT or other systemic administration starts within 30 minutes and reaches maximum within 1-2 hours [27]. In consonance with our study, Arora et al [28] also had similar observations regarding haemodynamic changes.

In contrast to our study, Anil Thakur et al [11] observed fall in blood pressure at 15-240 min and Dobrydnjov et al at 45-120 min whereas Grandhe et al [29] observed fall from 45 min to 8 hours after IT injection.

But Anil Thakur et al [11] has shown incidence of hypotension and bradycardia ,very similar to our findings. They observed 5 and 7 cases of hypotension in group BC_{15} and BC_{30} respectively and 2 cases of bradycardia in each group. Srivishnu et al [15] showed incidence of hypotension 12% and bradycardia as 27%with 30µg IT clonidine. But they observed 52% patients of hypotension and 21% of bradycardia, in control group. H Saxena et al [12] recorded hypotension as 10% and 20% in group BC_{15} and BC_{30} and bradycardia as15% and 30% patients, respectively. Higher doses of IT clonidine (75µg) in some studies recorded hypotension 24-29% and bradycardia 21%(Ranju Singh et al [16] and Olfa Kaabachi et al [17]).

Incidence of other side effects of IT clonidine was, sedation in 13% patients and that too in only group BC_{30}, in our study. Only one patient had nausea and vomiting. This is much less than in study done by H Saxena et al [12], who showed sedation in 15% and 40% patients in group BC_{15} and BC_{30} respectively, without any patient of nausea / vomiting, in either group. Shah Bhavini et al [14] observed sedation in 25% and 5% patients in BC_{15} and BC_{30} groups respectively. Even higher IT clonidine doses (75µg) inferred variable incidence of sedation, from 2% [17] to 40% [20] and nausea in 21% [17] and 14% [20] respectively.

Conclusion

From our results and above discussion, it is concluded that both doses of IT clonidine i.e. 15µg and 30µg with bupivacaine, produce equal prolongation of sensory and motor block alongwith time to first analgesic request. This prolonged effect also equals some of studies which have been done with higher doses of IT clonidine. So, clonidine15µg intrathecally with bupivacaine is preferred over 30µg or higher dose to achieve prolongation of desired sensory and motor block alongwith postoperative analgesia with clinically insignificant haemodynamic effects.

Financial or Other Competing Interests

None

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Original Research Article

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Effect of Dexamethasone as an Adjuvant to Ropivacaine in Supraclavicular Brachial Plexus Block for Upper Limb Surgeries

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Abstract

Background: Brachial plexus block is widely employed regional nerve block technique for upper extremity surgeries. Supraclavicular approach is most preferred as it is easy and gives consistency in results with minimal side effects. Various adjuvants have been added to local anesthetics to Prolong the duration of anesthesia. In our study, Dexamethasone has been added to ropivacaine to evaluate its effect on duration of analgesia. *Aim:* Evaluating the effect of adding dexamethasone to ropivacaine in supraclavicular brachial plexus block compared with ropivacaine alone. *Materials and Methods:* A Randomised prospective and double blinded clinical study. Seventy patients of ASA I and II of either sex, aged 20-65 years, undergoing various elective upper limb surgeries were equally divided into two groups and given supraclavicular brachial plexus block. Group A patients (n = 35) received 30 ml of 0.5% ropivacaine with distilled water (2 ml)control group whereas Group B patients (n = 35) received 30 ml of 0.5% ropivacaine with 8 mg dexamethasone (2 ml) made study group. The primary outcome measures were the onset of sensory and motor block, duration of analgesia and pain scores. *Results:* The onset of sensory and motor block was seen to be faster in Group B than Group A. Patients in group A required first rescue analgesia earlier (410.28± 38.70 min) thanthose of Group Bpatients (996.60 ± 56.60 min), which was found statistically significant (P < 0.002). The total dose of rescue analgesia was higher in Group A as compared to Group B, which was statistically significant (P < 0.00). *Conclusion:* Addition of dexamethasone (8 mg) to ropivacaine in supraclavicular brachial plexus approach significantly and safely prolongs sensory, motor blockade and postoperative analgesia more than that produced by ropivacaine alone.

Keywords: Dexamethasone; Ropivacaine; Local Anesthetics; Peripheral Nerve Blocks; Supraclavicular Block.

Introduction

Brachial plexus block is a very popular and useful technique for both as a sole regional anesthetic technique as well as additive to general anesthesia. It is widely employed as it is easier to perform and provides superior quality of analgesia and avoids the common side effects associated with general anesthesia as it offers better pain relief and also reduces the number of days of stay in the hospital. Supraclavicular approach is considered to be easier and also gives consistent results for surgeries of upper limb [1]. Few complications reported in this technique are pneumothorax and hemothorax. Various local anesthetics alone or in combination with different adjuvants have been tried to prolong the duration of postoperative analgesia in the recent times. Bupivacaine, lignocaine, Ropivacaine have been used singly or in combinations.

Ropivacaine is a long acting local anesthetic that is structurally related to bupivacaine. It is a S (-) enantiomer, unlike bupivacaine, which is a racemate, developed for the purpose of reducing potential cardio toxicity and improving relative sensory and motor block profiles [2]. Various adjuvants can be used with local anesthetics. Trials of mixinglocal anesthetic with adjuvant drugs like epinephrine, clonidine [3,4], opioids [5], midazolam

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[6] have been done and have met with limited success. Corticosteroids have all been studied previously in an attempt to prolong th eduration of analgesia after peripheral nerve blockade with varying degrees of success [7].

It is widely believed that dexamethasone improves the quality and duration of peripheral nerve blockade [8]. They produce analgesia by blocking transmission of nociceptive myelinated c-fibers and suppressing ectopic neuronal discharge. More recent studies indicate that 8 mgdexamethasone added to perineural local anesthetic injections augment the duration of analgesia in peripheral nerve block [9]. Dexamethasone is very potent and highly selective glucocorticoid, its potency is about 40 times that of hydrocortisone [10].

In this study, we evaluated the onset of sensory and motor blockade, duration and quality of postoperative analgesia of Dexamethasone 8 mg added to Ropivacaine 0.5%compared to plain Ropivacaine 0.5% for brachial plexus block by supraclavicular approach.

Materials and Methods

After obtaining Institutional ethical committee clearance, a randomized prospective double blind study was conducted in our medical college hospital between February 2016 to January 2017. Inclusion criteria were 70 patients of either sex aged between 20 to 65 years undergoing various upper limb surgeries under supraclavicular brachial plexus block. Exclusion criteria were Patient refusal for the block, ASA grade 3, 4 and 5 , infection at the site of injection, bleeding disorders, peripheral neuropathies, co-existing systemic diseases and hypersensitivity to study drugs were excluded from the study. An informed and written consent was obtained from all the patients. These patients were randomly divided into 2 groups.

Group A(n=35):Patients received 30ml of Ropivacaine 0.5% and 2ml Distilled water (control group). Group B(n=35): Patients received 30ml of Ropivacaine 0.5% and 2ml Dexamethasone (8 mg). A detailed pre-anaesthetic evaluation and appropriate baseline investigations were carried out prior to the surgery.

Patients were blinded to the study by random allocation by computer generated number table. On the day of surgery preoperative heart rate, SpO2, noninvasive blood pressure, respiratory rate readings were recorded. On the operation table I.V.access secured with 18G I.V. cannula and ringer lactate 500ml infusion was started. Basic non-invasive monitoring with Pulseoximeter , Blood pressure and electrocardiography connected.

Supraclavicular block was performed using nerve stimulation technique in the supine position with head turned 45^0 to the opposite side and arm placed by the side of chest. Under asepsis a peripheral nerve locator (Fisher and Paykel, Newzealand) connected to a 22 G, 50-mm-long stimulating needle (Stimuplex, Braun, Germany) was inserted almost perpendicularly to the skin in a caudal and posterior-lateral direction, 1-1.5cm above the midclavicular point and subclavian artery pulsation. After proper location of the brachial plexus which was appreciated by desired motor response at 0.6 Ma current, 32ml prepared coded drug solutions were injected with intermittent negative aspiration.

The Following Parameters were Studied

- Onset of sensory block was defined asthe time from injection to onset of analgesia in each of the major peripheral nerve distributions (ulnar, radial, medial and musculocutaneous). Sensory block was assessed by pinprick using the blunt end of a 27-gauge needle at 5 min intervals up to 30 min. Sensory block was graded according to the following scale:

  0 = no block (normal sensation)

  1 = partial block (decreased sensation)

  2 = complete block (no sensation).

- Onset of motor block defined as the time from injection to the inability of the patient to move his/her fingers or raise their hand. Motor block was measured at 10 min intervals for 30 min by assessing the following motor functions: flexion at the elbow (musculocutaneous nerve), extension of the elbow and the wrist (radial nerve), opposition of the thumb and index finger (median nerve), and opposition of the thumb and small finger (ulnar nerve). Motor block was graded according to the following scale: 0 = no block (full muscle activity), 1 = partial block (decreased muscle activity), and 2 = complete block (no muscle activity).

Post operative follow up was carried out in the recovery room and post operative ward. The duration of analgesia was noted using visual analogue score (VAS) which is numeric scale of 0-10 for pain at every half an hour for first 10 hours and then hourly till 24 hours. When the patients began to experience the worst pain (VAS >8), it

wasconsidered that analgesic action of the drugs was terminated and rescue analgesic (IM Diclofenac 1-1.5mg/kg) given.

Total duration of motor block postoperatively was assessed every hourly by asking the patients to move their fingers and to see whether they are able raise the hand or not and time was recorded.

Any side effects like drowsiness, pruritus, nausea, vomiting, Horner's syndrome, phrenic nerve palsy, pneumothorax, respiratory depression and sign and symptoms for local anaesthetic toxicity if any were looked for and noted. The above assessments were carried out by the principal investigator who was blinded to the drugs administered in the plexus block.

Statistical Analysis

Assuming Alpha-error of 0.05 and power (1-ß) of 90%, the effective sample sizeon the basis of duration of analgesia came out to be 34 so it was rounded off to 35 to increase the power of the study. The duration of analgesia was analysed by unpaired Student *t*- test. Categorical data were presented as mean and standard deviation. The results were considered significant if *P* value is <0.05 and highly significant if *P* value is < 0.001.All the statistical analysis was done with SPSS version 21.

Results

Seventy patients were enrolled and participated in the study. Demographic characteristics and duration of surgery were comparable in both the study groups [Table 1]. The mean duration of onset of sensory and motor block and the mean duration of peak of sensory and peak of motor blockade were comparable in both the groups [Table 2]. Duration of analgesia was taken as time from the onset of sensory blockade to the reappearance of pain. The mean duration of analgesia (sensory block) was longer in Group B as compared to group A (990.89±98.69 min versus 409.55±34.88 min), which was highly statistically significant (*P* = 0.002) [Figure 1].

VAS scoring was zero in both the study groups in the immediate postoperative period and remained as such up to 7 hours of postoperative period and had no statistical significance.

In Group A, patients required first rescue analgesia at 7 hr 23 min (410.28 ± 38.70 min) while in Group B, patients required first rescue analgesia at 16 hr 39 min (996.60± 56.60 min), which was found statistically significant in Group (*P* = 0.000) [Figure 2]. The amount of rescue analgesic was more in Group A versus Group B (98.75 mg versus 43.75 mg) which was again statistically significant.

Table 1: Demographic data

	Group A	Group B
Age (Years)	43.45± 5.67	40.90±3.89
Gender (M:F)	16:19	20:15
Weight (Kgs)	58.90±3.88	60.77±1.67
ASA I/II	14/21	18/17

Table 2: Block characteristics

	Group A	Group B	P Value
Onset of sensory Block(min)	3.45±0.66	3.22±0.24	<0.05
Onset of Motor Block(min)	5.66±0.87	4.56±0.97	<0.05
Duration of Sensory block(min)/Duration of analgesia(min)	409.55±34.88	990.89±98.69	<0.05
Duration of motor block(min)	318.65±50.45	825.60±70.65	<0.05
Time of first resue Analgesia(min)	410.28±38.70	996.60±56.60	<0.05

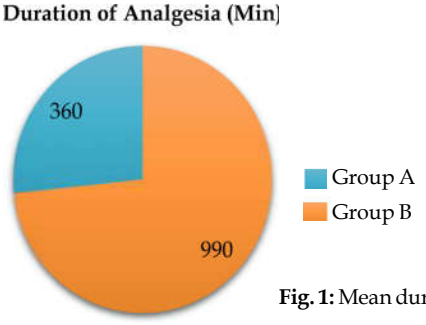

Fig. 1: Mean duration of Analgesia

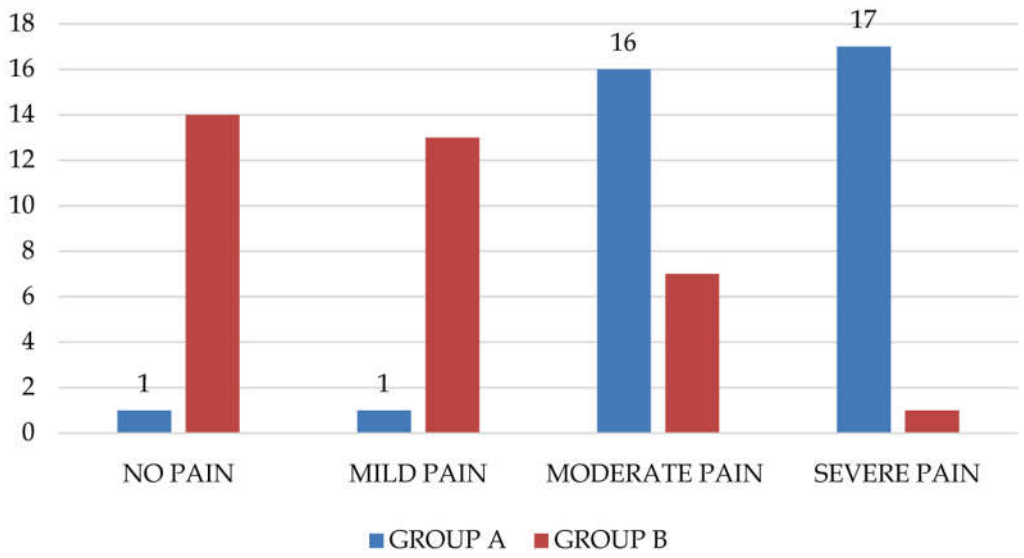

Fig. 2: Comparision of VAS Scores

Discussion

Brachial plexus block has emerged as a popular technique for upper limb surgeries. Peripheral nerve blocks not only provide intraoperative anaesthesia but also provide post operative analgesia. Several adjuvants like epinephrine, opioids, alpha2 agonists, dexamethasone etc. have been added to local anaesthetics to prolong the duration of action. Many studies have successfully proved the usefulness of dexamethasone as an effective adjuvant in peripheral nerve blocks [10]. The mechanism of action of corticosteroids in prolonging peripheral neural blockade may be secondary to a local action on nociceptive C-fibers mediated via glucocorticoid receptors and the up-regulation of function of potassium channels in excitable cells.

In our study the onset times of sensory and motor blockade was seen to be faster in the group with dexamethasone which is in support with one study by Shrestha BR et al [10] where onset of action was 10-30 minutes in local anesthetic group (mean 18.15±4.25) and 10-20 minutes (mean 14.5±2.10) in the local anesthetic plus steroid group. They found statistically significant difference between two groups.

However another study by Ali et al [11] found that the onset time of sensory and motor blockade was similar in both the groups. Our study showed prolonged duration of analgesia in Dexamethasone group when compared to plain Ropivacaine group. Kathrine Holte et al [12] found that addition of small amounts of dexamethasone to bupivacaine incorporated in microcapsules prolonged local analgesia compared with microcapsules with plain bupivacaine after subcutaneous administration in humans.

In another study by Droger C etal [13], it was found that incorporation of dexamethasone into bupivacaine microspheres significantly prolonged intercostal nerve block in sheep and the reason was believed to be due to a causative relationship between the suppression of inflammation and the remarkably longer duration of effect. The mechanism of the analgesia induced by corticosteroids is suspected to be mediated by their anti-inflammatory or immune-suppressive effects [14].

Few studies believe that the block prolonging effect of dexamethasone is due to its local action and not a systemic one [13]. They found that steroids produce analgesia by blocking transmission in nociceptive c-fibres and suppressing ectopic neuronal discharge. Local application of methylprednisolone has been found to block transmission in c-fibres but not in α and β fibres [15]. The effect was reversible, suggesting a direct membrane action of steroids. There are others who believe that analgesic properties of corticosteroids are the result of their systemic effect [16].

The safety of dexamethasone use in a nerve sheath may raise some concerns. Nerve injury is a rare complication of dexamethasone injection, and it usually occurs in the context of needle trauma.

Various doses of dexamethasone (4-16mg) as an adjuvant to local anaesthetics for peripheral nerve block have been used by various studies.We used a

dose of 8 mg because administration of this dose seems to be safe in adults and also used in many previous studies. Adverse effects with a single dose of dexamethasone are probably extremely rare and minor in nature, and previous studies have demonstrated that short-term (< 24 hours) use of dexamethasone was safe [17].

The main limitation of our study was that we could not use ultrasound guidance for the block procedure though it is recommended as gold standard due to non availability in our institution.

Conclusion

Our study concludes that addition of dexamethasone to ropivacaine as an adjuvant in supraclavicular brachial plexus significantly shortens the onset of sensory and motor blockade and prolongs the duration of postoperative analgesia in patients undergoing upper limb surgeries when compared to Ropivacaine alone. It was found to be well tolerated and cost effective method without the occurrence of remarkable adverse effects. Future scope of study is to evaluate the mechanism of action as well as the optimal dose before its routine use as a perineural adjunct that can be advocated to prolong block characteristics and also to study the side effects if any in late post-operative period.

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Original Research Article

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Comparison of Esmolol and Magnesium Sulphate for Attenuation of Hemodynamic Stress Response to Laryngoscopy and Intubation in Elective ENT Surgeries

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Abstract

Introduction: The sympathoadrenal response to laryngoscopy and intubation is hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease and intracranial pathology. Various drugs are used to attenuate this stress response. *Aim and Objectives:* This study compares the efficacy of Esmolol and Magnesium Sulphate in attenuating the hemodynamic stress response to laryngoscopy and intubation. *Methodology:* Randomized prospective single blinded study was designed. Ninety patients of ASA PS I and II were randomly allocated into three groups of thirty each. P—received normal saline, E—Esmolol 1.5mg/kg, M—Magnesium Sulphate 50mg/kg. *Statistical Analysis:* ANOVA and Pearson chi square test were used. A p value <0.05 was considered as statistically significant. Tukey's HSD was used to compare between groups. *Observations and Results:* The following observations were made. 1. Group E showed maximum attenuation of heart rate and blood pressure. 2. Group M also showed significant attenuation of blood pressure response but produced tachycardia on infusion of the drug. Heart rate response was not statistically significant compared to group E. 3. All patients recovered well. 4. Incidence of side effects was not significant between the groups. *Conclusion:* Esmolol is effective in blunting the intubation response followed by Magnesium Sulphate which blunts the hypertensive response but produces tachycardia during infusion of the drug. Placebo was ineffective in blunting hemodynamic stress response.

Keywords: Esmolol; Hemodynamic Stress Response; Intubation; Laryngoscopy; Magnesium Sulphate.

Introduction

The induction of anaesthesia, laryngoscopy, tracheal intubation and surgical stimulation evoke cardiovascular responses leading to alteration in heart rate, cardiac rhythm and blood pressure.

The response to laryngoscopy and intubation starts in 5 seconds, peaks within 1-2 minutes and returns to baseline in 5 minutes. This sympatho adrenal response is of little significance in healthy patients but hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease and intracranial pathology. Various drugs are used to attenuate this stress response like local anaesthetics, narcotics, vasodilators, beta blockers, calcium channel blockers, Magnesium and centrally acting sympatholytics. We have compared Esmolol and Magnesium Sulphate with placebo for attenuation of hemodynamic stress response to laryngoscopy and intubation.

Methodology

Ninety patients of age group 15-60 years of both sex with ASA physical status I and II undergoing elective ENT surgeries under general anaesthesia

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were included in the study. Institute ethical committee approval and informed written consent from the patient was obtained.

Inclusion Criteria

- Age: 15 – 60 years
- ASA: I & II
- Surgery: Elective ENT surgery
- Who have given valid informed consent.

Exclusion Criteria

- ASA III or IV
- Anticipated difficult airway
- known sensitivity to the drugs
- Emergency surgery
- Patients on alpha and beta blockers

Pre Anesthetic Preparation

Pre anaesthetic check up and investigations were done. All patients were given pre operative night sedation with tablet Alprazolam 0.5mg.

Method

The patients were allocated randomly into three groups of thirty patients. Monitors used were NIBP, ECG, $EtCO_2$ and pulse oximetry. Baseline heart rate and blood pressure was measured. They were premedicated with Inj. Glycopyrrolate 0.2mg and Inj.Midazolam 0.02mg/kg intravenous. Inj. Fentanyl 2µg/kg was given before induction. They were induced with Inj. Propofol 2mg/kg and intubation was done three minutes after Inj. Vecuronium 0.1mg/kg and mask ventilation with Nitrous oxide and Oxygen in a ratio of 66:33 and Sevoflurane 2%. Laryngoscopy and intubation was done in less than 15 seconds.

Group E received Esmolol 1.5mg/kg in 15ml normal saline over 15-20 seconds one minute after vecuronium and intubation was done after 2 minutes.

Group M received Inj.Magnesium Sulphate 50mg/kg in 100ml of normal saline infusion over 10 minutes before induction.

Group P received 15ml of normal saline after induction.

The hemodynamics was recorded at baseline, after premedication, after test drug, after induction, immediately after intubation, thereafter 1, 3 and 5 minutes following intubation.

Laryngoscopy duration and Cormack Lehane score were noted. Any incidence of hypotension, bradycardia or arrhythmias was noted. Anaesthesia was maintained with Nitrous Oxide and Oxygen, vecuronium 0.01mg/kg and sevoflurane 1-2% as needed.

All patients were reversed with Inj. Glycopyrrolate 0.01mg/kg and Neostigmine 50microgm/kg and extubated after reversal of neuromuscular blockade.

Primary Outcome Measures

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure.

Secondary Outcomes

Complications like bradycardia, hypotension, arrhythmias.

Data Analysis

ANOVA and Pearson chi square test were used. A p-value of <0.05 was considered as stastistically significant. Tukey's HSD was used to compare between the groups.

Observations and Results

There was no statistical significance between three groups in relation to age, sex, weight and basal hemodynamic parameters.

The modified Mallampati Score and Cormack Lehane grade and laryngoscopy duration were comparable between the groups.

Characteristics		Group P	Group E	Group M	p value
Age (yrs)		29.7±10.06	26.53±9.32	31.13±9.20	0.167
Sex	Male	11	13	11	0.829
	Female	19	17	19	
Weight (kg)		56.27±8.09	52.93±10.65	52.67±8.92	0.252

Heart Rate Changes (Beats/Min)

Table 1: Comparison of heart rate at various time intervals between the groups

Group	P	E	M	P Value
Baseline	79.80±14.44	86.67±9.79	81.47±14.47	0.112
After Premed	79.83±13.05	86.63±14.30	84.53±16.50	0.191
After Test Drug	77.30±11.30	77.70±13.14	93.27±18.45	0.001
After Induction	72.27±13.26	82.20±15.00	78.33±11.31	0.017
Immediately After Intubation	103.63±12.31	90.67±13.93	97.40±12.57	0.001
1 minute After Intubation	95.87±12.86	87.27±13.48	92.97±10.38	0.026
3 minutes After Intubation	87.83±12.50	84.30±12.79	90.07±9.82	0.167
5 minutes After Intubation	81.73±13.66	81.60±13.31	86.00±9.61	0.296

Systolic Blood Pressure Changes (mmHg)

Table 2: Comparison of systolic blood pressure at various time intervals between the groups

Group	P	E	M	p Value
Baseline	125.73±10.72	123.13±8.69	125.90±11.12	0.504
After Premed	123.47±10.54	120.67±9.05	120.30±9.56	0.391
After Test Drug	118.70±13.64	100.10±9.60	112.27±11.65	0.001
After Induction	109.97±13.63	107.70±9.23	98.97±9.74	0.001
Immediately After Intubation	138.57±17.25	114.43±8.76	124.90±17.76	0.001
1 minute After Intubation	128.73±17.04	107.60±9.23	116.80±15.66	0.001
3 minutes After Intubation	119.13±16.16	102.60±9.61	109.80±14.75	0.001
5 minutes After Intubation	111.23±14.34	100.20±9.44	105.47±10.84	0.002

Diastolic Blood Pressure Changes (mmHg)

Table 3: Comparison of diastolic blood pressure at various time intervals between the groups

Group	P	E	M	p Value
Baseline	81.33±6.70	80.00±6.50	81.33±8.12	0.707
After Premed	78.40±6.89	76.33±5.82	77.30±8.61	0.541
After Test Drug	76.93±7.38	61.90±8.22	69.70±9.63	0.001
After Induction	71.27±10.28	67.63±8.05	59.30±9.79	0.001
Immediately After Intubation	93.60±12.49	74.73±8.29	83.13±16.74	0.001
1 minute After Intubation	85.77±12.16	67.53±9.97	76.17±15.94	0.001
3 minutes After Intubation	79.80±12.27	62.63±10.19	71.07±14.29	0.001
5 minutes After Intubation	72.63±10.20	60.00±9.93	67.10±12.20	0.001

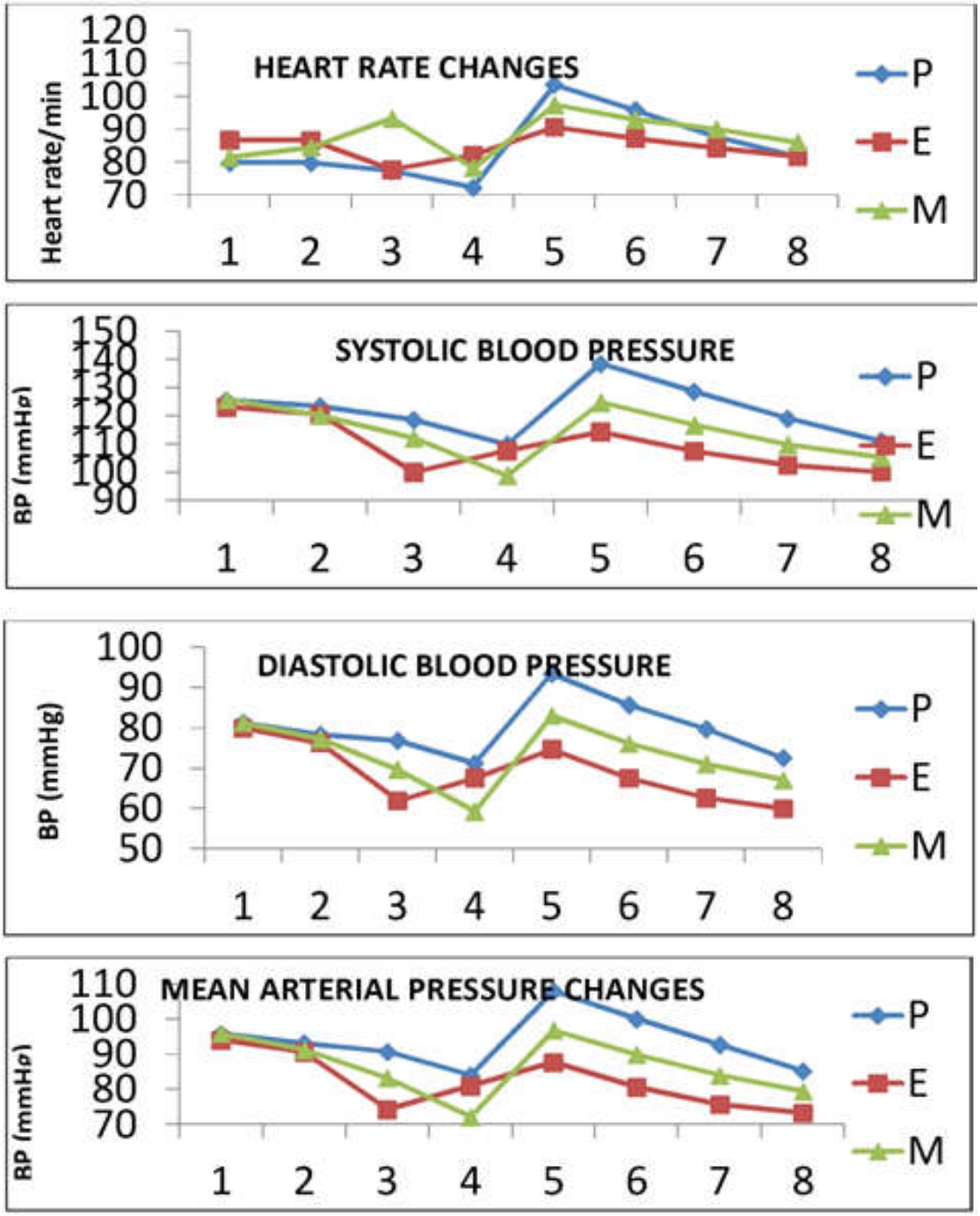
Mean Arterial Pressure Changes (mmHg)

Table 4: Comparison of mean arterial pressure at various time intervals between the groups

Group	P	E	M	p Value
Baseline	95.93±7.46	94.07±6.60	96.00±8.81	0.544
After Premed	93.20±7.49	90.63±6.76	91.30±8.73	0.412
After Test Drug	90.77±8.56	74.30±7.78	83.30±9.84	0.001
After Induction	84.00±10.36	81.00±7.34	72.23±9.34	0.001
Immediately After Intubation	108.10±14.19	87.70±8.01	96.87±16.72	0.001
1 minute After Intubation	100.10±13.49	80.67±9.19	89.97±15.64	0.001
3 minutes After Intubation	92.77±13.17	75.70±9.01	84.00±13.79	0.001
5 minutes After Intubation	85.30±11.17	73.30±8.69	79.50±10.73	0.001

Side Effects

	Hypotension		Bradycardia		Arrhythmia	
	Yes	No	Yes	No	Yes	No
Group P	0	30	0	30	0	30
Group E	1	29	1	29	0	30
Group M	4	26	1	29	0	30
P value	0.133		0.600			



1. Basal Value,
2. After Premedication
3. After Test Drug,
4. After Induction
5. Immediately after intubation,
6. 1 Minute after intubation
7. 3 Minute after intubation,
8. 5 Minute after intubation

Discussion

Laryngoscopy and intubation can produce hemodynamic stress response characterised by hypertension and tachycardia. It can lead to acute coronary events, arrhythmias, ventricular failure and rise in intracranial pressure. Many drugs have been reported to attenuate this response.

S.A. Aasim et al [1] compared Esmolol 1.5mg/kg and Magnesium sulphate 50mg/Kg in 60 patients. They did not have a control group. They stated that Esmolol group had significantly lower heart rate than MgSO4 group after intubation till five minutes. There was no significant difference in mean arterial pressure between both groups before and after intubation. They concluded that Esmolol is a better agent as it attenuates rise in both heart rate and blood pressure which is in accordance with our study.

Rajan Sunil et al [2] compared Magnesium Sulphate 50mg/kg and lignocaine for attenuating stress response in major head and neck surgeries Magnesium was administered as an infusion over 10 min before induction. They said preinduction HR following administration of magnesium sulphate increased significantly from the baseline values and concluded that magnesium sulphate effectively attenuated heart rate and blood pressure than Lignocaine.

In our study, comparison of Esmolol 1.5mg/kg, MgSO4 50mg/kg and placebo was done in attenuating haemodynamic stress response to laryngoscopy and intubation. The data was analysed using Microsoft Excel. Statistical significance was assessed by use of ANOVA and Pearson chi square test. TUKEYS HSD was applied to evaluate inter group comparisons. $p<0.05$ was considered statistically significant.

Heart Rate Changes

The heart rate immediately after intubation and one minute after intubation was significantly lower in group E than group M and group P.($p<0.05$). Magnesium infusion increased the heart rate. This was in correlation with the study by Santhosh Kumar et al [3] which stated that MgSo4 60mg/kg produced tachycardia and failed to attenuate the rise in heart rate compared to Esmolol 2mg/kg. Michael F M James et al [4] also concluded that MgSo4 60mg/kg pretreatment increased heart rate by 13±3.9 beats per minute but attenuated stress response. In our study heart rate increased by 11.8±3.98 beats per minute. Heart rate returned below baseline after three minutes in group E and to near baseline levels after five minutes in group M and group P.

Blood Pressure Changes

There were significant changes in systolic, diastolic and mean arterial pressure between the groups after test drug, after induction, immediately after intubation, at one, three and five minutes after intubation ($p=0.001$).

Systolic Blood Pressure (SBP) Changes

Immediately after intubation change in systolic blood pressure was significant between the groups ($p=0.001$). Systolic blood pressure was below the baseline value in group E, near baseline in group M and elevated in group P.

At one, three and five minutes after intubation there was significant fall in SBP between the groups ($p=0.001$). But there was no statistical significant difference in SBP between Esmolol and MgSO4 group at three and five minutes after intubation. The study of Juhi sharma et al [5] on controlled hypertensive patients showed no significant difference in systolic and diastolic blood pressure between the groups which received Esmolol 1.5mg/kg and MgSO4 40mg/kg .

Diastolic Blood Pressure (DBP) Changes

There was a statistically significant fall in diastolic blood pressure after intubation in group E compared to group M.($p<0.05$)

Mean Arterial Pressure (MAP) Changes

Immediately after intubation and one minute after intubation, MAP was increased in group P but there was a fall in MAP in group E and group M which was statistically significant ($p<0.05$).

We did not monitor serum magnesium levels and we had no clinical adverse effects related to magnesium infusion in our study.

Side Effects

One patient in group E and four patients in group M had hypotension (MAP<60mmHg). One patient in group M and one patient in group E had bradycardia (HR<60/min). There were no incidences of arrhythmia, prolonged neuromuscular

blockade or delayed recovery in any group. One patient in group M had complaints of hot flush in the lower abdomen when Magnesium Sulphate was being infused.

Conclusion

From this study, it is concluded that hemodynamic stress response to laryngoscopy and intubation can be attenuated by giving intravenous Esmolol 1.5mg/kg. Esmolol is effective in blunting the response followed by Magnesium Sulphate which blunts the hypertensive response but produces tachycardia during infusion of the drug. Placebo was not effective in attenuating stress response.

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Platelet Indices as Indicators of Severity of Sepsis

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Abstract

Aims: To compare Platelet indices with SOFA scores of patients with sepsis in order to assess the relationship between platelet indices like MPV and PDW and the severity of sepsis. *Settings and Design:* A total of 100 patients with sepsis or septic shock as cases and 95 patients as controls (with out sepsis) were considered for this study. *Patients and Methods:* The SOFA scoring of the patients (both cases and controls) was done at the time of admission. The relationship between platelet indices and severity of sepsis obtained by prognosis of the patient using admission SOFA score was assessed. *Statistical Analysis:* Statistical analysis was performed using SPSS for Windows version 17.0. *Results*: In patients with sepsis, there was a significant difference (P<0.05) between the baseline values of platelet counts as well as platelet indices amongst the two groups. *Conclusion:* The findings of this study suggest that platelet indices are significant indicators of severity of sepsis. Intense supervision and aggressive treatment of sepsis patients with higher baseline platelet indices may prevent progression of disease.

Keywords: Sequential Organ Failure Assessment (SOFA) Score; Mean Platelet Volume (MPV); Platelet Distribution Width (PDW); Platelet Indices; Sepsis.

Introduction

Sepsis is a major disease affecting millions of people worldwide each year [1,2]. It is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [3]. Septic shock is a subset of sepsis, in which, underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality [3].

Sepsis is the primary cause of death from infection, especially if not recognised and treated promptly and its recognition mandates urgent attention. The main differentiating factors between sepsis and any other infection are an aberrant host response and the presence of organ dysfunction [3].

The Sequential Organ Failure Assessment (SOFA) score is one of the most widely available scores, to describe organ dysfunction and predict survival [4]. It is a means to clinically characterize a septic patient. SOFA has widespread familiarity within the critical care community and a well-validated relationship to mortality risk. It can be scored retrospectively, either manually or by automated systems, from clinical and laboratory measures often performed routinely as part of acute patient management [3].

One of the systems frequently affected in sepsis is the haemostatic system.Thrombocytopenia (platelet count < 150,000/μl) is common in critically ill patients, with an estimated incidence of 20%–40% at some point during the intensive care unit (ICU) stay [5, 6]. Sepsis is a major risk factor for the development of thrombocytopenia.Generally, platelet production increases as platelet count decreases. An increased number of young platelets are also functionally more active than older platelets [1,7].

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In addition to their important role in haemostasis and thrombosis, accumulating evidence demonstrates that platelets contribute to the inflammatory process, microbial host defense, wound healing, angiogenesis, and remodeling [8].

Changes in the coagulation system are manifested by the prolongation of the Activated partial thromboplastin time (aPTT) and Prothombin time (PT), and decreased platelet (PLT) count [9]. The extent of the platelet fall is correlated to the prognosis in many studies, and platelet count has been shown to return towards normal values as the patient recovers.

Platelet indices like Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) are related to PLT and hence vary with variation in platelet counts.

Thus, a prospective study was conducted by us with an aim to compare Platelet indices with SOFA scores of patients with sepsis in order to assess the relationship between platelet indices like MPV and PDW and the severity of sepsis.

Materials and Methods

Eligible adult patients admitted in the ICU were considered for the study based on the following Inclusion and Exclusion Criteria:-

Inclusion Criteria

- Patients - Those in the ICU diagnosed as sepsis, severe sepsis, and septic shock at the first medical examination.
- Control Group - Patients in the ICU without sepsis.

Exclusion Criteria

- Pregnant women or women who had recently given birth
- Patients with active hemorrhage
- Patients with hematological diseases
- Patients who had infused with blood or platelets prior to their admission
- Patients who had used anti-platelet drugs prior to their admission.

A total of 100 patients with sepsis or septic shock as cases and 95 patients as controls were considered for this study.

Data Collection

After taking the patients' informed consent, their baseline characteristics, including demographic information were noted. The SOFA scoring of the patients (both cases and controls) was done at the time of admission based on assessment of the following systems – respiratory, coagulation, hepatobiliary, cardiovascular, neurologic and renal systems.

Blood samples were collected from the patients and platelet counts and indices were estimated at initial presentation of the patients to the hospital. All blood samples were obtained from the venous system and stored in tubes containing ethylenediaminetetraacetic acid (EDTA) and assayed automatically using internationally certified devices - Sysmex XE-2100 and Sysmex XT-2000i. These devices work by utilizing the power of fluorescent flow cytometry and hydrodynamic focusing technologies.

The relationship between platelet indices and severity of sepsis obtained by prognosis of the patient using admission SOFA score was assessed.

Statistical Analysis

All the quantitative variables like age, mean platelet volume, etc. are presented in terms of descriptive statistics such as Median and Interquartile range (IQR). All the qualitative variables are presented using Percentage.

Baseline characteristics as well as Platelet counts, MPV and PDW were compared between cases and controls using Mann-Whitney test. Chi square test was used to compare the categorical variables between cases and controls.

Patients were grouped into two categories based on their SOFA scores at the time of admission – a) those with SOFA scores < 9, and b) those with SOFA scores > 11. Platelet count, MPV and PDW between these two groups were compared independently using Mann-Whitney test.

Receiver operating characteristic (ROC) curve was used to find the cut off point for MPV and PDW for determining severity of sepsis. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for MPV and PDW.

All tests were two sided and a P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS for Windows version 17.0.

Results

A total of 100 sepsis patients were included in the study consisting of 64 males and 36 females. Also, 95 patients (64 males and 31 females) were included in the control group.

Age, gender and other baseline characteristics such as respiratory rate, heart rate, and haematocrit were statistically similar between the two groups (P>0.05). However, a statistically significant difference (P<0.05) was found in the temperature, white blood cell count, Prothrombin Time and Activated partial thromboplastin time between cases and controls [Table 1].

The cases exhibited a significantly lower baseline platelet count (P<0.05) when compared to controls at the time of admission. Patients with sepsis had higher values of platelet indices compared to controls at the time of admission to the ICU, however, this was not statistically significant (P>0.05) [Table1].

The cases and controls were further divided into two groups based on their SOFA score at the time of admission – those with a score < 9 and those with a score > 11. The trends in platelet count and indices in these two groups are shown in Table 2.

In patients with sepsis, there was a significant difference (P<0.05) between the baseline values of platelet counts as well as platelet indices amongst the two groups [Table 2].

There was no significant difference (P>0.05) observed between the platelet counts and indices amongst the two groups in case of controls [Table 2].

Figure 1 and Figure 2 show the results of ROC curve analysis for finding out the cut off point for

Table 1: Demographic characteristics and trends in baseline platelet counts and indices of cases and controls

	Cases	Controls	P Value
Age (years)			0.107
≤ 30	7.00%	17.90%	
31 – 45	21.00%	22.10%	
46 – 60	28.00%	26.30%	
≥ 60	44.00%	33.70%	
Sex			0.621
Males	64.00%	67.40%	
Females	36.00%	32.60%	
Period of stay in ICU (Days)	7.00 (5.00 - 11.00)	6.00 (3.00 - 11.00)	0.075
Temperature			0.001
Febrile	47.00%	23.20%	
Afebrile	53.00%	76.80%	
Respiratory rate (cpm)	21.50 (18.00 - 26.75)	20.00 (18.00 - 26.00)	0.052
Heart rate (bpm)	100.50 (88.00 - 110.00)	94.00 (82.00 - 108.00)	0.097
Hematocrit (%)	32.00 (28.25 - 38.00)	35.00 (29.00 - 42.00)	0.055
White cell count (/mm^3)	14015.00 (7802.50 - 18225.00)	10210.00 (7550.00 - 13740.00)	0.01
Prothrombin time (s)	14.20 (12.60 - 16.25)	12.80 (11.70 - 14.60)	0.001
Activated partial thromboplastin time (s)	38.75 (32.00 - 51.45)	30.00 (24.70 - 36.20)	<0.001
Platelet Count (lakhs/mm^3)	1.46 (0.595 - 2.15)	2.21 (1.34 - 2.935)	<0.001
Mean Platelet Volume (fl)	10.45 (9.40 - 11.30)	9.90 (9.15 - 10.80)	0.053
Platelet Distribution Width (%)	11.90 (10.0 - 14.35)	10.80 (9.95 - 12.20)	0.124

Table 2: Trends in platelet counts and indices among cases and controls

		SOFA score ≤ 9*	SOFA score ≥ 11*	P Value
Cases	Platelet count (lakh/mm^3)	1.715 (0.68 - 2.6475)	0.705 (0.35 - 1.1225)	0.002
	Mean Platelet Volume (fl)	10.00 (9.00 - 11.00)	11.90 (10.98 - 12.65)	<0.001
	Platelet Distribution Width (%)	11.15 (9.85 - 13.50)	15.80 (13.10 - 16.725)	<0.001
Controls	Platelet count (lakh/mm^3)	2.21 (1.425 - 2.92)	1.145 (0.375 - 3.48)	0.36
	Mean Platelet Volume (fl)	9.80 (9.20 - 10.80)	9.95 (6.30 - 10.90)	0.619
	Platelet Distribution Width (%)	10.90 (10.00 - 12.20)	10.70 (6.75 - 12.525)	0.452

*Data are median (IQR)

Table 3: Results of ROC curves of Platelet Indices

	Platelet Indices	
	Mean Platelet Volume	**Platelet Distribution Width**
Cut off point	11.2 fl	14.50%
Sensitivity	72.70%	72.70%
Specificity	84.60%	92.30%
Positive Predictive Value	57.10%	72.70%
Negative Predictive Value	91.70%	92.30%
Area Under Curve	85%	85.90%
P Value	<0.001	<0.001

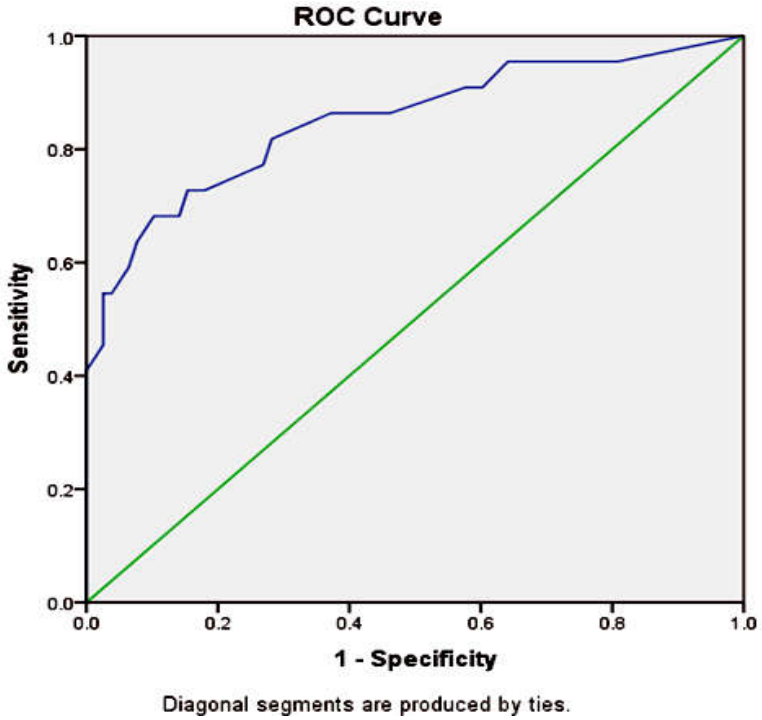

Fig. 1: ROC curve fo
Baseline Mean Platele
Volume

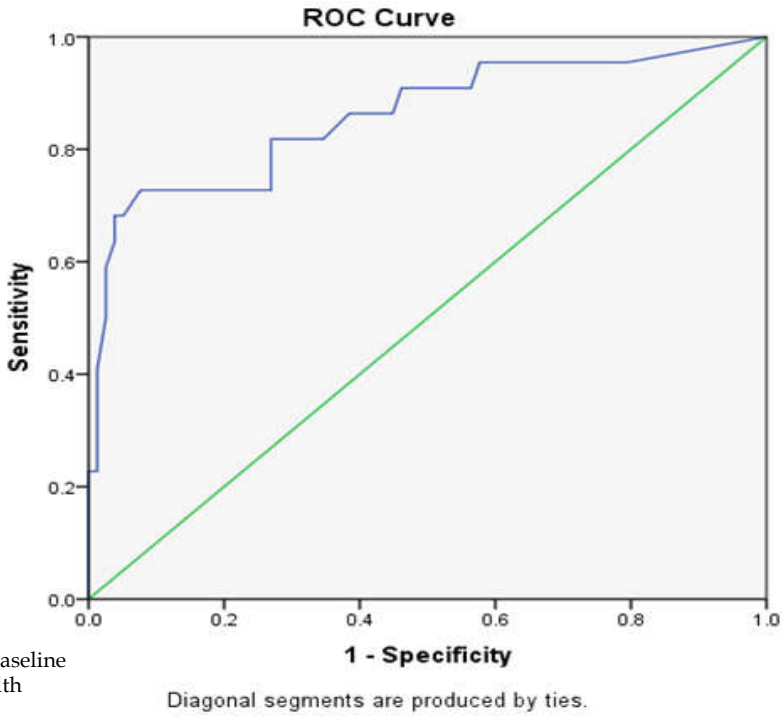

Fig. 2: ROC curve for Baseline Platelet Distribution Width

baseline platelet indices. A cut off point for MPV and PDW were 11.2 fl and 14.5% respsctively. [Table 3].

Discussion

Sepsis is a non specific inflammatory defence mechanism [10].The mortality rate of this condition varies from 25% to 80% depending on illness severity and the number of occurrences and the severity of organ failure [11,12,13]. Hence, early detection of sepsis will be useful for risk stratification and therefore, allocation of resources.

The present study is a prospective oneabout the prognostic value of changes in platelet indices in patients with sepsis or septic shock. The main findings of this study are mentioned below.

A comparison was made between the platelet counts and indices of the cases and controls. It was found that the patients with sepsis had significantly lower baseline platelet counts when compared to patients without sepsis. Also, their platelet indiceswere higher than the controls at the time of admission. This situation was probably due to endothelial damage, production of many cytokines, and bone marrow suppression in septic patients.Platelets release more than 300 proteins and small molecules from their granules, which can influence the function of the vascular wall and circulating immune cells [14]; and secrete microbicidal proteins and antibacterial peptides [8]. Platelets, also mediate leukocyte movement from the bloodstream through the vessel wall to tissues.They are capable of forming reactive oxygen species; the oxidative stress that accompanies inflammation can also activate platelets [15,16].

Their ability to influence other cells means that they can also play many principal roles in the pathophysiology of diseases [15].

Further, there was a significant difference in the platelet counts and indices between the sepsis patients with different SOFA scores. Patients with higher SOFA scores had higher MPV, increased PDW, and lower platelet count compared to patients with lower SOFA scores. Therefore, platelet indices and count can be used as a direct indicator of organ dysfunction and hence, predict mortality. MPV is a measurement of the average size of platelets found in the blood. It usually increases in cases of destructive thrombocytopenia. Normal value of MPV has been found to be between 7.5-11.5fl in previous studies [17]. The PDW increases during platelet depletion when turnover is accelerated and is an indicator of differences in platelet size. It is an indicator of variation in platelet size, which can be a sign of active platelet release. Normal values of PDW are between 10% and 17.9% [1,9].

It was found that greater baseline MPV levels, higher than 11.2fl, have moderate (72.70%) sensitivity and (84.60%) specificity can be used for determining sepsis severity.Similarly, at the time of admission, PDW levels, higher than 14.5%, with moderate (72.70%) sensitivity and high (92.30%) specificity can also be used. Amoderate positive predictive value (72.70%) supports this hypothesis too. Therefore, these indices can be used as an auxiliary test in the determination of severity of sepsis.

Findings in recent studies support our results. Van der Lelie et al showed that MPV was elevated in 13 of the 25 septicaemia patients, and returned to normal values as soon as the disease was under control [18].

Another study of 10 infected patients with thrombocytopenia, found that MPV rose at the beginning and subsequently decreased, following a biphasic change [19]. An elevation of MPV therefore suggested that the infection is invasive, systemic and uncontrolled and is related to the severity of the disease [9].

In a third study, it was concluded that MPV and PDW were significant parameters in the diagnosis of sepsis and in the differential diagnosis of sepsis and severe sepsis [1]. It was found that if PDW and MPV show increased trend while Platelet count shows a decreased trend, a poor prognosis maybe indicated in patients with septic shock [20].

The present study conducted in adults demonstrated that MPV and PDW levels were higher in sepsis patients. It was observed that PDW and MPV levels increased with increase in severity of sepsis patients. The low level of thrombocytopenia in patients with severe sepsis can explain the high levels of MPV and PDW.

Conclusion

The findings of this study suggest that platelet indices are significant indicators of severity of sepsis. Further studies are required to establish their role as prognostic markers of sepsis and septic shock. However, they can be used in addition to other established markers such as SOFA score, Acute Physiology and Chronic Health Evaluation

(APACHE) II score and C- reactive protein (CRP) to measure illness severity due to their low cost and easy accessibility. Intense supervision and aggressive treatment of sepsis patients with higher baseline platelet indices may prevent progression of disease.

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Original Research Article

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Comparative Study of Efficacy of Bupivacaine with Dexmeditomidine and Fentanyl as Adjuvant on Hemodynamic Changes in Lower Abdominal and Lower Limb Surgeries

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Abstract

Background: In regional anaesthesia and analgesia, maintaining better hemodynamic stability and minimal side effects is very much essential. A number of adjuvants have been combined with local anaesthesia's (LA) to improve the effectiveness of LA. Therefore, in the present study, the efficacy of Bupivacaine with dexmedetomidine or Fentanyl as adjuvant in maintaining better hemodynamic stability was studied. *Materials and Methods:* 60 patients of ASA group-I and II aged between 18-60 years undergoing elective lower abdominal, urologic, lower limb surgeries were selected and divided into two groups of 30 each. Group "BP" received intrathecally 12.5mg 0.5% of Bupivacaine +5 µg of dexmeditomidine while group "BF" received 0.5% Bupivacaine +12.5µg of Fentanyl. *Result:* Group-BD and in Group-BF did not differ significantly ($p>0.05$) with respect to heart rate, SBP and DBP at any interval of time. There was an insignificant variation in the side effects of anaesthesia.VAS was 0.03± 0.18 in group BD and 0.10 ± 0.31 in group BF, which was statistically in- significant. Whereas, VAS of patients anesthetized by Bupivacaine with Dexmeditomedine or Fentanyl as adjuvantwas statistically significant at 3 hours and 12 hours($p<0.05$). *Conclusion:* Bupivacaine with dexmeditomidine provided good quality of intraoperative analgesia with minimal side effectsandbetter hemodynamic stability.

Keywords: Bupivacaine; Dexmeditomedine; Fentanyl; Limb Surgeries.

Introduction

Though major advances have been made in local anaesthetic chemistry, synthesis of an ideal agent remains to be explored. An agent with a longer duration of action, shorter onset time, and a more selective site of action is sought. In lieu of finding such an ideal agent, a number of adjuvants have been combined with local anaesthesia's (LA) to improve the effectiveness of local anaesthesia's [1].

Subarachnoid block (SAB) is the most commonly used anaesthetic technique in patientsundergoing lower abdominal and lower limb surgeriesas it has the advantages of rapid onset, superior blockade, less failure rates and cost effectiveness. Being technically easier, SAB provides the optimal operative conditions with minimal intra-operative blood loss [2,3]. However post-operative pain control remains a concern as SAB using only local anaesthetic is associated with relatively short duration of action and thus early analgesic intervention is needed in the post-operative period [4].

Dexmedetomidine, an imidazole compound, exhibits a high ratio of specificity for the alpha-2 versus alpha-1 adrenergic receptor. This property makes it more effective hypnotic, sedative and analgesic agent with a more favourable pharmacodynamic profile [5]. This agent causes sedation, anxiolysis, and analgesia. Dexmedetomidine had been approved for sedation

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in adults during mechanical ventilation in intensive care unit settings [6]. There are few data addressing the use of this drug for regional anaesthesia. Further clinical trials are needed to fully determine the potential clinical application of both clonidine and dexmedetomidine in children [7].

Fentanyl is another more widely used opiates in conduction anaesthesia. This agent is combined with a local anaesthetic to act additively, if not synergistically, with LA to improve a variety of characteristics of the block. Fentanyl is a short acting opiate that is Adjuvants in Regional and Neuraxial Anaesthesia, which is stronger than morphine [8]. The side effects of using Bupivacaine are related to higher doses, as well as unintentional injection into alternative sites [9]. Absorption into the blood stream may lead to the side effects like low blood pressure, slow heart rate, strong or irregular heartbeat, and cardiac arrest, nausea, vomiting, faecal and urinary incontinence, loss of sexual function, blurred vision, ringing in the ears, and loss of joint cartilage [10]. Rare, but serious complications include decreased function of the nervous system, activation of the nervous systemresulting in seizures, paraplegia, nerve disorder, total block of spinal nerves, and respiratory arrest. Specific warnings exist about using the 0.75% dose in obstetrical anaesthesia as there have been reports of cardiac arrest [11].

Since, Bupivacaine, Dexmeditomidine and Fentanyl individually has disadvantageous as local anaesthetic agent, the present study was designed to study and compare the efficacy of Bupivacaine with Dexmeditomidine and Bupivacaine with Fentanyl as adjuvant on hemodynamic changes in lower abdominal and lower limb surgeries with the primary outcome measure as the quality of intraoperative analgesia and the secondary outcome measure as the side effects, duration and quality of post-operative analgesia.

Materials and Methods

This is a prospective observational study conducted on 60 patients of ASA physical status I/ II in the age group of 18year to 60 years of either sex, posted for elective lower abdominal, urologic, gynaecologic, lower limb surgeries, under spinal Anaesthesia after taking written informed consent. A sample size of 60 patients were recruitedin order to report significant difference with respect to efficacy of the drugs. Approval from the hospital ethical committee was taken prior to the study. Patients were randomly divided into two groups of 30 each by lottery method. Patients were divided into two groups. Group BD: Received intrathecally 12.5mg of 0.5% hyperbaric Bupivacaine with 5 μg of Dexmeditomidine as adjuvant. Group BF: Received intrathecally 12.5mg of 0.5% hyperbaric Bupivacaine with 25μg of Fentanyl as adjuvant. Maximum level of spinal anaesthesia was achieved in both the groups.

Patient refusal, ASA grade III & IV, Patients with dependency of narcotic, patients with gross spine anomalies and localized skin lesions, Patients with cardiac, Pulmonary, hepatic or renal disorders, Patients having inadequate subarachnoid blockade and who were later supplemented by general anaesthesia were excluded from the study.

Visual Analogue scores of patients, Heart Rate at different interval of time, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) in mm Hg and other side effects were recorded as end points in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant.

Post operatively, monitoring of vital signs, VAS scores were continued every 30 minutes until the time of regression of sensory block to L_1 dermatome. The duration of surgery was 45±5.0 minutes in any of the patients. The heart rate, Blood pressure and the side effects were recorded. Monitoring of Heart Rate, Systolic blood pressure and Diastolic blood pressure in postoperative period was recorded and reported as hypotension and bradycardia. The incidence of hypotension (arterial blood pressure <20% baseline) was recorded and treated with injection Mephenteramin 5 mg intravenous increments. Bradycardia (pulse rate <50/M) was recorded and treated by inj. Atropine 0.6mg intravenously. Catheterisation was done in all urological procedures.

Statistical Analysis

Thedemographic data were analysed by student 't' test and qualitative data were analysed by chi-square test. All values were expressed as mean±standard deviation. P<0.05 was considered statistically significant.

Results

The mean age of patient in group BD was 38.6±11.8 and in group BF was 38.3±12.8. This difference was insignificant (p=0.89). In both the groups, there were 20 males and 10 females. There

was no significant difference in Height and weight characteristics of patients (p>0.05, Table 1).

Intraoperative Visual Analogue Scale (VAS) score was 0.03±0.18 in group BD and in group BF it was 0.10±0.31, which was statistically not significant (p>0.05 Table 2). Whereas, VAS scores of patients anesthetized by Bupivacaine with Dexmeditomedine or Fentanyl as adjuvantwas statistically significant at 3 hours and 12 hours (p<0.05) implying that patients in group BD had better pain relief than the patients in BF group in postoperative period (Table 2).

The two groups did not differ significantly (p>0.05) with respect to heart rate at any interval. In group BD two patients had bradycardia which was treated by 0.6 mg atropine. No incidence of bradycardia in group BF (Table 3).

The two groups did not differ significantly (p>0.05) with respect to systolic blood pressure (Table 4) diastolic blood pressure (Table 5) at different interval of time. The usual side effects of anaesthesia like nausea, vomiting, pruritus, respiratory depression, hypotension, bradycardia and urinary retention were recorded in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant. These side effects did not show much variation between each group (Table 6).

Table 1: Demographic Profile of patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant N=60

Parameter	Group BD	Group BF	t	P value
Age (Y)	38.6 ±11.8	38.3 ±12.8	0.1335	0.89 NS
Sex M/F	20:10	20:10	-	-
Height (Feet)	5.49 ±0.31	5.46 ±0.35	0.37	0.71 NS
Weight (KG)	56.2 ±6.7	58.1 ±8.4	0.99	0.33 NS

Values are expressed as Mean ± S.D, NS = Not Significant.

Table 2: Visual Analogue Scale (VAS) scores of patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant N=60

Time	Group BD	Group BF	t	P value
Intraoperative VAS	0.03 ±0.18	0.10 ± 0.31	1.03	0.32 NS
Post op 3 hrs	0.07 ± 0.25	`0.73 ± 1.05	3.39	<0.05 S
Post op 6 hrs	2.93 ± 1.41	3.03 ± 0.89	0.33	0.75 NS
Post op 12 hrs	5.80 ± 0.89	6.30 ± 0.84	2.25	<0.05 S

Table 3: Heart Rate at different interval of time in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant. N=60

Time interval in (Minutes)	Group BD (mean ± SD)	Group BF (mean ± SD)	t	P value
0	82.0 ± 7.4	80.9 ± 11.6	0.43	0.67 NS
5	77.1 ± 8.7	78.5 ± 11.2	0.52	0361 NS
10	73.9 ± 7.8	74.8 ± 9.3	0.44	0366 NS
15	71.0 ± 7.5	73.3 ± 10.2	1.00	0.32 NS
20	70.5 ± 7.31	73.5 ± 12.4	1.12	0.27 NS
30	73.1 ± 5.4	73.9 ± 9.6	0.38	0.70 NS
120	75.2 ± 4.8	76.3 ± 8.8	0.58	0.56 NS

Table 4: Systolic Blood Pressure (SBP) in mmHg in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant. N=60

Time interval in (Minutes)	Group BD (Mean ± SD)	Group BF (Mean ± SD)	t	P value
0	130.0 ± 9.7	133.0 ± 12.5	1.00	0.32 NS
5	120.1 ± 12.1	123.1 ± 14.9	0.85	0.46 NS
10	112.5 ± 11.6	118.4 ± 15.0	1.70	0.09 NS
15	110.9 ± 11.7	114.6 ± 13.0	1.16	0.25 NS
20	112.4 ± 9.7	114.7 ± 10.8	0.87	0.39 NS
30	114.0 ± 9.0	116.7 ± 9.5	1.14	0.26 NS
120	120.5 ± 8.8	121.5 ± 9.3	0.43	0.67 NS

Table 5: Diastolic Blood Pressure (DBP) in mm Hg in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant. N=60

Time interval in (Minutes)	Group BD (Mean ± SD)	Group BF (Mean ± SD)	t	P value
0	81.2 ± 7.94	78.9 ± 7.9	1.12	0.27
5	72.5 ± 8.4	73.4 ± 6.7	0.46	0.65
10	67.5 ± 9.4	69.0 ± 7.4	0.72	0.47
15	66.5 ± 8.3	69.0 ± 7.6	1.22	0.23
20	68.5 ± 6.7	70.1 ± 6.8	0.92	0.36
30	71.0 ± 4.5	72.9 ± 6.0	1.44	0.16
120	76.5 ± 4.4	74.2 ± 6.8	1.56	0.12

Table 6: Side Effects recorded in patients anesthetized by Bupivacaine with Dexmeditomidine or Fentanyl as adjuvant. N=60

Adverse effects	Group BD N (%)	Group BF N (%)
Nausea	1 (3.33%)	2 (6.56%)
Vomiting	0	1 (3.33%)
Pruritus	0	1 (3.33%)
Respiratory Depression	0	0
Hypotension	3 (1. %)	2 (6.6%)
Bradycardia	2 (6.6%)	0
Urinary retention	1 (3.33%)	2 (6.6%)

Discussion

Opioids added to local anaesthetics for spinal anaesthesia improve the quality of intraoperative analgesia and also provide post-operative pain relief for longer duration [8]. There is antinociceptive synergism between intrathecal opioids and local anaesthetic during visceral and somatic nociception. Fentanyl, a lipophilic opioid has rapid onset of action following intrathecal administration. It does not tend to migratetofourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally. A common problem during lower abdominal surgeries under spinal anaesthesia is visceral pain, nausea, vomiting [9]. The addition of Fentanyl to hyperbaric Bupivacaine improves quality of subarachnoid block [10]. The disadvantages with opioids are pruritus and respiratory depression. The advantage of selective α-2 agonist is that it produces prolonged postoperative analgesia with minimal side effects [11-13]. There were no significant differences in the demographic profile of the studied groups.

The mean duration of effective analgesia (timeup to first pain medication) in BD group was 362.7 minutes while it was 210.8 minutes in BF group. These results are comparable with the previousstudies [4,5].

VAS at end of 3 hours in the group BD was 0.07 while it was 0.73 in group BF. VAS at the end of 12 in group BD was 5.80 while it was 6.30 in BF group. VAS scores were statistically significant at 3 hours and 12 hours implying that patients in group BD had better pain relief (lower VAS) in postoperative period than the patients ingroup BF. Addition of dexmedetomidine to intrathecal Bupivacaine results is significantly prolonged duration of analgesia and the time to first pain medication is longer with improved quality of analgesia and reduced requirement of analgesics postoperatively as compared to intrathecal Bupivacaine with Fentanyl.

Heart rate (HR). The two groups did not differ significantly with respect to HR at any interval. In group BD two patients had bradycardia which was treated by 0.6 mg Atropine intravenously. No incidence of Bradycardiaoccured in group BP. Rajni Gupta et al [14] in their study have concluded that one patient had developed bradycardia in dexmeditomedine group and no patient developed bradycardia in Fentanyl group. Gehan A Tarbeeh et al [15] showed in their study that there was no statistically significant difference in the groups. Al. Ghaneem SM et al [11] who have concluded that there was no significant difference in HR the groups where incidences of bradycardia were 2 and 3 in dexmeditomedine and Fentanyl groups respectively.

In our study, the two groups did not differ significantly with respect to mean systolic and mean diastolic pressure. Three patients in BD and two patients in BF group developed hypotension which was not statistically significant. Hypotension in both

the groups was treated with small doses of Mephenteramin. These results are comparable with the studies of Rajni Gupta et al [14], Ghaneem SM et al [11] and Gehan A. Jarbech et al [15]. Haemodynamic profile of the patients was found to be stable throughout the intra operative period in both the groups.

In group BD, 10% patients had hypotension, 6.5% patients had bradycardia, 1% had nausea and 1% patient had urinary retention. In group BF 6.6% had hypotension and urinary retention, 6% of patients had nausea, 3.3% of patients had vomiting and pruritus. Catheterisation was done in all urosurgical procedures. Studies of Rajni Gupta et al [14] and Al Ghaneem et al [11] also show similar side effects which are comparable with our studies. Though the inclusion criteria were up to 60 years, patients recruited in our study were below 50 years. So, absence of geriatricpopulationwas the limitation of the study.

Conclusion

Bupivacaine with dexmeditomidine provided good quality of intraoperative analgesia with minimal side effects, longer duration and excellent quality of post-operative analgesia than Bupivacaine with fentanyl. Therefore, from this study, it can be concluded that 5µg dexmeditomidine seems to be an attractive alternative to fentanyl as an adjuvant along with bupivacaine in surgical procedures of lower abdomen and lower limbs.

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Original Research Article

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Comparison of Nitroglycerine and Dexmedetomidine for Inducing Controlled Hypotension in Functional Endoscopic Sinus Surgery (FESS)

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Abstract

Background and Aims: Induced hypotension reduces blood loss during functional endoscopic sinus surgery (FESS), provides better surgical field visibility and minimizes the incidence of major complications. We aimed at comparing nitroglycerine (NTG) and dexmedetomidine for inducing controlled hypotension in patients undergoing FESS. *Material and Methods:* Sixty adult patients of ASA physical status I or II, undergoing FESS under general anaesthesia were randomly allocated to two groups of 30 patients each. Group N received NTG infusion at the rate of 0.5-5 mcg/kg/min while Group D patients received a loading dose of Dexmedetomidine 1mcg/kg/min followed by an infusion at the rate of 0.2-0.7 mcg/kg/hr. The infusions were titrated to maintain mean arterial pressure (MAP) in the range of 65-75 mm Hg in both the groups. The visibility of surgical field was assessed by the surgeon using Average Category Scale (ACS) scores. The haemodynamic parameters, rescue fentanyl usage, emergence time and time to first postoperative analgesic request were recorded. *Results:* The desired MAP (65-75mm Hg) could be achieved in both the groups. No significant intergroup differences were observed in ACS scores. The mean heart rate was significantly lower in Group D at various time intervals ($P<0.05$). Rescue fentanyl usage was significantly lower in Group D. Emergence time was significantly lower in Group N. Time to first analgesic request was significantly longer in Group D. *Conclusion:* Dexmedetomidine is comparable to Nitroglycerine for inducing controlled hypotension in FESS and provides good operative field visibility. Dexmedetomidine has the added advantage of reducing perioperative analgesic requirements.

Keywords: FESS; NTG; Dexmedetomidine; Controlled Hypotension; ACS Score.

Introduction

Functional endoscopic sinus surgery (FESS) is a minimally invasive surgical technique utilized to treat medically refractory chronic rhino sinusitis with or without polyps or recurrent acute rhino sinusitis [1]. Good visibility during FESS is necessary because of tiny nasal anatomical structures, which are full of vessels and limit the nasal endoscopic access. Major complications like Cerebrospinal fluid (CSF) leak, injury to orbit and its adnexa, ethmoidal artery transection etc have been reported for FESS under general anaesthesia resulting from impaired visibility due to excessive bleeding [2]. An important technique to reduce bleeding during the surgery is hypotensive anaesthesia which is a state of inducing controlled hypotension to reduce bleeding and improve the surgical site visibility, adjusted to the patient's age, preoperative blood pressure and past medical history [3]. In hypotensive anaesthesia, patient's mean arterial blood pressure (MAP) is reduced by 30% of baseline or kept at 60-70 mm Hg [3,4]. Various agents e.g., ganglion blocking drugs (hexamethonium [5], trimethaphan [6] and pentolinium [7]), vasodilators (sodium nitroprusside [8], nitroglycerine [9] (NTG)), high doses of potent inhaled anaesthetics [10], beta adrenergic antagonist [11], calcium channel blockers [12] and magnesium sulphate [13] have been used

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to achieve controlled hypotension. Of these agents, inhaled anaesthetics, short acting beta blockers and NTG are in common clinical practice at present. NTG has been used since many years to induce hypotension in developing countries in view of its easy titratability, limited interaction with anaesthesia drugs and low cost [14].

Dexmedetomidine is a potent and highly selective α_2 adrenergic receptor agonist. It has sedative, amnesic, analgesic, anaesthetic sparing effect and sympatholytic properties [15]. The central and peripheral sympatholytic action of dexmedetomidine is mediated by α_2 adrenergic receptors and is manifested by dose-dependent decrease in arterial blood pressure, heart rate (HR), cardiac output and nor epinephrine release [16,17].

We felt that dexmedetomidine would be a good addition to the list of drugs used for hypotensive anaesthesia because of its favourable pharmacological actions (reduction in BP and HR). Hence we conducted a prospective randomized study in which we compared the efficacy of dexmedetomidine to produce induced hypotension in FESS with that of NTG. The secondary goal was to compare the two agents with regard to visibility of surgical field, recovery profile and need for perioperative analgesia.

Materials and Methods

After obtaining Institutional Review Board approval and patients'written informed consent, this prospective, randomized study was conducted in Saveetha Medical College Hospital, on 60 healthy patients who underwent elective FESS under general anaesthesia. Patients of ASA physical status I & II of either sex, aged 18- 60 years were included in this study. Patients with major hepatic, renal or cardiovascular dysfunction, bleeding disorders, pregnancy and patients on anticoagulant medication were excluded from the study. Patients were allocated randomly to one of the two groups (Group N or D, n= 30 in each group) by a computer generated random number. Patients received NTG in Group N for controlled hypotension while in Group D, Dexmedetomidine was used for the same.

All patients were kept nil oral the night before surgery and received oral Diazepam 5 mg at night before surgery and 3 hours before surgery. In the operating room, patient was connected to electrocardiogram (ECG), non-invasive blood pressure (NIBP), end tidal carbondioxide ($ETCO_2$) and pulse oximetry (SpO_2) monitors. An 18G cannula was inserted with 3 way adaptor for infusion of intravenous fluids and dexmedetomidine / NTG. After preoxygenation for 3 minutes, anaesthesia was induced with fentanyl 2mcg/kg, propofol 2mg/kg and vecuronium 0.1mg/kg. Endotracheal (ET) intubation was done with a suitable cuffed ET tube. Oropharyngeal pack was kept. Patient was positioned in 15 degree reverse Trendelenberg position, mechanically ventilated and anaesthesia was maintained with isoflurane 1% along with 66% Nitrous oxide (N_2O) and 33% Oxygen (O_2). Muscle relaxation was maintained with vecuronium top ups.

In group D, all patients received a loading dose of dexmedetomidine 1mcg/kg (over10 minutes) before induction of anaesthesia followed by a maintenance infusion at the rate of 0.2-0.7 mcg/kg/hr which was started after the placement of oropharyngeal pack. In group N, NTG infusion was started after the placement of oropharyngeal pack and maintained at the rate of 0.5-5 mcg/kg/min and continued till the end of the procedure. In both the groups, infusions were titrated between ranges to attain target MAP of 65- 75mm Hg and signs of inadequate anaesthesia like increase in the MAP greater than the target MAP or somatic responses (movement, tearing or sweating) were treated with additional dose of fentanyl.

The systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, heart rate (HR), SpO_2 and $ETCO_2$ of all patients were recorded at baseline prior to drug infusion and during the hypotensive period every 5 minutes. The operation site was evaluated by the surgeon throughout the procedure. Intraoperative blood loss was estimated by assessment of suction bottle & swab counting. Quality of surgical field was assessed by the surgeon using Average Category Scale (ACS) based on previous studies by Fromme et al [18] and Boezaart et al [19].

Infusions and isoflurane were stopped at the end of surgery (nasal packing). Residual neuromuscular block was antagonized with neostigmine 50µg/kg & glycopyrrolate 10µg/kg. Awakening time following reversal was noted and patient was extubated awake with intact airway reflexes after thorough oropharyngeal suctioning. The time of requirement of first dose of post operative analgesia was also recorded.

Statistical Analysis

Sample size was estimated to be 20 in each group for a power of 80% at 5%significant level based on previous studies. This was increased to 30 in each

group to account for possible dropouts. Statistical analysis was done using SPSS 20 software. The parametric data (age, haemodynamic parameters [HR, SBP, DBP and MAP], duration of surgery, intraoperative blood loss, Average Category Scale for surgical field, first dose of post-operative analgesia requirement and emergence time) were expressed as mean and standard deviation and analysed using Independent unpaired t-test. Sex of the patients and intraoperative rescue fentanyl usage were expressed as percentage and analyzed using Chi-square test. P value of <0.05 was considered statistically significant.

Results

Patients in both the groups were comparable in terms of age, sex, height and weight (Table 1). There were no statistically significant differences between the two groups with regard to systolic, diastolic or mean blood pressures recorded and the duration of surgery. The heart rates recorded at various time intervals (15, 20, 30, 35, 40, 45, 50, 55, 60, 70, 80, 85, 90, 95 and 100 minutes after induction) were significantly lower in Group D compared to Group N. The amount of blood loss intraoperatively in group D was significantly lower compared to group N (31.67±6.47 ml versus 37.83±10.39ml). The Average Category Scale (ACS) for quality of surgical field was comparable in both the groups (2.07±0.25 in Group D versus 2.23±0.51 in Group N). Mean intraoperative rescue fentanyl usage was significantly lower in group D than group N (3.3% versus 20.0%). Time recorded to first analgesic request was significantly longer in group D than group N (62.17±22.46 min versus 32±10.22 min). Emergence time was significantly longer in group D than group N (19.03±6.57 min versus 10.93±4.89 min) (Tables 2 & 3, Figures 1& 2).

Discussion

In our prospective randomized study of comparing dexmedetomidine and NTG, we found that both drugs were effective in achieving a MAP of 65 to 75 mmHg and provided a dry surgical field as suggested by the ACS scores during FESS. In this study, we had chosen a target MAP of 65-75 mmHg to provide the best surgical conditions without the risk of tissue hypoperfusion based on a review of

Table 1: Demographic Data

	Group N (30)	Group D (30)	P value
Age (years) *	33.97±10.19	31.60±10.65	0.383
Sex male/female count	14/16	16/14	0.606
Height (cm) *	163.83±4.17	162.57±5.19	0.302
Weight (Kg) *	67.83±7.7	64.33±9.07	0.113

* Mean ± Standard deviation

Table 2: Intraoperative and Postoperative Parameters

	Group N (30)	Group D (30)	P value
Duration of Surgery (minutes) *	85±16.81	87.5±21.68	0.620
Intraoperative Blood loss (ml) *	37.83±10.39	31.67±6.47	0.008
Average Category Scale *	2.23±0.51	2.07±0.25	0.111
Rescue Fentanyl usage (number of patients & percentage)	6(20%)	1(3.3%)	0.044
Time to first analgesic request (minutes) *	32±10.22	62.17±22.46	0.000
Emergence Time (minutes) *	10.93±4.89	19.03±6.57	0.000

* Mean ± Standard deviation

Table 3: Average Category Scale

Grading	Explanation	Number of patients Group N	Number of patients Group D
0	No bleeding (cadaveric conditions)	0	0
1	Slight bleeding, no suctioning required	1	0
2	Slight bleeding, occasional suctioning required	21	28
3	Slight bleeding, frequent suctioning required; bleeding threatens surgical field a few seconds after suction is removed	8	2
4	Moderate bleeding, frequent suctioning required and bleeding threatens surgical field directly after suction is removed	0	0
5	Severe bleeding, constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible	0	0

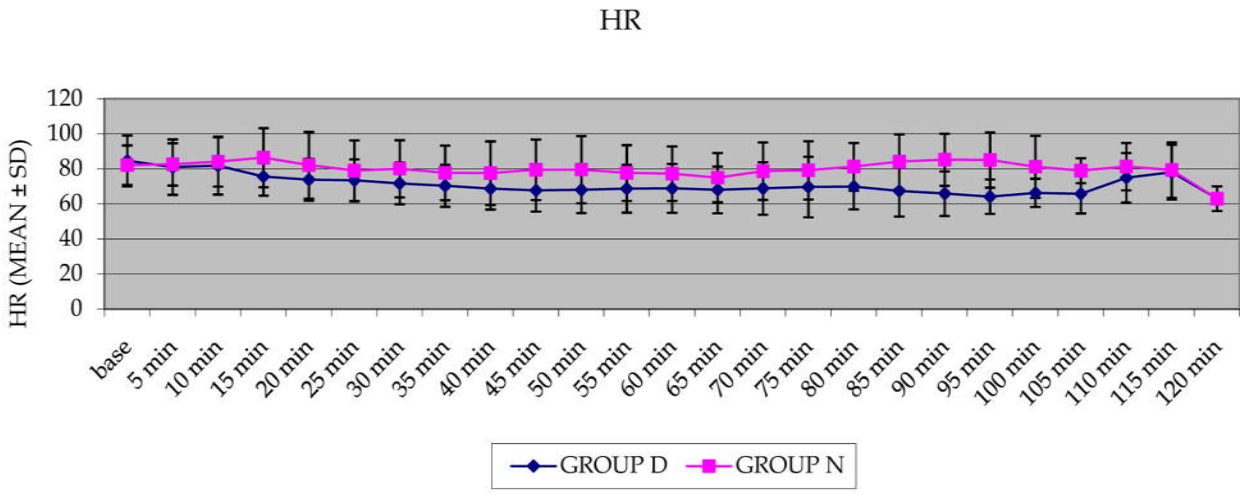

Fig. 1: Heart rate

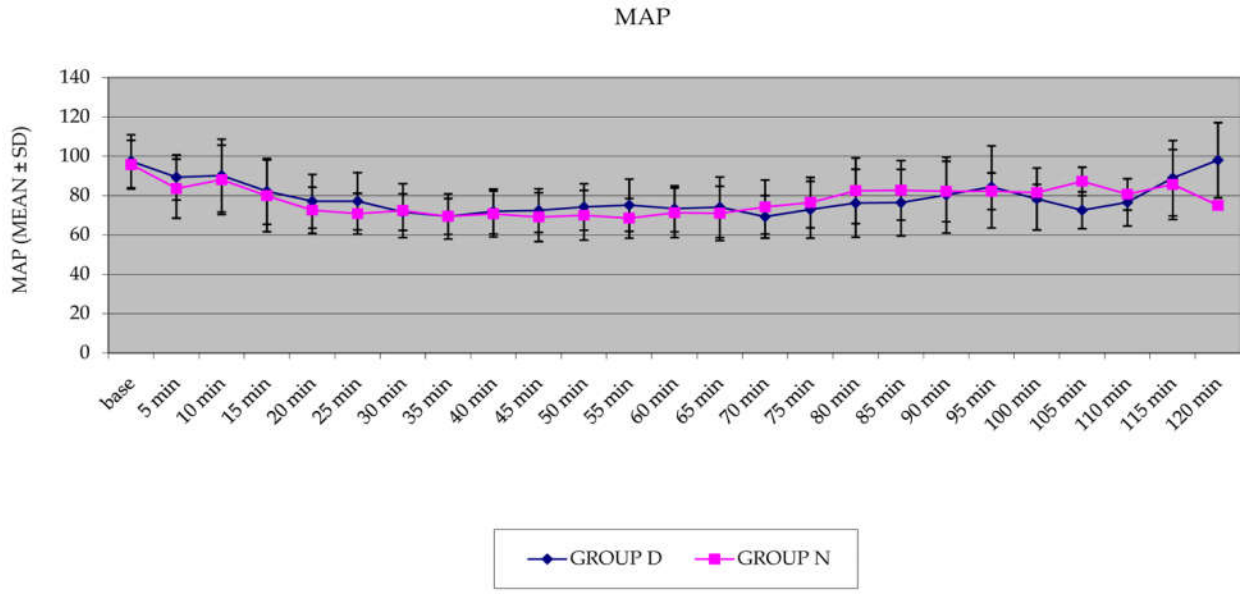

Fig. 2: Mean Arterial Pressure

literature published by Barak et al [20], in which the authors have recommended a MAP of 50 to 65 mmHg during major maxillofacial surgeries. Boezaart et al [19] demonstrated hypotensive anaesthesia induced by sodium nitroprusside or NTG in mandibular osteotomy to achieve MAP of 60-70 mm Hg and found to be absolutely safe and associated with no significant increase in pyruvate, lactate or glucose levels.

In our study, patients who were treated with dexmedetomidine (Group D), had hypotension comparable to Group N. However Group D patients had significant decrease in heart rates at various time intervals compared to Group N. This could be attributed to the known sympatholytic effect of α_2 agonists. Basar et al [21] investigated the effect of single dose of dexmedetomidine 0.5 mcg/kg administration 10 minutes before induction of anaesthesia and reported significant reduction in MAP and HR.

In a study conducted by Durmus et al [22], patients who received dexmedetomidine infusion for controlled hypotension during tympanoplasty and septorhinoplasty, had significant reduction in MAP and HR compared to placebo group.

The amount of blood loss intraoperatively in group D was significantly less compared to group N (31.67 ml versus 37.83 ml) in our study. Though there was a statistcally significant difference, the values clearly show that the difference was not clinically significant.

The ACS score for quality of surgical field was comparable in both the groups (2.07 in Group D versus 2.23 in Group N). The efficacy of dexmedetomidine in providing good surgical conditions and reduced blood loss during controlled hypotension has been previously reported by Durmus et al [22] during tympanoplasty and septorhinoplasty. Guven et al [23] reported better haemodynamic stability, visual analogue scale for pain and clear surgical field with lesser side effects in dexmedetomidine group than placebo group when FESS was done under either conscious sedation or local anaesthesia.

In our study, NTG administration provided a stable course of controlled hypotension and a good surgical field as evidenced by favourable ACS scores. Cincikas and Ivaskevicius [24] used NTG infusion (0.79±0.34 μg/kg/min) to maintain MAP of 50-60 mmHg during endoscopic nasal surgery and observed reduced surgical bleeding and improved surgical view quality.

Intra-operative rescue fentanyl usage was significantly less in dexmedetomidine group compared with N group. It has been previously reported by Scheinin et al [25] that premedication with dexmedetomidine reduces the intraoperative requirement of fentanyl.

Our study also demonstrated prolonged postoperative analgesia in dexmedetomidine group. This is in accordance with a study conducted by Gurbet et al [26] who reported that intraoperative infusion of dexmedetomidine reduces peri-operative analgesic requirements.

Dexmedetomidine has sedative and analgesic sparing effects via central actions in the locus ceruleus and in the dorsal horn of the spinal cord [27]. Dexmedetomidine group in our study was associated with significantly longer emergence time compared to NTG group. Delayed emergence associated with Dexmedetomidine has been previouslyreported by Kol et al [28] in tympanoplasty and by Bajwa et al [29] in FESS.

Conclusion

With the strength of literature evidence available and based on our study, we feel that dexmedetomidine is an effective alternative to NTG for inducing hypotension in FESS and thereby improving surgical visibility and surgeon satisfaction. Dexmedetomidine has the added advantage of reducing perioperative analgesic requirements.

Conflict of Interest: None to declare.

Key Messages

Dexmedetomidine improves surgical field visibility during FESS comparable to NTG and reduces perioperative analgesic requirements.

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A prospective Randomized Double-Blind Study Comparing Adrenaline vs. combination of Adrenaline and Dexmedetomidine in Local Infiltration Block for Ear and Nose Surgeries

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Abstract

Background and Aims: For the achievement of clear bloodless surgical field, local infiltration of adrenaline is used routinely in Ear, Nose and Throat (ENT) surgeries. The present study was intended to study effectiveness of the addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline and any adverse effect associated with it. *Methods:* We recruited 80 patients in the age group of 18-65years by randomization posted for tympanoplasty or septoplasty under general anesthesia and divided into two groups of 40 each. Group A received local infiltration of 11.5ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml normal saline while Group D received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml (50μg) of dexmedetomidine. Monitoring involved-Heart rate, Blood pressure, Intraoperative surgical bleeding and Surgeon's satisfaction score. Intraoperative isoflurane and fentanyl requirement was calculated. Student's *t*-test was used for analysing statistical significance in time related variables. *Results:* Intraoperative tachycardia and hypertension which was seen after infiltration of solution of lignocaine and adrenaline was found to be abolished by addition of dexmedetomidine. Also dexmedetomidine containing solution significantly decreased intraoperative bleeding and thus increased surgeon's satisfaction. Isoflurane and fentanyl requirement was significantly reduced in study group. *Conclusion:* Addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline in ear and nose surgeries provides a good quality surgical field with stable haemodynamics with decreased requirement of other agents for the purpose of clear field, enhancing safety of the procedure and patient and cost effectiveness.

Keywords: Adrenaline; Clear Bloodless Surgical Field; Dexmedetomidine; Hypotensive Anesthesia.

Introduction

Requirement of clear bloodless surgical field in ENT surgeries is gaining popularity day by day. Even a minor bleeding in the field can lead to loss of precision in these surgeries. Anaesthetist in addition to providing anesthesia has to provide a clear bloodless surgical field in these surgeries, which can be achieved with hypotensive anesthesia using various physical and pharmacological methods [1,2]. In addition to that local infiltration of adrenaline is used routinely in ENT operation theatre. But these methods have their own demerits like danger of tissue hypoxia in case of controlled hypotension and toxic circulatory effects like hypertension and arrhythmias that ensue after systemic absorption of local adrenaline [3]. So, to provide safe and satisfactory anesthesia, it is necessary to avoid systemic side effects of local adrenaline, avoid administration of hypotensive anesthesia and still to have better surgical conditions of operatability.

To satisfy above requirements, we studied the effectiveness of addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline after obtaining approval from the Hospital Ethics Committee along with written informed consent from the patients. The study was

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intended to study the effect on baseline heart rate, blood pressure, quality of surgical field and hence surgeon's satisfaction, requirement of anaesthetic and other agents and any other adverse effect of the drug.

Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic and analgesic properties [4,5] which has been described as a useful and safe adjunct in many clinical applications. Dexmedetomidine is the pharmacologically active dextro enantiomer of medetomidine, the methylated derivative of etomidine. It is considered primarily as α-2 adrenoceptor agonist, but also incorporates an imidazoline structure, thus having an agonist effect on imidazoline receptors.

Dexmedetomidine is chemically related to clonidine, but is approximately eight times more specific for α-2 adrenoceptors with α-2:α-1 selectivity ratio of 1600:1, compared with 220:1 for clonidine, especially for the 2a subtype, which makes dexmedetomidine more effective than clonidine for sedation and analgesia.

There are three types of α-2 isoreceptors - α-2a, α-2b, α-2c,which bind to α-2 agonists and antagonists with similar affinities and share an amino acid composition homology of approximately 70-75%. α-2a receptors appears to promote sedation, hypnosis, analgesia, sympatholysis, neuroprotection and inhibition of insulin secretion. Agonism at α-2b receptor suppresses shivering centrally, promotes analgesia at spinal cord sites and induces vasoconstriction in peripheral arteries. The α-2c receptor is associated with modulation of cognition, sensory processing, mood and stimulant induced locomotor activity and regulation of epinephrine outflow from the adrenal medulla. Inhibition of norepinephrine release appears to be equally affected by all 3α-2 subtypes [5].

Materials and Methods

After obtaining approval from the Hospital Ethics Committee along with written and informed consent from patients, 80 adults (18-65yrs) of either sex belonging to American society of Anaesthesiology (ASA) physical status class I and II and scheduled for Tympanoplasty and Septoplasty under general anesthesia, were enrolled in this prospective, randomized and double blind study. We excluded patients with organ dysfunction, allergy to any drug used, coagulation disorder, local infection at the site of block.

Patients were randomly divided into two groups of 40 patients each by computer generated random table number. Out of those 40 patients in each group, 20 underwent Tympanoplasty and remaining 20 underwent Septoplasty under general anesthesia. Patients of Group A received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml normal saline while Group D received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml (50μg) of dexmedetomidine. A standardized technique of infiltration administered by the same surgeon which provided reliable distribution of solution and eliminated operator bias was used. In case of tympanoplsty, infiltration was given in postauricular area to block greater auricular and lesser occipital nerves, in the incisura terminalis to block auriculotemporal nerve and the four quadrants of the external auditory canal and in case of septoplasty it was given under mucoperichondrium and mucoperiosteum.

All patients were admitted prior to the day of surgery and investigated for haemoglobin, bleeding and clotting time, urine examination, electrocardiogram (ECG). On arrival to the operation theatre, fasting of eight hours was confirmed. Written informed consent for surgery and anesthesia was taken. Intravenous (iv) line was secured by 18/20G cannula and ringer lactate solution was used as maintenance fluid. Baseline systemic blood pressure (BP), heart rate (HR), peripheral oxygen saturation (SpO2) and ECG were recorded using Philips MP 40 monitor. Patients were premedicated with Inj glycopyrrolate 5μg/kg intramuscular (im) 30 min before induction. Inj ondansetron 0.08mg/kg IV, inj midazolam 0.03mg/kg iv and inj fentanyl 1μg/kg iv were given just before induction of anesthesia. Inj hydrocortisone 2mg/kg and inj dexamethasone 0.2mg/kg iv was given in case of nasal surgeries.

After preoxygenation for 3 min, anesthesia was induced with inj thiopentone sodium 5mg/kg iv. Tracheal intubation with proper size endotracheal tube was facilitated with inj succinylcholine 2mg/kg iv under direct laryngoscopy.

Anesthesia was maintained with 50% nitrous oxide in oxygen and isoflurane dial concentration was titrated to achieve Fromme Boezaart scale of bleeding ≤2. Patients were ventilated manually with Bains circuit to maintain end tidal concentration of CO2 (EtCO2) between 30-35 mm Hg. Surgeon was asked to infiltrate locally at surgical site before tissue dissection. Operating surgeon or monitoring anaesthetist involved in data collection were not aware of the study solution.

Intraoperatively, heart rate, blood pressure, EtCO2, SpO2, temperature were monitored and recorded immediately after infiltration at 0min till 30min at 5min intervals and thereafter every 15min interval. Concentration of isoflurane was recorded in terms of percentage and total duration of set dial percent concentration was recorded. From these values total isoflurane volume required in ml was calculated by Dion's formula. Intraoperative surgical bleeding was assesed by Fromme Boezaart scale (0-6) and surgeon's satisfaction about field was graded as poor to excellent (1-5). Any adverse haemodynamic event was recorded and treated. Bradycardia (HR<50) was treated with atropine 0.6mg iv. Tachycardia (HR ≥ 20% of basal values) was treated with 50µgm increments of fentanyl. Hypotension or hypertension were defined as >30% changes in systolic blood pressure from basal values. Hypotension was treated with reducing isoflurane concentration to the minimum level of adequate plane of anesthesia (BIS 40-60) and if still not corrected iv fluids and mephentermine 6mg iv bolus were given. Hypertension was treated by increasing concentration of isoflurane.

Fromme Boezaart Scale for surgical bleeding [6,7] is; 0 – No bleeding, 1– Slight bleeding, no suctioning of blood required, 2– Slight bleeding, occasional suctioning required, surgical field not threatened, 3 –Slight bleeding, frequent suctioning required, bleeding threatens surgical field a few seconds after suction is removed, 4 – Moderate bleeding, frequent suctioning required, bleeding threatens surgical field directly after suction is removed, 5 – severe bleeding. Surgeon's Satisfaction was graded as; 1 – Poor, 2 – Good, 3 – Better, 4 – Best, 5 – Excellent. Dion's formula [8]- for calculation of total usage of volatile anaesthetics in ml = (Dialed conc. × Total fresh gas flow × Duration at that conc. × Mol. wt) / (2412 × Density).

(Conc = Concentration; Mol.wt= Molecular weight). In case of isoflurane, Molecular weight is 184.5 gm/mol and Density is 1.496 gm/ml. After surgery the residual neuromuscular blockade was antagonised with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg iv. Patients were extubated after observing adequate motor recovery and spontaneous breathing efforts. Patients were transferred to post anesthesia care unit for observation of any respiratory depression, haemodynamic changes, nausea and vomiting.

Statistical Analysis

The recorded data were tabulated and expressed in mean±standard deviation (SD). Statistical analysis was performed using SPSS for Windows software package (version 21.0, IBM Corp., Armonk, NY, USA). The demographic data for categorical variables were compared using Chi-square test. Student's *t*-test was used for analysing statistical significance in time related variables. $P < 0.05$ was considered as statistically significant.

Primary outcome of the study was quality of surgical field measured by Fromme Boezaart Scale. To detect 15% difference between two groups with 80% power and 5% significance level, sample size required was 32 patients in each group but considering dropout and to enable detection of potential variations, we included 40 patients in each group. This sample size was calculated based on a pilot study in the beginning of our study.

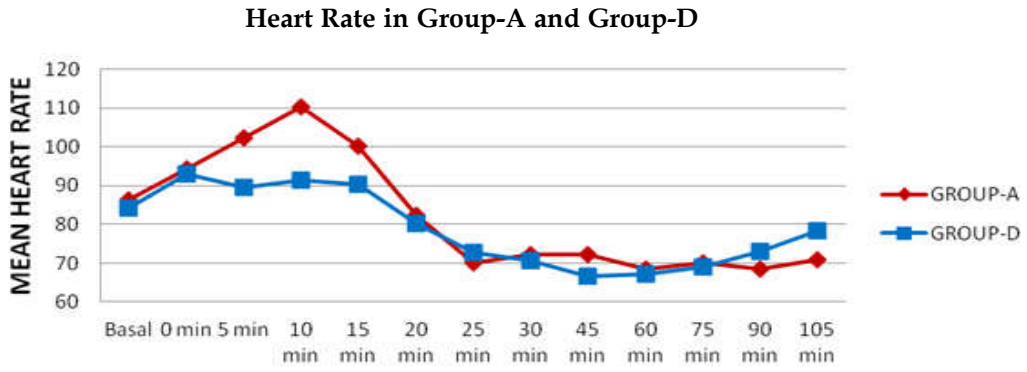
Results

The study was completed successfully in 80 patients. The demographic data of Patients i.e. age, Sex, weight, ASA physical status and surgical duration were comparable between the groups (Table 1). The baseline Heart Rate and Mean Arterial Pressures (MAP) were comparable between two groups. Heart Rate values were statistically significant at 5, 10, 15, 45 and after 90 minutes of surgeries in group-D (Figure 1). MAP were statistically significant at 5, 10, 15, 20, 30 and again after 90 minutes of surgeries in group-D (Figure 2).

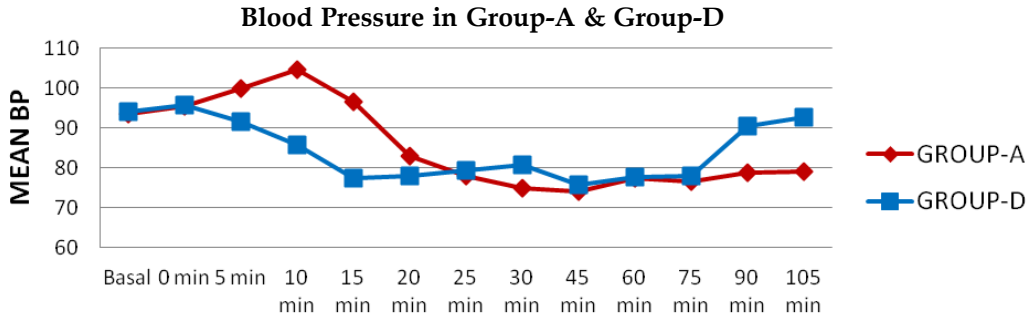
Table 1: Patients Demographic characteristics in Group-A and Group-D

Sr. No.	Parameters	Group-A (40 patients)	Group-D (40 patients)
1	Age (Mean± SD) yrs	39.27 ± 9.40	41.02 ± 9.42
2	Sex (M,F)	M=23,F=17	M=25,F=15
3	Weight (Mean± SD) kg	58.65 ± 8.47	57.37 ± 8.62
4	ASA Status (I,II)	I=33,II=7	I=32,II=8
5	Surgical Duration (Mean ± SD) min	109.55 ± 5.45	110.25 ± 4.45

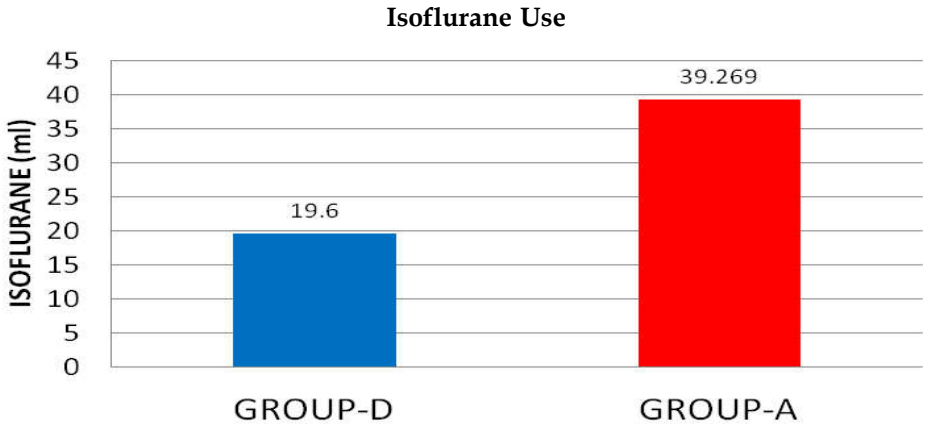
(SD –Standard Deviation, M-Male, F-Female)
Patient Demographic data were comparable between two groups



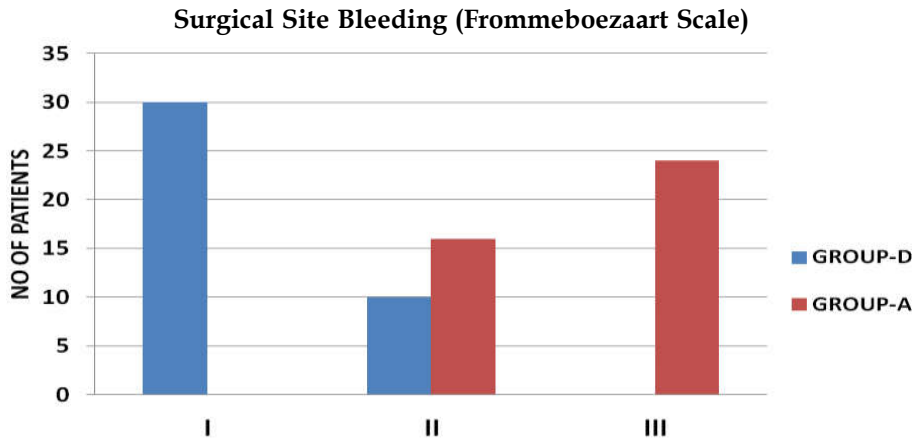
Graph 1: Mean Heart Rate in Group-A and Group-D



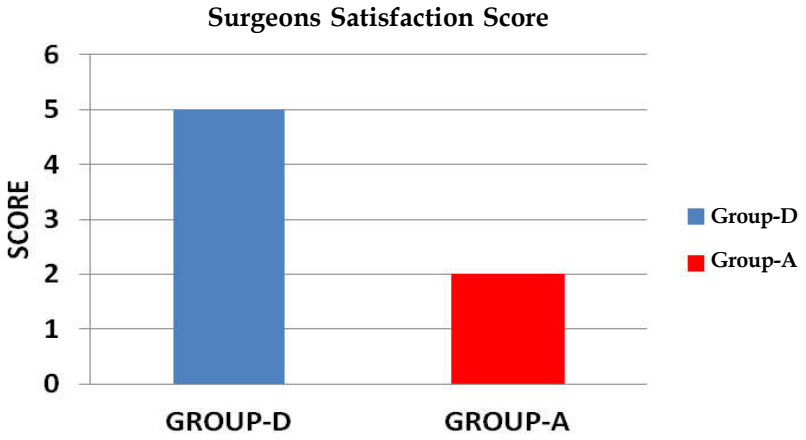
Graph 2: Mean arterial BP (MAP) mm/Hg in Group-A and Group-D



Graph 3: Isoflurane Use in Group-A and Group-D



Graph 4: Surgical site bleeding according to Frommeboezaart scale



Graph 5: Surgeons Satisfaction Score in Group-A and Group-D

Total intraoperative isoflurane requirement in order to achieve Surgical Field Grading ≤ 2 was significantly reduced in group-D patients (Figure 3). Group-A patients required additional fentanyl supplement intraoperatively. In case of Group-D, none of the patients required it additionally which was statistically significant. Majority of patients in Group-D had Grade-I surgical site bleeding which was Grade-III in case of Group-A (Figure 4). Due to better surgical field, Surgeon's satisfaction score was higher in Group-D which was statistically significant (Figure 5). None of the patients in study group had any adverse haemodynamic event, nausea or vomiting due to dexmedetomidine.

Discussion

We could not find the study assessing the effect of addition of dexmedetomidine to local infiltration solution in ENT surgeries to minimise surgical bleeding though studies showing role of iv dexmedetomidine to produce oligaemic field and decrease intraoperative anaesthetic and analgesic requirement are available. Gupta et al in a prospective randomized study proven that dexmedetomidine infusion during middle ear surgery under general anesthesia provide oligaemic surgical field [9].

There are various techniques to produce clear bloodless field. Various intravenous or inhalational agents have been used to produce controlled hypotension. We used dexmedetomidine in infiltration instead of by intravenous route to avoid systemic adverse effects of intravenous dexmedetomidine like initial hypertension, hypotension, nausea, dry mouth, and bradycardia. Overdose may cause first degree or second-degree atrioventricular block. Most of the adverse events associated with dexmedetomidine use occur during or shortly after loading dose [10,11]. At clinically effective doses, dexmedetomidine has been shown to cause much less respiratory depression than other sedatives [12]. However, coadministration of dexmedetomidine with anaesthetic agents, sedatives, hypnotics, or opioids is likely to cause additive effect [13]. Inspite of giving drug by infiltration, there was some systemic absorption of drug as there was moderate decrease in heart rate and blood pressure after some time (Figure 1 and 2), but this change was beneficial for surgery.

Tachycardia and hypertension caused by systemic absorption of adrenaline immediately after infiltration was suppressed after 5 min of infiltration in Group D, while in Group A that was sustained and surgeon started complaining of bleeding in the field. To overcome these systemic effects and bleeding, increased concentration of isoflurane and iv fentanyl were given in titrated dosages in an attempt to achieve clear field in Group A. In Group D patients we didn't need to change dial concentration of isoflurane.

Total isoflurane requirement was very less in Group D than Group A as calculated from Dion's formula. This formula is only a crude method for estimating the amount of isoflurane used. Nevertheless it is an easy and quick method to derive the amount of inhalational agent used at places where more sophisticated equipment like those used to calculate the end tidal concentration of inhalational agent are not available. Also it saves on the time for meticulous and lengthy calculations. Though not highly accurate, it definitely gives an objective value to indicate the anaesthetic sparing effect of dexmedetomidine.

In some patients of Group D there were higher values of heart rates and blood pressures than Group A after 80-90 min of surgery as Group A patients were managed on isoflurane and fentanyl for the purpose of clear bloodless surgical field. In spite of higher values of blood pressures and heart rates there was good surgical field in Group D patients and not required any additional measure. So there were less interruptions during surgery and hence excellent surgeon's satisfaction was achieved in Group D patients.

As there is no literature proposing the mechanism of action of local infiltration of dexmedetomidine to reduce surgical bleeding, it can be proposed as it is due to direct action of dexmedetomidine on peripheral α2b receptors which are present on vascular smooth muscles at the infiltration site causing local vasoconstriction in addition to adrenaline.

Simultaneously as local dexmedetomidine was absorbed systemically it was opposing the systemic effects of adrenaline by α2a receptors. These both effects were favourable for reducing surgical site bleeding. As this was the first study where dexmeditomidine was used by local infiltration to reduce surgical site bleeding, there was no study to compare the outcomes of the study. Secondly we didn't know exact optimal dose of dexmedetomidine for local infiltration which was derived from a pilot study done before. These are limitations of the study.

Conclusion

Addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline in tympanoplasty or septoplasty surgeries under general anesthesia provide good surgical field with excellent surgeon's satisfaction with haemodynamic variations within physiological range with decreased requirement of isoflurane and other agents reducing the cost of anesthesia.

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A Clinical Comparison between 0.5% Bupivacaine and 0.75% Ropivacaine in Brachial Plexus Block Through Axillary Approach

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Abstract

Aim: To compare 0.5% Bupivacaine and 0.75% Ropivacaine in patients for brachial plexus block through axillary approach. *Materials and Methods:* A prospective randomized study patients aged between 20 to 60 years with ASA class I and II posted for elective upper limb surgeries were included in the study. The study population was randomly divided using computer generated numbers into 2 groups with 30 patients in each group. Group B (n = 30) received 0.5% Bupivacaine, Group R (n = 30) received 0.75% Ropivacaine. *Results:* There is no statistically significant difference in the demographic profile of the patients in either groups. There is significant difference in the onset of sensory block in the dermatomes C_5 to T_1. The duration of sensory block was prolonged in group B with difference is statistically and clinically significant with a P value of <0.0001. Onset of motor block is faster in group R compared to group B with a p value of <0.0001 which is highly statistically significant. The duration of motor block in group B is longer than the duration of motor block in group R. It is a significant statistical difference in these values with a p value <0.0001. There is no statistical significant in the quality of sensory block in both the groups with a P value of 0.56. There is no significant difference in quality of motor block in both the groups with p value of 0.13. There is no significant statistical difference in changes in in the hemodynamic parameters. There was no occurrence of any dysrhythmias or any changes in the pattern of ECG during this study, all the patients had normal sinus rhythm. There were no adverse effects in this study. *Conclusion:* Faster onset of sensory and motor block and less cardiotoxic effects combined with the above said characteristics of Ropivacaine makes it a better choice than Bupivacaine for brachial plexus block through axillary approach for fore arm surgeries.

Keywords: Bupivacaine; Brachial Plexus; Axillary Approach.

Introduction

Anaesthesia has evolved into a specialty subject over decades with lot of improvements in the methods employed and drugs used to provide anaesthesia with least complications. General anaesthesia is one of the most common methods employed to provide anaesthesia for upper limb surgeries. With the introduction of newer and safer local anaesthetics and better advantages, regional anaesthesia has taken over as the principle technique for upper limb surgeries. There are many advantages of brachial plexus block for upper limb surgeries over general anaesthesia, namely effective analgesia with good motor blockade, awake patient, extended post operative analgesia, early ambulation, early resumption of oral feeding, minimal number of drugs used so that polypharmacy is avoided, no airway manipulation, less incidence of post operative nausea and vomiting, ideal operating conditions can be met [1]. Various approaches of brachial plexus block have been used for upper limb surgeries namely Interscalene approach, Supraclavicular approach, Infraclavicular approach, Axillary approach. Among these approaches Brachial block through axillary approach is technically easy compared to

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other approaches [1,2]. Various local anaesthetics have been used to produce brachial plexus block. Bupivacaine is one of the most popular drugs used because of its higher potency and prolonged duration of action. One of the drawbacks of Bupivacaine is its cardiotoxicity especially when injected intravascular accidentally [13].

This cardiotoxicity may be life-threatening as the dysrhythmias that are produced are resistant to all routinely used antiarrhythmics. Hence, there is a need for a drug which can have all the advantages of Bupivacaine without its cardiotoxicity. Ropivacaine is a new amino amide local anaesthetic which was introduced in western countries in the 1990s. It is a relatively new drug in India, not as used as commonly as Bupivacaine. Therefore, there is a need to study the effectiveness of Ropivacaine as a local anaesthetic for brachial plexus block through axillary approach. Hence a study was undertaken to compare the routinely used Bupivacaine with recently introduced Ropivacaine for brachial plexus block for elective upper limb surgeries.

Materials and Methods

A prospective randomized double blind clinical study entitled "A clinical comparison between 0.5% Bupivacaine and 0.75% Ropivacaine in brachial plexus block through axillary approach." was undertaken in Government General Hospital attached to Siddhartha Medical College, Vijayawada, Andhra Pradesh during the period from November 2014 to September 2016 for a period of 23 months. Sixty patients aged between 20 to 60 years with ASA class I and II posted for elective upper limb surgeries were included in the study. The study population was randomly divided using computer generated numbers into 2 groups with 30 patients in each group. Group B (n = 30) received 0.5% Bupivacaine, Group R (n = 30) received 0.75% Ropivacaine

Inclusion Criteria

Normal adult patients of either sex, aged between 20 to 65 years belonging to ASA class I and II, without any co-morbid disease, admitted for elective upper limb and wrist surgeries.

Exclusion Criteria

Patients with known hypersensitivity to study drugs, infection at the site of block, known coagulopathy or patients on anticoagulants, severe renal, hepatic, respiratory or cardiac disease, morbidly obese patients, pregnant women, neurological, psychiatric or neurovascular disorders, history of alcohol abuse, injury to any of the nerves of the upper limb.

All the patients underwent pre-anaesthetic check up. Pre-anaesthetic evaluation was done on the evening before surgery. A routine examination was conducted assessing general condition of the patient, airway assessment by mallampatti grading and rule of 1-2-3, nutritional status, weight and height of the patient, a detailed examination of the cardiovascular system, a detailed examination of the respiratory system and the surface anatomy where the block was going to be given. The following investigations were done in all the patients namely haemoglobin estimation, urine examination for albumin, sugar and microscopy, standard 12 lead ECG, X ray chest, fasting and post-prandial blood sugars and blood urea and serum creatinine. The anaesthetic procedure was explained to the patient and an informed consent was taken from the patient. All patients included in the study were given tablet alprazolam 0.5mg and ranitidine 150mg orally at 10 pm night before surgery and they were kept nil by mouth 6 hrs before surgery. On arrival of patients in the operating room, an 18 gauge intravenous cannula was inserted under local anaesthetic infiltration on the non operating hand and an infusion of lactated ringer was started. The patients were connected to multichannel monitor recording heart rate (HR), non invasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), continuous electrocardiogram (ECG) monitoring and pulse oximetry (SpO2). The baseline blood pressure and heart rate were recorded. The heart rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II. The patients and the observing anaesthesiologist as well as physicians and nurses of the acute pain service were blinded to the study drug used. All patients were premedicated with inj. Midazolam 1 mg iv. The patient is placed in the supine position. The operating arm is abducted at shoulder joint to 90p and elbow flexed to 90p and rested on a pillow. The axillary artery is palpated and marked with a skin marker. Under aseptic precautions, skin weal raised with 2 ml of 1% lignocaine. 22G needle is inserted above the artery at the proximal most point and after fascial sheath is pierced felt as a click, 10 ml of the study drug is injected after negative aspiration. Likewise a 22G needle is inserted below the artery and the needle is directed 45p towards the humerus and after the fascial sheath is pierced,

the study drug is injected after negative aspiration. Musculocutaneous nerve may be spared in this approach so 10 ml of the study drug is injected into the body of coracobrachialis muscle. An intercostobrachial nerve block was given if tourniquet is to be placed by using 5 ml 1% lignocaine. Immediately, after block placement, patients were evaluated every 2 minutes, for the assessment of onset of sensory and motor blockade, quality of sensory and motor blockade, duration of sensory and motor blockade and haemodynamic variables. Assessment of sensory onset is tested in the C5, C6, C7, C8 and T1 dermatomes. If the block was considered to be adequate, surgeons were allowed to apply the tourniquet and start the surgery. If the block was considered to be inadequate for surgery, the patient was given general anaesthesia with endotracheal intubation. During the surgery the time of application of tourniquet, haemodynamic variables like HR, SBP, DBP, MAP, SpO2, ECG were monitored base line value (0), 1st (immediately after the administration of block), 5th and 10th minute and then every 10 minutes till the completion of the surgery, Patients were monitored for any signs of cardiovascular or central nervous system toxicity (changes in HR/BP/ rhythm/ signs of CNS stimulation) throughout the study. Any hypersensitivity reaction for the drugs and other adverse events were also monitored. To evaluate the duration of sensory and motor block, patients were asked to document the time when discomfort at the site of incision began and the time when full power returned to the shoulder. In the post-operative period, when the patient complained of pain at the operative site, inj. Diclofenac Sodium 100 mg intra muscular was given and study was concluded. Data were obtained up to 24 hrs after the block placement.

Results

There were more male patients in the study with 71.2% than the female patients with 28.8% with a p value of 0.57. The gender of the subjects was not statistically significant,

Maximum number of the subjects in the study were in the age range of 21 to 40 years. About 60% of the patients in group B and 66.6% of the patients in group R were in age group of 21-40 years.

The mean weight of the patients in group B was 68.9 ±9.1 yrs and in group R was 72.5±9.5 yrs with a p value of 0.14 which was not statistically significant. Maximum number of the subjects in the study were in the weight group of 61 to 80 kgs.

The onset of sensory block in the dermatomes C_5 to T_1 was statistically significant. The duration of sensory block was prolonged in group B with difference which was statistically and clinically significant with a P value of <0.0001. Onset of motor block is faster in group R compared to group B with a p value of <0.0001 which is highly statistically significant. The duration of motor block in group B was longer than the duration of motor block in group R. The mean onset time of motor block in group B was 416.4±21.10 minutes and group R was 380.72±15.03 minutes. Hence, the mean onset of time of motor block was statistically significant with a p value <0.0001. The quality of sensory block in both the groups was not statistically significant with P value of 0.56. The quality of motor block in both the groups was not statistically significant with p value of 0.13. The hemodynamic parameters were also not statistically significant. There were no occurrence of any dysrhythmias or any changes in the pattern of ECG during this study, all the patients

Table 1: Demographic age wise distribution of study population range

Age	Group-B		Group-R		Total	
	Count	%	Count	%	Count	%
21-30	8	26.6%	8	26.6%	16	26.6%
31-40	10	33.3%	12	40.0%	22	36.6%
41-50	8	26.7%	6	20.0%	14	23.3%
51-60	4	13.3%	4	13.3%	8	13.3%
Total	30	100.0%	30	100.0%	60	100.0%
Weight in KGS						
51-60	8	26.7%	3	10.0%	11	18.3%
61-70	10	33.3%	12	40.0%	22	36.6%
71-80	9	30.0%	8	26.7%	17	28.3%
81-90	3	10.0%	6	20.0%	9	15.0%
91-100	0	0.0%	1	3.0%	1	1.6%
Total	30	100.0%	30	100.0%	60	100.0%

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

Sensory Block		Group B			Group R			P-Value
		N	Mean	SD	N	Mean	SD	
C_5		30	12.23	1.33	29	9.00	1.10	<0.0001
C_6		30	12.67	1.30	29	9.14	1.13	<0.0001
C_7		30	12.30	1.42	29	8.93	0.88	<0.0001
C_8		30	12.17	1.32	29	9.03	0.87	<0.0001
T_1		30	12.13	1.20	29	8.72	0.92	<0.0001
Total			12.3	1.3		8.96	0.98	
Duration of	B	30	390	550	461.5	32.0		<0.0001
sensory block	R	29	390	458	426.3	17.3		
Onset of motor	B	30	--	--	20.57	2.05		<0.0001
block	R	29	--	--	14.69	1.34		
Duration of	B	30	--	--	416.40	21.10		<0.0001
motor block	R	29	--	--	380.72	15.03		

Table 3: Quality of sensory block and motor block

QSB	Group-B		Group-R		Total		P-value
	Count	%	Count	%	Count	%	
			Quality of sensory block				
Excellent	22	73.3%	20	69.0%	42	70.0%	0.56
Good	8	26.7%	9	31.0%	17	28.3%	
Poor	0	0.0%	1	3.3%	1	1.6%	
Total	30	100.0%	30	100.0%	60	100.0%	
			Quality of motor block,				
II	10	33.3%	4	13.8%	14	23.7%	0.13
III	20	66.7%	25	86.2%	45	76.3%	
Total	30	100.0%	29	100.0%	59	100.0%	

Table 4: Comparison of ECG changes and adverse effects in both groups

ECG	Group-B Count	%	Group-R Count	%	Total Count	%
NSR	30	100.0%	29	100.0%	59	100.0%
Total	30	100.0%	29	100.0%	59	100.0%
Adverse Effects						
NIL	30	100.0%	29	100.0%	59	100.0%
Total	30	100.0%	29	100.0%	59	100.0%

had normal sinus rhythm. There were no adverse effects in this study.

Discussion

In our study, the drugs selected for brachial plexus block were Bupivacaine and Ropivacaine. Bupivacaine is being regularly used for brachial plexus block for upper limb surgeries in our hospital. Ropivacaine, another local anaesthetic with structural similarity to Bupivacaine without its cardiotoxic effects is a newer drug compared to Bupivacaine. Ropivacaine has been found to be equally effective as Bupivacaine for brachial plexus block by various authors [4,5,6]. Demographic data comparing age, sex, weight shows no statistically significant differences between both the groups in the present study which was in accordance to the reports of other studies. Mean onset time of sensory blockade in group B is 12.3±1.3 minutes and in group R is 8.96±0.98 minutes. There is faster onset time in group R with average time of onset being 9.2±1.5 in C5, 9.4±2.0 in C6, 8.9±0.9 in C7, 9.0±0.9 inc8 and 8.8±0.9 in T1 as compared to mean onset time of sensory block on 12.3±1.3 in C5, 12.7±1.3 in C6, 12.3±1.4 in C7, 12.2±1.3 in C8 and 12.1±1.2 in T8 in group B with p value of <0.0001 which is highly statistically significant. Similar results were observed in other studies as in the study conducted by Kaur A *et al* [4] reported the onset of sensory block was faster in Ropivacaine group compared to Bupivacaine group with mean onset time of 12.04±2.57 minutes in group B and 8.88±1.74

minutes in group R. These results were also comparable to those obtained by Bertini *et al* [5]. In the present study mean onset time was faster in group R when compared to group B. Tripathi D *et al* [6] study which reported a faster onset in 4.22±1.52 minutes and complete block by 11.70±6.40 minutes in Ropivacaine group. Onset of 13.83±3.49 minutes and complete block by 18.46±3.55 minutes in Bupivacaine group. Sirigeri S *et al* [7] observed the onset of sensory block was faster in Ropivacaine than Bupivacaine with mean value of 16.13±3.05 in 0.5% Ropivacaine group and 17.7±2.35 minutes in 0.5% Bupivacaine group. Casati *et al* [10] reported median onset of sensory block was 30 minutes in 0.5% Levobupivaine compared to 15 minutes of onset of sensory block in 0.5% Ropivacaine. Casati A. Fanelli G *et al* [8] reported that complete sensory block was achieved by 22 ± 8 minutes in Ropivacaine group compared to 28±15 minutes in Bupivacaine group. Hetal rathod *et al* [9] reported the onset of sensory blockade as 21.13 minutes in group B compared to 13.3 minutes in group R. Dr. P. Manohar *et al* [11], reported onset of sensory blockade of 15.66±1.82 in patients receiving 0.5% Ropivacaine as compared to 16.0±1.74 in patients receiving 0.5% Bupivacaine which is statistically insignificant. Sreeharsha Sirigeri *et al.* observed that Group R provided statistically significant rapid onset of sensory and motor blockade, prolonged duration of both sensory and motor blockade, prolonged duration of analgesia than Group B for upper limb surgeries. There were no significant differences in haemodynamic changes and complications. In Surendra Raikwar *et al* [12] study fifty patients were grouped equally and one group R received 0.5% ropivacaine (100mg) 20ml and another group B received 0.5% bupivacaine (100mg) 20ml. Onset & duration of sensory and motor blockade, duration of analgesia and associated complications & side effects were recorded. It was found that there were no significant differences in duration of sensory & motor blockade, in complications or any other side effects in both the groups. But ropivacaine provided rapid onset of action and better quality of surgical anesthesia than bupivacaine when used in supraclavicular brachial plexus blockade. Chandni M Soni *et al* [13] observed that in Group R the sensory and motor onset was 6.6 minutes and 12.93 minutes while that in Group B was 7.46 and 11.57 minutes respectively n Group R the sensory duration was 548.2±24.62 minutes while that in Group B it was 589.2±27.74 minutes and the duration of motor block in Group R was 534.4±27.65 minutes while in Group B it was 596.0±24.70 minutes. Group B showed prolonged sensory and motor block duration compared to Group R. The duration of analgesia in Group R, which was shorter, (555.4±20.73 minutes) in comparison to Group B (592.6±24.03 minutes) concluded that onset of sensory block was faster in ropivacaine. Duration of sensory block was longer in Bupivacaine. Tripathi D *et al* [6] observed that the mean onset time of sensory block was 4.22±1.52 min and 13.83±3.49min (P<0.01), peak developed in 11.70±6.40 min and 18.46±3.55 min (P<0.01), in group R and group B respectively. The duration of sensory block was 9.72±2.73 hrs and 8.77 ± 0.75 hrs respectively in group R and group B. (P >0.05). The mean onset time of motor block was 8.92±2.92 minutes and 15.86±3.72 min (P<0.05), peak developed in 27.26±8.93 minutes and 23.43±3.89 min (P<0.05) and duration of 8.53±1.02 hrs and 8.77±0.75 hrs (P>0.05) in group R and group B respectively.

Conclusion

It can be concluded that 0.5% Bupivacaine has slower sensory and motor onset compared to 0.75% Ropivacaine. While the duration of Sensory and motor blockade is longer in 0.5% Bupivacaine compared to 0.75% Ropivacaine. Accidental intravascular injection of local anaesthetic is a problem in spite of meticulous technique and particularly when large volume of anaesthetic is required for efficacy. Faster onset of sensory and motor block and less cardiotoxic effects combined with the above said characteristics of Ropivacaine makes it a better choice than Bupivacaine for brachial plexus block through axillary approach for fore arm surgeries.

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Comparative Study of Intravenous Lignocaine and Sublingual Nitroglycerine to Attenuate Stress Response to Laryngoscopy

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Abstract

Introduction: Laryngoscopy and intubation is associated with a reflex sympathetic pressor response resulting in elevated heart rate (HR) and blood pressures (BP). This may prove detrimental in high risk patients and may be in normal patients also. Several drugs Nitroglycerine (NTG), Lignocaine, Beta-blockers, Opioids, Calcium Channel blockers and Adrenergic agonists, have been used for attenuating the stress response. NTG sublingual spray is a new introduction to attenuate the stress response to intubation. *Aims*: Aim of this study was to compare the effects of sublingual NTG spray and intravenous (iv) Lignocaine on the haemodynamic response following laryngoscopy and intubation. *Patients and Methods:* Randomised control study involving sixty ASA I and II patients who are aged between 20 to 40 years posted for elective surgery were divided randomly into two groups of thirty each. 'Z' test was used for statistical analysis. All patients received premedication with Glycopyrrolate (0.01mg/kg), Midazolam (0.02 mg/kg)iv. Patients were induced with Thiopentone 5 mg/kg iv and muscle relaxant was used in the form of Vecuronium (0.1 mg/kg)iv. First group received iv Lignocaine 1.5 mg/kg, 5 min before intubation and second group received two puffs of NTG sub lingual spray, 400mcg/spray. HR and BP were recorded noninvasively before induction, post-induction, at intubation (0 min), 1,3,5,7 and 10 min from the onset of laryngoscopy. Pair wise comparison between the groups was done by `z' test. For all tests a `z' value of 1.96 was considered significant and a `p' value of 0.05 was considered significant. *Results*: In group N, the rise in systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) was not significant at 1, 3 and 5 min after laryngoscopy, the attenuation was statistically highly significant with p values of < 0.001. Where as in group L, there was significant increase in SBP, DBP and MAP till 7 min post laryngoscopy, after which the values reached the pre induction values. *Conclusions*: Pre-treatment with sublingual NTG spray provides a consistent and reliable attenuation of pressure response to laryngoscopy and intubation when compared to iv Lignocaine.

Keywords: Attenuation; Laryngoscopy; Intubation; Nitroglycerine; Lignocaine.

Introduction

Endotracheal intubation has become an integral part of anaesthetic management and critical care since its description in 1921 by Row Botham and Magill. In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation is noxious stimuli of the upper airway [1]. The rise in the pulse rate and blood pressure is usually transient occurring 30 seconds after intubation, lasting for less than 10min [2]. Usually these changes are well tolerated by healthy individuals. However, these changes may be fatal in Patients with Hypertension [3], Coronary artery disease [4], or Intracranial hypertension and also in normal patients. Numerous agents have been utilized to blunt these stimulatory effects on the Cardiovascular system induced by laryngoscopy and endotracheal intubation such as deepening of anaesthesia, pretreatment with vasodilators such as Nitroglycerin(NTG) [5], Lignocaine [6], Beta-blockers[7], Opioids [8], Calcium Channel blockers[9] and Alpha Adrenergic agonists [10].

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Lignocaine iv has traditionally been used to minimize the stress response. Hence, it is important to find an effective means of attenuating sympathetic responses to laryngoscopy and tracheal intubation. Many strategies have been advocated to minimise these hemodynamic responses and aimed at different levels of the reflex arc are topical application and infiltration of local anaesthetic to superior laryngeal nerve, block of central mechanism of integration and sensory input: i.e Fentanyl, Morphine, Block of efferent pathway and effector sites iv Lignocaine, Beta blockers, Calcium channel blockers, NTG. No single drug or technique is satisfactory [11].

NTG was the first practical explosive ever produced that was stronger than black powder. NTG was first synthesized by the chemist Ascanio Sobrero in 1846, who observed that a small quantity placed on tongue elicited severe headache. Sobrero initially called his discovery Pyroglycerine, and warned vigorously against its use as an explosive. It was later adopted as a commercially useful explosive by Alfred Nobel. Nobel experimented with several safer ways to handle the dangerous NTG. Following the discovery that Amyl nitrite helped alleviate chest pain, Dr William Murrell experimented with the use of NTG to alleviate angina pectoris and to reduce the blood pressure. He began treating his patients with small doses of NTG in 1878 [12]. NTG sublingual spray is a metered dose spray containing NTG. This product delivers NTG (400 mcg per spray) in the form of spray droplets under the tongue.

Aim

The purpose of the present study was to compare the effect of NTG sublingual spray with Lignocaine iv on the increase of blood pressure following laryngoscopy and intubation prior to surgery. The objectives of the present study were:

To compare the effect of NTG sublingual spray and Lignocaine iv in attenuating the stress response to laryngoscopy and intubation, with respect to changes in the heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial blood pressure(MAP). And to evaluate any side effects associated with the use of these drugs.

Subjects and Methods

A randomized control study of attenuation of sympathetic response to laryngoscopy and intubation was done in 60 patients posted for elective surgery. General anaesthesia was provided with endotracheal intubation for all patients. Patients undergoing various orthopaedic, ENT, General Surgical and Laparoscopic procedures were selected.

Ethical committee approval was obtained as per the protocol of the Ethical Committee Review Board of the institution. Informed consent was obtained from all the subjects included in the study. The Inclusion criteria were: Patients scheduled for elective surgeries, Age between 20 to 40 years, Patients with ASA grade I or II. The Exclusion criteria were: Unwilling patients, Emergency surgeries, Anticipated difficult intubation, Patients with ASA grade III or higher, Patients with cardiovascular diseases. Patients were selected after thorough preanaesthetic assessment. 60 cases were divided into two groups of 30 each. Group-L: Lignocaine group. In this group lignocaine iv, 1.5mg/kg was administered for attenuating sympathetic response to laryngoscopy and intubation. Group-N: NTG group. Here patients received sublingual NTG spray, 2 puffs of 400mcg each, before laryngoscopy and intubation. Anaesthesia was given after pre-oxygenation (6 liter/min) for 3 minutes. Midazolam (0.02mg/kg) and Fentanyl (2mcg/kg) was administered as premedication and induction with Thiopentone (5mg/kg). Vecuronium (0.1mg/kg) was injected after disappearance of eyelash reflex. At this time, patients in group L received Lignocaine intravenous (1.5mg/kg) 5min before intubation. Patients in group N, received NTG sub lingual spray two metered sprays (400mcg/spray) under the tongue, just prior to intubation by opening mouth and retracting the tongue to expose the ventral aspect of the tongue. The rest of the procedure was same for all patients, 3min after oxygenation with mask, patients were intubated by using Macintosh laryngoscope with PVC tube. Anesthesia was maintained in both groups equally using 1-1.5 MAC of isoflurane, N_2O and O2 (2: 1). HR, SBP and DBP, MAP were measured before induction, after intubation at 0,1,3,5,7,10min interval. During the surgery, occurrences of any types of arrhythmia, or cardiovascular complications were recorded. HR and BP values were taken from the monitor record by an independent observer who was blinded to the technique used in the patient. An observation was made related to adverse effects of drugs and anaesthesia related problems and were attended appropriately.

Descriptive data presented as Mean ± standard deviation in percentage. Pair wise comparison between the groups was done by 'z' test. For all

tests a 'z' value of 1.96 was considered significant and a 'p' value of 0.05 was considered significant. Statistical analysis were performed using the Statistical Package for the Social Sciences, version 19.0 (SPSS, Inc., Chicago, IL, USA).

Results

The mean value of age was 29.7±7.51 and 30.3±6.43 for group L and group N respectively. There was no significant difference between the two groups (p>0.05). No significant difference was observed in sex wise distribution between the two groups (p>0.05).

Mean value of weight is 61.33±7.17. In NTG group, mean of 61.6±7.95. No significant difference were observed between the two groups (p>0.05).

Heart rate (Figure 1): In the group L, pre induction HR was 91.18±8.23, after induction HR was 96.18±10.69. At onset of laryngoscopy (0 min) the rate was 98.2±8.4. At 1 min from onset of laryngoscopy the heart rate increased to 120±10 and remained higher till 3min with mean of 114.20 ±11.77. Subsequently decreased from 5min to 10min post laryngoscopy, 99.46±13.18 at 5 min, 98.94±11.47 at 7 min and 10 min it was 94.87±8.64. In the group N, the heart rate pre-induction was 89.3±6.80, post induction it was 91.76±6.27. At laryngoscopy the heart rate was 93.8±6.4 and 1 min after that the rate increased to 119.74±8.09 and remained high till 3min (113.48±8.74). Subsequently the mean heart rate decreased to 93.60±6.20 at 5min and to 92.6±9.86 at 7min and to 91.96±5.78 at 10min post laryngoscopy. The difference in heart rates between the two groups was statistically not significant (p > 0.05).

Systolic Blood Pressure (Figure 2): In group L, the mean pre induction values of SBP was 119.88±10.86

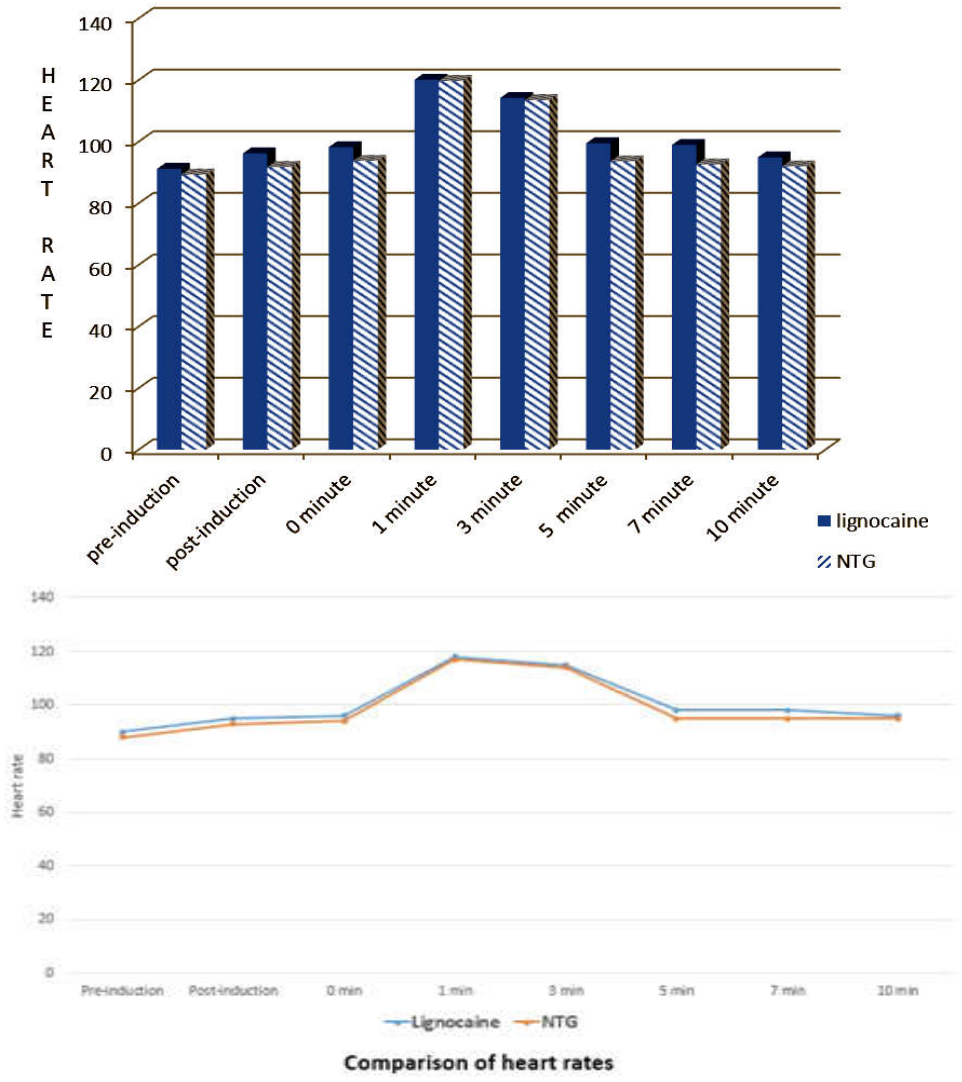


Fig. 1: Comparison of heart rates

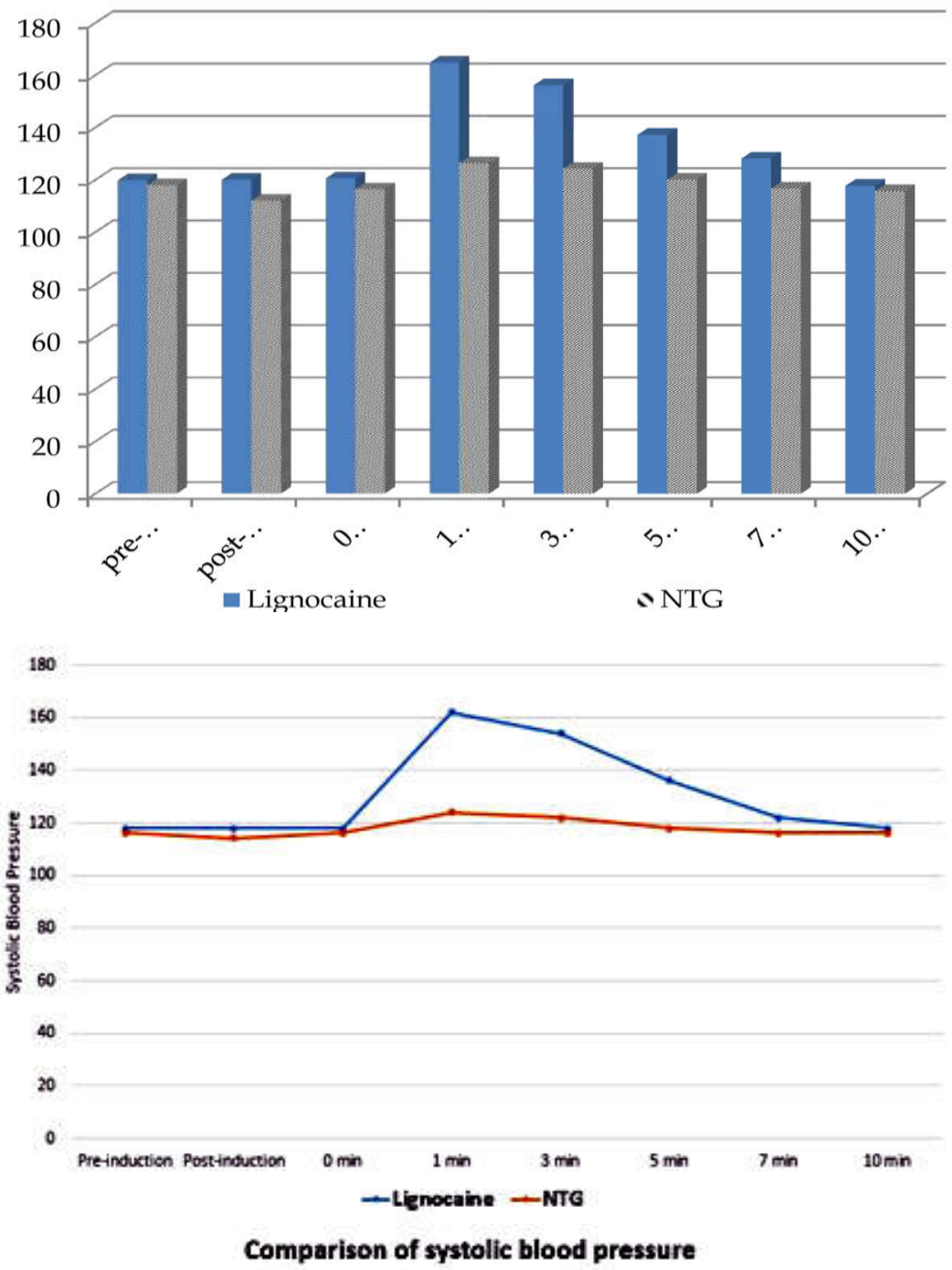


Fig. 2: Comparison of systolic blood pressure

and after induction it was 120.10±11.70. At onset of laryngoscopy (0 min) pressure was 120.64±10.60. At 1 min after the onset the pressure increased to 164.90±11.48 and at 3min it was 156.10±11.64. By 5 min the pressure started reduced 137.21±13.09, then at 7min it was 128.14±11.13 and at 10min it was 117.72± 10.01. In group N, the mean pre induction values of SBP was 117.96±12.22 and after induction 112.03±10.98. At onset of laryngoscopy (0 min) pressure was 116.42±11.60. At 1 min after the onset the pressure increased to 126.35±10.55 and at 3 min it was 124.22±10.13. By 5 min the pressure reduced 120.02±9.83, then at 7 min it was 116.67±9.49 and at 10 min it was 115.04±9.40. No significant variation was noted in both the groups at pre induction, post induction and at laryngoscopy (0 min). In

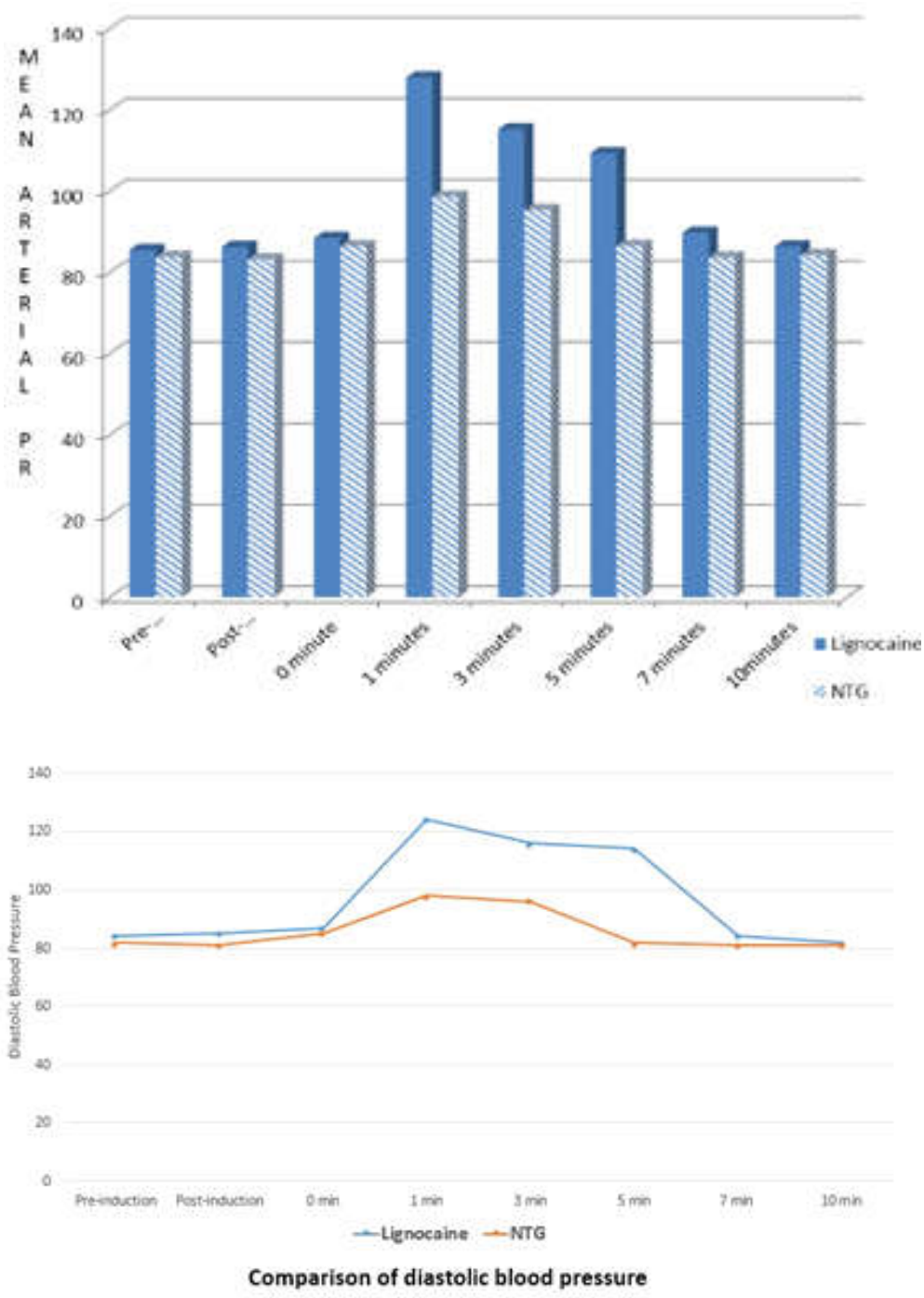
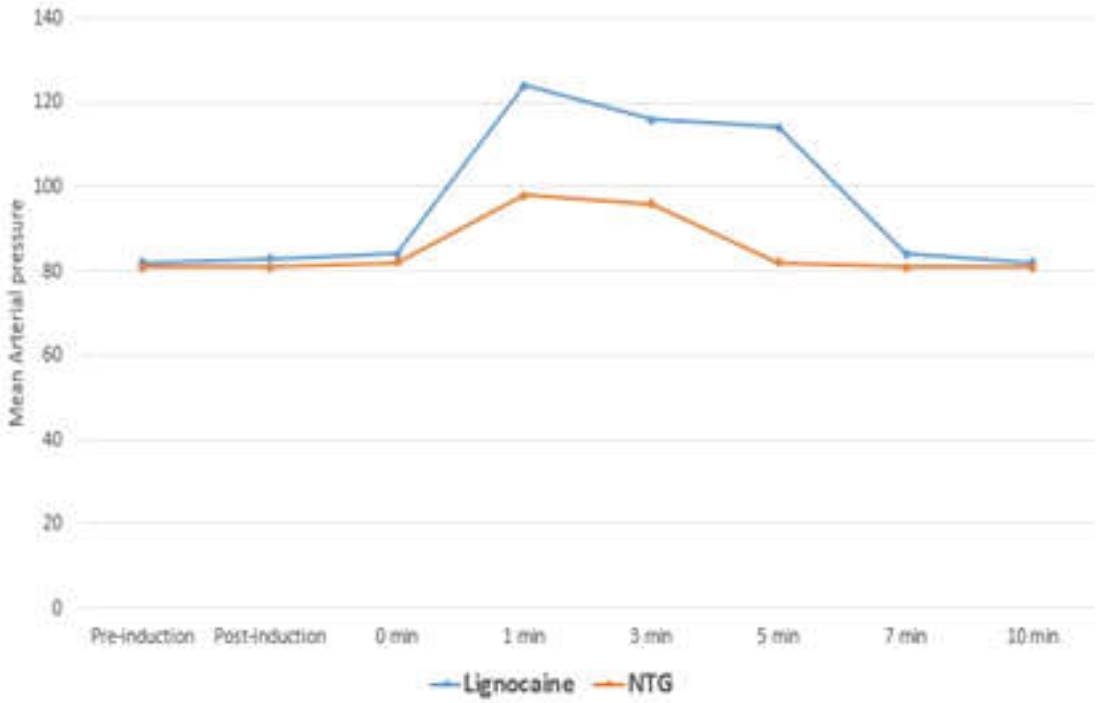


Fig. 3: Comparison of diastolic blood pressure

comparison with lignocaine, nitroglycerine group showed a statistically significant attenuation of systolic blood pressure at 1 min, 3 min and 5 min after onset of laryngoscopy with p values of <0.001 and by 5 min the values were almost equal to basal values.

Diastolic Blood Pressure (Figure 3): In the group L, the mean pre induction values of diastolic blood pressure was 68.28±6.12 and after induction it was 70.32±6.40. At onset of laryngoscopy (0min) pressure was 72.00±6.20. At 1 min after the onset the pressure increased to 109.40±5.18 and at 3 min it was 94.60±6.11. By 5 min the pressure started reduced 89.84±5.20, then at 7 min it was 76.60±5.47 and at 10 min it was 74.68±5.52.In the group N, the mean pre induction values of diastolic blood



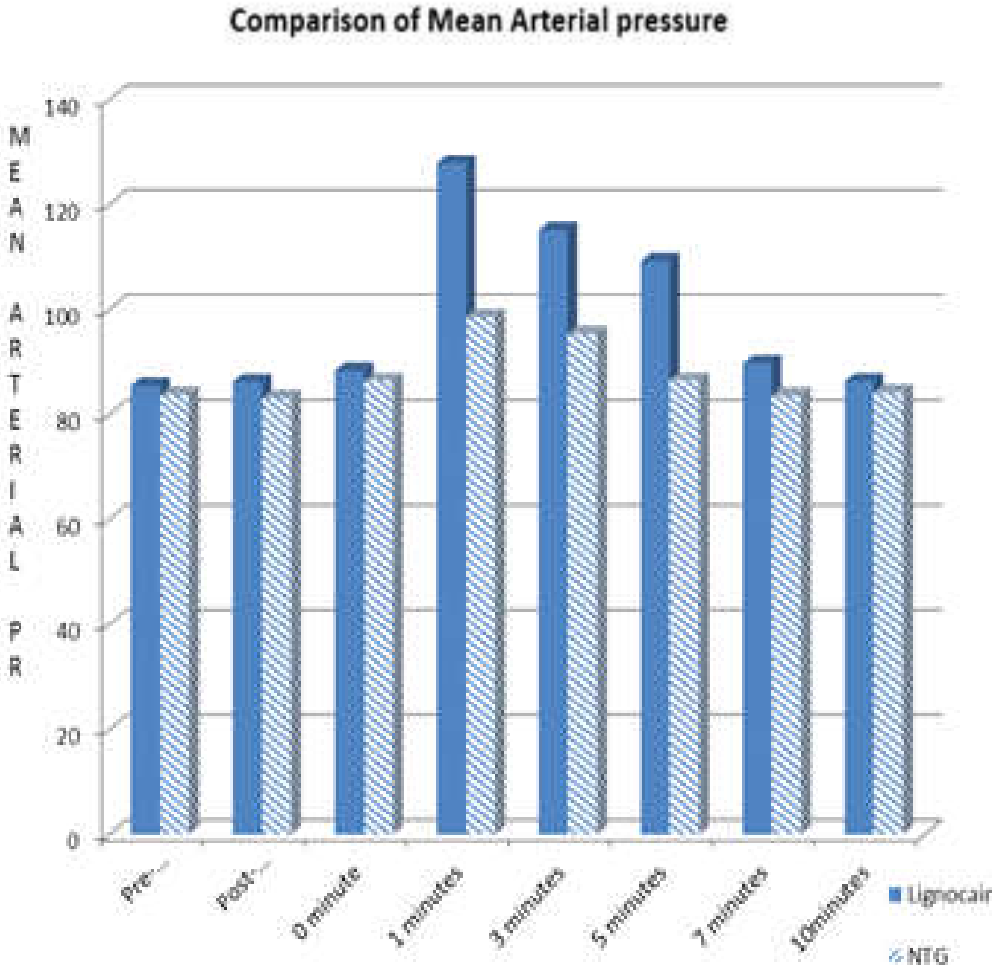


Fig. 4: Comparison of mean arterial blood pressure

pressure was 66.72±5.77 and after induction it was 68.82±5.37. At onset of laryngoscopy (0 min) pressure was 70.74±5.40. At 1 min after the onset the pressure increased to 84.92±5.22 and at 3 min it was 79.78±4.28. By 5 min the pressure started reduced 69.80±5.52, then at 7 min it was 67.10±4.80 and at 10 min it was 68.14±4.40. No significant difference was noted in diastolic blood pressure at pre induction, post induction and at onset of laryngoscopy. However the attenuation of diastolic systolic blood pressure with Nitroglycerine was statistically highly significant at 1 min, 3 min and at 5 min after the onset of laryngoscopy.

Mean Arterial Pressure (Figure 4)

In the group L, the mean arterial pressure before induction was 85.5±6.68 and after induction were 89.25±6.62. At laryngoscopy(0 min) the mean arterial pressure was 88.42±6.42. At 1 min after onset of laryngoscopy the map increased to 127.9±6.17 and subsequently the pressure at 3min was 115.20±6.17, at 5 min was 109.31±6.86 and by 7 min it was 89.75±6.33 almost equal to basal values and at 10 min it was 86.2±5.89.In the group N, the mean arterial pressure before induction was 83.80±5.75. After induction it was 83.17±5.16 and at laryngoscopy the pressure was 86.42±5.40. At 1 min, the mean arterial pressure increased to 98.61±5.24 subsequently at 3 min it was 95.34±4.72. At 5 min it was 86.5±4.66 reached almost to basal levels at 7 mins it was 83.62±4.42 and by 10 min it was 84.20±4.17.No significant difference was noted in mean arterial blood pressure at pre induction, post induction and at onset of laryngoscopy (0 min). However attenuation of mean arterial pressure with nitroglycerine was statistically highly significant attenuation at 1 min, 3 min and 5 min after onset of laryngoscopy.

Discussion

Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. These potentially dangerous changes disappear within 5min of onset of laryngoscopy [13]. Although these responses of blood pressure and heart rate are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease [4], increased intracranial pressure or anomalies of the cerebral blood vessels. An average rise in MAP of 25mmHg and 47.7mmHg has been documented [14]. A rise in mean heart rate of 29.9 beats/min has also been noted [2]. Many factors influence the cardiovascular changes associated with laryngoscopy like age, drugs, depth of anaesthesia, hypoxia, hypercarbia, etc., variations in HR decrease with age, young patients show more extreme changes [15]. Therefore we opted an optimal age group of 20–40 years.

Patients on antihypertensive drugs may exhibit a decrease in pressor response. We excluded the patients on antihypertensive medications from our study. Different drugs used for premedication, induction, relaxation, maintenance of anaesthesia influence the sympathetic response to laryngoscopy and intubation. Midazolam at a dose of 0.2mg/kg iv decreases the blood pressure and increases the HR similar to Thiopentone [16].

However premedication with of Midazolam has no effect on sympathetic response to laryngoscopy and intubation. Glycopyrrolate premedication can moderately increase the HR. Thiopentone was selected for induction since it still continues to be the most popular agent for induction. In normovolemic patients Thiopentone 5mg/kg iv can transiently decrease 10-20mm Hg of BP and increase the HR by 15-20 beats/min. There is increase in catecholamine levels, both Noradernaline and Adrenaline [17]. Nitrous oxide may increase the tone of sympathetic nervous system, Nitrous attenuates pressor response but did not affect the tachycardia response [18].

Laryngoscopy alone may produce most of the cardiovascular responses reported after laryngoscopy and tracheal intubation during anaesthesia [19].

The most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy [13]. A linear increase in HR and MAP during the first 45 seconds has been observed. Further prolongation has little effect. The force applied during laryngoscopy has only minor effect [20].

Attenuation of sympathetic response during laryngoscopy and intubation is of prime concern. Many strategies have been recommended but, no single drug or technique is satisfactory.

Each technique has advantages and disadvantages, the most obvious being that the prevention often outlasts the stimulus.

Bachofen M [21], stated the criteria for selection appropriate drug to prevent sympathetic response. The drug must be applicable regardless of patient collaboration, Prevent impairment of cerebral blood flow and avoid arousal of the patients, It should

neither be time consuming nor affect the duration and modality of ensuing anaesthesia.

In our study, both sublingual NTG spray and iv Lignocaine appear to fulfil the above criteria. Lignocaine though failed to attenuate cardiovascular response to laryngoscopy in a study by Miller and Warren [22], its efficacy was noted by others [6]. Its recommended dose 1.5mg/kg iv, optimum time is 3 min before intubation. NTG has been used intravenous [23], intranasal [24], topical [25] and sublingual tablets [26] successfully in a dose of up to 1mg to attenuate the laryngoscopic stress response.

In the present study NTG attenuated the increase in SBP and prevented a rise in DBP following intubation, though it failed to attenuate inotropic response to intubation. The reason for this could have been the tendency of NTG to cause tachycardia. This finding is similar to that of Singh et al [23] and Vanden Berg et.al [27], who also reported failure of NTG to attenuate increase in HR following intubation. One of the limitations of the present study is that the population enrolled comprised healthy patients of ASA grade I and II. Further studies are required to rule out any other short term or long term adverse effects in especially patients with comorbidities like hypertension, cardiovascular disease and intracranial pathology.

Conclusion

Pre-treatment with sublingual NTG spray provides a consistent and reliable attenuation of pressure response to laryngoscopy and intubation when compared to iv Lignocaine.

Acknowledgement

Conflicts of Interest: Nil

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Original Research Article

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Effect of Epidural Labour Analgesia on Maternal Body Temperature

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Abstract

Context: Epidural analgesia is an effective mode of labour analgesia. Few studies have shown that epidural analgesia is associated with an increase in maternal body temperature. The greatest impact of this increase in maternal body temperature lies in the need to eliminate the possibility of infection and subsequent use of antibiotics. This study was done to determine the relationship between epidural labour analgesia and maternal body temperature in Indian population. *Aims:* To determine the relationship between epidural labour analgesia and increased maternal intrapartum temperature. *Settings and Design:* A prospective randomised study in our institution. *Methods and Material*: Sixty ASA 1 or 2 consenting parturients scheduled for normal delivery were randomly allocated to 2 groups of 30 each to receive inj Fentanyl 50 mg intravenous or epidural boluses of 0.125% ropivacaine with 2 mg/cc of fentanyl after ethical committee approval. Baseline maternal and fetal vital parameters including maternal body temperature were recorded. *Statistical analysis used*: Data was analysed using student's unpaired t-test, Mann Whitney's U test and one-way ANOVA wherever indicated *Results:* Significant difference ($p< 0.05$) in the maternal body temperature between the groups at all intervals were noted. There was a significant rise in the temperature from baseline within the group as well ($p< 0.05$). *Conclusion*: The present study shows that maternal body temperature increases during labour and epidural labour analgesia only exaggerates it, albeit, without any apparent repercussions on the mother or infant.

Keywords: Epidural; Analgesia; Labour; Maternal Temperature.

Introduction

Epidural analgesia is an effective mode of labour analgesia. Few studies have shown that epidural analgesia been associated with an increase in maternal body temperature [1-3]. Though an increase in maternal intrapartum temperature may be an indication of chorioamnionitis, in many cases, it was not associated with any other signs of infection [4-7]. Though the exact mechanism is still largely unknown, the possibility of a change in maternal thermoregulation has been thought of [6]. The greatest impact of this increase in maternal temperature lies in the consequent maternaland neonatal evaluation performed to eliminate any possibility of infection and the increased use of antibiotic therapy [8]. The objective of the present study was to determine the relationship between epidural labour analgesia and increased maternal intrapartum temperature.

Materials and Methods

This study was conducted between october 2016 and june 2017 after approval from institutional research and ethics committee. Sixty American Society of Anaesthesiologists (ASA) physical status 1 or 2 parturients scheduled for labour analgesia were recruited for the study after obtaining a written

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informed consent. Parturients who had any contraindication for epidural technique and history of allergic reactions to any of the study drugs were excluded from the study.

The current study was designed to test the hypothesis that epidural labour analgesia increases maternal body temperature.

All the parturients were randomly assigned by picking lots into 2 groups of 30 subjects in each group: Control group (C) and ropivacaine groups (R). Parturients in control group received inj Fentanyl 50 μg intravenous boluses on request or when VAS score was above 3. Parturients in Ropivacaine group received epidural boluses of 0.125% ropivacaine with 2 μg/cc of fentanyl as and when required.

The parturients in labour, were encouraged not to have any solid food. Fruit juices (without pulp) and clear fluids were allowed. Ranitidine 150 mg and Metoclopramide 10 mg, was given orally (in patients in early labour, with 3-4 cm cervical dilatation).

In the labour room, after checking anesthesia machine and keeping all emergency drugs and airway equipment ready, monitors were connected and maternal baseline cardiorespiratory parameters - pulse rate, non-invasive blood pressure, oxygen saturation andelectro-cardiogram were recorded. Base line maternal body temperature (oral) and fetal heart rate were also recorded. An 18g i.v.cannula was secured and Ringer's lactate was started.

Epidural catheter was secured in all the parturients assigned to the study group. After taking adequate aseptic precautions, the catheter was placed at L2-3, L3-4 or L4-5 level and was secured at about 5 cms from the depth at which the epidural space was identified by loss of resistance technique to air using 18g Tuohy needle. First 10 ml bolus of the premixed solution acted as 'test cum therapeutic dose'. A total of 15 to 20 ml of the test drug was injected epidurally to achieve the desired level of block (T_{10}) over 30-45 min If analgesia was inadequate after 45 min, re-siting the epidural catheter would be considered.

After placement of epidural catheter, maternal blood pressure was monitored at 5 min intervals and continuous FHR monitoring for the first 45 minutes. Maternal BP and FHR would be monitored every 10 minutes thereafter. The attending nurse would check the sensory level once each hour. Also, maternal body temperature measured orally was recorded every hour for 6 hours.

Maternal hypotension was treated by avoiding aortocaval compression and placing the mother in full left lateral position. If there was no response, 3-6 mg bolus of ephedrine IV was given.

Statistics

Data was analyzed using the SPSS statistical software. Parametric and non parametric values were analyzed using student's unpaired t-test and Mann Whitney's U test respectively. Differences within the group for parametric variables at different time points were analyzed by one-way ANOVA with significance using Tukey's method. $P<0.05$ was considered significant.

Results

A total of sixty parturients were involved in the study. There were no drop outs and every body completed the study. There were no complications related to the study.

The demographic characteristics in both the groups were comparable (Table 1).

Both the groups were comparable with respect to parity (p=0.45), and duration of second stage of labour. The duration of first stage of labour was prolonged in the control group (p=0.01) which was clinically not significant (Table 2).

The maternal Heart rate, blood pressure and fetal heart rate were comparable between both the groups (Table 3).

The mean VAS in group C was 1.23 ±0.63 and in group R was 1.24±0.63 p-value of 0.95 which was statistically not significant.

The baseline temperature was comparable between the groups. There was significant difference

Table 1: Demographic characteristics

Characteristic	Control group (n=30) Mean (SD)	Ropivacaine group (n=30) Mean (SD)	P-value
Age(in years)	22.52(2.56)	22.89(2.87)	0.61*
Height(in cms)	153.43(3.234)	152.27(3.095)	0.159*
Weight(in kgs)	64.83(6.838)	60.13(6.976)	0.11*

*Not Significant

Table 2: Labour Characteristics

Characteristic	Control Group	Ropivacaine Group	P=value
Parity – primiparous (%)	65	70	0.450
Multipara (%)	35	30	
Duration of 1st Stage (median/25th-75th percentile)	240(180-300)	200(100-240)	0.04**
Duration of 2nd Stage (median/25th-75th percentile)	35(25-50)	32(20-45)	0.80

**Significant

Table 3: Maternal and fetal Hemodynamic Characteristics

Characteristic	Group C (n=30)	Group R(n=30)	p-value
Maternal Heart Rate (Mean +/- SD)	81.57 +/- 10.17	84.50+/- 9.38	0.250
Maternal Mean BP (Mean +/- SD)	86.86 +/- 5.00	91.65 +/- 6.94	0.06
Fetal Heart Rate	139.99 +/- 7.85	139.45 +/- 6.27	0.770

Table 4: Comparison of Mean Temperature between groups at various intervals

	Control group(n=30)	Ropivacaine (n=30)	p-value
Time 0	36.39	36.36	.063
Time 1	36.47	36.61	.000*
Time 2	36.57	36.78	.000*
Time 3	36.62	36.99	.000*
Time 4	36.65	37.11	.000*
Time 5	36.74	37.29	.000*
Time 6	37.10	37.33	.000*

* Significant

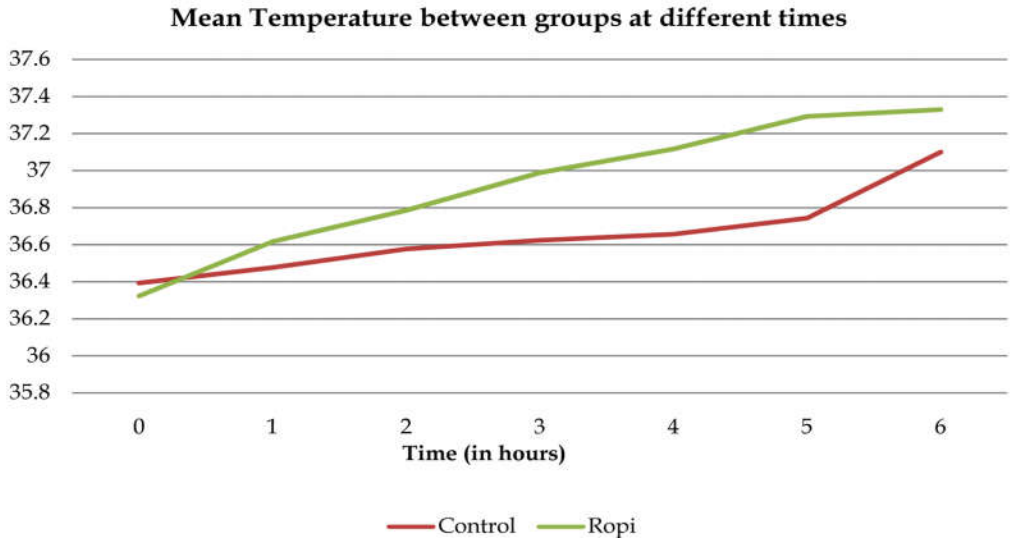

Fig. 1: Mean temperature between groups at different times

in the temperature between the groups at all other intervals (Table 4 and Figure 1).

Discussion

We observed that the mean maternal body temperature was significantly higher in the epidural group at all time interval of assessment. Nonetheless, no cases of maternal or neonatal infection were found and pharmacological analgesia was not associated with any adverse maternal or perinatal effects, as was found in the study done by F.A. De Orane et al [1]. However, we also noticed that there was statistically significant difference in the maternal body temperature from the baseline within the control group as well which was not so in the study done by F.A. De Orane et al [1]. This suggests that changes in the maternal body temperature occur during labour which may be due

to disturbance in the central thermoregulation and also due to an imbalance between heat production and elimination [4-7] and labour epidural analgesia only exaggerates this rise in temperature.

In their study F.A. de Orange et al observed that the hyperthermia seen in pregnant women receiving CSE anaesthesia was different from that found in women submitted to epidural anaesthesia, since the increase in temperature in their study appeared between the first and second hours after analgesia, continued throughout the first hours of labour and disappearedafter the sixth hour. Other investigators have published conflicting findings, reporting that 'epidural fever' is more common in prolonged labour, only 7% of women being affected in the first 6 hrs compared with over 36% when labour persists for more than 18 hrs [9].

Though the association of intrapartum fever with epidural anaesthesia has been demonstrated in several studies [1-3,10-12], their study [1] showed that CSE for pain relief during labour was associated with intrapartum maternal fever, although this fever was not indicative of any increased risk of maternal or neonatal infection.

But still, we have noticed that mere presence of intrapartum maternal fever results in major investigations, since both the mothers and the newborn infants are submitted more often to exams to screen for infection and to antibiotic therapy [10]. Hence, several authors propose a review of the obstetrical and neonatal criteria governing supplementary testing and antibiotic therapy in cases of intrapartum fever associated with anaesthesia [10,13]. Likewise, studies have shown that, despite the association between epidural anaesthesia and an increased risk of developing maternal fever, there are no repercussions on fetal well-being [14].

Several studies have reported an increase in the duration of the second stage of labour but no significant effects on the first stage [15,16,17]. A reduction in the duration of the first stage of labour was found in the present study, with no significant effect on the duration of the expulsion period.

Conclusion

The present study shows that maternal temperature increases during labour and epidural labour analgesia only exaggerates this increase in maternal temperature, albeit without any apparent repercussions on the mother or infant.

Acknowledgement

Nil

Conflict of Interest

Nil

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Original Research Article

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A Prospective Randomized Study on the Efficacy of Interpleural Analgesia in Reducing Post Operative Pain and Parenteral Analgesic Requirement in Patients Undergoing Upper Abdominal Surgery

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Abstract

Introduction: Administration of local anesthetics into the pleural space provides rapid onset and long duration of analgesia upper abdomen surgeries without respiratory depression as seen with opioids.in this study we attempt to find the efficacy of interpleural analgesia in reducing post operative pain and parenteral analgesic requirement in patients undergoing upper abdominal surgery. *Aim:* To analyze the efficacy of interpleural analgesia in reducing post operative pain and parenteral analgesic requirement in patients undergoing upper abdominal surgery. *Materials and Methods:* After ethics committee approval and written informed consent 36 patients undergoing elective upper abdominal surgeries were selected randomly based on computer generated random numbers. General anaesthesia administered as per routine in our hospital. When the surgery was over the patients divided into two trearment groups of 18 patients. 1. Pleural analgesia (bupivacaine) combined with Parenteral analgesics (Pentazocine). Forty milliliters of Injection bupivacaine 0.25%via intrapleural catheter. 2. Parenteral analgesics alone. (Pentazocine). *Results:* Consumption of pentazocine were higher in control group than in pleural group, for Day 1($P < 0.001$), Day 2 ($P < 0.01$) and Day1 + 2 ($P < 0.001$) Mean pain scores were significantly reduced 30 min after IP instillation of bupivacaine 0.25 % compared to control group. *Conclusion:* It is concluded from this study that intermittent interpleural analgesia with bupivacaine was more effective than intermittent intramuscular administration of pentazocine alone.

Keywords: Intrapleural Analgesia; Pentazocine; Bupivacaine; Upper Abdominal Surgeries**.**

Introduction

Surgical incision involving the upper abdomen decreases the diaphragmatic function resulting in reduced pulmonary compliance, muscle splinting, inability to breathe deeply or cough forcefully and in some cases may even cause hypoxemia and hypercarbia. The administration of local anesthetics into the pleural space provides rapid onset and long duration of analgesia without respiratory depression as seen with parenteral opioids. This study is chosen to investigate the efficacy of interpleural analgesia in treating postoperative pain in upper abdominal surgeries in comparison with parenteral opioids .

Aim of the Study

This study intends to prospectively analyze the efficacy of interpleural analgesia in reducing post operative pain and parenteral analgesic requirement in patients undergoing upper abdominal surgery.

Patients and Methods

After approval from local ethics committee and written informed consent 36 patients undergoing elective upper abdominal surgeries like open cholecystectomy, nephrectomy , pyelolithotomy and pyeloplasty at Government General Hospital, Chennai were enrolled in the study. The inclusion

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criteria were age 19 to 65 years ASA physical status 1 & 2 with no contraindications for the technique and drugs. These include pleural injury, pleural adhesion, fibrosis or effusion, COPD, local infection, bleeding diathesis and allergy to study drugs. The linear visual analog scales (VAS) were explained to the patients prior to the study.

Patients were premedicated with Inj glycopyrrolate 0.2mg and Inj fentanyl 100 micrograms IV just before induction. Patients were induced with Inj propofol 2mg /Kg, Inj Suxamethonium 100mg IV and intubated one minute later with appropriate size endotracheal tube orally. The anaesthesia was maintained with nitrous oxide –oxygen mixture 3:2, muscle relaxant Inj Vecuronium, Volatile agents.

When the surgery was over the patients were randomly assigned to two trearment groups of 18 patients in each.

1. Pleural analgesia (bupivacaine) combined with Parenteral analgesics (Pentazocine).
2. Parenteral analgesics alone. (Pentazocine)

In patient assigned in pleural group the catheter was inserted unilaterally on the side of incision. The patients were positioned laterally with operative site up and pleural catheter was inserted at the sixth intercostals space in the posterior axillary line just before anaesthesia was discontinued during spontaneous ventilation. Intercostal drainage tube was kept ready throughout the study period to manage any untoward pneumothorax occurrence..

Under aseptic precautions the 17G Tuohy needle loaded with 5ml syringe containing normal saline introduced in the sixth intercostal space and then walked off the superior edge of the rib . The loss of resistance to saline technique was used to identify the entry in to the pleural cavity. The catheter was then advanced posterosuperiorly past the tip of the needle and fixed in position close to the paravertebral space and the needle is withdrawn. Forty milliliters of Injection bupivacaine 0.25%, was injected through catheter after negative aspiration for blood. Patient was turned supine and after reversal extubated.

In patients in control group no analgesics were given before extubation.

One hour after extubation and every 6 hrs thereafter in both the groups pain was recorded using Visual analog scale (VAS). The patients were given pain relief medication on demand. In the control group patients were given Inj Pentazocine 30 mg intramuscularly. In the pleural group break through pain was treated similarly. Postoperatively, one hour after pleural puncture chest radiograph was obtained for detection of a possible pneumothorax in pleural group. Pain was evaluated with a 10 cm VAS in both the groups. Patients were continuously monitored with ECG. Blood pressure and heart rate were recorded noninvasively every 5 minutes up to 30 minutes after the bolus in both groups. The total parentral analgesic requirement in the initial 48 hrs postoperative period was recorded. The study was stopped after 48 hours because of concerns of the interpleural catheter displacement following mobilization of the patient and fear of catheter-related infection.

Statistical Analysis

Student t test was used to compare the pentazocine requirement and VAS scores between the pleural and control groups.

Data was analyzed with SPSS software.

Data are presented as means±SD. The P values were provided to indicate statistical significance. $P < 0.05$ was considered as significant.

Results

One patient was excluded from the study due to aspiration of blood in the pleural catheter. Demographic data were similar in both the groups. Mean age was 40.7yrs ± 11.30 (21 to 56 yrs) in pleural group and 44.6 yrs ± 11.9 (18 to 65 yrs) in control group. No episodes of hypotension or bradycardia were noted. Neither pneumothorax nor CNS (central nervous system) toxic reactions (tremor, perioral numbness, muscle twitches, metallic taste, and tinnitus convulsions) were noted. The catheter insertion using loss of resistance technique described above was easy to identify the pleural space and effective.

Consumption of pentazocine were higher in control group than in pleural group, for Day 1 ($P < 0.001$), Day 2 ($P < 0.01$) and Day 1 + 2 ($P < 0.001$) and was significant.It was found that difference was more significant on Day 1. Patients of control group received a mean dose of 114.9±20.7 mg of pentazocine in the first 48 hrs postoperatively in contrast to pleural group which received mean dose of 61.6±8.7 mgs.

Mean pain scores were significantly reduced 30 min after IP instillation of bupivacaine 0.25% compared to control group. The mean pain score of the pleural group is 2.96±0.72 and mean pain score

of the control group is 6.04±1.30 for 48 hrs.There was significant difference between the groups when comparing mean pain scores (P <0.001). When VAS scores were analyzed at each time point recorded showed significant difference between the groups at any time of measurement. Visual analogue scale (VAS) pain score versus time in patients assigned to pleural bupivacaine (=)or control group (+). Data are presented as mean±SD.

Table 1: Patient characteristics

	Pleural Group (18)	Control Group(18)
Age(yr)	40.7 ± 11.3	44.2 ± 11.9
Sex(male/female)	5/12	10/8
Weight(Kg)	55.4 ± 5.9	57 ± 6.8

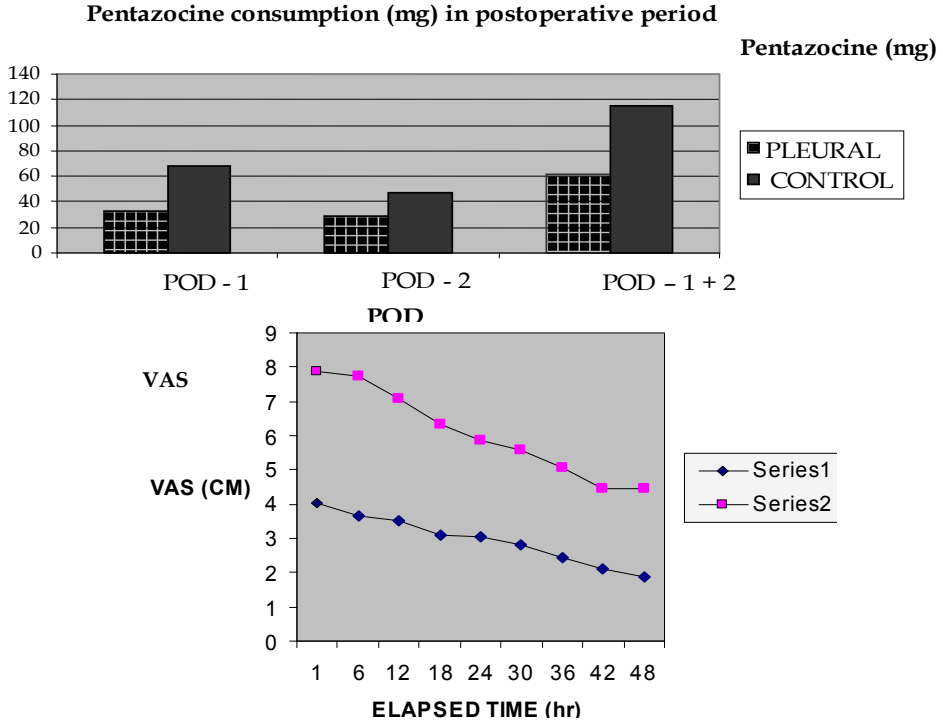
Table 2: Pentazocine consumption (mg) in the two groups recorded at Days 1 And 2 postoperatively and during whole study period (Day 1 + Day 2)

Group	Day1	Day 2	Day1+ 2
Pleural	33.3 ± 9.7	28.3 ± 7.0	61.6 ± 8.7
Control	68.3 ± 13.8	46.6 ± 21.1	114.9 ± 20.7
P Value	< 0.001	< 0.01	< 0.001

Table 3: Pain scores

Time	Interpleural Pain score	Control Pain score	P Value
1 Hour	4.0± 1.2	7.8 ± 0.7	< 0.001
6 Hour	3.6 ± 0.8	7.7 ± 0.7	< 0.001
12 Hour	3.5 ±1.0	7.0 ± 1.0	< 0.001
18 Hour	3.1 ± 1.3	6.3 ± 1.0	< 0.001
24 Hour	3.0 ± 1.4	5.8 ± 1.3	< 0.001
30 Hour	2.8 ± 1.4	5.5 ± 1.2	< 0.001
36 Hour	2.4 ± 1.1	5.0 ± 1.2	< 0.001
42 Hour	2.1± 1.2	4.4 ± 1.2	< 0.001
48 Hour	1.8 ± 1.1	4.4 ± 1.1	< 0.001
Total(48 hrs)	2.96 ± 0.72	6.04 ± 1.30	< 0.001

Bar Diagram Showing Pentazocine Consumption in Pleural & Control Group



Discussion

The Aim of postoperative pain management is to provide good subjective comfort and to contribute to early recovery and a good outcome after surgery.

In this prospective study we have investigated the efficacy of intermittent boluses of intrapleural bupivacaine compared to intramuscular pentazocine with regard to postoperative pain relief. Many clinicians avoid the closed chest technique for the placement of an interpleural catheter because of the high incidence of pneumothorax [3]. Using our technique, pneumothorax was not seen in our patients as determined by chest x-ray in the recovery room. We used a syringe filled with saline and a Touhy needle instead of a lubricated glass syringe to locate the interpleural space. This may eliminate false negatives caused by sticking between the piston and the syringe wall and thus prevent the needle from being accidently advanced too far into the thoracic cavity. Our technique is equally effective as the balloon method and it was easy to identify the pleural space.

We used pentazocine for comparison with interpleural bupivacaine because it has less propensity for causing spasm of spinchter of Oddi.

The intramuscular route was chosen because of the simplicity of administration by nurses in the post operative ward.

Nevertheless, the use of interpleural local anesthetics is not devoid of side effects that include pneumothorax (most common), systemic toxicity of local anesthetics, pleural effusion, Horner's syndrome, pleural infections, catheter rupture, and temporary phrenic nerve palsy [16,17]. No such complications were recorded in our patients. Pneumothorax and phrenic nerve palsy were excluded in our patients by chest X-rays. Furthermore, the use of a diluted local anesthetic solution decreased the propensity for phrenic nerve palsy and toxic reactions.

Parenteral opiods are similarily associated with risks, especially ventilatory depression and cognitive impairment that may restrict early postoperative ambulation. There is significant opioid sparing benefit by the interpleural analgesia.

We have chosen 40 ml of 0.25% bupivacaine every 6 hrs because this dose is unlikely to be associated with toxic plasma concentration [18].

In fact, postoperative alpha l-acid-glycoprotein increases, leading to an increase in protein binding of local anesthetics and to a reduction of free-fraction, thus diminishing the risk of potential central nervous system toxicity [19]. Moreover, Scott [20] suggests that the absolute toxic plasmacon centration may be more dependent on the rate of increase of the concentration than on any exact concentration of bupivacaine.Von Kleef et al also found no difference between the use of 0.5% and 0.25% bupivacaine for interpleural analgesia [21]. We used 0.25% bupivacaine which produced effective analgesia.

The quality of analgesia obtained in our study is consistent with that reported by others [2,3,4].

The results of this study demonstrate the effective analgesia obtained in the immediate postoperative period by the injection of interpleural bupivacaine after upper abdominal surgery.

Conclusion

It is concluded from this study that intermittent interpleural analgesia with bupivacaine was more effective than intermittent intramuscular administration of pentazocine alone, in reducing the severity of pain after upper abdominal surgery up to 48 hours postoperatively and can be recommended for sufficient pain control.

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Conflict of Interest: Nil

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Original Research Article

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Preemptive Antiemesis using Intravenous Ondansetron to Control Intrathecal Morphine Induced Nausea and Vomiting

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Abstract

Background: Morphine is an opioid and its intrathecal use for postoperative pain relief is well documented. Nausea and vomiting are the common adverse effects with intrathecal morphine and might be distressing in patients undergoing abdominal surgeries limiting its usage. Ondansetron is helpful in treating of nausea and vomiting but would be of greater help when administered pre-emptively. *Aims and Objectives:* Primary aim of study was to study the effect of pre-emptive ondansetron in controlling intrathecal morphine induced nausea and vomiting. Secondary aims was to assess its effectiveness in controlling pruritus. *Methods and Materials:* In this prospective, randomized study ninety patients undergoing abdominal hysterectomy were categorized into 3 equal groups receiving 15mg hyperbaric Inj.bupivacaine, in addition 0.5ml saline in Group-I, and 100µg and 200µg of intrathecal morphine diluted to 0.5ml respectively in Group-II and Group-III. All patients received 4mg of Inj.ondansetron intravenously 10 minutes before administering spinal drug preparation. Patients were assessed for duration of analgesia, nausea, vomiting, pruritus and other adverse effects of intrathecal morphine. *Results:* There was statistical significant difference with respect to age, body mass index and duration of surgery between three groups. Intrathecal morphine resulted in significantly longer duration of analgesia in patients receiving intrathecal morphine ($p<0.001$). Pre-emptive ondansetron effectively controlled intrathecal morphine induced nausea ($p=0.809$) and vomiting ($p=0.199$) and it was statistically insignificant when compared to control group, but did not decrease incidence of pruritus ($p=0.027$). *Conclusion:* Pre-emptive intravenous Inj.ondansetron (4mg) effectively controls intrathecal morphine induced nausea and vomiting but not pruritus.

Keywords: Preemptive; Ondansetron; Intrathecal Morphine; Nausea; Vomiting; Pruritus.

Introduction

Postoperative pain is one of the unpleasant experience a patient would experience during hospital stay and many treatment modalities have been employed since decades and individual treatment option has its own advantages and disadvantages.

Intrathecal morphine is one of the efficient and effective treatment modality for postoperative pain, has the advantage of longer duration of analgesia but its common adverse effects e.g. nausea, vomiting, pruritus are undesirable, limiting its usage [1,2]. Antiemetics when used preemptively, reduce the incidence of postoperativenausea and vomiting (PONV) [3,5] andwhen used for patients receiving intrathecal morphine would havethe advantage of its longer action while reducing the incidence of PONV [3].

Few studies have been done using prophylactic antiemetic to control PONV in patients receiving intrathecal morphine, but they showed conflicting results [3-5]. This study was undertaken to assess preemptive antiemeticaction of ondansetron in decreasing incidence of PONV in patients receiving intrathecal morphine for abdominal hysterectomy.

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Methods

This was a prospective, randomized, controlled study with double blinding of the patientsand procedure undertaken. After institutional ethics committee approval, written and informed consent were obtained and 90 patients of ASA l and ll who were scheduled for elective abdominal hysterectomy were included in the study. Primary aim of the study was to assess the effectiveness of preemptive use of Inj.ondansetron 4 mg i.v. in decreasing the incidence of nausea and vomiting in patients receiving intrathecal morphine. Secondary aim of the study was to assess the effectiveness in decreasing the incidence of pruritus.

Patients with history of respiratory disease e.g. bronchial asthma, chronic obstructive pulmonary disease, history of gastro-esophageal reflux disease, sleep apneapsychiatric illness, body mass index of more than 25kg/m^2, patients on opioid medications, known allergy to morphine or any other opioid medication were all excluded from the study.

Patients were asked to be nil oral eight hours before surgery. None of the patients in either groups received preoperative sedative, so as to have accurate assessment of intrathecal morphine induced sedation and respiratory depression and also to have frequent communication with patients. All patients were counselled and reassured preoperatively about the intraoperative events so as not to be apprehensive as they did not receive preoperative sedation. All patients received Inj.pantoprazole 40mg i.v. 1 hour before surgical procedure.

Patients were randomly allocated by envelope method into following three groups.All patients received 3ml of 0.5% hyperbaric bupivacaine in 8% dextrose and inaddition 0.5ml of the following: Group-l 0.9% normal saline, Group-ll 100 µg of morphine and Group-lll200 µg of morphine diluted to 0.5ml. Total volume of drug was made to 3.5ml. An anesthesiologist not involved in the study prepared the drug preparation. A 18.G. i.v. cannula was secured in holding room and patients were preloaded using 10ml/kg of Ringer's lactate. All patients received 4mg of Inj.ondansetron intravenously 10 minutes before injection of the spinal drug preparation.

Intraoperative monitoring included 5-lead electrocardiography (ECG), noninvasive blood pressure (NIBP) and plethysmography SpO_2. Under strict aseptic precautions in left lateral position, drug preparation was injected intrathecally using 27.G. Quinke's needle. To ensure safety of patients with regard to respiratory depression, oxygen by face mask 5 liters/min was administered for the first 24 hours irrespective of their SpO_2 reading.

Patients were observed and monitored for pain relief, nausea, vomiting, pruritus, bradycardia, hypotension, sedation, respiratory depressionin the first 24 hours-both intraoperatively and postoperatively. Respiratory depression was defined as rate < 10/min, bradycardia as heart rate < 50/min, hypotension as reduction of mean arterial pressure 20% from the baseline.Hypotension was treated using i.v. fluids and Inj.ephedrine, bradycardia using Inj.atropine, respiratory depression according to the severity. I.V. fluids and blood transfusion were undertaken on individual patient basis. All patients were catheterized for bladder because of surgical necessity (abdominal hysterectomy) and hence they were not monitored for urinary retention.

Patients who vomited more than once or havingunbearable nausea even after preemptive Inj.ondansetron received Inj.metaclopramide 10mg i.v. Pain was assessed using Visual Analogue Score (VAS), and a score more than 3 was treated using Inj.tramadol 2mg/kg as a rescue analgesic and pruritus was treated using Inj.pheniramine10 mg i.v. Postoperative monitoring of patients included ECG, NIBP and SpO_2. In addition patients were assessed for pain relief by time of rescue analgesic administered for a VAS >3, nausea, vomiting, pruritus, sedation, bradycardia, hypotension. As patients were catheterized urinary retention was not assessed.

After administration of spinal anesthesia all patients were assessed for level of sensory blockade using acold swab and the highest level achieved varied from T_4-T_8 level. There was no sparing action or incidence of failed spinal anesthesia in either of the groups. All patients were preloaded and received i.v. fluids according to the blood loss and hypotension. Two patients in Group-II and one patient in Group-I developed bradycardia and were treated using 0.6 mg Inj.atropine intravenously. Surgery was completed with spinal anesthesia technique alone and none of the patients, intraoperatively received any adjuvant medications for pain. Duration of surgery did not vary significantly between the three groups. Patients were reassured for intraoperative anxiety.

Statistical analysis was done using SPSS 17.0.2. Descriptive and inferential statistical analysis has been used in our study. Results on continuous measurements are presented on Mean±SD

(Minimum-Maximum) and results on categorical measurements are presented in percentage numbers (%). 'p' value of less than 0.05 was considered to be significant. The following assumptions on data were made - dependent variables were normally distributed, random sampling from the population was ensured and the cases of the samples were independent.

Student t test (two tailed, independent) and Chi-square/ Fisher Exact test were used to assess the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters and categorical scale between two or more groups respectively. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance and $p \leq 0.01$ was considered to be strongly significant.

Results and Observation

The three groups did not vary significantly with respect to age, body mass index and duration of surgery (Table 1). Spinal anesthesia was successful in all patients and there was no incidence of failed spinal anesthesia. The mean duration of analgesia in Group-I, Group-II and Group-III were respectively 3.4 hours, 16.15 hours and 24.9 hours (Table 2) and the difference was statistically significant when compared to control group ($p<0.001$). The duration of analgesia was dose dependent and it was higher in Group-III when compared to Group-II.

The three groups did not vary significantly with respect to incidence of nausea (p=0.809, Table 3) and vomiting (p=0.199, Table 3). The incidence of PONV

Table 1: Patient characteristics among the three groups. Data are mean (range) or Mean ± SD*

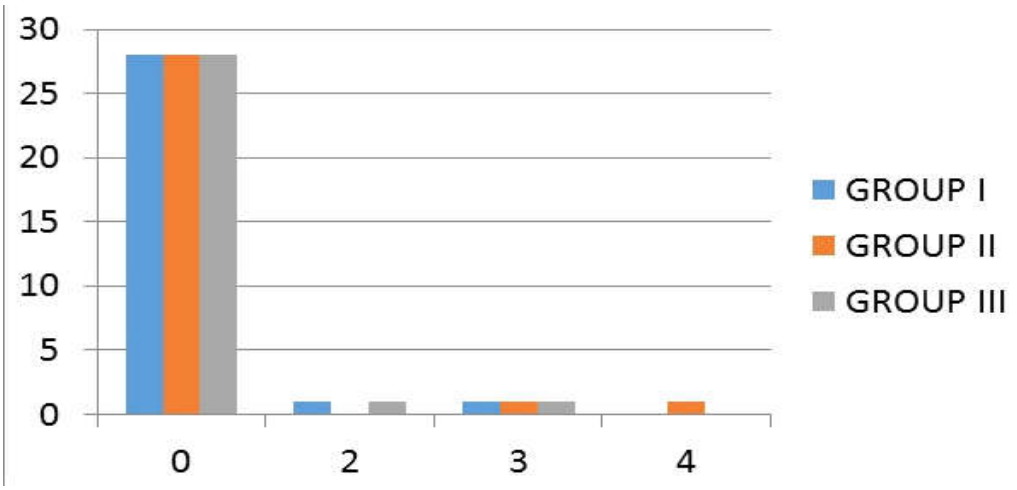
	Group I (n=30)	Group II (n=30)	Group III (n=30)	p-value
Age (years)	48.50 ± 2.17	49.40 ± 3.22	48.73 ± 2.18	0.377 (ns)
Body Mass Index (kg/m²)	21.72 ± 2.43	22.33 ± 1.89	22.26 ± 1.57	0.781 (ns)
Mean duration of surgery (in minutes)	97.50 ± 3.20	95.10 ± 3.03	94.86 ± 3.08	0.814 (ns)

Abbreviations: ð SD = standard deviation, $p<0.05$ significant, ns= statistically not significant

Table 2: Comparison of Duration of Analgesia (hours) among the three groups

	Sample number (n)	Duration of Analgesia (hours)	p-value
Group I	30	3.43 ± 0.40	
Group II	30	16.15 ± 2.26	<0.001 (hs)
Group III	30	24.90 ± 2.26	

$p<0.05$ is significant, Abbreviations: hs= highly significant



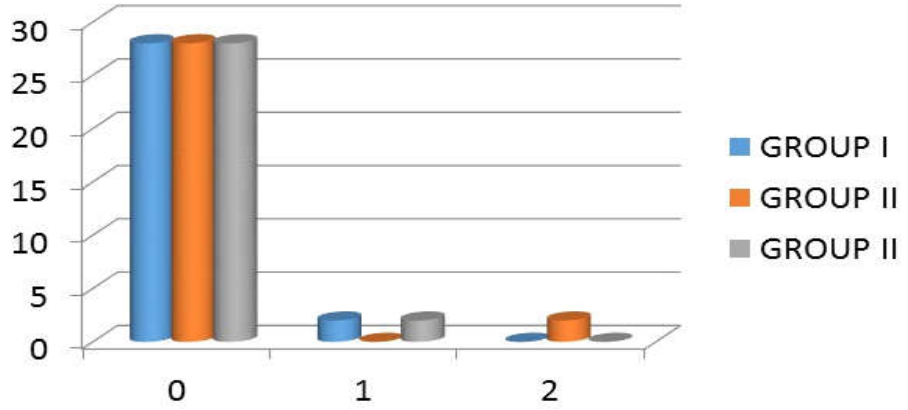
x-axis= number of episodes, y-axis= number of patients

Fig. 1: Comparison of incidence of Nausea among the three groups

Table 3: Comparison of adverse effects among the three groups

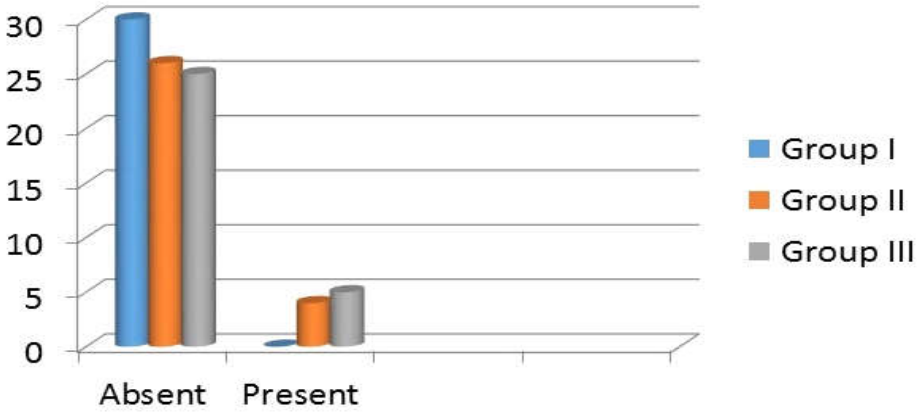
Adverse Effects		Group I (n=30)	Group II (n=30)	Group III (n=30)	p-value
Nausea	2*	1	0	1	0.809 (ns)
(number of episodes)	3*	1	1	1	
	4*	0	1	0	
Vomiting	1*	2	0	2	0.199 (ns)
(number of episodes)	2*	0	2	0	
Pruritus		0	5	5	0.027 (ns)
Sedation		0	3	2	0.227(ns)
Bradycardia		0	2	1	0.725 (ns)

Abbreviations: ð number of episodes complained by the patient, $p < 0.05$ is significant, ns= statistically not significant



x-axis= number of episodes, y-axis= number of patients

Fig. 2: Comparison of incidence of Vomiting among the three groups



x-axis= pruritus present (or) absent, y-axis= number of patients

Fig. 3: Comparison of incidence of Pruritus among the three groups

was not related to the dose of intrathecal morphine received.Incidence of pruritus was significant in Group II and Group III when compared to Group I (p=0.027) (Table 3).

Sedation scores were similar between Group-II and Group-III and it was statistically insignificant (p=0.227, Table 3).

Discussion

Postoperative nausea and vomiting (PONV) is one of the common symptoms patients would experience in perioperative period. This may be related to patients own risk factors, drug induced or the surgical procedure patient has undergone.

Irrespective of the cause, PONV delays recovery and prolongs the duration of stay in postoperative anesthesia care unit (PACU) and at times it would be very distressing for the patient [6].

Intrathecal morphine provides good pain relief having the advantage of longer duration of action. However, PONV is a common adverse effect noted after the use of intrathecal morphine for perioperative pain relief [2]. PONV reduces the quality of recovery and increases the duration of stay in PACU [6]. Higher incidence of PONV with the use of intrathecal morphine, prolonging PACU stay and decreasing the quality of recovery is the main drawback of its use, especially when used for intraabdominal surgeries.

5-HT_3 antagonists have been used frequently to decrease the incidence of nausea and vomiting, and ondansetron is one of the common medication used in this class of drugs [7]. Dolasetron, ramosetron and palanosetron are other medications of the same class which are used more recently [3,8-10].

Morphine is a hydrophilic opioid and hence its action with regard to pain relief and adverse effects are delayed in onset when compared to other lipophilic opioids [11,12]. Hence, intrathecal morphine induced nausea and vomiting occur more frequently in postoperative than intraoperative period. 5-HT_3 antagonists like ondansetron have been used to treat intrathecal morphine induced PONV. Ondansetron when administered pre-emptively, would reduce the incidence of intrathecal morphine induced nausea and vomiting [3,13,14]. This would improve the quality of recovery and decrease the stay in postoperative unit.

Ondansetron when usedpre-emptively has been shown to reduce nausea and vomiting in patients receiving intrathecal morphine [2,14]. In our study, all patients received 4 mg of intravenous ondansetron, 10 minutes before injection of spinal drug preparation. Patients were monitored and treated for nausea and vomiting intraoperatively and postoperatively. We observed statistically insignificant difference in incidence of nausea (p=0.809) and vomiting (p=0.199) in patients receiving intrathecal morphine when compared to control group (Table 3). Incidence and frequency of nausea and vomiting were not related to the dose of intrathecal morphine used.

There are many risk factors for patients to develop perioperative nausea and vomiting e.g.- GERD, peptic ulcers, obesity, gastropathy, NSAIDs, opioids, abdominal surgeries etc. and different treatment medications have been used. Each factor would contribute collectively to cause PONV. In our study we excluded patients who had risk factors to develop PONV so as to avoid bias on the results with the use of intrathecal morphine. We maintained the uniformity of the patients chosen and limited our study for abdominal hysterectomy patients.We did not notice any significant difference between control group and intrathecal morphine group. In addition, PONV was not related to dose intrathecal morphine used (100 μg versus 200 μg) and correlates with the study conducted by other authors [2,14].

Pre-emptive use of ondansetron to reduce incidence of pruritus have been studied by various authors and have been observed to be effective [3,5,15,16] by few authors while others have found it to be ineffective [4,14]. In our study incidence of pruritus was statistically significant (p=0.027) in Group II and Group III when compared to Group I. None of the patients in control group developed pruritus, whereas 5 patients each in Group-II and Group-III developed pruritus (Table 3).

Sedation as an adverse effect with the use of intrathecal morphine was statistically insignificant (p=0.227) and it was mild (Table 3). Respiratory depression associated with the use of intrathecal morphine is dose dependent and higher incidence was observed when dose exceeded 300 μg and safe when used less than 300 μg [2]. We used 100 μg and 200 μg in Group-II and Group-III respectively and hence did not observe respiratory depression.

Bradycardia and hypotension are observed less frequently with the use of intrathecal morphine.[2]In our study we noted bradycardia in two patients in Group-II and one patient in Group-III which responded to 0.6mg Inj.atropine i.v. (Table 3). Incidence of bradycardia in our study was more likely because of dilution of the spinal drug preparation using normal saline, reducing the baricity of the drug preparation resulting in higher level of blockade than expected. It was unlikely to the doses of intrathecal morphine used.

Conclusion

Preemptive antiemesis with ondansetron 4 mg administered intravenously 10 minutes before injection of intrathecal morphine, reduces the incidence of intraoperative and postoperative nausea and vomiting. Duration of analgesia was significant and dose dependent in patients receiving intrathecal morphine, and better tolerated because of lesser incidence of PONV. Pruritus was higher in patients receiving intrathecal morphine and did not decrease with the use of preemptive ondansetron.

Conflicts of Interest

Nil

Acknowledgement

Nil

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Intravenous Dexmedetomidine versus Dexmedetomidine and Midazolam Combination for Paediatric Sedation in MRI Room: A Randomized Study

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Abstract

Background: Sedation is a necessity for MRI (Magnetic Resonance Imaging) procedures in children for alleviating anxiety and to avoid movements during the procedure. Dexmedetomidine a selective alpha-2 adrenoreceptor agonist is very useful for such procedures. *Aims and Objectives:* To analyze and compare the sedative, hemodynamic and respiratory effect of Intravenous (IV) dexmedetomidine with IV dexmedetomidine and midazolam combination in children undergoing magnetic resonance imaging (MRI) examination. *Material and Methods:* Total of 60 patients were studied, 30 in each group, group D and group DM. Group D received inj. Dexmedetomidine 2mcg/kg, Group DM received dexmedetomidine 2mcg/kg and inj. Midazolam 0.03 mg/kg intravenously. The level of sedation was assessed by the Ramsay sedation scale and quality of MRI was assessed using the 3 point scale. During the procedure, respiratory rate, heart rate, oxygen saturation and blood pressure were continuously monitored and recorded using MRI compatible monitors. The data were analysed using SPSS version 24.0. *Results:* There was significant difference in onset of sedation; the mean values ranged 6.3±2.28 minutes (mins) and 3.23±3.02 minutes for D and DM group respectively ($p < 0.05$). There was significant difference in the Level of sedation; the mean values ranged 4.57±0.57 and 5.27±0.52 for D and DM group ($p < 0.05$). There was no significant difference in blood pressure values at various time periods between the two groups. The quality of MRI is better in Group DM than group D. There was no significant difference in heart rate, respiratory rate, oxygen saturation values at various time periods between the two groups. 4 patients in Group D received supplementation, whereas none in group DM received supplementation. *Conclusion:* Addition of midazolam to dexmedetomidine for sedation helped in decreasing the onset of sedation and also offered a better quality of MRI study without any haemodynamic or respiratory disturbances.

Keywords: Dexmedetomidine; Hemodynamic; Midazolam; MRI; Respiratory; Sedation.

Introduction

Sedation is frequently necessary for children less than 10 years of age undergoing MRI. We mainly aim to attain anxiety relief, pain control and the restriction of excessive movement during imaging procedures without compromising patient safety [1]. The choice of drug that we administer depends on the type of sedation as well as the depth of sedation required. For CT Scanning, for instance, modern multislice scanners allow for rapid image acquisition; therefore, moderate sedation can be employed. Children need deeper levels of sedation to stay still in noisier environments like MRI room. We have opioids, benzodiazepines, barbiturates, ketamine, propofol and alpha2 adrenergic agonists as options. These drugs are able to provide a very good level of sedation [2].

The success of sedation for MRI depends on the safety of the sedation and the successful completion of the diagnostic examination. But the usage of these drugs such as thiopental, propofol, ketamine, morphine, diazepam, etc is associated with some of the unwanted effects like hypoventilation, apnea,

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sialorrhea, airway obstruction, hyperventilation, hypotension or bradycardia [3]. Due to the lack of immediate and easy access to the patients with instruments that would help in securing the airway and stabilization of the circulatory function, it is necessary to utilize drugs such as dexmedetomidine, midazolam etc. so as to provide an adequate sedation level without severe adverse reactions [4].

Dexmedetomidine an alpha-2 adrenergic agonist at therapeutic doses provides profound levels of sedation without affecting cardiovascular and respiratory stability [5,6]. It also provides anxiolysis and analgesia [7]. The purpose of this randomized study is to compare between the effects of dexmedetomidine alone and its combination with midazolam and see if the combination would help in a faster induction and to know if the need for supplementation is reduced for the entire MRI study without compromising patient safety.

Material and Methods

This prospective randomised study was undertaken in tertiary care medical college hospital, during the period November 2015 to May 2017 after obtaining ethical committee clearance as well as informed consent from all the guardians of the patients. 60 children who were scheduled for magnetic resonance imaging study under IV sedation and belonging to ASA class I and II were included under this study. All children of ASA III and IV, children with congenital heart disease, gastroesophageal reflux disease and respiratory tract infection were excluded from the study. The study population was randomly divided into two groups group D and group DM, with 30 patients in each group using sealed envelope technique. The envelope was opened by a senior anaesthesiologist who was not involved with the study. Group D received Inj. Dexmedetomidine (2mcg/kg IV), Group DM received Inj. Dexmedetomidine (2mcg/kg) + inj. Midazolam (0.03 mg/kg). A routine pre-anaesthetic examination was done in all the participants.

All the children were premedicated with syrup phenergan 0.5 mg/kg at night. They were advised to maintain a nil per oral protocol as per 2–4–6 fasting rule [8]. Topical application of EMLA cream is done to the dorsum of the hand 1 hour prior to the procedure to facilitate the venous cannulation. Pre-sedation behavior was assessed on a 4 point scale by a senior anaesthesiologist who did not know which drug would be administered: 1 = calm, cooperative; 2 = anxious but assurable, 3 = anxious and not assurable; 4 = crying or resisting. After obtaining IV access inj. Metoclopramide 0.3 mg/kg and inj.Glycopyrrolate 0.005 mg/kg were given 3 mins prior to the sedation of the patient. Solution of dexmedetomidine, 1 ml at a concentration of 100 mcg/ml, was diluted with 49 ml normal saline to a concentration of 2 mcg/ml. To group D children, the dose of dexmedetomidine at 2 mcg/kg is administered as a slow infusion over 10 mins. Solution of midazolam, 1 ml at a concentration of 1 mg/ml was diluted with 10 ml sterile water to a concentration of 100 mcg/ml. To the group DM children, the combined dose of dexmedetomidine at 2 mcg/kg and midazolam at 0.03 mg/kg is administered as a slow infusion over 10 mins by a blinded anaesthesiologist.

Ramsay sedation scale was used to measure sedation levels by a blinded anaesthesiologist. The Ramsay scale assigns a score of 1–6 as follows: 1 = anxious, agitated, restless; 2 = awake, but cooperative, tranquil, orientated; 3 = responds to verbal commands only; 4 = brisk response to loud noises or glabellar taps; 5 = sluggish response to loud noises or glabellar taps; 6 = no response to loud noises or glabellar taps [8,9]. Score 3 was accepted as a level to start the procedure, whereas score 5 was accepted as level of deep sedation. The children were then transferred after both a Ramsay score of 5 was achieved and haemodynamic and respiratory stability was ensured. If patient movements were observed in between the procedure, then the same supplementation (with dexmedetomidine 1 mcg/kg) is given depending on the duration of the procedure remaining. If in the case the procedure is interrupted repeatedly (cut off twice), then the procedure is cancelled and considered as a failure. Inadequate sedation was defined as difficulty in completing the procedure as a result of the child's movement during MRI examination [8,9].

Blood Pressure 5 minutes after the completion of the administration of drug was noted. Heart rate (HR), peripheral oxygen saturation (SpO_2), blood pressure and respiratory rate (RR) were recorded continuously using MRI compatible monitors. If there was significant hypotension (SBP<20% of baseline), fluid at 10 ml/kg body weight would be administered. Patients were allowed to breathe spontaneously through a Hudson face mask with oxygen at 4 L/min. Ventilator function was continuously being assessed by the blinded anaesthesiologist by observation of the child's respiratory function. If the SpO_2 level decreased

below 95% for 30 seconds, the MRI procedure would be interrupted and the child shifted out of the MRI tunnel for stabilization.

Quality of the MRI was evaluated by a radiologist, who is not a part of the study, using a three-point scale: 1 = no motion; 2 = minor movement; 3 = major movement necessitating another scan. At the end of the procedure, the child was shifted from the imaging center to the post-anaesthesia recovery room in the left lateral position and then the vitals are continuously monitored until the child recovers completely from sedation and reaches a Ramsay Score of 2.

The onset of sedation time was defined as "the period of time between the beginning of study drug administration and reaching a Ramsay score of 5" [8,9]. Recovery time was accepted as the period of time taken for the patient to recover to the Ramsay score 2 from sedation. The patient was maintained in the nil per oral status for 6 hours while supplemented with IV fluid of plasmalyte-P at a maintenance rate based on the Holiday Segar formula of 4:2:1 [10]. Statistical analyses were made using SPSS®24.0. Results are presented as mean (sd) or their confidence interval (CI). Analysis of variance for repeated measures was performed on hemodynamic and respiratory variables, with compensation for post hoc comparisons using the Bonferroni correction. Intergroup statistical analyses were performed using Student's *t*-test, and nonparametric data were analyzed using chi^2 test. Statistical significance was considered at p value < 0.05. The power of the study was calculated based on the onset of sedation time. Setting a significance level of P <0.05, it was calculated that a group size of 30 patients allowed detection of a difference of 4 min between groups with a power of 100%.

Results

There were no statistically significant differences in the demographic profile of patients in either group in terms of age, weight and gender (p>0.05). (Table 1).

There was no significant difference in baseline Pulse Rate and respiratory rate between two groups. (Table 2).

There was significant earlier onset of sedation and level of sedation in group DM compared to group D. (p value – 0.001) (Table 3).

There was no significant difference in blood pressure values at various time periods between the two groups (p > 0.05) (Table 4).

There was no significant difference in Heart Rate values at various time periods between the two groups (p > 0.05) (Table 5).

There was no significant difference in Respiratory Rate values at various time periods between the two groups (since p > 0.05) (Table 6).

There was no significant difference in SpO_2 values at various time periods between the two groups (p > 0.05) (Table 7).

Table 8 describes that 4 patients received supplementation in group D which is statistically significant. (p = 0.04) (Table 8).

This showed that there were no untoward effects in both the groups, both group D and group DM. (Table 9).

The quality of MRI was significantly better in Group DM compared to Group D. (p < 0.05). (Table 10).

Table 1: Demographic Characteristics of study population

Variable	Group D	Group DM	P value
Age	6.57 ± 2.62	7.07 ± 2.61	0.4
Weight	20.08 ± 8.89	23.49 ± 7.87	0.12
Gender (M/F)	21/9	19/11	0.5

Table 2: Comparison of Baseline Measurements in both groups

Variable	Group D	Group DM	P value
Pulse Rate	102.7 ± 9.09	99.27 ± 19.47	0.38
Respiratory Rate	22.9 ± 3.52	21.03 ± 5.88	0.14

Table 3: Comparison of Sedation between D and DM group

Variable	Group D	Group DM	P value
Pre sedation Behavior	2.33 ± 0.55	2.1 ± 0.71	0.16
Time Sedation	6.3 ± 2.28	3.23 ± 3.02	0.001
Level of sedation	4.57 ± 0.57	5.27 ± 0.52	0.001

Table 4: Comparison of Blood Pressure at various time points

Variable	Group D	Group DM	P value
Baseline			
SBP	92.07 ± 6.96	94.8 ± 9.96	0.22
DBP	58.47 ± 5.65	60.73 ± 4.87	0.1
Before drug			
SBP	95.87 ± 7.43	98.47 ± 8.43	0.21
DBP	59.73 ± 4.45	60.27 ± 3.43	0.6
5 Mins			
SBP	90.6 ± 6.5	92.87 ± 9.26	0.28
DBP	58.47 ± 4.22	59.6 ± 4.28	0.3
Recovery			
SBP	96 ± 7.86	99.67 ± 10.58	0.13
DBP	59.6 ± 4.28	59.47 ± 3.48	0.8

Table 5: Comparison of Heart Rate (mins) in both groups over the time

Heart Rate	Group D	Group DM	P Value
0 Min	126.8 ± 9.35	124 ± 20.18	0.49
5 Mins	116.2 ± 9.19	113.6 ± 20.2	0.52
10 Mins	109.5 ± 8.97	107.1 ± 19.36	0.54
15 Mins	105.83 ± 8.96	101.93 ± 18.93	0.31
20 Mins	103.1 ± 9.98	97.3 ± 18.54	0.13
25 Mins	99.93 ± 9.25	93.37 ± 18.04	0.08
30 Mins	98 ± 9.46	90.7 ± 17.97	0.15
35 Mins	95.53 ± 8.39	89.6 ± 17.88	0.1
40 Mins	93.06 ± 9.47	89.21 ± 18.44	0.43
45 Mins	94.83 ± 11.5	82 ± 20.2	0.23

Table 6: Comparison of Respiratory Rate (mins) in both groups over the time

RR	Group D	Group DM	P Value
0 Min	24.47 ± 6.66	24.87 ± 4.24	0.78
5 Mins	22.07 ± 6.07	22.27 ± 4.05	0.88
10 Mins	20.8 ± 5.79	21.37 ± 3.76	0.66
15 Mins	20.43 ± 5.64	19.83 ± 4.14	0.64
20 Mins	20.43 ± 5.98	19.03 ± 4.07	0.29
25 Mins	19.57 ± 5.43	18.07 ± 4.33	0.24
30 Mins	19.23 ± 5.24	17.8 ± 4.39	0.25
35 Mins	18.58 ± 5.09	17.43 ± 3.92	0.36
40 Mins	19.67 ± 5.19	17.36 ± 4.19	0.16
45 Mins	17.5 ± 4.73	18.25 ± 4.59	0.79

Table 7: Comparison of SPO_2 (mins) in both groups over the time

SPO_2	Group D	Group DM	P Value
0 Min	99.83 ± 0.53	99.8 ± 0.66	0.83
5 Mins	99.9 ± 0.3	99.9 ± 0.4	0.99
10 Mins	99.93 ± 0.25	100	0.15
15 Mins	99.93 ± 0.25	100	0.15
20 Mins	99.93 ± 0.3	100	0.32
25 Mins	99.97 ± 0.18	100	0.32
30 Mins	99.97 ± 0.18	100	0.32
35 Mins	99.88 ± 0.33	100	0.14
40 Mins	99.89 ± 0.32	100	0.14
45 Mins	99.71 ± 0.49	100	0.22

Table 8: Comparison of Supplementation between D and DM group

Supplementation	Group D	Group DM	Total	P
No	26	30	56	0.04
Yes	4	0	4	
Total	30	30	60	

Table 9: Comparison of untoward effects between D and DM group

Un toward Effects	Group D	Group DM	Total
No	30	30	60
Yes	0	0	0

Table 10: Comparison of Quality of MRI between D and DM group

Quality of MRI	Group D	Group DM	P Value
1	26	30	0.04
2	4	0	
3	0	0	

Discussion

Sedation is seen as a depressed state or level of consciousness of a patient. It can vary from various stages. It can exist from a very light plane of sedation to a very deep plane of sedation. The level or plane of sedation that is required for any particular investigation or procedure mainly depends on the type of procedure, the location where it is being held, the duration of the procedure and if any interference is present during the undergoing investigation. At concious sedation we find that the patient is able to retain the ability to independently and consciously maintain a patent airway and is also able to respond properly to verbal commands. The patient might have ante grade amnesia, but the protective airway reflexes are normal or minimally altered.

A variety of drugs have been used for MRI sedation. Pentobarbital has been used very frequently for MRI sedation due to being a short acting barbiturate. Rooks, et al conducted a study comparing pentobarbital and chloral hydrate among 498 children and found no significant differences between the two groups [10]. The common side effects associated with pentobarbital were respiratory depression, cardiovascular depression and need for active airway interventions. Lower doses were associated with no sedation or lighter planes of sedation leading to repeated interruptions or delay of the imaging study and even postponement of the scan [12]. Chloral hydrate was also associated with the stimulation of nausea and vomiting in children due to its property of gastric irritation [13]. No intrinsic analgesic effect was appreciated with this drug. Chloral hydrate can also cause respiratory depression [14].

Barbiturates such as thiopental were also in usage. Filner BF et al found that 5 mg/kg IV of thiopental in normovolemic patients caused a transient and mild decrease in blood pressure of 10- to 20- mm Hg and was followed with a rise of heart rate around 15- to 20- beats per minute [15]. It also resulted in a dose related depression of medullary and pontine ventilatory centers. These cases required active airway management in the form of laryngeal mask airway or intubated with an endotracheal tube along with active ventilation till spontaneous breathing occurred. These facilities are difficult to manage in the MRI settings and hence active management of the patient in response to drug induced ventilatory depression is cumbersome and dangerous. Methohexital a potent sedative is not recommended by Pomeranz et al as a rectal route due to the high frequency of apnea or desaturation [16].

Propofol, administered at 1.5 – 2.5 mg/kg in < 15 seconds, produces unconsciousness in 30 seconds. Awakening is also rapid when compared with other drugs [17]. But large doses reduce the SBP significantly. It also decreases the cardiac output and systemic vascular resistance [18]. Baroreceptor reflex of the heart is also depressed as seen by Deutschman CS et al [19]. Bradycardia and asystole was observed in many cases requiring active airway management and assisted ventilation. Tidal volume and frequency of breathing is also decreased

Dexmedetomidine, an alpha-2 agonist, is a drug with safe therapeutic window in relation to respiratory depression [20,21,22]. This is a very positive point with respect to its usage for procedural sedation. In case of MRI study, it has an advantage over the other medications due to the child not being immediately accessible to the medical team. Many studies demonstrate dexmedetomidine as a good option for procedural sedation [8,9,23,24]. Previous studies show that low dose dexmedetomidine of rates 0.1 – 0.7 mcg/kg/min as an safe and effective sedation dose [3,25]. But, this dosage will not be sufficient in conducting MRI sedation as higher levels are required for children. There have been several trials clinically to compare between dexmedetomidine and propofol usage for IV sedation in pediatric age groups during

MRI studies [8,9,26]. 83% sedation with dexmedetomidine and 90 % sedation with propofol, was observed in a study conducted among 60 children undergoing MRI [26]. Shorter means were noticed in the propofol group with respect to onset, recovery and discharge time. Studies evaluated the safety and efficacy of dexmedetomidine during noninvasive radiological procedures [27]. Use of high dose dexmedetomidine as a sole sedative was found to provide higher quality radiological imaging and lesser use of rescue medications [5,28]. But there were incidences of bradycardia during these studies. In our study, we have compared the advantage of adding midazolam in combination with dexmedetomidine in hope to further prolong the time as well as improving the quality of the MRI. It is seen that, adding midazolam (0.03mg/kg) to dexmedetomidine (2 mcg/kg) is effective in completing a MRI study with no interruptions or need for supplementation in the form of pentazocine 0.5 mg/kg or ketamine 1-2 mg/kg and with a success rate of 100%. This study also showed that plain dexmedetomidine 2 mcg/kg IV bolus over 10 mins could provide an uninterrupted MRI study in 86% of cases.

In our study, there was no significant fall in the heart rate from baseline during sedation. It could be explained also by the fact that the anxiolytic action of dexmedetomidine was countered by the prophylactic administration of glycopyrrolate in both groups at the dose of 0.005 mg/kg IV. Other studies showed the heart rate to decrease to a value < 20% from baseline, which is considered to be insignificant [3,24]. In this study, the incidence of bradycardia is 0% of the total, which is less than 4% as noticed by Mason et al [24] or 3.9% as reported by Ahmed et al [28]. Our study, it was noticed that the blood pressure and oxygen saturation was maintained in the normal range throughout the entire MRI study period. One study showed that there was a fall in blood pressure immediately after stopping the dexmedetomidine infusion at the end of the MRI procedure which reverted to the baseline without any intervention [28]. Such infusion can be avoided by adding midazolam at 0.03 mg/kg to the dexmedetomidine drug at 2 mcg/kg.

The limitation of our study was the absence of recording the recovery time and duration of sedation for the two groups, group D and group DM. It has been reported in a previous study, the average recovery time of 38 minutes with dexmedetomidine [29]. By this study, we have come to the interpretation that during an MRI study within the pediatric age group, the usage of dexmedetomidine for the purpose of sedation is highly advocated and that addition of midazolam to dexmedetomidine helped in decreasing the time for the onset of sedation and also offered a better quality of MRI study. Thus, we come to the final conclusion that the combination of dexmedetomidine and midazolam is better and equally safe from the respiratory and haemodynamic perspective when compared with plain dexmedetomidine for the successful completion of MRI study in the pediatric age group.

Conclusion

Thus with this study, we have come to the findings that during an MRI study within the pediatric age group, the usage of dexmedetomidine for the purpose of sedation is highly advocated and that addition of midazolam to dexmedetomidine helped in decreasing the onset time for sedation and also offered a better quality of MRI study. It was also noted that a single bolus dose of dexmedetomidine at 2 mcg/kg iv and midazolam 0.03 mg/kg iv over 10 mins allowed us to perform the complete test without any disturbance or break and without requiring any additional supplementation.

Also the initial dose was not associated with any significant hypotension or bradycardia. Thus, by this study, we come to the final conclusion that the combination of dexmedetomidine and midazolam is safe without any haemodynamic or respiratory compromise in children, and it also provides adequate level of sedation for the entire MRI study to be conducted without any interruptions or requirements of additional supplementation.

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Pre-Emptive Analgesic Efficacy of Preincisional I.V. Low Dose Ketamine (0.15mg/kg) in Patients Posted for L.S.C.S. Under Spinal Anaesthesia

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Abstract

Introduction: Inadequate pain relief after caesarean section delivery impairs mother's ability to optimally care for her infant and to breastfeed in the immediate postoperative period. Pre-emptive analgesia is an antinociceptive treatment that prevents the establishment of altered processing of afferent input which amplifies postoperative pain. The lower dose of ketamine is not associated with neonatal depression and complication is minimal with high patient acceptance. *Aim and Objectives:* To assess the pre-emptive analgesic efficacy of pre-incisional i.v. low dose ketamine in patients posted for L.S.C.S under spinal anaesthesia. *Material and Methods*: The present clinical prospective study was carried out in Department of Anesthesiology, during Dec. 2011 to Oct. 2013. Sixty parturients of ASA Grade I and II were randomly divided into two groups of 30 each, every even number patient received IV ketamine (group K) and every odd patient received normal saline (group B). *Results*: Highest level of sensory block reached in group B was T_2 in 7% of patients and 10% of patients in group K. All patients had excellent sensory analgesia. Mean time of total duration of sensory block was 234.27±24.23min in group B and 230±28.8min in group K. Mean time of effective analgesia was 126±17.6 min in group B and 161.6±24.2 min in group K. Hypotension was noted in 12 (40%) in group B and in 9 (30%) in group K. Shivering was observed in 3 patients in group B. *Conclusion*: The pre-incisional administration of low dose intravenous ketamine delayed the time to first analgesic request in parturients. The study could not substantially demonstrate the preemptive analgesic property of ketamine.

Keywords: Ketamine; Caesarian; Spinal Anesthesia; Pre-Emptive Analgesia; Low Dose.

Introduction

One of the primary aims of anaesthesia is to render adequate pain relief, thereby permitting the performance of surgical procedures without stress and discomfort. Inadequate pain relief is associated with undesirable physiological and psychological consequences. Inadequate pain relief after caesarean section delivery impairs mother's ability to optimally care for her infant and breast feed in the immediate postoperative period. Hence, it is necessary that pain relief with mother's ability to move around and care for infant with no adverse effect on the neonate.

Pre-emptive analgesia is an antinociceptive treatment that prevents establishment of altered processing of afferent input which amplifies postoperative pain. This concept was formulated by Crile [1] on the basis of clinical observation, he advocated the use of regional blocks in addition to general anaesthesia to prevent intraoperative nociception and formation of painful scar caused due to changes in central nervous system during surgery.

Many drugs are used for the study of pre-emptive analgesia but ketamine is a direct blocker at N-methyl-D-Aspartate (NMDA) receptors involved in central sensitisation [2-4]. Blocking NMDA receptors may improve the efficacy of opioid and

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reduce the development of chronic pain syndrome. Low dose ketamine is defined as a bolus dose of ketamine ≤ 2mg/kg when administered intramuscularly and ≤ 1mg/kg when administered via intravenous or epidural route [5]. The lower dose of ketamine (0.2-0.5mg/ kg iv) is not associated with neonatal depression and complication was minimal with high patient acceptance [5,6]. In India, Ketamine is commonly employed anaesthetic because it is cheap and perceived to be safe. In this study, we have selected patient for elective L.S.C.S. under regional anaesthesia rather than in general anaesthesia to study about the Pre-emptive analgesic efficacy of pre-incisional I.V. low dose ketamine.

Aim and Objectives

1. To assess the pre-emptive analgesic efficacy of pre-incisional i.v. low dose ketamine in patients posted for L.S.C.S under spinal anaesthesia
2. Comparison of time to first request for analgesia in the postoperative period.

Material and Methods

After obtaining Institutional Ethical Committee approval the present clinical prospective study was carried out in Department of Anesthesiology, during the period of December 2011 to October 2013. Sixty parturients of ASA Grade I and II undergoing elective LSCS by taking low transverse (modified Pfannenstiel) incision without medical or obstetric complications formed subjects.

Exclusion

Patients having respiratory, cardiovascular disease, bronchial asthma, history of allergic reactions to drug or food, patients with extremes of height (below 140 cm and above 165 cm) and weight (below 45 kg and above 65 kg) , patients with shock and coagulation disturbances ,patients with a local skin infection, any spinal deformity, spinal tenderness or neurological deficit were excluded. These patients were divided into two groups of 30 each by systematic randomization, every even number patient received IV ketamine (group K) and every odd patient received normal saline (group B).

Group (B) - Patients receiving hyperbaric bupivacaine (0.5%) 10mg (2ml) and normal saline for injection 10cc IV

Group (K) -Patients receiving hyperbaric bupivacaine (0.5%) 10 mg (2 ml) and 0.15mg/kg ketamine diluted upto 10cc IV. Routine investigations like Hemoglobin, urine examination for sugar and albumin, blood grouping and Rh typing were carried out in all patients. The procedure was explained to the patient, written informed consent for anaesthesia, surgery and blood transfusion was obtained. Baseline pulse rate, respiratory rate, blood pressure [systolic/ diastolic], oxygen saturation [SpO2], were recorded after placing the patient in 15^0 left lateral tilt. Preloading was done with 10 ml/kg body weight with ringer lactate solution in operation theatre before administration of spinal anaesthesia. The position of the table was kept horizontal. The patient was given left the lateral position and under all aseptic precautions, lumbar puncture was performed with lumbar puncture needle of 23 gauge at L_3 - L_4 space. After ensuring the free flow of clear cerebrospinal fluid the desired drug was injected. The patient was immediately turned supine and the wedge was given below right flank for left uterine displacement.

Hypotension was defined as a decrease in systolic blood pressure of more than 30% of baseline value. Hypotension was treated with leg elevation, O_2 supplementation, pushing IV fluids (200 ml bolus), Inj. Mephenteramine 3 mg IV and repeated every 3 min until hypotension was corrected.

Bradycardia was defined as a fall in pulse rate below 50 beats per minute. Atropine was kept ready for bradycardia. Inj. Ondansetran 4 mg IV was given for nausea and vomiting.

Sensory characteristics such as onset of sensory block, maximum level of sensory block, time required to achieve maximum sensory block, time required for two segment dermatome regression, total duration of sensory block and request for first dose of rescue analgesics were studied.

Analysis of data was performed using student's unpaired t-test (for finding the significance of difference between means of two independent samples. Chi -Square test (a test of association between two events in binominal samples). P value less than 0.05 was considered to be significant.

Results

In the present study 60 parturients ASA I and II those underwent caesarean section under subarachnoid block for LSCS were studied. The mean age of patients in group K was 25±3.5 years

Table 1: Showing demographic data and surgical duration

Variable	Group B (mean ± SD)	Group K (mean ± SD)	P value
Age (yrs)	24.8±3.57	25±3	0.80
Weight (kg)	54.3±4.57	53±6	0.99
Height (cm)	151±3.87	151±4.9	0.99
Duration of surgery (min)	52.6±7.2	52.5±5.3	0.91

Table 2: Showing maximum level of sensory block.

Maximum Sensory Level	Group B	Group K
T2	02	03
T3	00	0
T4	08	10
T5	05	02
T6	15	17
Total	**30**	**30**

Table 3: Degree of sensory block (quality of sensory analgesia)

Degree of Analgesia	Group B	Group K
I	0	0
II	0	0
III	0	0
IV	30	30
Total	30	30

Table 4: Showing Time Required For regression of block to S_1 in min

Total duration of sensory block(min)	Group B	Group K
121-180	02	03
181-240	23	20
241-300	07	07
Total	30	30
Mean ± SD(min)	234.27±24.23	230±28.8

Table 5: Showing Duration of Effective Analgesia in min

Duration of Effective Analgesia (Min)	Group B	Group K
90-120	15	00
121-150	15	13
151-180	00	14
181-210	00	03
Total	30	30
Mean ± SD(min)	126±17.6	161.6±24.2

Table 6: Comparison of side effects in both groups

Side effects	Group B	Group K
Nausea/ vomiting	0	0
Hypotension	12	09
Bradycardia	2	0
Pruritis	0	0
Respiratory depression	0	0
Shivering	3	0

Table 7: Showing blood pressure variations

Systolic BP	Group B Mean ± SD	Group K Mean ± SD	P Value
Preoperative	122±8.4	120±8.8	0.37
After 15 Min	89±13	88±9.8	0.57
After 90 Min	114±10.2	113±15	0.76
After 180 Min	118±10	118±7.1	0.99

and in group B was 24.8±3.3 years. The mean height of patients in group K was 151±4.9 cms and in group B was 151±3.87 cms. The mean weight of patients in group K was 53±6 kg and in group B was 54.3±4.5 kg. The mean time of duration of surgery was 52.5±5.34 min in group K and 52.6±7.2 min in group B. Highest level of block reached in group B was T_2 in 7% of patients and 10% of patients in group K. these findings were comparable in both groups (p=0.8, p>0.05).

Degree of Analgesia (Bromage PR1964)

I. Required general anaesthesia for completion of surgery.

II. Pain that required addition of analgesic drug.

III. Mild discomfort but did not required systemic analgesic.

IV. No discomfort at all during procedure.

All patients in group B and group K had excellent sensory analgesia. No patients from both the groups required general anaesthesia (Grade I). Time Required For regression of block to S_1(total duration of sensory block) Mean time of total duration of sensory block was 234.27±24.23min in group B and 230±28.8min in group K. it is comparable in both the groups (p=0.57, p>0.05).

Time Required for First Dose of Analgesic (Effective Analgesia)

Mean time of effective analgesia was 126±17.6 min in group B and 161.6±24.2 min in group K. Duration of effective analgesia between both the groups was statistically significant (p=0.0004 P<0.001).

Comparison of Side Effects in Both Groups

Hypotension was noted in 12 (40%) of patients in group B and in 9 (30%) of patients in group K, bradycardia was noted in 2 patients of group B and no bradycardia in group K. Shivering was observed in 3 patients in group B and no episode of shivering in K group. As all patients were catheterized urinary retention could not be monitored. Pruritus was not seen in any patients of both groups. Respiratory depression was not seen in any patient of both groups. There was fall in systolic blood pressure following spinal anaesthesia in both groups. Magnitude of fall was similar in both groups and it was not clinically or statistically significant (p>0.05). Statistical analysis of arterial oxygen saturation values for two groups at preoperative, intraoperative, postoperative shows that there was no statistically significant difference in two groups at these four periods (p>0.05).

Table 8: Showing SpO_2 variations

SpO_2	Group B Mean ± SD	Group K Mean ± SD	P Value
Preoperative	98±0.7	99±0.8	0.9
After 15 Min	98±0.7	99±0.8	0.9
After 90 Min	98±0.8	99±0.8	0.9
After 180 Min	98±0.7	99±0.8	0.9

Discussion

The present study is a prospective, double-blind, randomized study done at a tertiary hospital from December 2011 to September 2013.

Multimodal therapy for postoperative pain control is now widely practiced due to the advantage it provides in blocking multiple pain pathways while minimizing side effects of each individual pain medication [7]. Adverse effects such as nausea and vomiting often limit postoperative pain management. There are a number of reasons for postoperative nausea and vomiting (PONV), and these have been exhaustively discussed in the anaesthetic literature.

One possible factor is the use of opioids and adjuvant treatment with opioid-sparing drugs such as ketamine may be of value in giving better analgesia with fewer adverse effects (Schmid 1999) [8]. This research work studied the effect of low dose intravenous ketamine as a pre-emptive analgesia in patients undergoing caesarean section under spinal anaesthesia.

Demographic Data

In the present study the mean age of patients in group K was 25 years and in group B was 24.8±3.3 years. The mean weight of patients in group K was 53±6 kg and in group B was 54.3±4.5 kg. The mean time of duration of surgery was 52.5±5.34 min in group K and 52.6±7.2 min in group B. The difference observed in above demographic data and duration of surgery was statistically and clinically not significant (P- 0.05).

Sensory Block

The meantime required for the onset of sensory block was comparable in both the groups (p=0.41,p>0.05). The highest level of block reached in both groups was comparable (p=0.8, p>0.05). The mean time required to reach maximum sensory level was both statistically and clinically not significant (p=0.55, p>0.05). While the meantime for two segment dermatome regression was 84.33±4.58 min in group B and 84.9±5.76 min in group K that was comparable in both the groups (p=0.99, p>0.05). The meantime of total duration of sensory block was comparable in both the groups (p=0.57,p>0.05). These results were similar to studies carried out by Sen S et al [9] and Ebong EJ et al [10].

Above results show that onset, duration and spread of sensory block is similar in both ketamine and control group. As peripheral human NMDA receptors have been identified and ketamine has local anaesthetic like properties, but the peripheral effect in small dose does not provide sufficient analgesia when used alone [11].

The observed effect of prolonged first dose of analgesic is inhibition of central sensitization and not due to the peripheral action of ketamine. Demonstration of pre-emptive analgesia with systemic but not spinal suggests that supraspinal effect predominates with systemic ketamine administration and has a similar effect as opioid. Antinociceptive effect of systemic ketamine involve activation of the mono aminergic descending inhibitory system, and this effect does not occur after spinal administration [12,13].

First Dose Analgesic Requirement

In the present study, it was noted that time to first request for analgesic was significantly delayed in ketamine group than the control group. This finding is same as in the study of Amanor-Boadu et al in which ketamine prolong the time for the first analgesic [14]. It has been demonstrated in other studies that ketamine delayed the first request for analgesic by approximately 10-30 min compared to control group [15].

Our results are similar to Sen S et al [9] who demonstrated that time for first dose analgesic requirement was significantly longer in ketamine(197min) group than Fentanyl (165min) and control(144 Smin) group. Since in this study 3cc hyperbaric bupivacaine was used hence the time for first dose analgesic requirement was more in all the groups than our study but the difference in control and ketamine group is clinically significant; difference between TFA in both studies is due to different dose of hyperbaric Bupivacaine.

Evidence has shown that postoperative pain is the product of both peripheral and central sensitization [16]. Following stimulation of free nerve ending by incision, cutting, and traction, the chemical mediator of pain such as bradykinin and prostaglandins maintain the pain longer resulting in primary hyperalgesia.

To achieve sustained pre-emptive analgesia, the pain of initial injury must be blocked and since chemical mediators continue to be released for longer than the initial insult, their effect must be prevented for a longer time than the duration of action of a single dose of analgesia administered unfortunately our study cannot demonstrate the sustained pre-emptive effect. But the study demonstrated that first dose requirement was significantly prolonged in the group that has received low dose ketamine.

Studies of Himmelseher S et al [11] show that small dose of ketamine reduced opioid requirement for postoperative pain

Comparison of Side Effect

In the present study, hypotension was noted in 12 (40%) patients in group B and in 9 (30%) of patients in group K. Shivering was observed in 3 patients only in group B. Respiratory depression was not seen in any patient. In our study episode of hypotension in ketamine group was 30% and in control group, it was 40% that difference may be attributed to the sympathomimetic activity of ketamine.

In the present study, only 6.33% of the women in the placebo group developed some bradycardia and none in the ketamine group. Ketamine is well known to cause a rise in blood pressure and heart rate due to its sympathomimetic activity. This could be the reason for the less incidence of bradycardia observed in the group that received low dose ketamine.

Postspinal shivering was a complication that was prominent amongst the placebo group. None of the women in the ketamine group developed shivering. This observation is similar to the study carried out by Ebong EJ et al [10]. Ketamine, a competitive NMDA receptor antagonist, also inhibits postoperative shivering [17]. Psychometric response to a small dose of ketamine is not found troublesome [11]. The absence of characteristic sedation, dreams

and hallucination observed in this study is similar to that observed by Amanor-Boadu SD et al [14]. None of the patients who had ketamine scored more than zero on Ramsay sedation scale. This could be due to the small dose used during the study [12,13].

Haemodynamic

Pulse Rate

In comparison, there was no statistically significant difference found in both groups with respect to pulse rate (P value>0.05). Bradycardia was reported in 2 (6.33%) patients in group B. No statistically significant difference was found between the two groups (p-value 0.6120).

Blood Pressure

In comparison, there was no statistically significant difference found in both groups with respect to mean blood pressure (P value>0.05). Hypotension was reported in 12 (40%) patients in B group and 9 (30%) in ketamine group with no statistically significant difference in both the groups (p-value-1.0000).

Oxygen Saturation (SpO_2)

The SpO_2 monitoring was done with pulse oximetry. None of the patients developed respiratory depression in our study.

Conclusion

The pre-incisional administration of low dose intravenous ketamine delayed the time to first analgesic request in parturients who had caesarean section under bupivacaine spinal anaesthesia. The study could not substantially demonstrate the preemptive analgesic property of ketamine.

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Original Research Article

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Efficacy of Epidural Clonidine as an Adjuvant to Local Anesthetic in Lower Abdominal Surgeries: A Randomized Control Clinical Trail

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Abstract

Introduction: Management of both intraoperative anaesthesia and post operative pain by neuraxial block demands addition of additives which gives good and prolonged postoperative analgesia with minimal side effects. Among various choices of additives, alpha 2 agonists are one among the preferred drugs. *Aim of the Study:* To compare the efficacy of a mixture of 0.5% bupivacaine and clonidine 150 micrograms with 0.5% bupivacaine used alone in lumbar epidural anaesthesia for lower abdominal surgeries. *Materials and Methods:* Fifty patients belonging to ASA I or ASA II category were selected for the study. All patients were randomly divided into two groups of 25 each. Group I, the control group received 10-15 ml 0.5%of bupivacaine and 1 ml of normal saline and Group II. Clonidine group received 10-15 ml of 0.5% bupivacaine and 150µgm of clonidine. Onset and duration of sensory and motor block and duration of post-operative analgesia along with adverse effect were studied. Statistical analysis was performed using student unpaired t –test and chi- square test. *Results:* Epidural clonidine in the dose of 150 µgm combined with 0.5% bupivacaine produced an effective anaesthesia with rapid onset, intensified and prolong blockade and an extended duration of post operative analgesia with minimum side effects.

Keywords: Clonidine; Bupivacaine; Extradural; Analgesia.

Introduction

In the clinical situation of regional anaesthesia and postoperative pain management , neuraxial drugs with additives or synergistic interaction is more desirasble to improve anaesthesia and analgesia. Since the discovery of an adrenergic pain modulating system in the spinal canal, the extradural analgesic potential of alpha adrenergic agonist has been in the focus as an alternative to opioids [1]. Clonidine, apartial alpha 2 adrenergic agonist has been shown to produce analgesia of variable intensity and duration in both acute and chronic pain [2]. Clonidine exerts its analgesic effect through the activation of adrenergic receptors at the peripheral, spinal and brainstem sites.

Clonidine produces analgesia by activation of postsynaptic alpha 2 receptors in the spinal canal and exerts action on the descending inhibitory monoaminergic tracts, resulting in ant nociceptive effect. It also potentiate the effect of opioids and local anaesthetic agents [3,4].

The main side effect of extradural administration of clonidine are dose dependent hypotension, bradycardia, and sedation which are rarely severe and easily treated [3,5].

Main aim of the study is to compare the effects of extradurally administered clonidine and bupivacaine with those of extradural bupivacaine, with particular emphasis on postoperative pain and hemodynamic changes. The dose of extradural clonidine is chosen 150 µgms as this has been shown

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to produce significant analgesic benefit with minimal adverse effect [6].

Materials and Methods

After obtaining approval from the institutional ethics committee and written informed consent , fifty adult patients belonging to ASA I or II scheduled for lower abdominal procedure under lumbar epidural anaesthesia were included in the study.

Exclusion criteria included, patient refusal for regional anesthesia, patients with coagulopathy, obstetric patients, neurosurgical cases and patients with cardiac, kidney and liver pathology, history of hypersensitivity and patients belonging to ASA III and above.

All patients were randomly allocated in to two group of 25 each.

Meterial and Method

Group 1 Control group 10 to 15 ml of 0.5% bupivacaine and 1 ml of normal saline

Group 11 clonidine group 10– 15 ml of bupivacaine and 1 ml of clonidine [150 micro grams]

Details of the Parameters Studied

1. Sensory Blockade

Sensory blockade was assessed at 1 minute interval until peak effect, beginning from completion of epidural injection.

Assessment done by hollmens scale

Grade 0 normal sensation at pin prick

Grade 1- pinprick felt as sharp pointed but weaker as compared to same area in upper extremity.

Grade 3- pinprick recognized as touch with a blunt object.

Grade 4- no pinprick perception to touch.

2. Time of Onset of Sensory Analgesia at T 10.

Time of completion of epidural injection to the occurrence of grade 3 sensory block on hollmen scale at the level of umbilicus at T 10.

3. Duration of sensory blockade

The time from the maximum cephalad spread of analgesia to the time at which sensory block has regressed by two segments.

4. Motor Blockade

Motor blockade was assessed every minute till peak effect and every 5 minutes thereafter till complete motor blockade, by testing the power of a specific joint movement of both lower limbs which are regarded as equivalent to the corresponding myotomes using seow decimal score.

5. Time of Onset of Complete Motor Blockade

Time from completion of epidural injection to the time at which complete spread of motor blockade occurred.

6. Intensity of Motor Blockade

Number of myotomes blocked, expressed as myotome score on *Seow decimal score.*

Table 1:

	Right	Left
Hip flexion [L2]	1	1
Knee extension [L3]	1	1
Ankle dorsiflexion[L4]	1	1
Great toe dorsiflexion[L5]	1	1
Plantar flexion[s1]	1	1
	5	5=10

7. Duration of Motor Blockade

Time from complete motor blockade to the recovery of complete power of all joint movements.

Intraoperatively blood pressure and pulse rate were recorded every two minute for first 30 minutes and every 5 minutes thereafter till the end of procedure. Any complications like adverse reactions and failure of analgesia were noted.

In the post operative ward the patient were monitored for haemodynamic changes.

8. Duration of Analgesia

The intensity of pain was charted on visual analogue scale every hour and the duration to reach a visual analogue score of 4 cm was noted for patients in both the groups.

Time taken for VAS to reach 4 from the time of injection of drug or for the patients request for analgesia from the time of injection of drug is taken as duration of analgesia for that particular group. Top up of 0.125% bupivacaine 5-8 ml was administered for analgesia

8. Sedation RAMSAY SEDATION SCORE was used

1. Anxious, agitated and restless
2. Awake, cooperative, oriented and tranquil
3. Semi asleep but responds to commands
4. Asleep with response to stimuli
5. Asleep with sluggish response to stimuli
6. No response

Statistical Analysis was performed using students unpaired t test for mean age, height, weight distribution, haemodynamic variables. Time of onset of sensory block, motor block, duration of sensory and motor blockadeand duration of analgesia. *Chi – square test* was used for analysis of intra operative adverse effects. p< 0.005 suggest statistically significant .

Results

I. Onset Time

Mean onset time of sensory block at T10 in control group was 9.6+3.09 mins and in clonidine group was 6.16+2.59, which was statistically highly significant.

Complete motor blockade was not achieved in 2 patients in clonidine group and in control group out of 25 patients in each group. Mean time for onset of complex motor block was 22.82+4.22 compared to 17.39+5.44 in control group, which was statistically highly significant.

II. Duration Time

The mean time of duration of sensory blockade was 102.26+10.89 mins in control group in comparison to 145.86+22.31 in clonidine group, which was highly significant.

Table 2: Mean time of onset of sensory and motor blockade

Parameter	Group	N	Mean	SD	t
Sensory	Control	25	9.60	3.095	4.258
Blockade (T_{10})	Clonidine	25	6.16	2.592	P=0.001 vhs
Motor	Control	23	22.82	4.228	3.782
Blockade	Clonidine	23	17.39	5.441	P=0.001 vhs

Table 3: Mean time of duration of sensory and motor blockade

Parameter	Group	N	Mean	SD	t
Sensory	Control	23	102.26	10.897	8.421
Blockade (T_{10})	Clonidine	23	145.86	22.316	P=0.001 vhs
Motor	Control	22	204.27	23.417	16.205
Blockade	Clonidine	25	366.48	41.456	P=0.001 vhs

Table 4: Myotome Score

Parameter	Group	N	Mean mins	SD	t
2 (L_2)	Control	25	6.160	2.426	0.14300
	Clonidine	25	6.040	3.421	P>0.05 ns
4(L_3)	Control	25	10.720	3.482	1.631
	Clonidine	25	17.39	5.441	P>0.05 ns
6 (L_4)	Control	25	14.880	3.844	2.545
	Clonidine	25	11.960	4.257	P<0.05 sig
8 (L_5)	Control	25	18.360	3.795	3.457
	Clonidine	25	14.240	4.594	P<0.001vhs
10 (S_1)	Control	23	22.826	4.228	3.782
	Clonidine	23	17.391	5.441	P<0.001vhs

The mean time of duration of motor blockade was 204.27+ 23.41 in control group in comparison to 366.48+41.45 in clonidine group, which was highly significant.

III. Intensity of Motor Blockade

No significant difference was observed between the two groups in the time to attain myotome score 2 and 4. The time to attain the particular myotome score, thereafter was significantly shorter in the clonidine group compared to the control group.

IV. Sedation

Patients in clonidine group had higher sedation score 3 or above in comparison to the control group and was statistically significant. Onset of sedation noticed within 30 minutes of administration and was observed throughout the intraoperative period. Patients were easily arousable and responded to verbal commands.

There was no depression in ventilation as evidenced by pulse oximetry. One patient in clonidine group had snoring and drop in oxygen saturation from 100% to 96% .

Table 11: Intraoperative sedation score

Time	Group	N	Mean	SD	T
30	Control	25	2.00	0	12.970
	Clonidine	25	3.52	5859	P=0.001 vhs
60	Control	25	2.00	0	15.087
	Clonidine	25	3.68	5567	P=0.001 vhs
90	Control	25	1.96	2000	14.241
	Clonidine	25	3.52	5099	P=0.001 vhs

V. Duration of Analgesia

Duration of analgesia was significantly increased in the clonidine group (598.68+110.91 mins) compared to the control group as they required additional 0.5% bupivacaine in the intropertive period.

Group	N	Mean	SD	T
Control	22	270.636	36.350	13.245
Clonidine	25	598.680	110.916	P=0.001

VI. Visual Analogue Scale

Table 13: Vas Score

Time (hrs)	Group	N	Mean	SD	T
½	Control	22	0.272	455	2.996
	Clonidine	25	.0	.0	P=0.001vhs
1	Control	22	1.636	.847	9.666
	Clonidine	25	.0	.0	P=0.001 vhs
2	Control	22	3.636	1.093	16.659
	Clonidine	25	.0	.0	P=0.001vhs
3	Control	16	5.187	.655	28.551
	Clonidine	25	0.160	.472	P=0.001 vhs
4	Control	2	6.0	.0	-
	Clonidine	25	0.480	.714	
5	Control	0	-	-	-
	Clonidine	25	1.320	1.030	
6	Control	0	-	-	-
	Clonidine	25	2.210	1.103	
7	Control	0	-	-	-
	Clonidine	25	2.850	1.387	
8	Control	0	-	-	-
	Clonidine	25	3.500	1.095	
9	Control	0	-	-	-
	Clonidine	25	4.330	1.303	
10	Control	0	-	-	-
	Clonidine	25	4.500	1.915	

Discussion

For Post operative pain control various adjuvants like opioids, neostigmine, clonidine, midazolam, ketamine etc has been tried with local anesthesia to potentiate its action. Alpha agonists like Clonidine is in focus when we think about any alternative to opioids. Enough evidences exists to implicate the role of clonidine in the inhibition of nociceptive transmission when administered epidurally in humans [1,3].

Our study demonstrated that epidural clonidine when administered with bupivacaine produced effective anaesthesia with a rapid onset of action of both sensory and motor blockade, with a prolonged and intensified block. T zeng et al reported that epidural clonidine when administered with lidocaine produces effective anaesthesia with a rapid onset, longer duration of action and more profound block [7].

On the other hand previous studies by Engel et al reported no change in the onset of sensory and motor blockade by epidural clonidine. Only difference between their and our results might be because their study used Ropivacaine, which has a slower onset and shorter duration of action than bupivacaine.

Our study demonstrates prolonged analgesia with almost 2 fold increase in the duration of analgesia with administration of clonidine [598±110.91 compared to 290.63±36.35 in control]. Previous studies show similar prolonged analgesia with use of epidural clonidine. Engel et al reported analgesia of 513±92 minutes duration and it is shorter than our study as Ropivacaine was used in their study.

Studies by Kalia et al, Carabine et al, O Meara et al, Tzeng et al, all demonstrated similar findings. The duration of analgesia obtained in their studies were shorter due to the use of lower concentration or lesser volume of bupivacaine or lidocaine in comparison with our study [6,9,10].

VAS scores were lower with epidural administration of clonidine and complete relief was observed in the initial four hours of postoperative period, providing satisfactory analgesia. Studies by Carabine et al, O Meara et al, Anzai et al reported lower pain scores and satisfactory analgesia with epidural administration of clonidine [6,10,11].

In our study, no significant difference was observed in the incidence of hypotension, bradycardia, with epidural administration of clonidine. However mean arterial pressure were lower with the use of clonidine than with plain bupivacaine. Also in the postoperative period, patients who received clonidine showed a lower mean arterial pressure and lower heart rate. This might be either due to the central effect of clonidine on sympathetic outflow or due to decreased analgesia in the patients receiving plain bupivacaine.

In our study, sedation was observed following epidural clonidine and the onset was observed within 30 minutes. All previous studies on clonidine have shown that it produces sedation with minor or no effect on ventilation. By a central neuraxial blockade, sedation may be a desired action as it reduces the need of any other sedatives and anxiolytics. Incidence of shivering was lower significantly with the use of clonidine. Studies done by Zhao et al have demonstrated that clonidine possess anti shivering properties and has been used clinically in the prevention of shivering [12].

Conclusion

Epidural clonidine in the dose of 150 µgm combined with 0.5% bupivacaine produced an effective anaesthesia with rapid onset, intensified and prolonged blockade and an extended duration of post operative analgesia with minimum side effects.

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Original Research Article

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Single Injection versus Double Injection Ultrasound Guided Supraclavicular Brachial Plexus Block: A Randomised Comparative Study

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Abstract

Background: Ultrasound guided (USG) supraclavicular brachial plexus (SPB) block can be performed either by a single injection (SI) technique, injecting the entire volume of drug in the corner pocket or by a double injection (DI) technique, whereby half the volume of the drug is injected in the corner pocket and remaining half directly into the neural cluster. We conducted this study to compare thesuccess rates of the two techniques. *Methods:* A comparative two group study was carried out in 120 patients who underwent elective upper limbsurgeries (excluding the shoulder) under USG guided SPB in M.S. Ramaiah Hospital, Bangalore. Patients were randomly allocated in two groups (SI & DI). Both the groups received 30 ml 0.5% ropivacaine. SI group received the entire volume in the corner pocket, whereas DIgroup received 15 ml in corner pocket and the remaining 15 ml in the neural cluster. The blocks were assessed every 5 mins upto 30 mins forboth sensory and motor blockade using cold test and motor movements respectively, in the musculocutaneous, median, radial and ulnar nerves distribution. Each nerve was allocated a maximum of 2 points for complete blockade. Hence a maximum composite score of 16 could be achieved. To label a block successful a minimum of 14 points were required. We compared the success rate of blockade and total anaesthesia related time between the two groups. *Results:* The success rate of the blockade in the SI and DI group was 96.7% and 91.7% respectively at 30 min of performing the block which was not statistically significant. All the seven patients who had failure in both the groups had ulnar nerve sparing. The mean total anaesthesia related times in the two groups were 21.42±3.29 and25.17±2.45 in DI and SI groups respectively with P<0.001. During the first 25 minutes, the DI group displayed a higher proportion of patients with minimal composite score of 14 points. Fifty eight patients(96.7%) in DI achieved a composite score of 14 points and above within the first 25 minutes. The mean onset times were 17.25±2.83 and 22.72±2.47 in DI and SI group respectively. No adverse events were seen in both the groups. *Conclusions:* The success rates in both the SI and DI techniques were comparable. The DI technique results in a faster onset and hence a shorter total anaesthesia related time, which however may not be clinically relevant.

Keywords: Corner Pocket; Supraclavicular; Ultrasound.

Introduction

The Supraclavicular block (SCB) provides a complete and reliable blockade for upper limb surgeries [1]. A precise needle position and proper delivery of the local anaesthetic (LA) solution ensures successful blockade. Without the use of ultrasound (USG), it is difficult to verify the precise location of the needle tip in relation to the nerve bundles as well as the distribution of the local anaesthetic.[2] Use of real time USG has improved block success rates, shortened the latency time for onset, and has reduced the volume of the local anaesthetic required for the successful block [1].

Ultrasound guided SCB can be performed either by the single injection (SI) technique, whereby the entire volume of the drug is injected at the corner pocket [3] (intersection of the first rib and the subclavian artery) or by the double injection (DI) technique, whereby half the volume is deposited at

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the corner pocket and half is injected inside the neural cluster [4,5,6,7].

Intraneural injection while performing peripheral nerve blocks is a dreaded complication and hence many practitioners are conservative while performing such blocks [8]. Ultrasound has shown to reduce such intraneural injections but it depends on the practitioners' skill and the imaging characteristics of the needle and the tissues [9].

Reducing the needle maneuvering inside the neural cluster decreases the incidence of neural injury and this has been the goal of many practitioners. This forms the rationale behind single rather than multiple injections.

However, cadaver and patient studies using dye have shown that a single location injection does not ensure the spread of the dye into all the compartments [10].

Septae and muscular membranes found between the scalene muscles might prevent the spread of the local anaesthetic [11]. Several studies have been conducted comparing single injection versus multiple injection techniques with the conclusion that the latter is more successful, with faster onset times and no increased complications. However, consistent results regarding the onset of the block or the nerves blocked were not demonstrated.

Hence, the aim of this study was to compare the block success rate of SI and DItechnique, USG guided SCB for upper limb surgery.

Methods

After obtaining ethics committee approval and written informed consent, this prospective randomized studywas undertaken in M.S. Ramaiah medicalcollege, Bangalore, in 120 patients undergoing upper limb surgeries not involving shoulder. The sample size was calculated based on the study done by Amr M.A. Sayed et al [7] using a power of 80%, alpha error 5% and confidence interval of 95%.

Inclusion criteria were age between 18 and 70 years, body mass index between 20 and 35 kg/m2 and ASA physical status I to III. Exclusion criteria were preexisting neuropathy, coagulopathy, hepatic or renal failure, allergy to LA, pregnancy and previous surgery in the supraclavicular fossa.

Patients undergoing upper limb surgeries not involving shoulder surgeries receivedultrasound-guided supraclavicular block with 0.5% ropivacaine. Patients were monitored byECG, pulse oximetry and NIBP. Intravenous midazolam (1-2 mg) was given to all the patients before the surgery. All blocks were performed by using an ultrasound machine (GE Logitech Venue 40) with an 8-12 MHz linear type probe. The surface of the ultrasound probe was covered with sterile coupling gel and covered with sterile transparent film.

The patients were randomised into two groups of 60 each, using computer generated randomisation numbers. The patients were placed in supine position with head turned to the opposite side. The ultrasound probe was placed in the supraclavicular fossa and a transverse view of the subclavian artery and the brachial plexus was obtained. The brachial plexus lie superolateral to the subclavian artery and appear as a 'bunch of grapes'. A skin wheal was raised with lidocaine 2%. Once the artery, rib, pleura and plexus were simultaneously in view, theneedle was guided, using an in-plane technique, towards the "corner pocket" [3] between the firstrib inferiorly, the subclavian artery medially and the nerves superiorly. Confirming that thelocation of the needle tip is not in hypo echoic nodules (in nerves), 0.5 ml of LA was injectedas a test dose to avoid intra neural injection. If the patients did not complain of paresthesia orpain or there was no excessive resistance to injection, the LA was injected. A total volume of 30 ml of local anesthetic was injected. This volume was derived from a study conducted byAmr M.A. Sayed [7].

In group SI the entire 30 ml was injected in the corner pocket (image 1). In group DI the volume wasdivided, where 15 ml was deposited in the corner pocket and during withdrawal of the needlethe remaining 15 ml was injected superior and lateral to the subclavian artery in the centre ofbrachial plexus (image 2).

Data was collected by an assessor blinded to the patient's volumeassignments. For both techniques, the following were recorded:

Imaging time: The time interval between contact of the ultrasound probe with thepatient and obtaining of a satisfactory picture.

The needling time: The temporal interval between the start of the skin wheal andthe end of local anaesthetic injection.

Performance time: The sum of imaging and needling times. The extent of sensory and motor blockade was tested by a blinded observer, every 5 minutesuntil 30 minutes.

Sensory blockade of the musculocutaneous (lateral part of forearm), median (palmar surface of

2nd finger), radial (dorsal surface of the hand between thumb and 2nd fingers), and ulnar nerves (5th finger) was gradedaccording to a 3-point scale using a cold test. GRADE 0 = no block, 1 = analgesia (patient can feel touch, not cold), 2 = anesthesia (patient cannot feel touch) [6].

Motor blockade was also graded on a 3-point scale. GRADE 0 = no block,1 = paresis, 2 = paralysis [6]. Motor blockade of the musculocutaneous, radial, median, and ulnar nerves were evaluatedby elbow flexion, thumb abduction, thumb opposition and thumb adduction, respectively [6].

Overall, the maximal composite score were 16 points. The block was considered successfulwhen a composite score of 14 was achieved. Composite score less than 14 was considered asfailure of blockade and was converted to general anaesthesia and excluded from the study. Onset time was defined as thetime required to obtain 14 points [6].

The primary outcome was to compare the success rate of blockade in SI versus DI groups.The secondary outcome was to measure the total anesthesia related time.

Total anesthesia related time was defined as the sum of performance time plus time for onset ofblock.Patients with Horner's syndrome, voice change and chest discomfort (dyspnea) were noted. The patients with failed blockades and those with severe complications such as arrhythmias, hypotension, and desaturation received general anesthesia.If in case surgery was unduly prolonged and the effect of the block wore off, rescue analgesiawas given in the form of intravenous Fentanyl 1 mcg/kg and infusion of Propofol 50-100mcg/kg/min.

Statistical Analysis

Statistical Methods

Descriptive and inferential statistical analysis has been carried out inthe present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance was assessed at 5% level of significance.

The following assumptions on data were made,

1. Dependent variables should be normally distributed.
2. Samples drawn from the population should be random, cases of the samples should beindependent.

Student 't ' test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between the two groups (inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters oncategorical scale between two or more groups and non-parametric setting for qualitative dataanalysis.

Significant Figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value:0.01<P ? 0.05)

** Strongly significant (P value: P?0.01)

Statistical Software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver. 2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

The study was carried out on a total of 120 patients operated under USG guided supraclavicular brachial plexus block. Demographic data, success rate, imaging time, needling time, performance time, onset time, total anaesthesia related time, adverse perioperative events and complications werecompared between Group SI and Group DI.There were no significant differences in the patient characteristics including age, gender, weight, height, BMI and ASA grade (Table 1).

Our primary endpoint was the success rate of blockade (composite score>14). In all, 113 patients had successful blockade. Five patients in SI and 2 patients in DI failed to achieve a composite score of 14 and hence were labelled as failure and excluded from the study. All the 7 patients who had failure of block couldn't achieve a composite score of 14 due to ulnar nerve sparing. The success rate of blockade in both the SI and DI groups were 91.7% and 96.7% respectively at 30 minutes of performing the block which was not statistically significant (Tables 2-5).

Our secondary endpoint was to compare the total anaesthesia related time between the two groups.The total anaesthesia related time was less than 20 mins in 24.1% of patients in DI and none of the patients in DI grouptook more than 30 minutes. The mean total anaesthesia related times in the two groups were 21.42±3.29 and25.17±2.45 in DI and SI

groups respectively with P<0.001. There was no difference in the imaging time between the two groups. However, the needling time was significantly longer in the DI group and consequently the performance time was also significantly longer in the DI group (Tables 6 & 8).

During the first 25 minutes, the DI group displayed a higher proportion of patients with minimal composite score of 14 points. Fifty eight patients (96.7%) in DI achieved a composite score of 14 points and above within the first 25 minutes. In comparison, 6 patients in SI group had onset time of more than 25 minutes. Eleven patients in DI had

Table 1: Demographics

	DI (Mean ± SD)n=60	SI (Mean ± SD) n=60	P value
Age(Yrs)	49.37±16.79	45.35±16.25	0.186
Gender(F/M)	20/40	20/40	1.000
Weight(kgs)	67.90±10.23	68.4±8.57	0.757
Height(cms)	166.15±6.72	164.20±13.53	0.319
BMI(kg/m^2)	24.79±3.31	24.85±3.30	0.920
ASA grade 1/2/3	27/13/20	31/15/14	0.478

Table 2: Comparison of sensory blockade in group DI and SI

Sensory blockade	Group DI (n=60)	Group SI (n=60)
Musculocutaneous		
0	0(0%)	0(0%)
1	3(5%)	6(10%)
2	57(95%)	54(90%)
Median		
0	0(0%)	0(0%)
1	0(0%)	1(1.7%)
2	60(100%)	59(98.3%)
Radial		
0	0(0%)	0(0%)
1	2(3.3%)	0(0%)
2	58(96.7%)	60(100%)
Ulnar		
0	2(3.3%)	5(8.3%)
1	3(5%)	0(0%)
2	55(91.7%)	55(91.7%)

Table 3: Comparison of motor blockade in both groups

Motor blockade	Group DI (n=60)	Group SI(n=60)
Musculocutaneous		
0	0(0%)	0(0%)
1	3(5%)	6(10%)
2	57(95%)	54(90%)
Median		
0	0(0%)	0(0%)
1	0(0%)	1(1.7%)
2	60(100%)	59(98.3%)
Radial		
0	0(0%)	0(0%)
1	2(3.3%)	0(0%)
2	58(96.7%)	60(100%)
Ulnar		
0	2(3.3%)	5(8.3%)
1	3(5%)	0(0%)
2	55(91.7%)	55(91.7%)

Table 4: Comparison of the composite point in each group

Composite point	Group DI (n=60)	Group SI(n=60)
12	2(3.3%)	5(8.3%)
14	7(11.7%)	7(11.7%)
15	2(3.3%)	0(0%)
16	49(81.7%)	48(80%)
Total	60(100%)	60(100%)

P= 0.382, not significant, Fischer exact test

Table 5: Blockade failure in both the SI and DI groups

Blockade Failure	Group DI (n=60)	Group SI(n=60)	Total (n=120)
No	58(96.7%)	55(91.7%)	113(94.2%)
GA	2(3.3%)	5(8.3%)	7(5.8%)
Total	60(100%)	60(100%)	120(100%)

P=0.439, not significant, Fischer exact test

Table 6: Performance Time

	Group DI (n=60)	Group SI(n=60)	Total	P value
Imaging time(min)	1.83±1.17	1.67±5.65	1.75±4.10	0.84
Needling time(min)	2.36±1.15	1.43±0.71	1.89±1.06	<0.001**
Performance time(min)	4.25±2.28	2.40±0.99	3.32±1.99	<0.001**

student t test

Table 7: Onset time

Onset time	Group DI (n=58)	Group SI(n=55)	Total (n+113)
<15 min	11(19%)	0(0%)	11(9%)
15-25 min	47(81%)	49(89%)	96(85.5%)
>25 min	0(0%)	6(11%)	6(5.5%)
Total	58(100%)	55(100%)	113(100%)
Mean±SD	17.25±2.83	22.72±2.47	19.91±3.81

P<0.001**, significant, student t test

Table 8: Total anaesthesia related time

Total anaesthesia related time	Group DI (n=58)	Group SI(n=55)	Total (n+113)
<20 min	14(24.1%)	0(0%)	14(12.4%)
20-30 min	44(77.5%)	53(96.4%)	97(85.8%)
>30 min	0(0%)	2(3.6%)	2(1.7%)
total	58(100%)	55(100%)	113(100%)
Mean±SD	21.42±3.29	25.17±2.45	23.24±3.47

P<0.001**, significant, student t test

Table 9: Adverse Perioperative event

Adverse preoperative event	Group DI (n=60)	Group SI(n=60)
None	60	60
Yes	0	0
Total	60	60

onset time of <15 minutes. The mean onset times were 17.25±2.83 and 22.72±2.47 in DI and SI group respectively (Table 7). The DI group hada significantly faster onset with a p value <0.001. None of the patients in both the groups developed any perioperative adverse events (Table 9).

Discussion

In this prospective randomized trial we compared the DI technique with the SI technique forperforming USG guided supraclavicular brachial

plexus block.In ourstudy we found thatboth the techniques provided similar success rates of surgical anaesthesia. The performancetime was longer in group DI in comparison with group SI probably because group DI requiredmore needle maneuvering. However, the additional needle maneuvering did not lead to anincrease in the incidence of vascular puncture, paraesthesia or post operative neurologicdeficits.

In comparison with a study done by Amr M.A. Sayed, Amr Sobhy [7], our current studydemonstrated a shorter total anaesthesia related time in DI technique, despite having a longerperformance time in view of a shorter onset time.The results of our present study are in agreement with a study conducted by Techasuk W et al [12]. They compared the DI technique with TII and concluded that the total anesthesia relatedtime was shorter with TII group. The two methods achieved comparable rates of surgical anesthesia and the DI group required fewer needle passes as well as shorter needling andperformance time.

Injection of the drug directly into the brachial plexus could lead to the formation of smallersatellite clusters, resulting in the increase in the surface area of exposure of the nerves to the local anaesthetics [12]. This could explain the faster onset of the blockade in the DI group observed in thestudy.

However, safety regarding the direct placement of the needle in the brachial plexus cluster isnot established. In an observational study conducted by Bigeleisen et al, it was opined that60the positioning of the needle tip in the cluster was equivalent to intra neural placement [13]. Thus they concluded that DI technique posed a larger risk of adverse neurological deficits. Inanother contrasting study done by Franco it was opined that intra cluster injection of LA didnot amount to true intra neuronal injection [14]. Irrespective of the fact whether LA injected intothe neural cluster amounts to true intra neuronal injection, recent evidence supports the safetyof DI technique [15]. There was no incidence of paraesthesia or any other adverse neurological outcome in our study, thus confirming the safety of DI technique.

Our study has some limitations. First, we found that the decrease in the total anaesthesia related time in the DI technique was approximately 4 mins. In a hospital with a busy set upwhere large number of upper limb surgeries are performed under regional anaesthesia, such areduction could result in a clinically relevant reduction in anaesthesia related time over the course of the day. However, we agree that such a difference may not be clinically relevant in acentre that performs lesser number of cases per day. Second, we did not restrict to a single type of surgical procedure. In a study done by Arab etal [16] they focused on a single type of surgical procedure to eliminate any confounding factorsarising from the surgical stimulus or location of the surgery. Third, the blocks were performed by both senior anaesthesiologists trained in USG andresidents. The DI technique required needle redirections thus increasing the level of difficulty among the residents and hence could have led to a longer performance time. There were no complications such as hypotension, arrhythmia and desaturation noted ineither of the groups. None of the surgical procedures in both the groups required rescueanalgesia.

Conclusion

In conclusion, this study demonstrated that the success rates in both the SI and DI techniques are comparable. The DI technique results in a faster onset and hence a shorter total anaesthesia related time, which however may not be clinically relevant.

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Haemodynamic Changes in Laryngoscopy with Endotracheal Intubation and Laryngeal Mask Airway Insertion: A Comparative Study in General Surgery Patients

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Abstract

Introduction: Airway management is must during delivery of general anaesthesia. Previously, laryngoscopy and endotracheal tube (ETT) insertion has been the mainstay in providing adequate airway management and delivering anaesthesia. The laryngeal mask airway (LMA) offers a much less invasive way of maintaining the airway as it does not pass through the glottis but is placed over the glottis. It does not require the use of the laryngoscope. *Objective:* To determine the haemodynamic response elicited by laryngoscopy and endotracheal intubation and compare it with that elicited by laryngeal mask insertion in ASA I and ASA II patients, undergoing elective general surgeries. *Methods:* A hospital based prospective randomized comparative study was conducted to determine the haemodynamic response, elicited by laryngoscopy and endotracheal intubation and compare it with that elicited by laryngeal mask airway insertion in ASA I and ASA II patients, undergoing elective general surgeries. After induction of anaesthesia either an ETT or LMA was inserted. Evaluations included measurement of blood pressure and heart rates before insertion, and 1 minute, 3 minutes and 5 minutes after insertion. *Results:* There was an increase in HR, SBP and DBP seen after laryngoscopy and ETT insertion as well as after laryngeal mask airway insertion. The change in haemodynamic parameters after laryngoscopy and ETT insertion were significantly greater than those elicited by LMA insertion. *Conclusion:* A significant haemodynamic response consisting of an increase in HR, SBP and DBP was seen after the insertion of both the LMA and ETT in this study. It was also concluded that the haemodynamic response to laryngoscopy and ETT insertion is significantly greater than that to LMA insertion.

Keywords: Endotracheal Intubation; Laryngeal Mask Airway; Haemodynamic Response.

Introduction

Airway management is of most important during delivery of general anaesthesia. Patients who have been anaesthetized are unable to maintain an adequate airway on their own and artificial airway maintenance devices are employed [1]. Previously laryngoscopy and endotracheal intubation has been the mainstay in providing adequate airway management, delivering anaesthesia and avoidance of aspiration in anaesthetized patients. Though intubation has many advantages including provision of a reliable airway, prevention of aspiration and delivery of anaesthetic gases, it is not without complications. These can be seen during insertion, after insertion and during extubation. These complications are airway trauma, physiological reflexes like hypoxia, tachycardia and hypertension, malposition, laryngospasm, narrowing and increased airway resistance as well as negative pressure pulmonary edema [2]. The laryngeal mask airway offers a much less invasive way of maintaining the airway as it does not pass through the glottis but is placed over the glottis. It does not require instrumentation like use of the laryngoscope. It acts as an intermediate between the endotracheal tube and the oropharyngeal airway and offers some of the advantages of the endotracheal tube while surpassing the

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disadvantages like stimulation of the laryngopharyngeal reflex [2].

Laryngoscopy and tracheal intubation or laryngeal mask airway insertion are noxious stimuli which provoke a transient but marked sympathetic response manifesting as hypertension and tachycardia. In susceptible patients particularly those with systemic hypertension, coronary heart disease, cerebrovascular disease and intracranial aneurysm, even these transient changes can result in potentially deleterious effects like left ventricular failure, arrhythmias, myocardial ischaemia, cerebral haemorrhage and rupture of cerebral aneurysm [3,4,5]. There are a number of ways to blunt these haemodynamic changes. They include minimizing the duration of laryngoscopy, the use of intravenous narcotics, lidocaine, vasodilators and beta - blocking agents, but most of these have produce variable results [6]. Laryngeal mask airway insertion involves lesser mechanical manipulation of upper airway than endotracheal intubation does, but it has its own limitations as it is contraindicated in patients who are at risk for aspiration, those with low pulmonary compliance and those with pharyngeal obstruction.

Objectives

To determine the haemodynamic response elicited by laryngoscopy and endotracheal intubation and compare it with that elicited by laryngeal mask airway insertion, in ASA I and ASA II patients undergoing elective general surgery cases

Materials and Methods

Study Design

A prospective randomized comparative study was conducted during the period of July 2014 to July 2015.

Study Population

This study done in adult patients who fulfils the inclusion and exclusion criteria and between the age of 18 to 55 years who were ASA I and ASA II patients of both sexes presenting for elective general surgeries.

Sampling Procedure

Patients those not meeting the inclusion criteria or those refusing to participate were excluded. The patients were then randomly allocated to one of the two groups: ETT group and LMA group. They were then randomly assigned to anesthetists experienced in handling both devices. A total of 50 patients in the LMA group and 50 patients in the ETT group were completed in a span of 12 months.

Inclusion Criteria

1. Patients undergoing elective surgeries
2. Aged between 18- 55 years
3. Mallampatti I and II
4. ASAI and ASAII
5. Willing to participate in the study by giving written informed consent

Exclusion Criteria

1. History of respiratory problems
2. History of angina, palpitations, syncopal attacks
3. Baseline heart rate< 60 per minute
4. Baseline systolic pressure >140 mm of Hg

Study Tools

Laryngeal mask airways for airway management in the LMA group and endotracheal tubes with laryngoscopes for the ETT group. I.V. cannulae, drugs including propofol, pentazocin, suxamethonium, midazolam, oxygen and isoflurane for the induction and maintenance of anaesthesia. Monitoring of HR, SBP and DBP of the patients was done using multipara monitors. The data sheets used to collect information contained demographic data, proposed surgery, type of airway management tool, ease of insertion, haemodynamic variables including heart rate, non invasive systolic and diastolic pressure before induction, preinsertion/intubation, immediately after laryngoscopy with intubation or insertion of laryngeal mask, 1, 3 and 5 minutes after intubation or insertion of laryngeal mask.

The patients were then premedicated with injection midazolam 0.05mg/kg and pentazocine 0.5 mg/kg, 3 minutes prior to induction. Pre-oxygenation was done during these three minutes after which, induction of anaesthesia using I.V. propofol 2 mg/kg was done. For the ETT group muscle relaxation for intubation was facilitated by the use of injection succinylcholine 1.5-2 mg/kg. Patients were then ventilated with 100 percent oxygen for a period of 1 minute prior to intubation with the aid of Macintosh laryngoscope or insertion of laryngeal mask airway. Duration of intubation/

insertion was defined as the time from the start of laryngoscopy/LMA insertion, until cuff inflation. Monitoring Heart rate, non invasive blood pressure which included systolic, and diastolic blood pressure were monitored throughout the study and recorded at the following time points a) Pre insertion/intubation. b) Immediately after laryngoscopy and intubation or insertion of laryngeal mask. c) One minute after intubation or insertion of laryngeal mask. d) Three minutes after intubation or insertion of laryngeal mask e) Five minutes after intubation or insertion of laryngeal mask.

Results

All the patients that met the inclusion criteria were included in the study. In the ETT group, 2 patients were excluded as they needed more than 2 attempts for intubation. Each group had a total of 50 participants. The ETT group had 30 males and 20 females and the LMA group had 30 males and 20 females. The ages ranged from 18 to 55 years and 22 to 54 years in the ETT and LMA groups respectively. The range for weight was 44 to 82 kg and 52 to 80 kg in the ETT and LMA groups respectively. The two groups were comparable in terms of demographic data as there were no significant differences between the 2 groups in terms of age, sex, weight and ASA classification (As shown in Table 1).

It was seen from Table 2 that heart rates of the 2 groups were comparable at induction. At insertion, the heart rate increased significantly in both groups, but the increase was substantially higher in the ETT group as compared to the LMA group. The elevation in heart rate significantly persisted for a longer period of time in the ETT group.

It was seen from Table 3 that systolic blood pressure in the two groups was comparable at baseline. An increase in SBP was noted just after insertion of either the LMA or ETT, but the increase elicited by the ETT was significantly higher.

It was observed from Table 4 that diastolic blood pressure was comparable between the 2 groups at baseline. After insertion, both groups showed an increase in DBP that was statistically significant within and between the groups. The values returned

Table 1: Demographic and clinical characteristics of study participants

	LMA (n=50)	ETT (n=50)	P- value
Mean Age (years)	37.5	38.8	0.568
Mean Weight (kg)	65.7	63.8	0.278
Sex - Male	20	20	1.000
Female	10	10	
ASA - I	23	20	0.137
II	07	10	

Table 2: Mean heart rate at different times among ETT and LMA study participants

	ETT Mean±SD	P value for difference within ETT group	LMA Mean±SD	P value for difference within LMA group	P value for difference between ETT and LMA groups
Pre-insertion	93.0±13.5	-	90.8±11.8	-	0.383
Insertion	111.9±13.6	<0.0001	106.9±11.1	<0.0001	0.047
1 minute	106.5±13.4	<0.0001	97.8±9.2	<0.0001	0.0001
3 minute	99.5±13.1	<0.0001	88.5±6.8	0.592	0.0001
5 minute	92.2±11.4	0.664	85.4±6.5	0.059	0.066

Table 3: Mean systolic blood pressure at different time points among the study participants

	ETT Mean±SD	P value for difference within ETT group	LMA Mean±SD	P value for difference within LMA group	P value for difference between ETT and LMA groups
Preinsertion	121.2±10.8	-	117.0±11.9	-	0.067
Insertion	146.4±16.4	<0.0001	127.7±12.9	<0.0001	<0.0001
1 minute	135.4±12.8	<0.0001	121.5±11.4	<0.0001	<0.0001
3 minute	128.5±11.5	<0.0001	117.6±10.5	0.487	<0.0001
5 minute	122.0±11.8	0.665	115.4±9.1	0.147	0.002

Table 4: Mean Diastolic blood pressure at different times among ETT and LMA study participants

	ETT Mean±SD	P value for difference within ETT group	LMA Mean±SD	P value for difference within LMA group	P value for difference between ETT and LMA groups
Preinsertion	76.4±7.2	-	75.7±7.1	-	0.618
Insertion	90.1±11.7	<0.0001	83.5±8.6	<0.0001	<0.001
1 minute	85.2±10.4	<0.0001	78.0±7.4	0.012	<0.0001
3 minute	80.7±10.0	0.007	75.5±8.0	0.793	0.005
5 minute	76.1±9.8	0.813	74.7±7.3	0.310	0.447

to baseline by 3 minutes in the LMA group and by 5 minutes in the ETT group. The difference between the groups was lost by 5 minutes.

Discussion

This study conducted on a total of 100 patients, aimed at comparing the haemodynamic changes elicited by laryngoscopy with endotracheal intubation, to those elicited by laryngeal mask airway insertion. This study demonstrated that there is a haemodynamic response consisting of an increase in heart rate, SBP, and DBP that comes with laryngoscopy with ETT insertion as well as with LMA insertion [7]. However, the response caused by laryngoscopy with ETT insertion is significantly greater than that caused by LMA insertion. It was also observed that insertion of an LMA is easier and takes a shorter time compared to laryngoscopy with ETT insertion.

The heart rates in both groups showed an increase from the pre induction values. These results were similar to those observed in a study done in Scotland, where it was shown that arterial pressure decreased significantly and heart rate increased significantly after induction of anaesthesia. The same effects were also observed in several other studies done previously [8-12]. This effect could be attributed to the hypotensive effect of the induction drugs used [9]. The HR, SBP, and DBP were significantly elevated after the insertion of the endotracheal tube in the ETT group of the study compared to the pre intubation values. The elevation persisted for a period of 5 minutes by which the parameters returned to the pre intubation values. These results are similar to those found by Miller and co workers who found that in normotensive patients, laryngoscopy and insertion of a tracheal tube is immediately followed by an average increase in mean arterial pressure of 25 mmHg [10]. The study done by Russell and colleagues also demonstrated a significant increase in arterial blood pressure after intubation [11].

The observed changes are probably due to the sympathoadrenal response caused by stimulation of the supraglottic region and that of the trachea. The LMA group in this study also showed a significant increase in HR, SBP, and DBP after insertion of the LMA. These results are similar to those of a study done to investigate the cardiovascular effects related to insertion of the Brain laryngeal mask airway compared to those after insertion of a Guedel oral airway, a significant increase in arterial pressure and in heart rate followed insertion of the laryngeal mask and the Guedel airway [12]. The changes in haemodynamics in the LMA group were significantly lower compared to those seen with the ETT group. Similar findings were reported by the study done by Anita and colleagues who demonstrated that endotracheal intubation was associated with a significant increase in heart rate and arterial pressure compared to LMA insertion. Several other studies have shown results similar to those of this study [13,14,15].

The attenuated response shown by LMA could be due to the fact that the LMA avoids the sympathoadrenal response caused by insertion of the endotracheal tube through the trachea. This explanation is supported by the study done in Japan, which showed that direct stimulation by a tracheal tube induces greater cardiovascular responses than stimulation of the glottis by laryngoscopy alone [16]. SBP and DBP were almost twice as high in the ETT study group compared to the LMA study group after instrumentation. These findings are similar to those of Wilson and colleagues [17]. However, the difference in HR in our study was significantly higher in the ETT group compared to the LMA group unlike in their study where there was an increase in heart rate in both groups with no significant difference between the groups. The difference might have been picked by our study due to the larger sample size compared to that of their study. The haemodynamic changes in the LMA group took about 3 minutes to return to pre insertion values while it took about 5 minutes for the changes to return to pre intubation values in the ETT group.

Several other studies have demonstrated that the haemodynamic response to LMA is short lived compared to that to ETT [15]. The greater and more persistent changes in cardiovascular parameters seen with ETT as compared to LMA insertion probably reflect higher catecholamine levels in the ETT group as seen in previous studies. The longer time needed in the ETT group could translate to a longer stimulation period, leading to a greater haemodynamic response. This was shown by the study done by Stoelting who stated that time required to perform endotracheal intubation, directly correlates with an increase in MAP [17].

Conclusions

A significant haemodynamic response consisting of an increase in HR, SBP, and DBP was seen after the insertion of both the LMA and ETT in this study. It was also observed that the haemodynamic response to laryngoscopy and ETT insertion is significantly greater than that to LMA insertion. The response is also short lived in the LMA group compared to ETT group. This response might be of no clinical importance in the healthy, normotensive patients, but might be harmful in patients with hypertension, aortic or cerebral aneurysm, raised intracranial pressure or other cardiovascular diseases. In such cases, the attenuated response of the LMA might be desirable. Time taken to insert an LMA was significantly shorter and insertion was easier as compared to laryngoscopy and ETT insertion. These factors might be contributory to the higher haemodynamic changes seen with laryngoscopy and ETT insertion.

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A Comparative Study of Spinal and General Anaesthesia on Maternal and Foetal Outcome in Cases of Elective Caesarean Section

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Abstract

Background: International health care community is more worried about the rates of cesarean sections throughout the world. Cesarean sections are associated with temporary benefits but are associated with short and long term risks which can extend beyond many years after delivery and affect the health of the mother, child and future pregnancies. An ideal anesthetic technique, for minimizing the surgical morbidity among mothers and neonates has yet to be described in literature. *Objectives:* Hence our objective of the study was to compare the effects of spinal and general anesthesia on maternal hemodynamic status and foetal outcome by comparing the APGAR scores of the newborn. *Materials and Methods:* A prospective cross sectional study was conducted at ACSR tertiary care hospital for a period of one year.120 cases that fulfilled inclusion criteria were divided into two equal groups (50 each) and one group administered general anesthesia and other spinal. Maternal hemodynamic parameters were recorded and foetal outcome with regard to APGAR score at 1 and 5 minute interval was recorded. SPSS version 10 for windows was used for statistical analysis. P value <0.05 was considered significant. *Results:* In our study, statistically significant differences between the two groups were observed in relation to APGAR scores of the neonates at 1 and 5 minute intervals. APGAR score readings were higher in general anesthesia group. Significant differences were also observed in readings of HCO_3 and PCO_2 levels between the two groups and patients in general anesthesia group were more tachycardic than patients in spinal anesthesia group. *Discussion:* To conclude in our study, we observed that umbilical artery pH and APGAR scores of neonates who received general anesthesia were lower than the neonates born under regional anesthesia. Spinal anesthesia is effective than general anesthesia, foetal outcome is favorable in cases of spinal than general anesthesia. This study can be further evaluated in cases of emergency cases of cesarean section which covers all the risk factors.

Keywords: APGAR Score; General Anesthesia; Spinal Anesthesia; Cesarean Section.

Introduction

For nearly 30 years, the international health care community is more worried about the rates of cesarean sections throughout the world. However an expert panel on reproductive health has considered the ideal rate of cesarean sections to be between 10-15% at a meeting organized by WHO [1]. Since then there has been an absolute surge in the number of cesarean sections throughout the world in both developed and developing countries.

Cesarean sections are associated with temporary benefits but are associated with short and long term risks which can extend beyond many years after delivery and affect the health of the mother, child and future pregnancies [2]. With increased patient care and practices, cesarean procedures have become safe but are still associated with significant maternal and perinatal mortality and morbidity. The overall post operative morbidity rate associated with cesarean birth is 35.7% [3]. The reasons for this increase are multifactorial and less understood as there is a gross variation in the cultural and social aspects of the different regions throughout the

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world. For many years general anesthesia was preferred type of use in cesarean sections. Moreover complications like maternal aspiration syndrome and intubation failure, which may occur during general anesthesia may contribute towards maternal mortality have been reported. In view of these, rates of cesarean section using regional anesthesia have been increasing and has become preferred technique to avoid maternal and foetal complications. Most of the reports earlier have shown, identical indexes for both general and spinal anesthesia, most of the anesthesiologists have preferred regional anesthesia under elective conditions. However, some reports point out that regional anesthesia related hypotension syndrome due to sympathetic blockade may affect neonatal outcomes by impairing utero placental perfusion. Hence, an ideal anesthetic technique, for minimizing the surgical morbidity among mothers and neonates has yet to be described in literature [4], Hence, today the choice of anaesthesia is depending upon the mothers request, obstetric reasons and experience of the anaesthecian. Most of the studies published various reports regarding the foetal outcomes with comparison to general and spinal anesthesia by reading the APGAR scores. The reports are variable and studied retrospectively and in variable cases [5].

Hence our objective of the study was to compare the effects of spinal and general anesthesia on maternal hemodynamic status and foetal outcome by comparing the APGAR scores of the newborn.

Materials & Methods

A prospective cross sectional study was conducted at A.C.S.R government medical college and hospital, a tertiary care hospital in south India by the department of Anesthesiology and department of Gynecology & obstetrics for a period of one year from January 2015 to December 2015. The study protocol was accepted by the institutional ethical committee and all the ethical committee guidelines were followed strictly.

Study Design

A total of 120 consecutive pregnant women after completion of 37 weeks and posted for elective cesarean section, without any complications and singleton pregnancy were selected for the study. Indications for cesarean delivery may be previous history of cesarean section, primary infertility, Cephalo-pelvic disproportion, Precious pregnancy etc. All the cases were informed about the study and written informed consent was obtained. 120 cases of the study were divided equally (60 each) into two groups, Group A (General anesthesia) and Group B (Spinal anesthesia).

Inclusion Criteria

Women who completed 37 weeks of gestation and with cephalic presentation of a singleton foetus.

Exclusion Criteria

Pregnant women with any medical and Obstetric complications.

Pregnant women not consenting to participate in the study.

All the cases in both groups were evaluated preoperatively and socio demographic data was collected by interviewing, obstetric history was noted and detailed physical examination (Heart rate, systolic and Diastolic Blood pressure recordings) was done. Detailed laboratory investigations including Hb%, coagulation profile, fasting blood glucose, Prothrombin time, International normalized ratio (INR), and renal profile were done and noted for every cases in the study. Preoperative medications were administered as per protocol. All the cases were kept in 15^0 left lateral position till delivery to protect against supine hypotension syndrome.

Technique: On arrival in the operating room every case received ECG and non invasive blood pressure monitoring continuously, pulse oximetery and capnography for group A patients after induction. For cases of Group A general anesthesia was administered by standardized anesthesia technique by performing rapid sequence induction and intubation with Inj.propofol 2mg/kg, inj. Suxamethonium 1.5mg/kg, application of Sellick's maneuver, confirmation of endotracheal tube, inj.atracurium0.5mg/kg and then maintenance on 0.25% -0.5% isoflurane in oxygen. Controlled mechanical ventilation with 100% oxygen, and 1.0 minimum alveolar concentration of isoflurane. End tidal carbon dioxide pressure kept at 35 mm Hg. For cases of group B, all cases were preloaded with crystalloid solution. Bupivacine 0.5%, 1.5 ml with 25µg fentanyl was given at L3-4 or L4-5 interspaces in sitting or lateral position and all patients were placed in supine position. A 15^0 Trendelenburg position was assumed to optimize cephalic spread of anesthetic drugs. Adequate anesthesia was defined as an upper sensory spread to a level of T4

and not requiring epidural supplementation. Emergency drugs Atropine 1mg/ml and Ephedrine hydrochloride 3mg/ml were prepared for both groups. Heart rate, systolic and diastolic blood pressure of every case was recorded at an interval of 5 min, 15 min, 30 min and 45 minutes and every 30 minutes in the recovery room till discharge.

Newborn Management

APGAR score of the neonates was assessed by the pediatrician at the end of 1 minute and 5 minutes. Umbilical artery blood gas analysis for PH. $PCO_{2,}$ HCO_3 were determined and compared between both the groups. Anesthesia was labeled as effective if APGAR score was ≥ 7 and blood pH was≥ 7.2.

Statistical Analysis

Data was presented as mean±SD. Categorical variables were assessed using chi-square test when appropriate. P value <0.05 was considered significant. The software SPSS v10 for windows 10 was used for analysis.

Results

In the present study, total 120 cases were selected for cesarean section and divided into two equal groups. Group A was administered general anesthesia and Group B spinal anesthesia as per the route of administration of anesthesia. The most common indication for cesarean section was previous cesarean section accounting to 64% of cases with precious pregnancy (18%) the next. The mean maternal age of the participants in the Group A was 32±7.1years with range of 21-36 years and gestational age was 37±5.4 weeks. The mean maternal age of the participants in Group B was 33±5.24 years with range of 22-38 years and gestational age was 37±3.9. No statistical significance was observed with respect to maternal age and gestational age in both the groups of the study. ('P' value >0.05) [Table 1].

Table 2 summarizes the parameters of hemodynamic status of the cases in Group A and Group B. Preoperatively the heart rate, systolic and diastolic blood pressures were monitored in both the cases. The differences in the parameters were not statistically significant in both the groups preoperatively with Heart rate (p value -1.251), systolic blood pressure (p value -0.987) and diastolic blood pressure (p value -0.869). The parameters were recorded at intervals of 5, 15, 30, 45, 60 and 120 minutes postoperatively until transfer to the ward. To determine the changes in the heart rates in both groups, repeated measures ANNOVA was used. Based on the values of means and standard deviations in both the groups, it was observed that Group A patients were significantly tachycardic at all the time intervals when compared to Group B patients and were statistically significant (p value <0.05). The repeated measurement test ANNOVA was used to study the trend of changes in systolic blood pressure in both the groups. The table 2 shows that differences in the systolic blood pressure between the two groups was statistically significant and lower in group B compared to Group A at an

Table 1: Demographic data (Mean ±SD) of the study groups

Demographic Variable	Group A (General Anesthesia) (n=60)	Group B (Spinal anesthesia) (n=60)	P value
Maternal age (Years)	32 ± 7.1	33 ± 5.24	0.69
Gestational age (weeks)	37 ± 5.4	37± 3.9	0.78

Demographic data expressed as number, mean and standard deviation. P value ≤ 0.05 considered significant

Table 2: Maternal Vital signs of cases in the study with preoperative and post operative evaluation

	Group A (General Anesthesia) (n=60)	Group B (Spinal anesthesia) (n=60)	P value
Preoperative			
Heart rate	104 ± 12.015	101.54 ± 14.25	1.251
Systolic blood pressure	122 ± 13.54	120 ± 8.24	0.987
Diastolic blood pressure	76 ± 9.8	75.12 ± 10.35	0.869
After 5 minutes			
Heart rate	118 ± 13.15	94.34 ± 16.025	<0.05
Systolic blood pressure	127 ± 15.64	108.14 ± 11.24	<0.05
Diastolic blood pressure	80.50 ± 13.8	65.10 ± 8.125	<0.05

After 15 minutes			
Heart rate	109 ± 11.98	98.42 ± 14.125	<0.05
Systolic blood pressure	110.15 ± 11.20	116.04 ± 9.24	<0.05
Diastolic blood pressure	71.50 ± 10.815	72.12 ± 11.12	<0.05
After 30 minutes			
Heart rate	101.1 ± 10.5	89.2 ± 10.1	<0.05
Systolic blood pressure	108.05 ± 9.20	117.14 ± 4.24	<0.05
Diastolic blood pressure	74.5 ± 13.41	74.1 ± 12.12	<0.05
After 45 minutes			
Heart rate	94.12 ± 8.52	80.12 ± 8.5	<0.05
Systolic blood pressure	101.21 ± 4.65	108.11 ± 3.56	<0.05
Diastolic blood pressure	75.9 ± 10.24	76.12 ± 10.56	<0.05
1 hour postoperative			
Heart rate	84.10± 4.56	82.12 ± 9.5	<0.05
Systolic blood pressure	111.12 ± 6.12	104.01 ± 4.35	<0.05
Diastolic blood pressure	77 ± 6.28	77.25 ± 9.41	<0.05
2 hour postoperative			
Heart rate	78.21± 3.89	74.25 ± 8.5	<0.05
Systolic blood pressure	118.25 ± 4.85	108.11 ± 5.36	<0.05
Diastolic blood pressure	79 ± 5.69	78.15 ± 8.24	<0.05

Table 3: Foetal outcome: APGAR score at 1 and 5 minute interval; ABG at birth and after 5 minutes

	Group A (General Anesthesia) (n=60)	**Group B (Spinal anesthesia) (n=60)**	**P value**
APGAR score at 1 minute	8.4 ± 1.68	9.6 ± 01.9	< 0.05
APGAR score at 5 minute	9.9 ± 1.1	10.2 ± 1.1	< 0.05
ABG at Birth			
PH	7.26 ± 0.19	7.28 ± 0.9	0.19
PCO_2	46.92 ± 4.98	48.21 ± 5.25	0.21
HCO_3	21.21 ± 3.98	22.14 ± 3.12	< 0.05
ABG after 5 minutes			
PH	7.44 ± 0.10	7.49 ± 0.09	0.074
PCO_2	43.28 ± 1.44	46.14 ± 2.87	0.654
HCO_3	24.11 ± 2.50	25.11 ± 1.58	< 0.05

Data expressed as number, mean and standard deviation. P value ≤ 0.05 considered significant

interval of 5 minutes from induction of anesthesia. Repeated measures ANNOVA was used to study the trends in changes of diastolic blood pressure between both the groups. Values of the mean and standard deviations indicate that there were significant differences in both the groups at all the intervals and lower in group B than group A. (p value<0.05).

Table 3 summarizes the APGAR scores of the newborn at intervals of 1 and 5 minutes in both group A and group B. Mean APGAR score in group A at 1 minute interval was 8.4±1.68 and in group B was 9.6±01.9 and the difference was found statistically significant (p value<0.05). Mean APGAR score at 5 minute interval in group A was 9.9±1.1 and in group B was 10.2±1.1 and the difference was found statistically significant (p value<0.05). PH and PCO_2 levels were recorded in both the groups at 1 and 5 minute intervals and compared. However, there was no statistically significant difference in both the groups at both the intervals. With regard to the levels of HCO_3, recorded at 1 and 5 minute interval, mean HCO_3 levels in group A at 1 minute interval was 21.21±3.98 and in Group B was 22.14±3.12 and the difference was found to be statistically significant (p value<0.01). The level of HCO_3 at 5 minute interval in Group A was 24.11±2.50 and in group B was 25.11±1.58 and the difference was found statistically significant (p value < 0.01).

Discussion

Cesarean section has become one of the most common and prevalent surgical procedure throughout the world. This procedure is associated with the outcome of the mother and the foetus. Hence there is an obvious need to minimize the maternal morbidity and mortality along with

favorable foetal outcome. In this regard the necessity of administering the best anesthetic procedure has gained importance. General anesthesia was the preferred anesthetic procedure in older days but with the observation of few maternal complications and adverse foetal outcomes, regional anesthesia is nowadays the preferred technique but with lot of studies reporting variable results.

In our study, the effects of general anesthesia and spinal anesthesia were compared in elective cases of cesarean section and maternal and foetal outcome was recorded and reported. In our study no cases of maternal and neonatal mortality were recorded, but findings of Haller G et al and Fenton PM et al who recorded maternal and foetal mortality in their studies [6-7]. This can be explained as the pre and perioperative patient care and follow up care was better and advanced. It was observed in our study, that there was a significant mean difference regarding mean systolic and diastolic blood pressure between the two groups respectively. This difference in blood pressure may be due to inadequate preloading of mothers who underwent spinal anesthesia and extensive sympathetic blockade. In our study, no significant difference was observed in the pH in both the groups, but a study by Seneter et al found that umbilical vein pH and arterial PO2 were higher in cases of epidural anesthesia than general anesthesia [8]. A recent study reported no differences in umbilical artery pH values [9].

Our study also determined the effects of anesthesia on foetal outcome with APGAR scores evaluation. In our study, APGAR scores of newborn at 1 minute and 5 minute was significantly high in women who received spinal anesthesia (9.6±01.9 & 10.2±1.1) in the present study as compared to general anesthesia. Similar findings with relating to APGAR score was reported by Kolatat et al and Alfredo M et al in their studies [10-11]. Findings of our study in relation to all the maternal and foetal parameters were in consistent with the findings of Manusco and colleagues who compared the general and spinal on 179 cases of elective cesarean section and found that spinal anesthesia was superior to general anesthesia in foetal outcome and maternal status [9]. Bloom SL et al in her study reported that no significant difference was observed at 1 minute APGAR scores in cases of general and spinal anesthesia but more neonates in the general anesthesia group appeared depressed and required free flow oxygen [12]. It is widely believed that regional anesthesia is safest for neonates and mothers the reason being less exposure of neonates to depressant drugs, decrease risk of maternal pulmonary aspiration and it is easy to perform, rapid with more intensive block [13].

Some of the studies mention that umbilical artery pH was found more accurate method to assess foetal wellbeing. In the present study, average pH was high in neonates of group A (7.44±0.10) than in group B (7.49±0.09). In our study it was observed that fetuses born under general anesthesia had higher incidence of academia and lower APGAR scores. These findings are in comparison with findings of Sendag et al [14].

To conclude in our study, we observed that umbilical artery pH and APGAR scores of neonates who received general anesthesia were lower than the neonates born under regional anesthesia. Spinal anesthesia is effective than general anesthesia, foetal outcome is favorable in cases of spinal than general anesthesia. This study can be further evaluated in cases of emergency cases of cesarean section which covers all the risk factors.

Acknowledgements

NIL

Conflict of Interest

Nil

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Study of Prescription Pattern of Analgesics in Terminally Ill Cancer Patients with Solid Tumors in a Tertiary Care Centre: A Retrospective Study

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Abstract

Background: This study evaluated the prescribing pattern of analgesics in very terminal ill cancer patients who succumbed to their illness in a tertiary care hospital. *Methods:* This retrospective study was conducted in the Medical Records Department by observing for the type of cancer and previous treatment, details on recurrence/metastasis, co morbidities, pain when got admitted and the analgesics prescribed. The details were tabulated and subjected to frequency and percentage analysis. *Results:* In total, there were 173 deaths due to cancer during the study period (48% female, and 52% males). Most patients were in the age group of 41 to 50 and from town background (44.5%). Co morbidity was observed only in 24.6% of the patients and hypertension was the most commonly observed (13.3%). Most of the admission was due to complications of advanced cancer and metastasis. A range of analgesics were used to mitigate the pain. Tramadol alone (31.2%) was used in the maximum number of cases followed by morphine (26%). Combination of paracetamol and tramadol, tramadol and morphine and all the three were also used. Morphine alone (26%) and or in combination with other analgesics (7.4%) was also used. Morphine tables were the most prescribed over the injections. *Conclusions:* Analgesics have been increasingly prescribed in very terminally ill people with cancer. However, morphine was relatively under-prescribed. Relevant studies need to be carried out to determine the barriers for using morphine through prospective studies.

Keywords: Very Terminally Ill Cancer Patients; Pain; Analgesic; Paracetamol; Tramadol Morphine.

Introduction

In cancer, pain is a major issue and reports indicate that up to 86% in patients with advanced disease and 35% of the cancer survivors endure unbearable pain [1-3]. Under these circumstances, effective pain relief is of cardinal importance and also a primary ethical obligation of the treating doctors [3]. In these situations, opioids and morphine is specific is the pharmacologic sine qua non of intolerable pain management and the mainstay analgesic in treating end of life patients [2-4]. Unfortunately, the use of morphine has often been crowded with controversy and the misconception and numerous misunderstandings present a barrier to effective pain management [4]. Some of the most common misconceptions are that morphine is addictive, has a narrow therapeutic range, is not effective when administered orally, induces nausea and causes respiratory depression [4].

Consequentially these misconceptions have lead to inadequate pain management and suffering to the patient [4]. In reality, morphine are very ideal analgesics as they are available world-wide are relatively cheap, safe when used judiciously and most effective pain medicine for most moderate to severe pain [4]. To substantiate this innumerable studies have now shown that morphine are useful as potent analgesic and in 1986, the World Health

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Organization (WHO) recommended its judicious use as the drug of choice for the treatment of severe chronic pains, including in cancer pain [1-3].

Drug utilization studies that focus on the factors related to prescription and dispensing the medication, administration and intake of medication, and the associated events are vital in end of life care [5]. Additionally, the World Health Organization (WHO) has prescribed a set of core drug use indicators that are useful for studying patterns of drug prescribing in health care facilities [6]. These studies help evaluate if the drugs used are rational or not and also help to take right decision by the treating physician and the hospital [5]. In this retrospective study, we analyzed the prescription pattern of morphine in people who were terminally ill and succumbed to their disease in the hospital.

Materials and Methods

This was a retrospective data based study and was conducted with the support of Medical Records department of Father Muller Medical College Hospital Mangalore. The study was approved by the institutional ethics committee. The inclusion criteria were that the patient had to be admitted for their advanced cancer and had been treated for a minimum of one day in the inpatient services before succumbing to their illness in the calendar year of 2015. The exclusion criteria include patients who succumbed to other ailments, suicide or death due to accidents, cancer patients who were brought dead to the facility and ones who recovered and got discharged. The MRD provided the list of cancer patients who succumbed to their illness. The files that satisfied the inclusion criteria were selected and were thoroughly reviewed by two student investigator and a senior pharmacologist. The necessary details were entered in a present proforma sheet. The data were then entered in Microsoft excel program and imported in to statistical program (SPSS version 23) for descriptive statistics analysis.

Results

The results of the study are represented in Table 1 to 4 and Figures 1 to 3. As observed majority of the patients were from urban area (86%), men (52%) and in the age group of 41 to 60 (55%) group (Table 1). The previous treatment availed by the patients before being admitted in end of end of life/terminal stages is depicted in Figure 1. Majority of the patients admitted were of breast cancer (38.2%) followed by cancer of the gastrointestinal system (30.6%) (Table 2). The details and number on people afflicted with one or more co-morbiditis are enlisted in Table 2. The details on regrowth and metastasis and cause of death are enlisted in Table 3 and Figure 2-3. The details on the pain and the array of analgesics used, either alone or in combination are all enlisted in Table 4.

Table 1: Sociodemographic and other details

	Details	Frequency (Percent)
Gender	Females	83/173 (48.0)
	Men	90/173 (52.0)
Age	Less than 40	20/173 (11.6)
	41-50	50/173 (28.9)
	51-60	45/173 (26.0)
	61-70	36/173 (20.8)
	More than 70	22/173 (12.7)
Place	Village	24/173 (13.9)
	Town	77/173 (44.5)
	City	72/173 (41.6)

Table 2: Details on cancer and co morbidities

	Details	Frequency (Percent)
Cancer	Breast	66/173 (38.2)
	Gastrointestinal (Head and Neck, Esophagus, Liver, Pancreases, Gastric, Colon, Rectum)	53/173 (30.6)
	Lung	49/173 (28.3)
	Urogenital (Bladder, prostate, cervix)	5/173 (2.9)
Co morbidities	No co morbidity	130/173 (75.1)
	TB	4/173 (2.3)

	Malaria	1/173 (0.6)
	DM	16/173 (9.2)
	HTN	23/173 (13.3)
	IHD	7/173 (4.0)
	Asthma	1/173 (0.6)
	CVA	3/173 (1.7)
	CKD/renal dysfunction	2/173 (1.1)
	COPD	3/173 (1.7)
	SVS syndrome	1/173 (0.6)
	Neuro disorder/ seizure	2/173 (1.1)
Number of co morbidities	Nil	130/173(75.1)
	People with co morbidities	43/173 (24.9)
	One co morbidity	26/43 (60.5)
	Two co morbidities	15/43 (34.9)
	Three co morbidities	1/43 (2.3)
	Four co morbidities	1/43(2.3)

Table 3: Details on cancer regrowth, metastasis

	Details	Frequency (Percent)
Details on Regrowth and Metastasis	Recurrence/regrowth	35/173 (20.2)
	Metastasis	87/173 (50.3)
	Metastasis to one site	13/87 (14.9)
	Multiple metastasis	74/87 (85.1)
	Metastasis to Bone	60/87 (69.0)
	Metastasis to Lung	34/87 (39.1)
	Metastasis to Liver	46/87 (52.9)
	Metastasis to Brain	11/87 (12.6)
	Metastasis to other parts	18/87 (20.7)

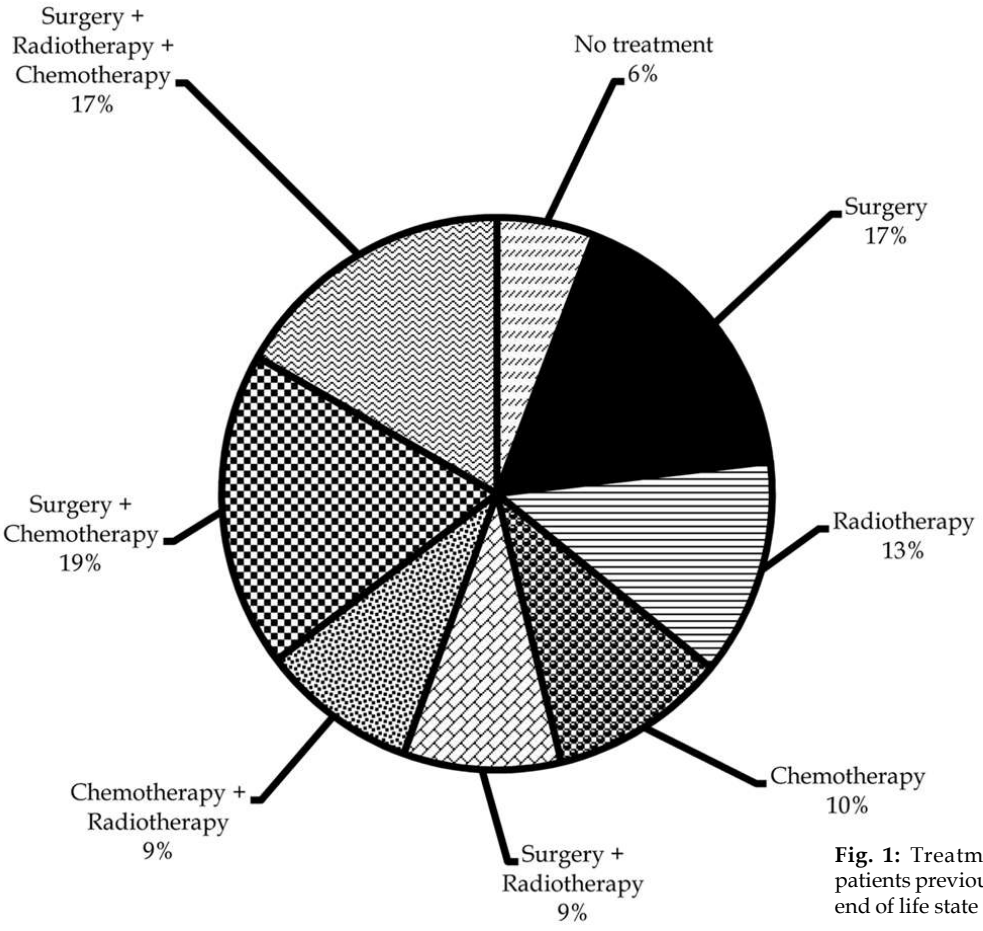

Fig. 1: Treatment undertaken by the patients previous to being admitted with end of life state (n = 173)

Table 4: Details on pain and analgesic use

	Details	Frequency (Percent)
Pain	Medium	113/173 (65.3)
	Severe	9/173 (5.2)
	Very severe	51/173 (29.5)
Analgesic	Paracetamol only	1/173 (0.6)
	Diclofenac only	31/173 (17.9)
	Tramadol only	54/173 (31.2)
	Morphine only	45/173 (26.0)
	Paracetamol + Tramadol	28/173 (16.2)
	Tramadol + Morphine	11/173 (6.3)
	Paracetamol + Tramadol + Morphine	2/173 (1.1)
Morphine	No morphine	115/173 (66.5)
	Tablets	40/173 (23.1)
	Injection	18/173 (10.4)
Morphine + Other analgesics	Morphine	45/173 (26.0)
	Tramadol + Morphine	11/173 (6.3)
	Paracetamol + Tramadol + Morphine	2/173 (1.1)

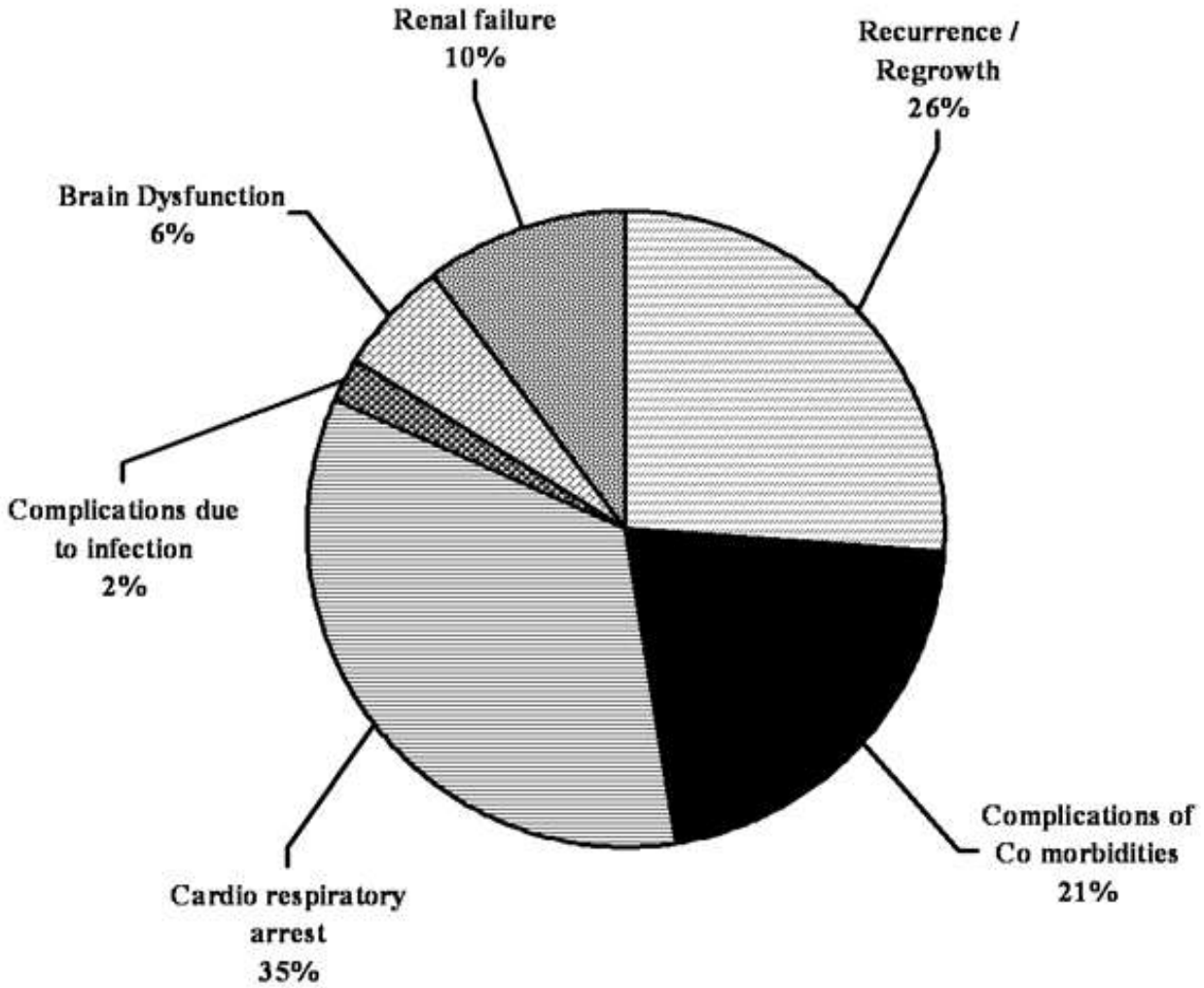

Fig. 2: Details on the cause of death in the study population (n = 173)

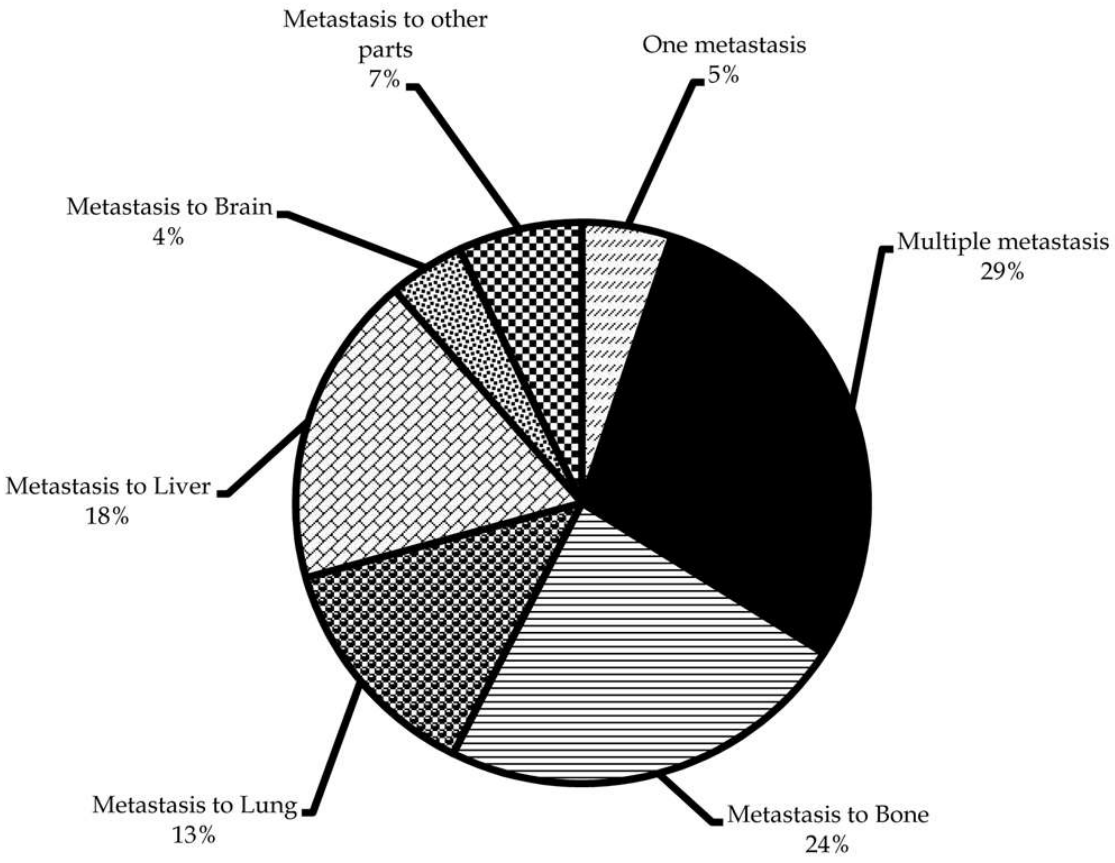

Fig. 3: Details on Metastasis in the study population (n = 87)

Discussion

Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time and at the lowest cost to them and their community [WHO, 1987] [7,9]. Suboptimal pain control can be very debilitating [1]. Patients and their families tend to be under great distress after the diagnosis of cancer [2]. Although many of these patients carry a very poor prognosis, prompt and effective pain control can prevent needless suffering, may significantly improve the quality of their lives, and may potentially spare families the feeling of helplessness and despair [1-4]. Although cancer can be a terminal disease, there should be no reason to deny a patient the opportunity to live productively and free of pain [7,8].

Severe pain can interfere with physical rehabilitation, mobility, and proper nutrition. A significant number of cancer patients are subsequently diagnosed with depression. Therefore, the goals of pain control in any patient with cancer should be to optimize the patient's comfort and function while avoiding unnecessary adverse effects from medications [5-8]. The correct use of opioids for managing cancer pain must be balanced against opioid fears, especially with concerns about an epidemic of abuse and overdose deaths involving prescription opioids [9]. In the United States, the medical use of opioids has increased 10-fold since 1990 [10].

Drug use at the end of life widely varies at each setting, in cases of both potentially appropriate and inappropriate medications [11]. Hospices specialize in symptom management and in providing the best palliative care for dying patients [1-2]. Culture-based differences in hospice management of end-of-life care patients have been observed. In some countries a substantial number of patients are sedated when approaching death [12]. In Finland the practice in the use of terminal sedation may be more conservative. Palliative care and end-of-life care has only come to focus during the last years on a national level. More training and education in this area is required [13].

The present study was conducted in order to improve the understanding between practices in specialized cancer care and hospice management of terminal cancer and in particular to study trends in pain management with approaching death. In this study it was observed that the analgesic use pattern was different and that morphine was used only in 35% of the patients and under-prescribed. This is an aspect that needs great attention.

The major limitations of our study are as follows: The study was retrospective, and could not evaluate analgesic prescriptions in relation to pain prevalence and intensity because data availability was restricted. Second it was a study from a single center and included consecutive patients. Thirdly, we took into consideration the last prescribed opioid dose before death rather than the actual dose received because the majority of our patients died at home.

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Efficacy of Airway Assessment Variables as Predictors of Difficult Intubation among Northeastern Population in India: A Hospital Based Prospective Study

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Abstract

Background and aim: Difficult intubation is an important cause of mortality in surgical patients; even more so when it is unanticipated. Predicting difficult intubation with the help of different airway parameters has been the endeavor of all anesthesiologists. However, there are variations in the accuracy of these airway parameters due to differences in race and ethnicity. The present study was aimed to assess the efficacy of various airway parameters in predicting difficult intubation in the northeast Indian population. *Methods:* Four hundred adult American Society of Anesthesiologists physical status I and II patients scheduled for elective surgery under general anaesthesia requiring tracheal intubation were assessed preoperatively for different predicting factors of difficult laryngoscopy and intubation. Intubation difficulty was assessed by the Intubation Difficulty Scale. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. The association between different variables and difficult intubation was evaluated using Fishers exact test; p-value < 0.05 was considered significant. *Results:* The mean age of the patients was 43.40±12.49 years; 60% patients were male. 23 (5.75%) patients were having difficult intubation. While all the parameters were strongly able to predict difficulty, thyromental distance < 6 cm and Cormack Lehane grade ≥ 3 were having the most strong relative risk (8 and 100.22 respectively; p < 0.0001 for both). Only Cormack Lehane grade ≥ 3 was having both good sensitivity and specificity (95.65% and 86.74% respectively). *Conclusion:* Difficult intubation rate is not different in northeastern Indian population. Thyromental distance , Modified Mallampati score and Cormack Lehane view were the strongest predictors of difficult intubation in the study population.

Keywords: Laryngoscopy; Airway Management; Intubation; Prediction.

Introduction

A difficult airway has been defined as the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with facemask ventilation of the upper airway, difficulty with tracheal intubation, or both [1]. Difficult of failed endotracheal intubation under general anaesthesia (GA) may bring on fatal outcomes. Up to 30% of anesthetic deaths were being attributed to a compromised airway [2]. The importance of prior airway assessment as a means to decrease complications in anesthesia has been well recognized. Several clinical systems were developed a few decades ago for predicting difficult intubation [3,4,5] .

The majority of studies of difficult laryngoscopy and intubation have been performed in western population [3,4,6]. Anthropometrically, Indians, especially the north east Indians are different compared to them. Adequate data of values in a given population may help the clinician to identify patients who are outside the range and therefore potentially challenging. Investigators have henceforth attempted to predict difficult intubation by using simple bedside tests (airway assessment parameters) like Modified Mallampati score (MMS), thyromental distance (TMD), sternomental distance

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(SMD), neck circumference, receding mandible etc. Nevertheless, the diagnostic accuracy of these screening tests has varied from trial to trial which is probably because of differences in the incidence of difficult intubation, inadequate statistical power, different test thresholds, or differences in patient characteristics [7,8]. The objective of the present study was to assess the efficacy of various bedside airway parameters including Cormack and Lehane grade in predicting difficult intubation in patients of northeast India.

Methods

After the approval from the institutional ethics committee, the present prospective observational study was conducted in a tertiary care teaching hospital during (May, 2015 to February, 2017). The incidence of difficult intubation is around 8% [9]. The present study was planned with an absolute precision of 3% for an indefinite population which gave us the required sample size 315. A design effect of 1.25 was taken based on the non randomized nature of sampling which gave a total required participant as 393. Four hundred adult American Society of Anaesthesiologists (ASA) physical status I and II patients scheduled for elective surgery under GA requiring endotracheal intubation were included after obtaining written informed consent from the participants (patients). Patients with obvious anatomical and pathological abnormality of the airway, those at increased risk of aspiration, inter-incisor distance < 2 cm and unstable cervical spine were excluded from the study. The age, sex and body mass index (BMI) etc. were noted. All patients were assessed in the evening day before surgery by a single observer for collecting data of airway assessment variables. The modified Mallampati class (MMC), inter-incisor distance (IID) < or ≥ 3.5 cm, thyromental distance (TMD) < or ≥ 6 cm, sternomental distance (SMD) < or ≥12.5 cm, range of head and neck movements (Grade I ≥ 90°, II = 80° - 90° and III < 80°), ability to prognoth (Class I- lower incisors can bite the upper lip above the vermilion line, II- can bite the upper lip below the vermilion line and III- cannot bite the upper lip), protruding incisors etc. were noted.

All intubations were facilitated with and attempted after 3 minutes of injecting vecuronium 0.1 mg/kg intravenously after standard GA induction. Intubation was performed using appropriate sized Macintosh blade with the patient's head in sniffing position by anaesthesiologists with more than five years experience in anaesthesia. Laryngoscopic glottis view was graded by Cormack and Lehane grading [3]. Intubation difficulty was assessed by using the scores from Intubation Difficulty Scale (IDS). IDS score = 0 represented easy intubation, 1-5 represented slight difficulty and IDS score ≥ 6 represented major difficulty in intubation [10]. Alternative techniques included patient repositioning, change of blade or tracheal tube, use of stylet, laryngeal mask airway (LMA), intubating LMA, fibreoptic intubation or intubation through LMA. The study ended after successful tracheal intubation was confirmed by assessment of chest movement, auscultation and capnography. If tracheal intubation was not possible by any means, it was noted as impossible.

Data was calculated in absolute numbers and presented in percentage scale. The measures of central tendencies were also calculated for metric data. Sensitivity, Specificity, positive and negative predictive value and accuracy for each airway predictor was calculated using standard formula. The association between different airway assessment variables and difficulty in intubation was evaluated using the Fishers exact test and $p < 0.5$ was considered as significant. INSTAT software (Graphpad prism software, Inc,. La Zolla, CA. USA) was used for statistical analysis.

Results

All the 400 participants completed the study and were included in the study. Majority (60%) of the participants were male. The participants were in the range of 18 to 76 years of age with median ASA physical class I. The demographic parameters of the study participants are presented in Table 1.

Twenty three (5.75%) patients were having MMS 3 or more while 6.5% of the patients were having TMD less than 6 cm. The numbers of patients and respective percentage scale for different airway parameters assessed are presented in Table 2. 318 (79.5%) of the patients had easy intubation, 59 (14.75%) had slight difficulty and 23 (5.75%) patients were having moderate to major difficulty in intubation. No intubation was found to be impossible.

The MMS 3 and more, TMD < 6 cm, SMD < 12.5 cm, restricted neck extension, inability prognath up to vermilion line, higher Cormack and Lehane class showed a strong relation with difficult intubation ($p \leq 0.001$) in univariate analysis (Table 3). Thyromental distance < 6 cm followed by MMS 3

Tables 1: Demographic measures of the participants (SD- standard deviation, BMI – Body mass Index, ASA – American Society of Anaesthesiologists, (q3 – q1) – third and first quartile range)

Patient characteristics	Mean ± SD or n (%) or median (q3 – q1)
Male	240 (60.0)
Female	160 (40.0)
Age (years)	43.40 ± 12.49
Age groups	
18 – 40	118 (29.50)
40 – 65	223 (55.75)
>65	59 (14.75)
Weight (kg)	66.26 ± 17.71
Height(centimeters)	158.44 ± 6.19
BMI(kg/m2)	23.93 ± 3.79
ASA physical class	1 (2 – 1)
ASA I	239 (59.75)
ASA II	161 (40.25)

Table 2: Distribution of the participants with regard to the different airway variable assessed. (IQR – inter quartile range)

Airway Parameters	n (%) / Median (q3 – q1)
Modified Mallampati Score	1 (2 – 1)
Class I	231 (57.75)
Class II	146 (36.5)
Class III	13 (3.25)
Class IV	10 (2.50)
Inter incisor distance	
Class I > 3.5 cm	384 (96)
Class II< 3.5 cm	16 (4)
Thyromental distance	
Class I > 6 cm	374 (93.5)
Class II< 6 cm	26 (6.5)
Sternomental distance	
Class I > 12.5 cm	376 (94)
Class II< 12.5 cm	24 (6)
Head & Neck movements	
Class I > 90 degree	352 (88)
Class II > 80 – 90 degree	48 (12)
Class III < 80 degree	0
Protruding incisors	
Yes	12 (3)
No	388 (97)
Ability to prognath	
Yes (class I & II)	388 (97)
No (class III)	12 (3)
Cormack and Lehane grade	1 (2 – 1)
Grade I & II	328 (82.0)
Grade III & IV	72 (18.0)

Table 3: Relationship of airway assessment variables with intubation difficulty analyzed using Fishers exact test. (IDS – intubation difficulty scale, RR – relative risk, CI – confidence interval)

Airway assessment Variables	Intubation as per IDS		RR (95% CI)	Two tailed p
	Difficult [N= 23]	Easy + slight difficult [N = 377]		
Modified Mallampati			8.742	<0.0001
Class III & IV	8(2%)	15(4%)	(4.13-18.46)	
Class I & II	15(4%)	362(91%)		
Inter incisor distance			5.053	0.0096
Class II< 3.5 cm	4(1%)	12(3%)	(1.943-13.136)	
Class I > 3.5 cm	19(5%)	365(91%)		
Thyromental distance			8	<0.0001
Class II< 6 cm	8(2%)	17(4%)	(3.754-17.051)	
Class I > 6 cm	15(4%)	360(90%)		

Sterno mental distance			5.529	0.0012
Class II < 12.5 cm	6(2%)	18(5%)	2.400-12.737	
Class I > 12.5 cm	17(4%)	359(90%)		
Head & Neck movements Class II &			9.533	<0.0001
III	13(3%)	35(9%)	(4.425-20.537)	
Class I	10(3%)	342(86%)		
Protruding incisors			4.850	<0.0260
No	20(5%)	368(92%)	(1.665-14.128)	
Yes	3(1%)	9(2%)		
Ability to prognath			8.981	0.0002
No (class III)	18(5%)	370(93%)	4.006-20.13	
Yes (class I & II)	5(1%)	7(2%)		
Cormack & Lehane			100.22	< 0.0001
3 & 4	22(6%)	50(12%)	13.725-731.86	
1 & 2	1	327(82%)		

Table 4: Accuracies of different airway assessment parameters assessed in predicting difficult intubation. (PPV – positive predictive value, NPV- negative predictive value)

Variable Assessed	Sensitivity	Specificity	PPV	NPV
Modified Mallampati	34.78	96.02	34.78	96.02
Inter incisor distance	17.39	96.82	25	95.05
Thyromental distance	34.78	95.49	32	96
Sterno mental distance	26.09	95.23	25	95.48
Head & Neck movements	56.52	90.72	27.08	97.16
Protruding incisors	13.04	97.61	25	94.85
Ability to prognath	21.74	98.14	41.67	95.36
Cormack & Lehane view	95.65	86.74	30.56	99.70

and above was found to be the highest predictor among the external airway parameters assessed.

All the external parameters assessed had very well (> 90%) in terms of specificity, only Cormack and Lehane showed very good sensitivity and negative predictive value too to predict difficult intubation (Table 4). Inter incisor distance had the lowest sensitivity while inability to prognath was having the highest specificity. The sensitivity, specificity, positive and negative predictive values of individual variables is presented in Table 4.

Discussion

Difficult laryngoscopy and intubation in the operation theatre can lead to major morbidity and mortality. Unanticipated difficult intubation is an even greater risk. The ASA has defined difficult tracheal intubation as when "proper insertion of the endotracheal tube with conventional laryngoscopy requires more than three attempts, or more than ten minutes."[11]. However this definition is not much objective. The IDS has a scoring system for different components and parameters related to tracheal intubation which gives objectivity.

The incidence of moderate to major difficult intubation in the present study was 5.75%. The incidence of difficult intubation in our study was nearly similar to the findings of other similar studies [8,12,13]. No intubation was impossible in our study. It was found that despite having good glottis view (i.e. Cormack & Lehane grade 1 or 2) tracheal intubation was having major difficulty in two cases which state that glottis exposure alone is an incomplete reflection of intubation difficulty. Similar findings were found in the study conducted by Adnet et al too [13].

The different airway assessment parameters assessed as predictors showed significant association with the outcome i.e difficult intubation as measured by IDS. However the sensitivity, specificity, positive predictive value, negative predictive values indicate that most of the external airway parameters are having average to poor sensitivity except TMD. Although Cormack & Lehane grade 1 or 2 glottic view does not completely exclude difficult intubation; Cormack & Lehane grade ≥ 3 do have a very good accuracy in terms of sensitivity and specificity in predicting difficult intubation.

The MMS showed sensitivity of only 34.78% which was nearly similar to the result of El-Ganzouri et al. (44.7%) [14]. The specificity of MMS was also comparable to that study of El-Ganzouri et al and Merah et al [14,15]. This indicates that the MMS ≥ 3 has poor capacity to correctly predict difficult

intubation but MMS ≤ 2 is better in correctly predicting easy intubation. Among the external bedside airway assessment parameters, we found the TMD and MMS had the highest sensitivity however, all the predictors had high specificity (>90%). These findings were similar to the other studies conducted in different populations [16,17, 18]. Our findings also concur indirectly with the meta analysis of Shiga et al who inferred that a combination of the Mallampati classification and thyromental distance had the highest discriminative power among currently available tests for predicting difficult intubation [7].

The present study is however limited with the fact that this is a single centre study. Although the study was planned with 80% power and was conducted in a tertiary care referral hospital, only 400 participants do not represent the huge diverse population very well too.

Conclusion

The MMS ≥ 3, TMD ≤ 6 cm, SMD ≤ 12.5 cm, restricted neck extension, inability prognath up to vermilion line are having significant relation with difficult intubation as measured by IDS in northeastern Indian population; MMS ≥ 3 and TMD ≤ 6 cm were having the highest discriminative power. Cormack and Lehane ≥ 3 view is the best the predictor of difficult intubation having very good sensitivity, specificity and relative risk.

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Original Research Article

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Effect of Administration of Magnesium Sulphate, Clonidine or Dexmedetomidine on Hemodynamics Due to Pneumoperitoneum in Patients undergoing Laparoscopic Procedures under General Anesthesia

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Abstract

Title: Effect of administration of Magnesium sulphate, Clonidine or Dexmedetomidine on hemodynamics due to pneumoperitoneum in patients undergoing laparoscopic procedures under general anesthesia. *Background*: Pneumoperitoneum and the positioning during laparoscopy induce pathophysiological changes which potentially complicate anesthetic management and require some intervention. *Aim:* To compare the effects of Magnesium sulphate ($MgSO_4$), clonidine, or dexmedetomidine on hemodynamic changes occurring after pneumoperitoneum in laparoscopic procedures. *Material and Method*: 60 adult, ASA Grade I & II, patients undergoing laparoscopies were randomly divided into three groups: Group M (magnesium sulphate), Group D (Dexmedetomidine) & Group C (Clonidine). In each group, boluses of study drugs were given before induction of anesthesia, followed by infusion prior to pneumoperitoneum. Heart rate, systolic/diastolic/mean blood pressure, end tidal CO_2, sedation score, VAS score for pain were recorded. Mean and standard deviation for each parameter was calculated using ANOVA. Sedation and pain (VAS) Score were calculated by Kruskal Willis test, p value<0.05 was considered statistically significant'. *Results:* Intraoperative heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were below baseline & comparable in all three groups ($p<0.05$) but minimally disturbed in dexmedetomidine group. Most of the patients were pleasantly sedated at the extubation with maximum patients responding to verbal commands quickly in clonidine group. VAS Pain score were minimal in dexmedetomidine group.

Keywords: Laparoscopy; Pneumoperitoneum; Hemodynamic; Magnesium Sulphate; Dexmedetomidine; Clonidine.

Introduction

Laparoscopic surgical procedures, having the benefits of minimally invasive, are being successfully performed and accepted worldwide.[1,2] However, pneumoperitoneum and the position of the patient required for laparoscopy induce pathophysiological changes that may potentially complicate anesthetic management [3,4]. These changes include increases in blood pressure, end-tidal carbon dioxide ($EtCO_2$) pressure, and central venous pressure, which are the result of the increase in intrathoracic pressure and postural changes [5] Hypercapnia and pneumoperitoneum cause stimulation of the sympathetic nervous system leading to release of catecholamine and vasopressin [6]. Different pharmacological agents like α_2 adrenergic agonists [1], beta-blockers [7] and opioids [8] are often used to attenuate circulatory response due to pneumo-peritoneum. Use of α_2 adrenergic agonists such as clonidine or dexmedetomidine and beta blocking agents significantly reduce hemodynamic changes and anesthetic requirement [12]. The intraoperative stress response, however can be reduced by preoperative administration of α_2-agonist [12].

Clonidine, an α_2- adrenergic agonist, and dexmedetomidine, a new generation highly selective alpha-2 adrenoreceptor agonist, are well known to inhibit catecholamine release. Magnesium

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also is known to inhibit catecholamine release and attenuate vasopressin-stimulated vasoconstriction and intravenous administration of magnesium sulphate before pneumoperitoneum attenuates arterial pressure increases during laparoscopic cholecystectomy. Although magnesium sulfate 50 mg/kg produces hemodynamic stability comparable to clonidine 1μg/kg, clonidine in doses of 1.5μg/kg blunts the hemodynamic response to pneumoperitoneum more effectively [9].

Dexmedetomidine is a more selective alpha 2 adrenoceptor agonist with sedative and analgesic properties. Though approved for intensive care unit sedation, studies are being conducted on its off-label uses [10]. Dexmedetomidine, an α2 agonist, when used as an adjuvant in general anesthesia attenuates stress response to various noxious stimuli, maintains perioperative hemodynamic stability and provides sedation without significant respiratory depression postoperatively [11].

We have designed this randomized controlled study to compare the effect of clonidine, dexmedetomidine and magnesium sulphate in patients undergoing laparoscopic procedures. We got our study registered with clinical trial of India registration number CTRI/2016/-09/007325.

Aims & Objectives

1. To observe and compare the hemodynamic changes occurring after administration of magnesium sulphate, clonidine, or dexmedetomidine before and after creation of pneumoperitoneum in laparoscopic procedures.
2. To observe and manage other pharmacological effects if any.
3 To observe and manage any side effect and complication if any.

Material and Method

After approval from institutional ethical committee, All patients belonging to ASA I & II and well controlled hypertensive patients (on regular drugs) scheduled to undergo laparoscopic procedures lasting up to 2 hrs were included in the study.

Exclusion Criteria

Age ≤ 20 Yrs. and ≥ 65 yrs.

Uncontrolled hypertension

Any degree of heart block

Cardiac dysfunction (low ejection fraction state)

Impaired Kidney function

Impaired hepatic function

Patients on clonidine, alpha methyl dopa, Mao inhibitors

Patients allergic to Magnesium sulphate, clonidine, or dexmedetomidine

Total of 60 patients were included in study. Power calculations suggested that a minimum of 16 subjects per group was required to detect 10% difference in arterial pressure between groups (taking type I or α error of 5%, type II or â error of 20% and Standard Deviation=10).

Patients were admitted one day prior to the scheduled surgery, examined, interviewed and written informed consent was taken. No hypnotic medication was given on the evening before surgery. Upon arrival in the operating room, monitors were attached and baseline parameters, e.g. heart rate, NIBP, oxygen saturation and ECG, were recorded.

Patients were randomly divided into three groups by computer generated number system. We planned not to incorporate a control group in our study as hemodynamic alterations due to pneumoperitoneum and postural changes in laparoscopic surgeries are well documented and confirmed phenomena and leaving them untreated would not serve any purpose and might be unethical.

Group M

Received Magnesium sulphate bolus 30mg /kg, Infusion @10 mg/kg/hr.

$MGSO_4$ 6ml (3000mg) +44 ml of0.9% Normal saline (1ml =60mg).

(Total volume of 50 ml).

Group C:

Received clonidine bolus 2 mcg/kg, infusion @1mcg/kg/hr.

Clonidine 2ml (300mcg) +48 ml of 0.9%normal saline (1ml=6 mcg).

(Total volume of 50 ml).

Group D

Received Dexmedetomidine bolus 1 mcg/kg, infusion @0.5mcg/kg/hr.

Dexmedetomidine 2 ml (200mcg) +48 ml of 0.9% normal saline (1ml= 4mcg)

(Total volume of 50 ml)

All the study drugs were made in 50 ml normal saline and given by syringe pump. The preparation and labeling of the study drugs were performed by an anesthesiologist who was not involved in administration of study drugs.

The bolus of drug according to group was administered over 10 minutes before induction .A standard premedication of butorphenol 0.2 mg / kg, Glycopyrolate 0.02 mg/kg was administered. After pre-oxygenation for 3 minutes, anesthesia was induced with a standard anesthetic protocol using intra venous injection of Propofol till loss of eyelash reflex (1- 2mg/kg), and tracheal intubation was facilitated by vecuronium bromide 0.1 mg/kg intravenously.

Anesthesia was maintained by N_2O:O_2 (60:40) with controlled ventilation. After surgical field has been draped, infusion of the drug was started before creation of pneumoperitoneum as above mentioned.

Any decrease in mean arterial pressure more than 20% below baseline was considered hypotension .A bolus of 3-4 ml /kg of crystalloid over 5 -10 minutes was to be given to treat hypotension and over a period of 10 minutes. If no response, then rate of infusion of study drug was reduced to half. In case mean arterial pressure fell below 60, infusion was stopped.

Any increase in mean arterial pressure more than 20 % above baseline was considered hypertension. In that case the rate of infusion was increased. In case of no response, the depth of anesthesia was increased. Heart rate less than 50 beats per min was treated with increments of 0.3 mg of atropine. Heart rate more than 100 or 20% increase from baseline was treated by increasing the depth of anesthesia (increasing conc. of isoflurane).

Infusion was stopped at deflation of abdomen. Throughout the laparoscopic surgery, carbon dioxide pneumoperitoneum was established and maintained to a pressure of 14 mm Hg and $ETCO_2$ was maintained between 35-45 mm Hg.

Ringer lactate solution was administered intravenously at a rate of 15 mL/kg in the first hour, followed by 7.5 mL / kg / hr until the end of surgery in all patients. At the end of operation, neuromuscular blockade was antagonized with injection of neostigmine 0.05 mg/kg and Glycopyrolate 0.02 mg/kg intravenously and patient was extubated when respiration was deemed sufficient and they were able to obey verbal commands.

Observations

Arterial pressures and heart rates were measured upon arrival in the OT (baseline), at start of infusion, at induction of anesthesia, after intubation, and after every 10 minutes till release of CO_2, after deflation of pneumoperitoneum, and at extubation. Postoperative vitals were recorded in recovery room upon arrival and 20 minutes thereafter up to one hour. Time from switching of anesthetic agents to extubation and response to verbal commands were also noted. Intraoperative observations were recorded by anesthesiologist who was blinded to study drug and not directly involved in study. In post operative period sedation level, VAS score for pain, VAS for nausea and any episode of vomiting were recorded in addition to pulse rate, blood pressure and oxygen saturation one hour at interval of twenty minutes. Post operative observations were recorded by nursing staff posted in recovery room.

Statistical Analysis

Intraoperative and postoperative parameters among three groups were compared by using one way analysis of variance (ANOVA). The statistical data was expressed as mean and standard deviation. Categorical data were compared using Kruskal Willis test. A p -value of less than or equal to 0.05 was considered as statistically 'significant'.

Results

There were no significant differences between three groups with regard to demographic data such as age, sex, weight, ASA grade and duration of surgery, duration of anesthesia (Table1). Out of 60 patients, 33 patients underwent laparoscopic cholecystectomy,17 underwent laparoscopic appendecectomy, 5 had laparoscopy assisted vaginal hysterectomy and rest 5 underwent total laparoscopic hysterectomy.

Baseline heart rate was comparable among all three groups. After administration of bolus of study drug, there was fall in heart rate in all groups. Heart rate in group D showed maximum fall from baseline (8%) as compared to group C (5%) and group M (4.8%). Though there was noticeable increase in response to intubation as compared to pre

intubation heart rate in group M (3.9%) and group C (4.0%). There was hardly any change in heart rate in group D (0.13%). The difference in heart rate post intubation among groups was not statistically significant (p>0.05). Since study drug infusion was continued after intubation throughout surgery, so even after creation of pneumoperitoneum, heart rate remained below baseline throughout surgery. Though heart rate was comparable among groups, lowest pulse rate was recorded in dexmedetomidine group at all time intervals. As infusion of study drugs were stopped at deflation of pneumoperitoneum, increase in heart rate was noted at time of extubation in all three groups. Though difference in heart rate was not statistically significant among groups (p-0.14) but heart rate in group D show minimal increase at extubation (7.9%) as compared to group M (10%) and group C (10%) (Graph 1).

Preoperative baseline systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable among groups. After administration of bolus of study drugs there was fall in blood pressure below baseline. Fall in systolic blood pressure from baseline to pre-intubation was maximum in group D (15.5%) as compared to group M (12.1%)and group C (12.3%). Similar trend was seen in mean arterial pressure in group D (17.1%), group M (13.2%) and group C (12.8%) (Graph 2) Though there was slight increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure after intubation as compared to pre intubation value but it was below baseline value and fluctuation was minimal in group D again. Blood pressure remained below baseline among three groups throughout procedure till extubation because of continuous infusion of study drugs. Even at extubation blood pressure was below base line in all three groups but there was rise in mean arterial pressure from pre extubation value (7.8%) in group M, (6.1%) in group D and (5.9%) in group C) Difference in systolic blood pressure, diastolic blood pressure and mean arterial pressure among groups was not significant at this time (p>0.05).

None of the patients had hypotension. Only one patient in group D had bradycardia that responded to 0.6mg of atropine.

Modified Ramsay Sedation Scale

Sedation score	Clinical response
0	Paralyzed, unable to evaluate
1	Awake
2	Lightly sedated
3	Moderately sedated, follow simple commands
4	Deeply sedated, responds to non painful stimulus
5	Deeply sedated, responds to painful stimulus
6	Deeply sedated, unresponsive to painful stimulus

Table 1: Demographic variables

Variables	Group M	Group D	Group C	p-Value
Age(years)	45.7 ±7.47	42 .0 ± 6.19	41.2 ±10.5	0.22
Gender				
M	10(47)	9(42)	5(27)	0.42
F	11(52)	12(57)	13(72)	
Weight(kgs)	59.6 ±8.36	60.4 ±8.36	60.65 ±9.06	0.93
ASA Physical status				
I	13	12	10	0.91
II	8	9	8	
Duration of surgery (minutes)	71±14.5	68.7±15.2	66±16	0.59
Duration of anesthesia (minutes)	101±14.5	97±16.7	96±16	0.57

Table 2: Recovery characteristics

Variables	Group M	Group D	Group C	p- Value
Extubation time(minutes)	9.4± 1.11	9.1± 0.85	6.9 ± 0.94	0.0001*
Eye opening to verbal commands(minutes)	10.1 ±0.78	10.4±1.10	7.9.±0.85	0.0001*

Recovery from anesthesia was smooth; there was no undue coughing on endotracheal tube. Time from Switching off of anesthetic agents to extubation and eye opening time was minimal in group followed by group D and group M ($p<0.05$) (Table 2). Out of all, patients in group D had sedation score 3 at extubation, maximum (17), followed by Group M(16) and 14 patients in group C (Table 3).

Post operative period was uneventful. Patients were calm during postoperative period. Heart rate, blood pressure remained within normal range with no hypotension and bradycardia. Most of our patients after extubation had Ramsay sedation score 3.Extubation time and eye opening to verbal commands was minimal in group C, followed by group D and group M ($p<0.05$). Sedation scores were statistically significant immediately on arrival in recovery room ($p< 0.05$). Patients in group C were least sedated among three groups on arrival in recovery room. Sedation score were comparable among groups after 20minutes, though still least in clonidine group. After 60 minutes, more number of patients start becoming awake in group D and group M ($p>0.05$).

VAS score for pain were comparable from arrival in recovery room up to 20 minutes and most of patients were pain free. At 40 and 60 minutes in recovery room, there was statistically significant

Table 3: Comparison of Sedation score in post operative recovery room

Time interval	Group M (sum of ranks)	Group D (sum of ranks)	Group C (sum of ranks)	p-Value
T0minute	28.5	40	23	0.0072*
T20 minutes	32.5	34.3	24.4	0.15
T40minutes	31.5	34.5	25.5	0.25
T60minutes	30	34	27	0.39

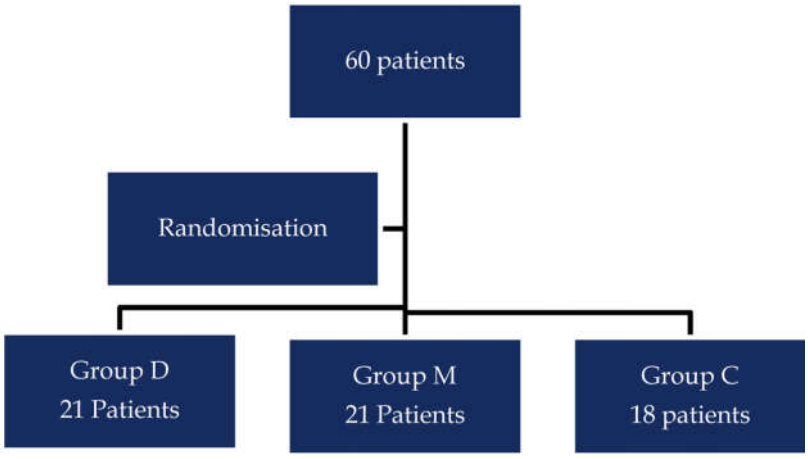
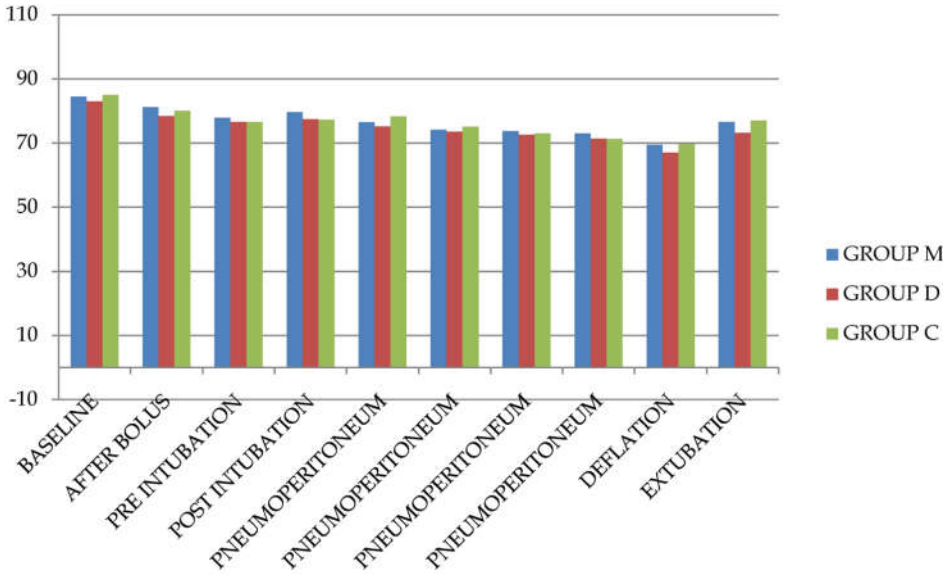
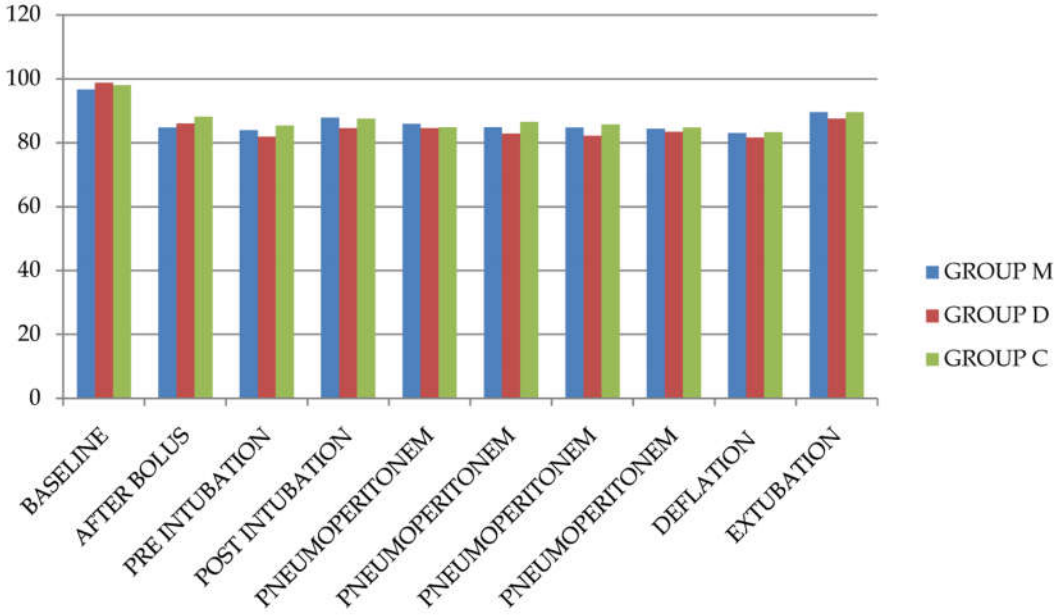


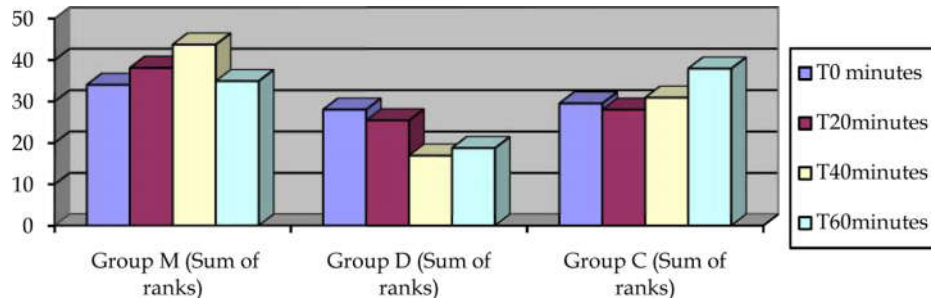
Chart 1: Consort chart



Graph 1: Comparison of Intraoperative Heart Rate among Groups



Graph 2: Comparison of intraoperative Mean Arterial Pressure Among Groups



Graph 3: Comparison of VAS score for pain in post operative period

difference in pain score ($p<0.05\%$). Pain scores were least (1-4) in group D followed by group M (2-6) and group C (2-5) (Graph 3). Only one patient in group M required analgesic. Only two patients complained of nausea in postoperative period in group M.

Discussion

Currently most preferred modality for abdominal surgeries is by laparoscopy. The preferred technique of anesthesia for laparoscopic abdominal surgeries is general anesthesia with tracheal intubation and muscle paralysis with intermittent positive pressure ventilation.

The hallmark of laparoscopy is the creation of pneumoperitoneum with carbon dioxide (CO_2). The pneumoperitoneum results in pathophysiological changes characterized by increase in arterial pressure and systemic and pulmonary vascular resistance (SVR and PVR). At intra-abdominal pressure of 15 mm Hg, Joris et al [13] found a 35% increase in mean arterial pressure, a 65% increase in systemic vascular resistance, a 90% increase in pulmonary vascular resistance, while there was a 20% decrease in cardiac output. Various pharmacological agents like magnesium sulphate, clonidine, dexmedetomidine, nitroglycerin, beta-blockers have been used to ameliorate pathophysiological changes during laparoscopy under general anesthesia. Perioperative use of α-2 adrenoceptor agonists' decreases sympathetic tone attenuates the stress responses to anesthesia and surgery, sedation and postoperative analgesia. Dexmedetomidine is a highly specific α-2 adrenergic receptor agonist [14]. We designed present study to compare magnesium sulphate, dexmedetomidine and clonidine during laparoscopic abdominal surgeries.

Clonidine, is a centrally acting selective partial α_2-agonist (α_2: α_1 = 220: 1). a α_2 agonist, inhibits the release of catecholamine and vasopressin hence causes decrease in heart rate and arterial pressure. This mechanism explains modulation of hemodynamic changes induced by pneumoperitoneum [15].

As bolus of study drugs was administered before induction of anesthesia, pressor response to laryngoscopy was also attenuated in all three groups. After administration of bolus of study drugs, heart rates start decreasing from baseline in all the groups. Heart rate in group D showed maximum fall from baseline (8%) as compared to group C & group M. Immediately after intubation there was rise in heart rate as compared to pre intubation value but remained below baseline in all three groups. Heart rate was minimally disturbed in group D. Jaakola et al [14] found decreased BP and heart rate during intubations following the administration of 0.6 μg/kg bolus of dexmedetomidine preoperatively. Perioperative use by Ray M [15] showed that of both clonidine and magnesium sulphate was able to attenuate the hemodynamic response to tracheal intubation.

Dexmedetomidine, with an elimination half life of 2 to 3 hours is a highly selective, potent and specific α_2-agonist (α_2: α_1 = 1620: 1), and is 7 to 10 times more selective for α_2 receptors compared to clonidine with a shorter duration of action [15]. Dexmedetomidine decrease sympathetic outflow from the locus coeruleus and this sympatholytic effect causes decrease of mean arterial blood pressure (MAP) and heart rate (HR) due to reduction of norepinephrine release. Further it causes release of substance P from the dorsal horn of the spinal cord and therefore exerting analgesic effect [16].

The effect of magnesium on hemodynamics is due to activation of membrane Ca-ATPase and Na-K-ATPase, enzymes involved in transmembrane ion exchanges during depolarization and repolarization phases, therefore behave as cell membrane stabilizer and intracytoplasmic organelles stabilizer [17]. This calcium inhibitory effect of Mg causes central arteriolar vasodilatation. The reduction of catecholamine release with sympathetic stimulation could be another mechanism responsible for amelioration of stress response to surgery. Magnesium exerts analgesic effect by blocking N-methyl-D-aspartate (NMDA) receptor which plays a significant role in the mechanisms underlying central sensitization in the spinal cord and is crucial for the establishment of several pain states [17,18].

In our study we did not notice significant hemodynamic disturbances during pneumoperitoneum. Heart rate remained below baseline throughout surgery. Infusion of study drug was stopped at deflation of pneumoperitoneum. At extubation there was increase in heart rate as compared to pre extubation value, rise was minimal in group D. There was no statistically significant difference among groups in heart rate at extubation ($P>0.05$).

Similarly, systolic blood pressure, diastolic blood pressure and mean arterial pressure start declining after bolus of study drugs (13.2% in group M,17.10%in group D and 12.8% in group C), though statistically no significant difference among groups. Though there was slight increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure after intubation as compared to pre intubation value but it was below baseline value and fluctuation was minimal in group D again. Blood pressure remained below baseline among three groups throughout procedure till extubation because of continuous infusion of study drugs. There was slight rise in systolic blood pressure, diastolic blood pressure and mean arterial pressure at extubation because infusion was stopped at deflation of pneumoperitoneum. Statistically significant difference was not seen among all three groups in blood pressure at extubation. Observations in our study similar to those in a study conducted by Kalra et al [19] who assessed that which of magnesium or clonidine attenuates hemodynamic stress response to pneumoperitoneum better and found that systolic blood pressure was significantly higher in control group as compared to study groups during pneumoperitoneum with no significant difference between magnesium and clonidine given in dose of 1μg/kg.

Bryskin and Weldon [21] used a combination of dexmedetomidine and magnesium sulfate for hemodynamic control during laparoscopic resection of pheochromocytoma and reported that cardiovascular stability was achieved. In our study we used magnesium sulphate and dexmedetomidine individually in two different groups and found hemodynamic stability in both the groups.

Administration of clonidine or dexmedetomidine in a study by Rajdip Hazra et al [22] showed that before commencement of pneumoperitoneum effectively attenuates hemodynamic response to pneumoperitoneum.

Our findings concur with those of Pierre Zarif [23] et al, who stated in their study that Intraoperative infusion of either dexmedetomidine or magnesium sulfate could ameliorate the pressor responses to anesthetic and surgical manipulations

during laparoscopic colectomy under pneumoperitoneum in 30° Trendelenburg position.

Only one patient in group D had bradycardia. Otherwise there were no hemodynamic disturbances during procedure and no episode of bradycardia and hypotension.

In another study by Manjushree et al [24] administration of clonidine 3 μg/kg intravenously 15 minutes before induction and reduction of the infusion to 1 μg/kg/hour intraoperatively and observed significant incidences of bradycardia and hypotension. In our study, we reduced bolus of clonidine to 2 μg/kg and infusion @1μg/kg/hr. Hence, we did not find any significant bradycardia and hypotension in clonidine group in our study.

Use of $MgSO_4$ 40 mg/kg intravenously by Elsharnouby and Elsharnouby [25] over a period of 15 minutes before induction and 15 mg/kg/hour by continuous infusion intraoperatively resulted in more episodes of severe hypotension. In our study, we reduced the dose of $MgSO_4$ to 30 mg/kg before induction and 10 mg/kg/hour by continuous infusion intraoperatively. The dose selected by us resulted in a steady and smooth reduction of MAP and heart rate, with no episodes of severe hypotension and bradycardia. Most of our patients after extubation had Ramsay sedation score 3. Variation in sedation score was not significant though maximum patients in group D had score 3($p<0.05$). Extubation time and time for eye opening to verbal commands was minimal in clonidine group, followed by group D and group M ($p<0.05$).

Magnesium sulfate potentiates neuromuscular blockade induced by non-depolarizing neuromuscular blocking agents and this possibly was the cause of the prolongation of extubation time [10]. Difference in sedation scores among groups were statistically significant immediately on arrival in recovery room ($p< 0.05$).

Patients in group C were least sedated among three groups on arrival in recovery room. Sedation score were comparable among groups after 20minutes, though still least in clonidine group. After 60 minutes, more number of patients start becoming awake in group D and group M ($p>0.05$). Recovery time and sedation score were significantly higher in groups D (dexmedetomidine) and M (magnesium sulphate) as compared to control group during laparoscopic colectomy in a study by Pierre Zarif [23].

VAS score for pain were comparable from arrival in recovery room up to 20 minutes and most of patients were pain free. At 40 and 60 minutes in recovery room, there was statistically significant difference in pain score ($p<0.05\%$). Pain scores were least (1-4) in group D followed by group M (2-6) and group C (2-5). Only one patient in group M required analgesic. This effect of dexmedetomidine can be attributed to high selectivity for α_2 receptors.

Conclusion

Use of magnesium sulphate, dexmedetomidine and clonidine results in smooth and steady hemodynamic during laparoscopic abdominal surgeries under general anesthesia, clonidine being superior in terms of early extubation and responsiveness at given dosages. Dexmedetomidine exerts a tight control on hemodynamics and best postoperative analgesia.

Limitations of the Study

Use of BIS and end tidal isoflurane concentration, would have been ideal and more informative, especially in the terms of the depth as well as, whether any significant changes in requirement of the inhalational anesthetic agent. Some authorities have shown reduction in amount of anesthetic agents with use of these drugs.

Conflict of Interest

There is no conflict of interest.

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Original Research Article

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A Comparative Study of the Effects of Intrathecal Levobupivacaine Vs Ropivacaine for Inguinal Hernioplasty

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Abstract

Objective: To compare the onset and duration of sensory and motor block, haemodynamic responses, side effects associated with administration of intrathecal isobaric levobupivacaine (0.5%) and isobaric ropivacaine(0.75%) for inguinal hernioplasty. *Place and Duration of Study*: Rajah Muthaih Medical College, Chidambaram, 2016-17. *Methodology*: After obtaining approval from institutional ethics committee and written informed consent from all patients, a randomized controlled double blinded clinical trial was conducted on 50 ASA 1 and 2 adult patients undergoing elective inguinal hernioplasty. Patients were randomly allocated into two groups, group L and group R of 25 each. Patients in group L were to receive isobaric levobupivacaine 0.5% and group R 0.75% ropivacaine. Haemodynamic variables (heart rate, systolic and diastolic BP) and onset and duration of sensory and motor block, sensory regression time were recorded and compared.

Keywords: Levobupivacaine; Ropivacaine; Randomized Control Trial; Double Blinded Study.

Introduction

The quest for searching newer and safer anaesthetic agents is always present in anaesthesiology practice. The introduction of levobupivacaine and ropivacaine has satisfied the need of a drug with superior pharmacokinetic profile and equally efficacious as bupivacaine.

Levobupivacaine, an aminoamide local anaesthetic exerts its pharmacological actions through reversible blockade of neuronal sodium channels. It is S–enantiomer of bupivacaine with low cardiovascular and neurological toxicity [1]. Its long duration of sensory and motor blockade has led to its wide application as local anaesthetic.

Ropivacaine, synthesized by Ekenstam in 1957, introduced in clinical practice in 1996, is an aminoamide local anaesthetic [2], an almost pure S–enantiomer (>99% pure) of Propivacaine. It is less lipophilic than bupivacaine resulting in relatively reduced motor blockade and its less neuro and cardiotoxicity. This greater degree of motor sensory differentiation could be useful when motor blockade is undesirable [3].

Methodology

The study population was randomly divided into two groups with 25 patients in each group. The study was carried out as a randomized double blinded study. The study drugs were prepared and numbered and the register was maintained by another faculty member.

Group L consisting of 25 patients were to receive 0.5% isobaric levobupivacaine intrathecally. Group R consisting of 25 patients were to receive 0.75%

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isobaric ropivacaine intrathecally. A thorough preanaesthetic evaluation was done to rule out any systemic disease. ASA 3 and ASA 4 patients were excluded from the study. Tab. Diazepam 10mg and Tab. Ranitidine 150mg were given on the night before surgery. Patients were maintained nil by mouth for a duration of 8 hours prior to the surgery.

On the day of surgery patient was shifted to the operating room. Intravenous access was secured. A multichannel monitor consisting of pulse oximeter, electrocardiogram, heart rate, noninvasive blood pressure was connected. The baseline heart rate, oxygen saturation, electrocardiogram, systolic, diastolic and mean arterial blood pressures were recorded. An observer new to the group assignments recorded the evolution of sensory block (using the pin prick sensation test) and the motor block (by modified bromage scale).

Modified Bromage Scale

0 – no impairment.

1 – unable to raise extended legs but able to move knees.

2 – unable to raise extended legs, as well as unable to flex knees, able to move the feet.

3 – unable to flex ankle, feet or knees.

The levels of sensory and motor block were recorded every 2mins. Maximum sensory and motor block levels were also recorded.

It was planned to treat bradycardia (HR < 50/min) with inj. Atropine 0.01mg/kg and hypotension (decrease in systolic arterial BP 30% < baseline) with Inj. Mephentramine (6-12mg). Patients were not sedated during surgery.

Observation

In the present study, the mean age(in yrs) in both group R and L is above 50 years.

The mean heart rate in group R is 75.76 and in group L is 74.64

The mean height in group R is 155.40 and in group L is 157.32

The preoperative mean systolic BP in group R is 128.72 and in group L is 126.08

The intraoperative mean systolic BP in group R is 109.52 and in group L is 112.56 and diastolic BP in group R 70.00, group L 69.12.

The onset of sensory block is between 3-5.30mins in group R and 2-3.30mins in group L.

The mean duration of sensory block is 162.80mins in group R and 211.20mins in group L.

The onset of motor block is between 5-6mins in group R and 2-3mins in group L.

The mean duration of motor block in group R is 112.40mins and 209.60mins in group L.

Side effects like hypotension, nausea, vomiting and other adverse effects were not encountered in both the groups.

There is no significant change in age and height distribution between the two groups (Group L and Group R) and majority of patients are above 50 years in both groups.

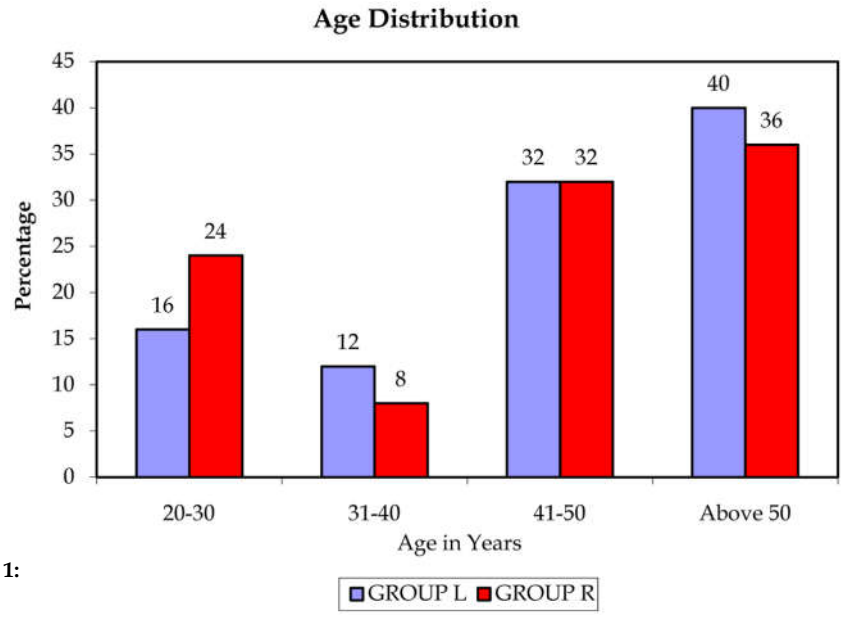
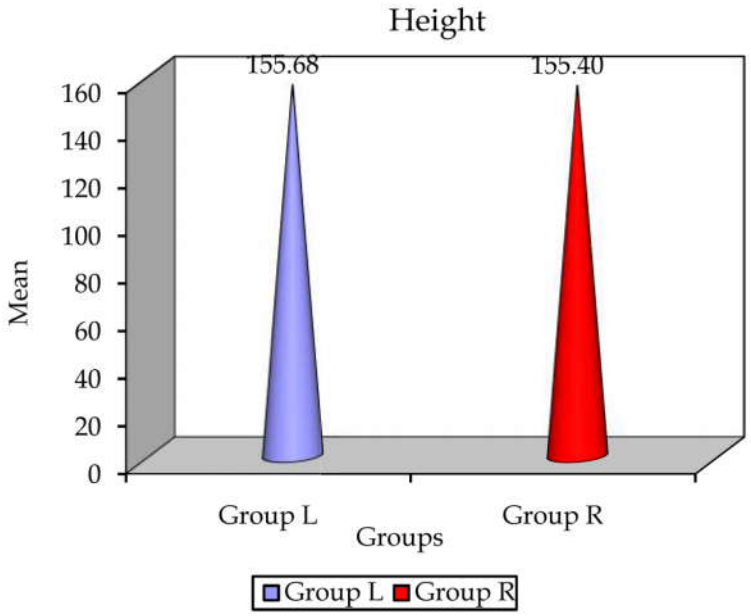


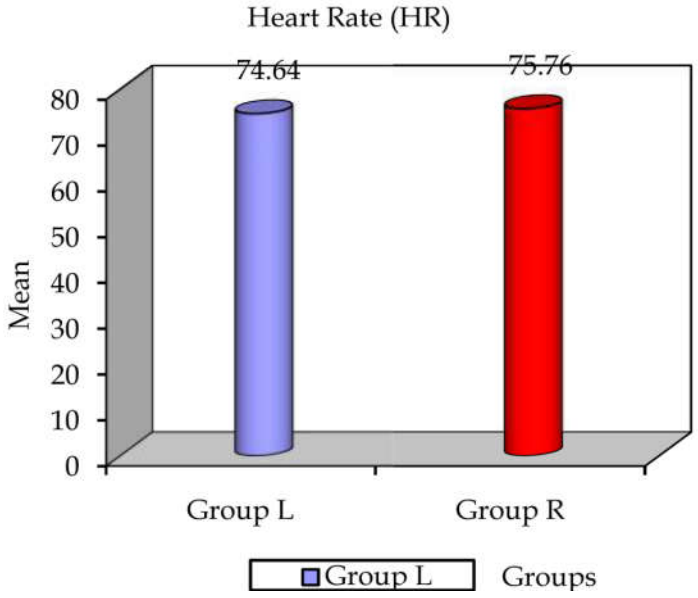
Fig. 1:

Fig. 2:



Calculated t-value	P Value	Level of Significant
0.348	0.731	Not Significant

Fig. 3:



Calculated t-value	P Value	Level of Significant
0.698	0.492	Not Significant

There is no significant change in heart rate between the two groups (Group L and Group R)

	Pre-op Systolic	Pre-op Diastolic	Intra-op systolic	Intra-op Diastolic
t-value	1.826	0.532	1.470	0.515
p-value	0.080	0.600	0.153	0.611

Blood Pressure Changes

There is no significant change in pre-operative and intra-operative systolic, diastolic blood pressures between the two groups (Group L and Group R)

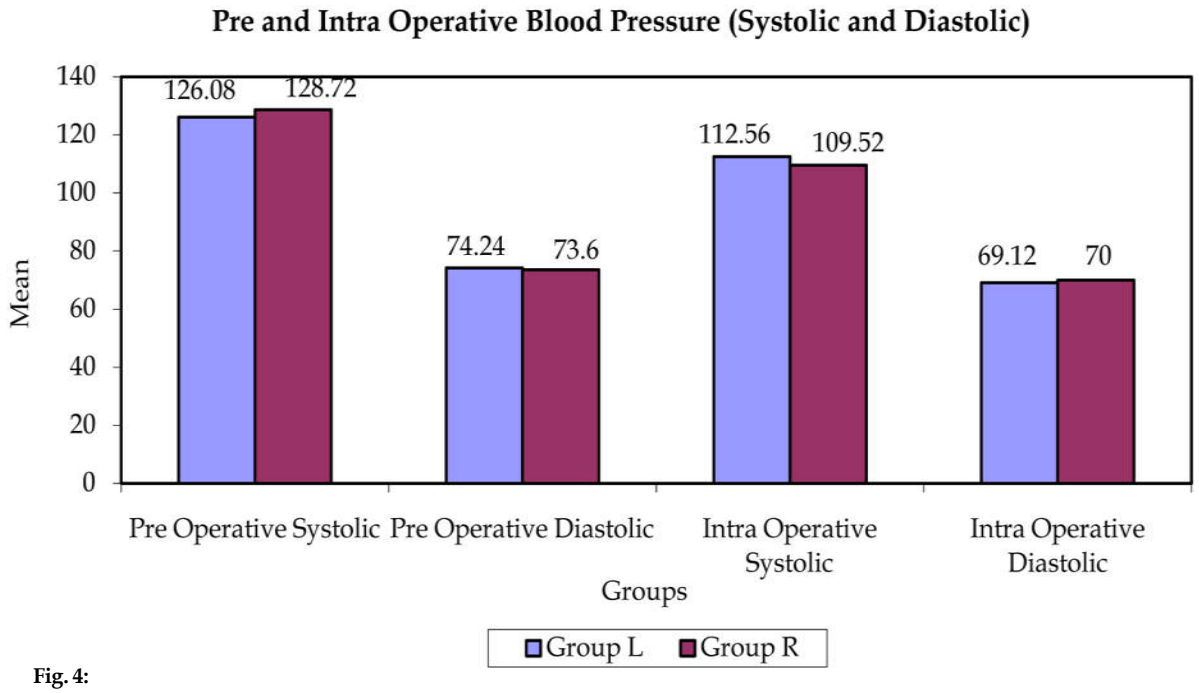


Fig. 4:

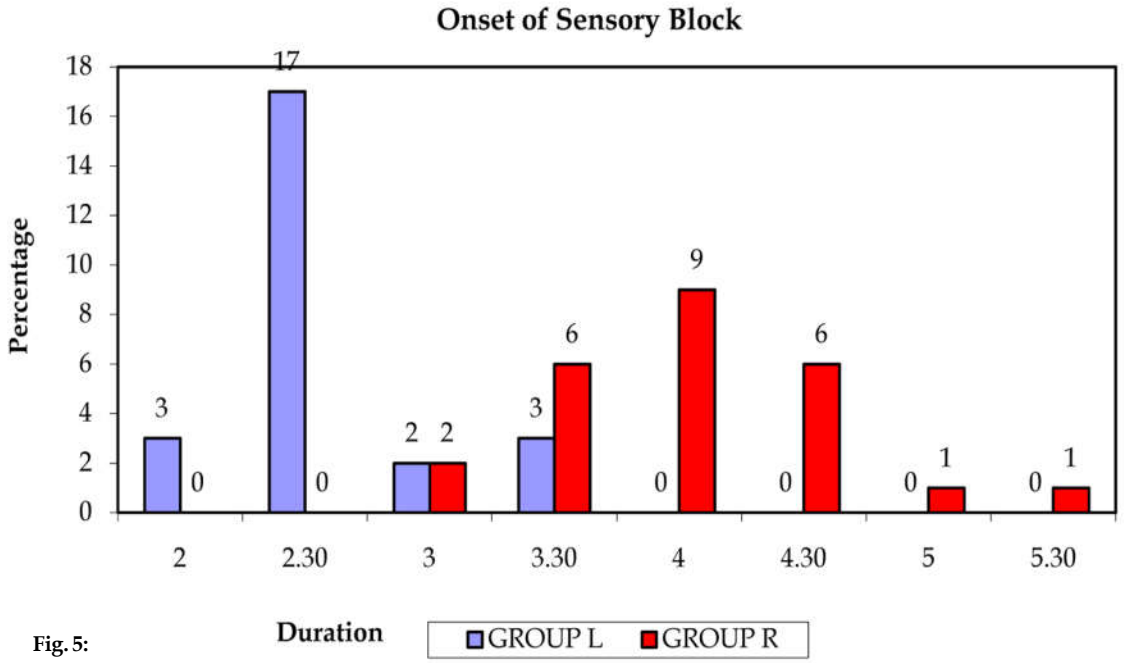


Fig. 5:

Calculated Chi-square Value	Degrees of Freedom	Probability Value
38.00	7	0.0001

Group L has a quicker onset of sensory block as compared to group R.

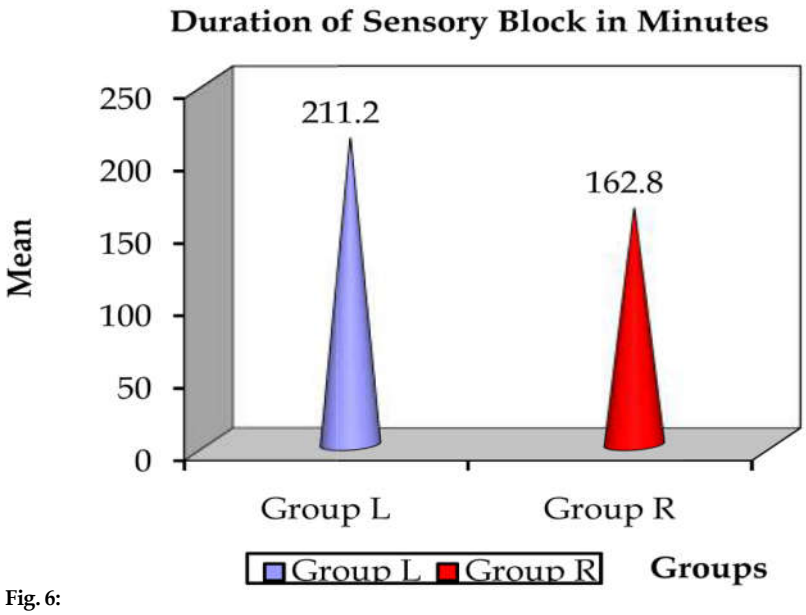


Fig. 6:

Calculated t-value	P Value	Level of Significant
11.894	0.001	Significant

P<0.01

Group L has longer duration of sensory block as compared to group R.

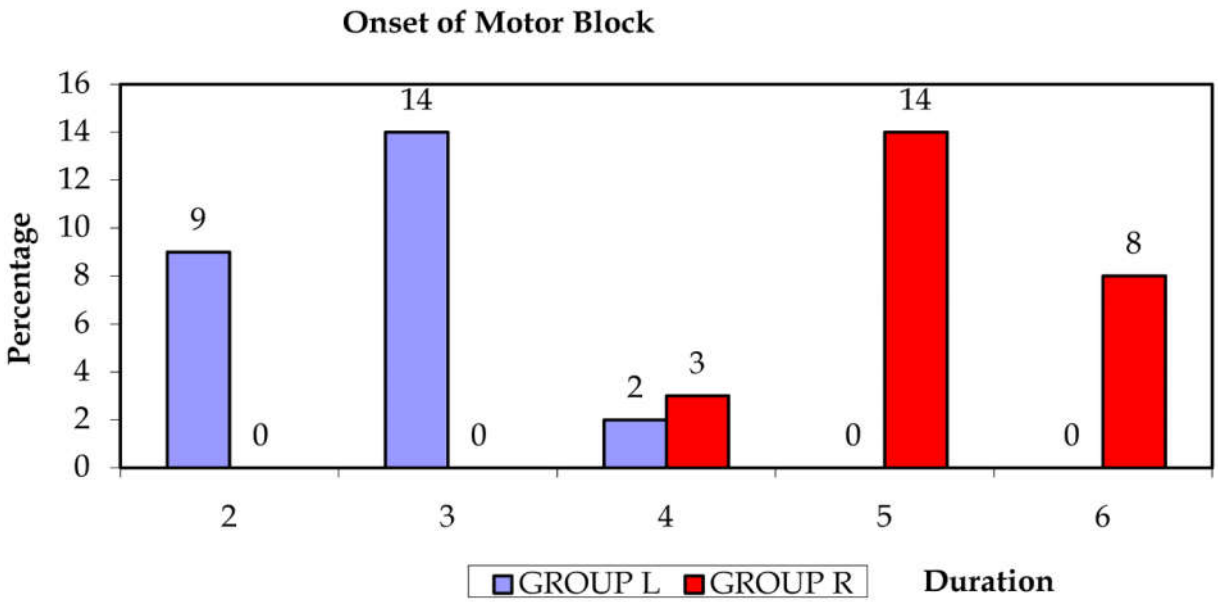


Fig. 7:

Calculated Chi-square Value	Degrees of Freedom	Probability Value
45.20	4	0.0001

Group L has quicker onset of motor block as compared to group R.

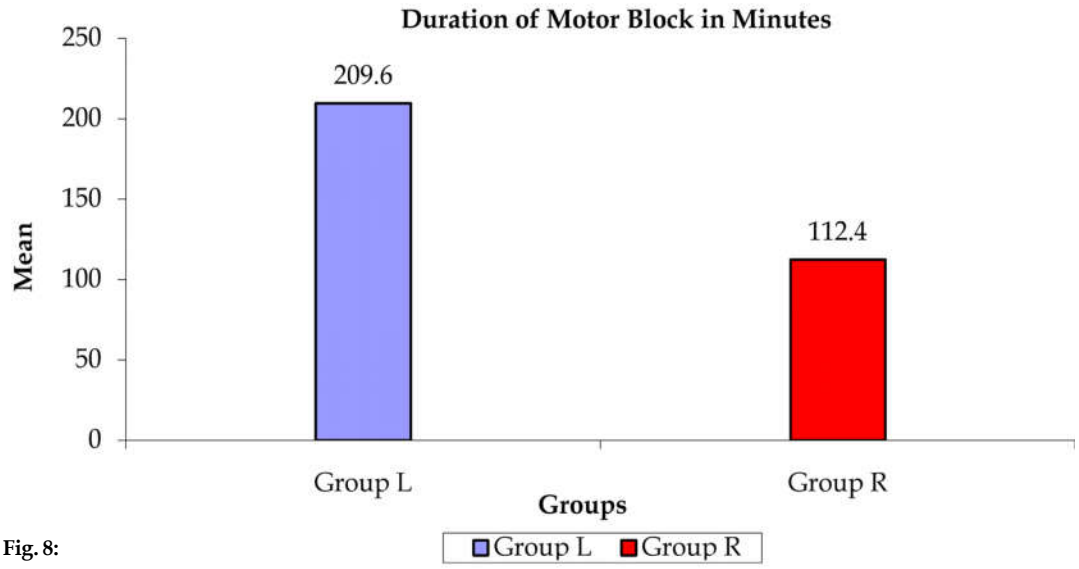


Fig. 8:

Calculated t-value	P Value	Level of Significant
31.525	0.001	Significant

P<0.01

Group L has significant longer duration of motor block as compared to group R.

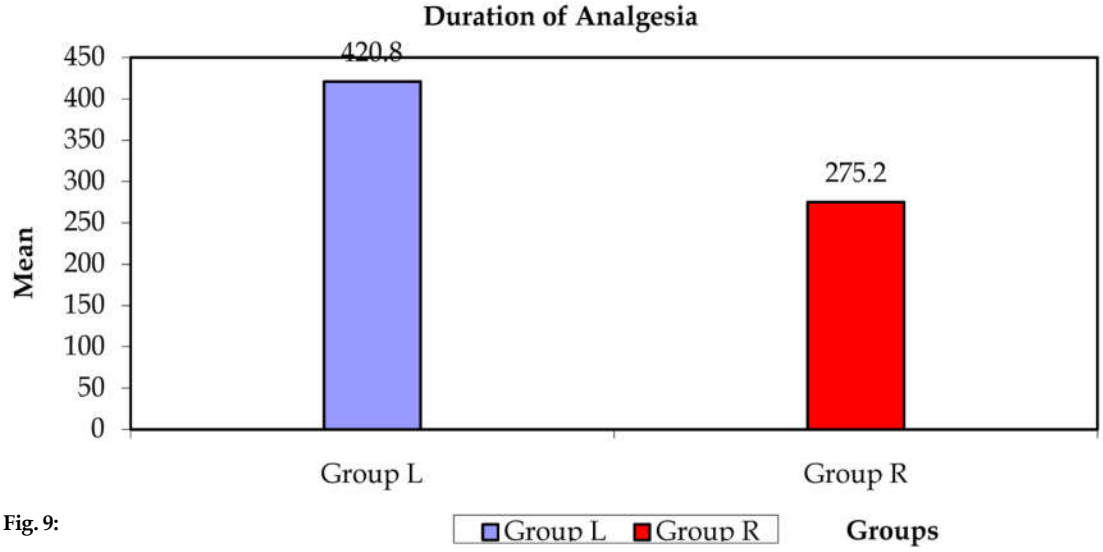


Fig. 9:

Calculated t-value	P Value	Level of Significant
23.307	0.001	Significant

P<0.01

Group L has significant longer duration of analgesia as compared to group R.

Discussion

The intrathecal administration of local anaesthetic agent is commonly employed to avoid the risk of general anaesthesia which involves airway management, aspiration and polypharmacy. It is safe inexpensive and easy to administer, offers high level of postanaesthetic satisfaction for patients. The quality of sensory blockade, motor blockade,

haemodynamic changes and side effect profile are some considerations in selecting a drug for spinal anaesthesia.

Levobupivacaine, a newer local anaesthetic used for lower limb [10], abdominal (inguinal Hernia) surgeries [4,5,6] has long duration of action and minimal cardiovascular and neurological toxicity [7].

Ropivacaine, another new agent is being increasingly used for spinal anaesthesia in caesarean section, labour analgesia [8,9], lower abdominal and perineal surgeries including lower limb surgeries [10]. Advantages claimed are shorter duration of motor block and lesser cardiotoxicity, minimizing the psychological discomfort of being immobile for longtime.

Conclusion

The onset of sensory and motor block is fast in group L than in group R. the mean duration of motor block is prolonged in group L than in group R.

Haemodynamically, both the drug groups showed comparable and stable results. None of the patients needed any intraoperative analgesic topups. We conclude that both 0.5% levobupivacaine and 0.75% ropivacaine can be successfully used in inguinal hernioplasty. Both the drugs in their respective concentrations are equally potent. The side effects are minimal in both the drug groups and both the drugs exhibited stable and comparable results.

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Original Research Article

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Feasibility of Hematoma Block for Closed Reduction of Fractures of Distal End of Radius: A Comparison with General Anesthesia

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Abstract

Background: Fractures of distal radius are common and there are different modes of anesthesia to obtain pain relief prior to closed reduction. The aim of this study was to prospectively compare hematoma block alone and general anesthesia for the reduction of distal radius fractures, with respect to pain perception before and after manipulation using a visual analogue scale (VAS), patients' acceptance and surgeons' acceptance. *Methods:* In this randomized, controlled study, 60 ASA-I and II patient were divided into HB group (n=30) who received Hematoma block, compared with GA group(n=30) who received general anesthesia. Pain was assessed preoperatively and postoperatively by VAS, and intraoperatively by change in heart rate and mean arterial blood pressure from the baseline levels. Patients' and surgeons' acceptance with the nature of procedure were assessed using patients score and surgeons score respectively. *Results:* Intraoperatively, HB group patients had better hemodynamic variables when compared to GA group. The mean of postoperative VAS of HB group and GA group were 2.1 and 3.83 respectively which was statistically significant. The difference of mean score between the two groups with respect to surgeons' score ($p<0.001$) and patients' score ($p<0.001$) were statistically significant. Post-manipulation pain was significantly greater in patients who received general anesthesia (VAS=3.83±0.64). *Conclusion:* Patient acceptance and surgeons' satisfaction is greater with a correctly performed hematoma block and is a safe and effective alternative to general anesthesia.

Keywords: Closed Reduction; Distal Radius Fracture; Hematoma Block; General Anesthesia; Visual Analogue Scale.

Introduction

Over 5-16% of all fractures treated at trauma unit of emergency department are distal radius fractures and are common in all age groups especially elderly people [1-4]. Various techniques of anesthesia for fracture reduction include intravenous sedation, general anesthesia, intravenous regional anesthesia, nerve blocks and hematoma block [2,5-10]. Hematoma block is achieved by administering local anesthetic within the hematoma in between the fracture ends [9,10]. Several studies were done comparing different techniques and each has its own associated risk and drawbacks [7,8]. Comorbidities and drug interactions additionally add risks to the patient who is undergoing fracture reductions under any of the above mentioned techniques. Hematoma block serves to block the free and open nerve endings in between the fracture ends resulting in effective blockade and analgesia [9].

Methods

This prospective, randomized study was undertaken after obtaining ethics committee approval and written informed consent from the patients. A total of sixty ASA-I, II patients in the age range of 20 to 60 years, scheduled forisolated closed reduction of distal radius fracture were

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selected for the study. Patients with injury more than 96 hours, analgesic consumption during the past 8 hours, any associated injuries, systemic illness, patients with smoking or alcoholism and those with coagulopathy were excluded from the study.

All patients were randomly allocated by envelope method into two groups. First group received hematoma block (HB group) whereas second group received general anesthesia (GA group). Pre-anesthetic evaluation of the patients was done in both the groups assessing for systemic illness and airway examination, compartment syndrome and neurological deficits secondary to fracture. After fulfilling inclusion and exclusion criteriaa minimum of 8 hours of nil per oral for solids and 4 hours for clear waterwas obtained. Preoperative visual analogue scale (VAS) were noted in both the groups before administering anesthesia. Patients rated their pain from 0 (no pain) to 10 (severe pain) prior to fracture manipulation. Duration from the time of injury and analgesic consumption 8 hours prior to induction of anesthesia technique were noted. Intradermal test dose was administered 30 minutes prior to institution of hematoma block.

In all patients intravenous access was secured using 20G i.v. cannula in non-operating limb. Intraoperative monitoring in both the groups included electrocardiography, non-invasive blood pressure and plethysmography.Under strict aseptic precautions, patients in HB group received hematoma blockusing a 22G needle and by injecting 10 ml of preservative free 2% Inj.lignocaine in the dorsal aspect of forearm in between the fractured ends. An elastic bandage was applied above the fracture site for 10 minutes after administration of hematoma block for proper anesthesia. After lapse of 10 minutes,pain at the fracture site was assessed, elastic bandage removed and it was manipulated and reduced by surgeon.

Patients in GA group received general anesthesia using Inj.fentanyl 2µg/kg, Inj.propofol 2 mg/kg and according to the response and anesthesia was maintained using N_2O:O_2 in 66:33 ratio and Isoflurane(1-1.5%). Patients were monitored for heart rate and mean arterial blood pressure at 0, 5, 10, 15, 20, 25 and 30 minutes. In majority of the patients fracture was reduced within 5 minutes and in all patients by the end of 10 minutes.

At the end of procedure after the application of cast and when patients were fully awake, patients visual analogue scale (VAS), patients' satisfaction about the anesthesia technique used (patients' score) and surgeons' satisfaction on the reduction of the fractured ends, radiological correction of fracture and anesthesia technique administered (surgeons' score) were noted.

Descriptive and inferential statistical analysis has been used in our study. Results on continuous measurements are presented on Mean±SD (Minimum-Maximum) and results on categorical measurements are presented in percentage numbers (%). 'p' < 0.05 was considered to be significant. The following assumptions on data were made-dependent variables were normally distributed, random sampling from the population was ensured and the patients chosen were independent.

Student t test (two tailed, independent) and Chi-square/Fisher Exact test were used to assess the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters and categorical scale between two or more groups respectively. Levens test for homogeneity of variance has been performed to assess the homogeneity of variance and $p \leq 0.01$ was considered to be strongly significant. Data was collected and statistics done using 17.0.2 version of SPSS.

Results

The two groups did not vary significantly in age, sex, ASA grade and duration from the time of injury (Table 1). Baseline (0 min) heart rateand mean arterial pressure were statistically insignificant between the two groups and also at 5^{th} and 10^{th} minute (Tables 2,3 Figure 1,2). Following manipulation and reduction of fracture the mean heart rateand mean arterial blood pressure between the two groups at 15, 20, 25 and 30 minutes varied significantly (Tables 2,3 Figure 1,2).

The average duration since the time of injury (p=0.337) (Table 1) and preoperative Visual Analogue Scale(VAS) did not vary significantly between the two groups(Table 4, Figure 3). The mean of postoperative VAS of HB group and GA group were 2.1 and 3.83 respectively and there was statistically significant difference between the two groups (Table 4, Figure 3). Within the group there was significant reduction in VAS from preoperative to postoperative period in both groups and the difference was higher in HB group (5.10±0.711) when compared to GA group (3.36±0.927) and it was statistically significant (p<0.001) (Table 4). The mean surgeons' score of GA and HB group were 7.26 and 8.1 respectively (Table 4, Figure 4). The mean patients' score of GA and HB group were 6.8

and 7.9 respectively (Table 4, Figure 4). The difference of mean score between the two groups with respect to surgeons' score ($p<0.001$) and patients' score ($p<0.001$) werestatistically significant (Table 4).

Hematoma block resulted in good pain relief and surgeons' could reduce the fracture with ease. There was no incidence of failed hematoma block. Post-manipulation pain was significantly greater ($p<0.001$) in patients who received general anesthesia (Postoperative VAS=3.83±0.64) (Table 4). There were no complications related to eitherof the anesthetic methods used.

Table 1: Patient characteristics (n=30). Data are mean (range) or Mean ± SD*

Time	**Group-HB** (n=30)	**Group-GA** (n=30)	p-value
Age (years)	46.66±4.84	48.03±4.37	0.085(ns)
Sex (Male:Female)	10:20	9:21	0.781(ns)
ASA (I:II)	19:11	19:11	1.000(ns)
Mean duration since time of injury (hours)	10.53 ± 2.09	11.03± 1.90	0.337(ns)

Abbreviations: SD=standard deviation, $p<0.05$ significant, ns=statistically not significant

Table 2: Comparison of mean heart rate (bpm) changes in response to manipulation and closed reduction of radius fracture between Group:HB and Group:GA

Time	Group-HB	Group-GA	p-value
0 min	93.06±3.77	91.26±3.94	0.076(ns)
5 min	89.66±4.00	87.73±3.95	0.065(ns)
10 min	85.06±4.25	84.00±4.48	0.349(ns)
15 min	89.40±4.14	95.00±3.85	<0.001(hs)
20 min	86.46±4.19	92.80±3.80	<0.001(hs)
25 min	84.13±3.96	91.06±3.43	<0.001(hs)
30 min	81.60±4.14	89.66±3.79	<0.001(hs)

T-time intervals as mentioned in the Methods of study. ns= statistically not significant, hs=highly significant

Table 3: Comparison of mean arterial pressure changes (MAP in mm Hg) in response to manipulation and closed reduction of radius fracture between Group:HB and Group:GA

Time	Group-HB	Group-GA	p-value
0 min	97.66±3.79	96.30±2.71	0.114(ns)
5 min	94.26±3.92	93.80±2.69	0.593(ns)
10 min	91.13±3.47	92.33±2.73	0.142(ns)
15 min	92.26±3.81	95.36±2.23	<0.001(hs)
20 min	90.20±3.72	93.20±2.38	<0.001(hs)
25 min	89.06±3.55	91.73±2.39	<0.001(hs)
30 min	87.33±3.76	91.33±2.42	<0.001(hs)

T-time intervals as mentioned in the Methods of study. ns= statistically not significant, hs=highly significant

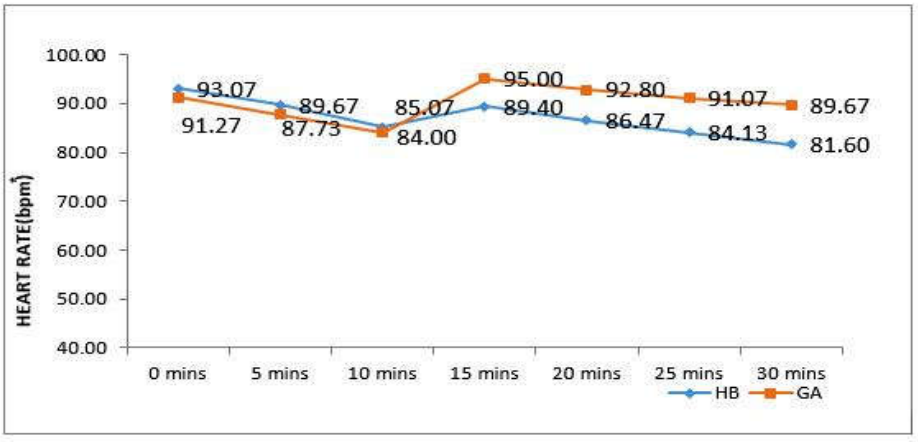

Fig. 1: Comparison of heart rate between HB group and GA group at various intervals of time

Table 4: Comparison of Visual Analogue Score (VAS), Surgeons' score and Patients' score between Group:HB and Group:GA

TIME	Group-HB	Group-GA	p-value
Preoperative VAS	7.18±0.92	7.42±0.24	p=0.92 (ns)
Postoperative VAS	2.10±0.48	3.83±0.64	p<0.001 (hs)
Pre-Post VAS*	5.10±0.711	3.36±0.927	p<0.001 (hs)
Surgeons' score	8.10 ± 0.661	7.266±0.583	p<0.001 (hs)
Patients' score	7.90 ± 0.711	6.80±0.846	p<0.001 (hs)

p<0.05 significant, ns=statistically notsignificant. *difference of preoperative and Postoperative VAS

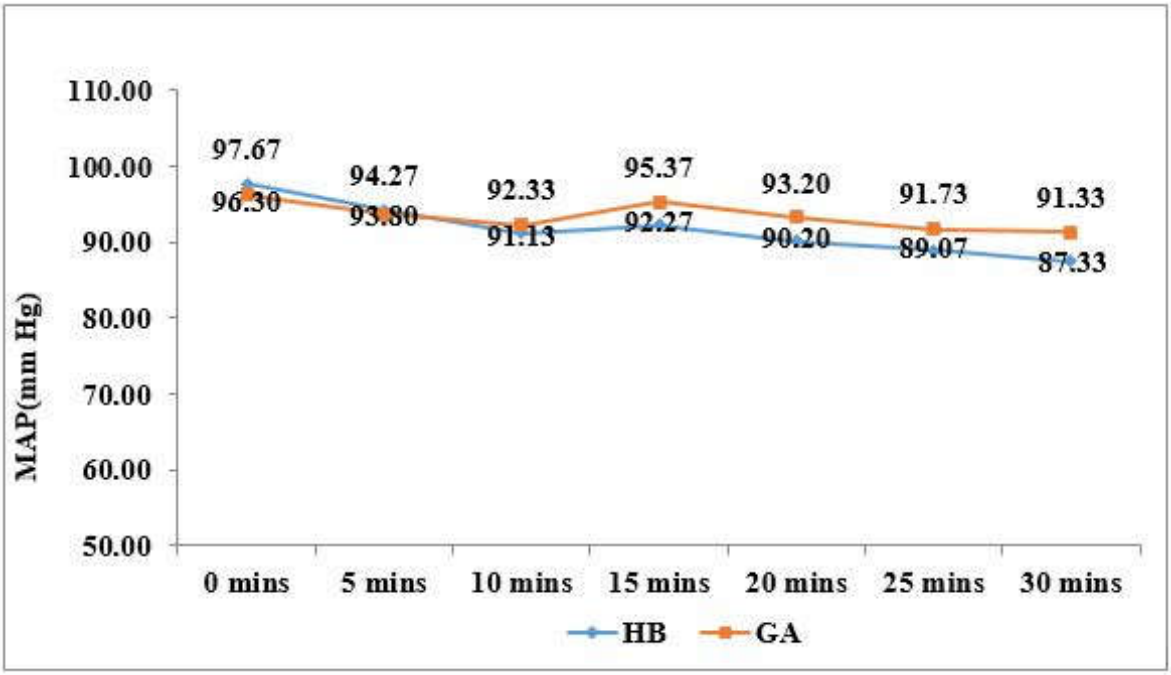

Fig. 2: Comparison of mean arterial blood pressure between HB group and GA group at various intervals of time

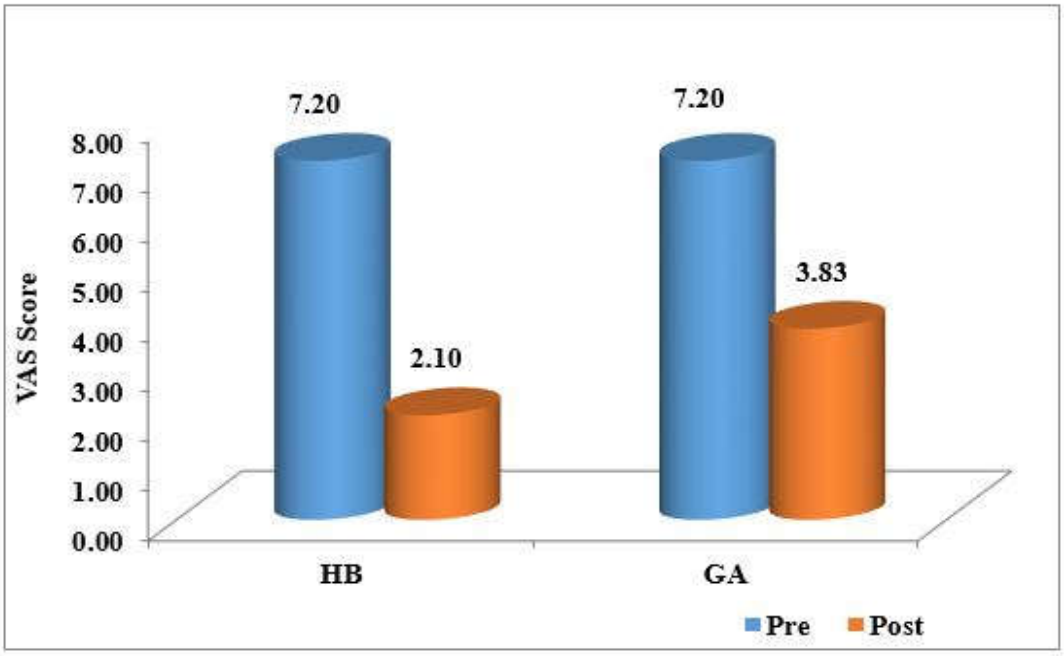

Fig. 3: Comparison of preoperative and postoperative VAS in between HB group and GA group

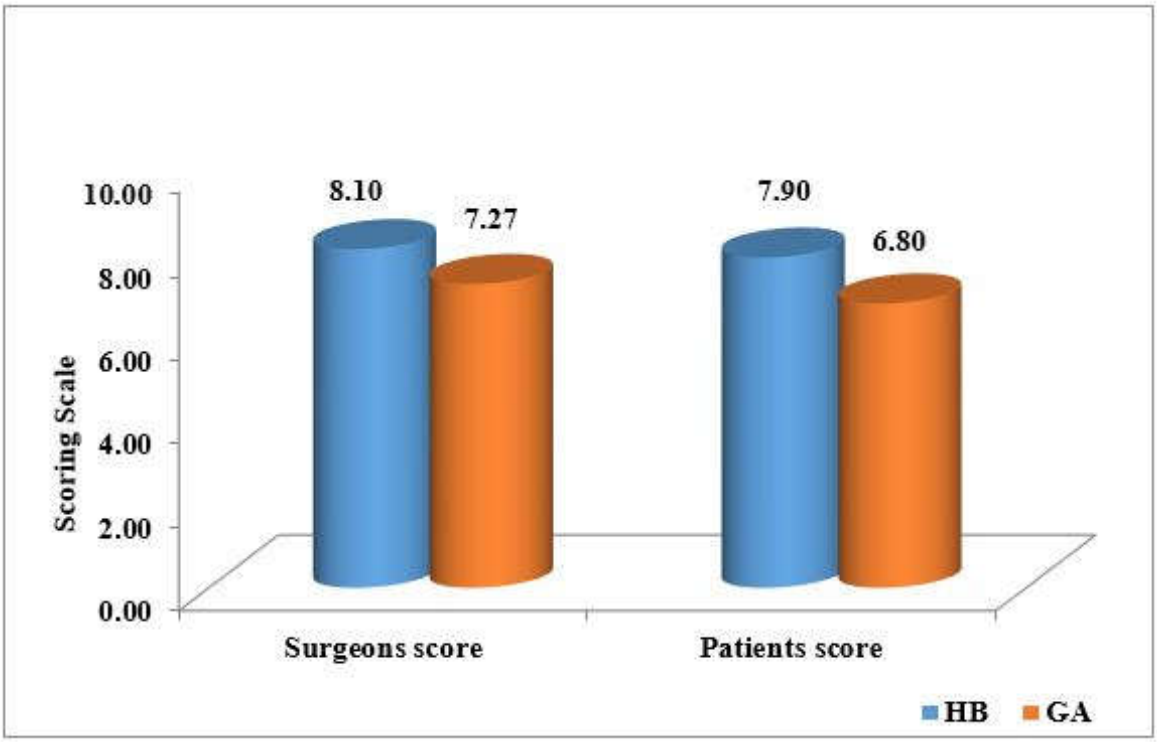

Fig. 4: Comparison of Surgeons' score and Patients'score between HB group and GA group

Discussion

Fractures of the distal radius are common and methods of obtaining pain relief prior to their reduction include general anesthesia, intravenous regional anesthesia, drugs e.g. midazolam and ketamine [11], modified forearm intravenous regional anesthesia, brachial plexus block and local infiltration of the fracture hematoma (hematoma block) [5-10]. Studies have been done comparing these techniques (general anesthesia, sedation alone, sedation with hematoma block, hematoma block alone) but with varying results [5,7-9]. Major advantages of regional anesthesia are early recovery, early ambulation and cost-effectiveness [12].

Hematoma block is commonly used for closed reduction of distal radius fractures. Studies have done have using lignocaine as common drug. The infiltration of local anesthetic agent within the fracture site serves to block the nerve fibers of the surrounding soft tissues and the periosteum around the fracture [9]. Recently ultrasonography has been used to assist in institution of hematoma block [13]. Studies have been done using buffered lignocaine and hyaluronidase but with no added resultant advantage [11,14].Study concluded that if appropriate precautions are taken hematoma block is safe with no increased risk of infection [15]. Advantages of hematoma block are shorter waiting time, manipulation time, early recovery, early ambulation, good patient acceptance and cost-effectiveness [7].

Funk et al [7] studied by administering hematoma block and general anesthesia in 40 people and concluded that patients experienced pain during manipulation with hematoma block while patients under general anesthesia had no pain. Myderrizi and Mema [9] conducted a study and concluded that there is no significant difference between two modes of anesthesia in pain intensity after hematoma block and 10-15 minutes waiting for analgesic effect induction. In our study, we waited for 10 minutes for analgesia to be inducted for hematoma block action and its effectiveness. Application of an elastic bandage above the fracture site before administration of hematoma block would limit the spread of local anesthetic and result in better blockade. None of these studies used elastic bandage before hematoma block was given. But in our study we used elastic bandage. This could have resulted in better pain relief as assessed by patients' hemodynamic variables intraoperatively and VAS scores post-reduction.

In our study following reduction of fracture, patients who received hematoma block had better

pain relief when compared with those who received general anesthesia. Patients had better acceptability of hematoma block (Patients' score= 7.90±0.711) ($p<0.001$, Table 4, Figure 4) as their choice because they could be awake during procedure, had good pain relief during and following reduction of fracture and early discharge from hospital. Surgeons too had better acceptability of hematoma block (Surgeons' score= 8.10±0.661) ($p<0.001$, Table 4, Figure 4) as their choice because of equally good radiological correction of fracture, early ambulation and early discharge from the hospital. We did not use sedation in addition to hematoma block so as to assess the effectiveness of this technique alone. Previous studies done showed that general anesthesia or hematoma block with sedation as their technique of choice when compared to hematoma block alone. Patients who received analgesics within 8 hours prior to reduction were excluded because this could bias the results obtained. Hematoma block may fail or be ineffective when, the time since injury is beyond 96 hours as the clot organizes.[6] In our study we excluded patients who had their injury beyond 96 hours.

Pain reduction was significant ($p<0.001$) (Table 4) following hematoma block (Pre-Post VAS=5.10±0.711) during manipulation and reduction of fracture compared to presentation during admission. Following reduction of fracture, pain was significantly greater ($p<0.001$) in GA group (Postoperative VAS=3.83±0.64) when compared to HB group (Postoperative VAS=2.10±0.48) (Table 4, Figure 3). We did not notice any adverse events/ effects in either groups. A correctly performed hematoma block will have good patients' acceptance compared to general anesthesia.Even though a formal cost-effectiveness analysis was not done in our study, the difference in expenses was obvious, with significant savings in the HB group.

Infection at the injection site [16], local anesthetic toxicity[17] and compartment syndrome [18] are the possible complications with hematoma block but the probability is very low. Dorf E et al [17] recorded a case of lignocaine toxicity after hematoma block by injecting 10 ml of 2% Inj.lignocaine. Younge D et al [18] documented a case of compartment syndrome after hematoma block used for wrist fracture. There were no complications associated with any of the procedures in our study.

Conclusion

Hematoma block using 2% Inj.lignocaine is a safe and effective alternative to general anesthesia in reducing fractures of distal end of radius. Patient acceptance is greater with a correctly performed hematoma block compared to general anesthesia. It would be beneficial in clinically high risk patients in whom administration of general anesthesia would be detrimental.

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Nil

Conflicts of Interest: Nil.

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Original Research Article

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A Comparative Study of Dexmedetomidine (1 mcg/kg) and Fentanyl (2 mcg/kg) with Dexmedetomidine (1 mcg/kg) Alone for Sedation during Awake Fiberoptic Intubation

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Abstract

Aim of Study: Many drugs are used for providing favorable intubation conditions during awake fiberoptic intubation (AFOI). However, most of them cause respiratory depression and airway obstruction leading to hypoxemia. The aim of this study was to compare intubation conditions, and incidence of desaturation between dexmedetomidine in combination with fentanyl and dexmedetomidine alone. *Material and Methods:* This randomized double-blind prospective study was conducted on a total of 60 patients scheduled for maxillo facial surgeries who were randomly allocated into two groups: Group DF received dexmedetomidine 1 mcg/kg along with fentanyl 2 mcg/kg and Group D received dexmedetomidine 1 mcg/kg over 10 min. Patients in both groups received glycopyrrolate 0.2 mg intravenous, nebulization with 2% lidocaine 4 ml over 15min and 10% lidocaine spray before undergoing AFOI. Adequacy of intubation condition was evaluated by Incidence of desaturation, cough score and post-intubation score, hemodynamic changes and sedation using Ramsay sedation scale (RSS) were noted and compared between two groups. *Results:* Cough score <2 was considered as favourable intubation condition, which was achieved in 27 out of 30 patients in Group DF, but only in 5 out of 30 patients in Group D which is statistically significant. ($P < 0.0001$) Better tolerance score (Score 1) was found in 21 patients of Group DF and only 4 patients in Group D. This difference was also statistically significant ($P < 0.0001$). higher RSS was achieved in Group DF(3.7±0.79)than in Group D (1.7±0.65) ($P < 0.0001$). We observed that 8 patients of Group DF and 28 patients in Group D were able to maintain SpO_2 (≥95%) ($P < 0.0001$) during the procedure *Conclusion:* Dexmedetomidine with fentanyl provides good intubation conditions than Dexmedetomidine alone during AFOI.

Keywords: Awake Fiber Optic Intubation (AFOI); Dexmedetomidine; Fentanyl; Cough Score; Intubation Conditions.

Introduction

Oral or nasal flexible fiber optic intubation (AFOI) is usually the gold standard method for airway management in the expected difficult airway. Success of the fibre optic intubation is highly dependent on adequate preparation and sedation techniques [1].

A patient who is comfortable, cooperative, free of oropharyngeal blood and secretions, and able to maintain his/her airway with spontaneous ventilation are the adequate conditions for AFOI. In order to achieve controlled sedation and analgesia, the pharmacologic agents which are short acting, easily titratable, provide the required amount of sedation with little suppression of spontaneous ventilation should be used.

Dexmedetomidine is a centrally acting, selective alpha-2 agonist which was approved in 1999 by the Food and Drug Administration (FDA) as a short term sedative and analgesic (<24 hours) for critically ill or injured people on mechanical ventilation in the intensive care unit (ICU) [2,3], for intraoperative sedation during surgery under regional anesthesia [4], for awake craniotomies [5], and for sedation of pediatric patients in different settings [6]. More recently, there have been several case reports of dexmedetomidine being used for AFOI [7-10].

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Opioids like as fentanyl and remifentanil are helpful for attenuating hemodynamic response and discomfort during fibre optic intubation but incidence of hypoxia is very high due to their respiratory depressant action [11,12]. Fentanyl in high dose may cause apnea and loss of tone of upper airway producing difficulty during the negotiation of the bronchoscope beyond epiglottis [13,14].

In the present study, we compared dexmedetomidine alone and dexmedetomidine with fentanyl for conscious sedation during AFOI in adult patients scheduled for oro maxillo-facial surgeries. The aims of our study were to compare between these two groups: Intubation condition by cough score, tolerance to intubation bypost-intubation score, hemodynamic parameters and incidence of oxygen desaturation (SpO_2).

Materials & Methods

After obtaining institutional ethical committee approval and written informed consent from study subjects, this double blinded randomized prospective study was conducted on 60 patients from march 2017 to august 2017 at narayana medical college, Nellore with each group having 30 patients of either sex, aged 20-60 years, belonging to American Society of Anesthesiologists physical status (ASA-PS) I and II, and posted for elective maxillofacial surgeries. Exclusion criteria for study was patients with bradycardia (baseline HR <60 beats/min), any type of atrioventricular block, heart failure, having significant neurological, hepatic, renal and pulmonary disease, emergency surgeries, any contraindication for nasal intubation like thrombocytopenia or coagulopathies.Patients were allocated by computer generated random numbers and were divided into two groups. Group DF – dexmedetomidine+fentanyl group (n = 30) and Group D-dexmedetomidine group (n = 30). Dose of study drug was calculated according to patient's body weight, diluted with normal saline to make equal volume of 50 ml and enveloped according to patient's inclusion number. The anesthesiologist preparing the study drug and the observer anesthesiologists were blinded to each other. Bronchoscopy was performed by a single anesthesiologist in all patients.

Patients were pre-medicated with tab alprazolam 0.5 mg, tab ranitidine 150 mg night before surgery. In the operating room, intravenous line (i.v.) was secured with wide bore cannula (18G) and multichannel monitor was applied to record baseline Heart rate (HR), Mean arterial pressure (MAP), SpO_2 and electrocardiogram. Injection glycopyrrolate 0.2 mg i.v. was given. Patency of both nostrils was tested and the nostril with better patency was chosen for awake nasal fiberoptic intubation. Topicalization of both the upper and lower airway was accomplished by nebulization with 2% lidocaine 4 ml (80 mg) for 15 min. Xylometazoline nasal drops and lidocaine jelly were applied to both the nostrils. Tongue and hypopharynx were sprayed with two puffs of 10% lidocaine (20 mg). After that dexmedetomidine (1 mcg/kg over 10 min) and fentanyl (2mcg/kg) in DF group, dexmedetomidine (1 mcg/kg over 10 min) in D group was infused according to the subject's inclusion number. After lubrication bronchoscope was loaded with appropriate size cuffed polyvinyl chloride endotracheal tube. At the end of the study drug infusion, sedation was evaluated by Ramsay sedation scale (RSS) [15]. Bronchoscopy was performed through nasal approach.

After proper placement of tube in trachea general anesthesia was induced and surgery was allowed to proceed. Intubation condition was evaluated by cough score during bronchoscopy as Score 1 = no cough, 2 = slight cough (no more than two cough in sequence), 3 = moderate cough (3-5 cough in sequence), 4 = severe cough (>5 cough in sequence) [16]. Tolerance to intubation was evaluated by post-intubation score after placement of tube in the trachea as: 1 = Co-operative, 2 = minimal resistance, 3 = severe resistance [17]. Level of sedation was evaluated by Ramsay sedation score (RSS) just after completion of infusion of study drug as: 1 = Anxious, agitated or restless, 2 = cooperative, oriented and tranquil, 3 = sedated but responds to command, 4 = asleep, brisk glabellar reflex responds to loud noise, 5 = asleep, sluggish glabellar reflex or responds to loud noise, 6 = asleep with no response to a painful stimulus. MAP and HR were noted as a baseline and immediately after intubation. SpO_2 was monitored throughout the procedure and lowest one was noted. Hypotension (reduction of MAP >20% from baseline) was treated with i.v. fluid and/or phenylephrine 50 mcg i.v. bolus, repeat dose after 5 min. Bradycardia (HR <60 beats/min) was treated with atropine 0.6 mg i.v. Oxygen desaturation (SpO_2 < 95% for >10 s) was treated with oxygen supplementation either through a nasal cannula or oxygen port of bronchoscope.

Statistical Analysis

Numerical data were expressed as mean with a standard deviation and categorical data were put

into tables. Statistical analysis were carried out using the statistical package for the social sciences 16.0 statistical software packages.

Numerical data were compared between two groups using independent *t*-test. Categorical data were compared between two groups using Chi-square test and P value < 0.05 was considered statistically significant.

Results

Demographic characteristics like age, weight and ASA-PS (I/II) were comparable between two groups as shown in (Table 1, Figure 1 & 2).

Cough score <2 was considered as favourable intubation condition, which was achieved in 27 out of 30 patients in Group DF, but only in 5 out of 30 patients in Group D. The difference was statistically significant ($P < 0.0001$) as shown in(Table 2 & Figure 3).

Better tolerance score (Score 1) was found in 21 patients of Group DF and only 4 patients in Group D. This difference was also statistically significant ($P < 0.0001$) as shown in (Table 2 & Figure 4).

At the end of study drug infusion, higher RSS was achieved in Group DF (3.7±0.79) than in Group D (1.7 ± 0.65) ($P < 0.0001$) as shown in (Table 2 & Figure 5).

We observed that 8 patients of Group DF and 28 patients in Group D were able to maintain SpO_2 (eH 95%) ($P < 0.0001$) during the procedure. 2 patients in Group D and 8 patients in Group DF suffered from significant desaturation (SpO_2 dH 94%), which was managed by administration of oxygen through the port of the bronchoscope as shown in (Table 2 & Figure 6).

There was a rise of MAP compared with baseline values in both groups. The increase of MAP was minimal in Group DF as well as Group D as shown in (Table 3 & Figure 7). There was no episode of hypotension in both groups.

There was a significant increase in HR in the post-intubation period (77.30±5.98 beats/min) in comparison with the baseline value (65.50±7.25 beats/min) in Group D. The post-intubation HR (73.10±5.62 beats/min) increased in comparison with baseline value (64.39±4.31 beats/min) in Group DF as shown in (Table 3 & Figure 8). However, no patient developed bradycardia (HR <60 beats/min) requiring atropine.

Table 1:

	Group DF Mean±SD	Group D Mean±SD	P value
Age (in Years)	42.40±10.07	40.63±10.10	**0.500**
Weight (Kgs)	67.33±9.14	66.10±8.48	0.590
ASA-I_II	1.17±0.37	1.13±0.35	0.72

Table 2:

	Group DF Mean±SD	Group D Mean±SD	P Value
Cough Score	1.1±0.31	2.2±0.89	<0.0001
Tolerance Score	1.3±0.45	2.27±0.69	<0.0001
Ramsaysedation Score	3.7±0.79	1.7±0.65	<0.0001
Oxygen Saturation	92.2±3.89	98.10±1.78	<0.0001

Fig. 1:

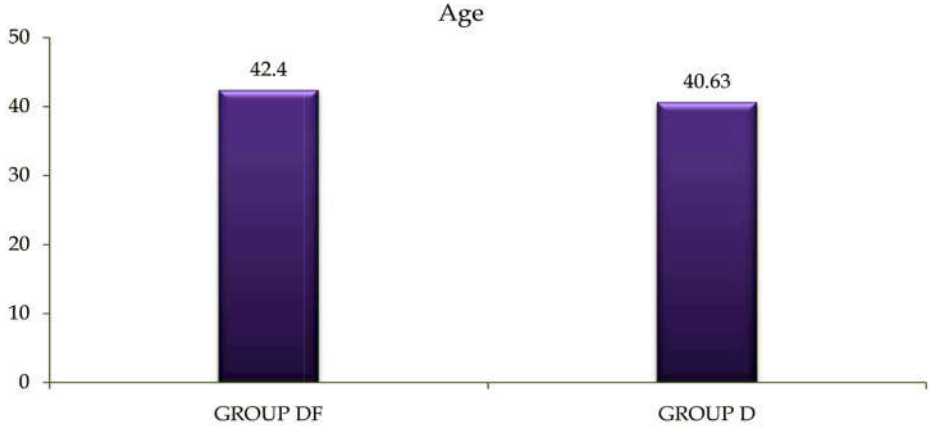


Table 3:

	Group DF Mean ± SD	Group D Mean ± SD	P Value
Baseline MAP	72.43±4.53	74.32±4.36	0.112
Post Intubation MAP	73.93±4.91	75.0±4.37	0.387
Baseline HR	64.39±4.31	65.50±7.25	0.294
Post Intubation HR	73.10±5.62	77.30±5.98	<0.0001

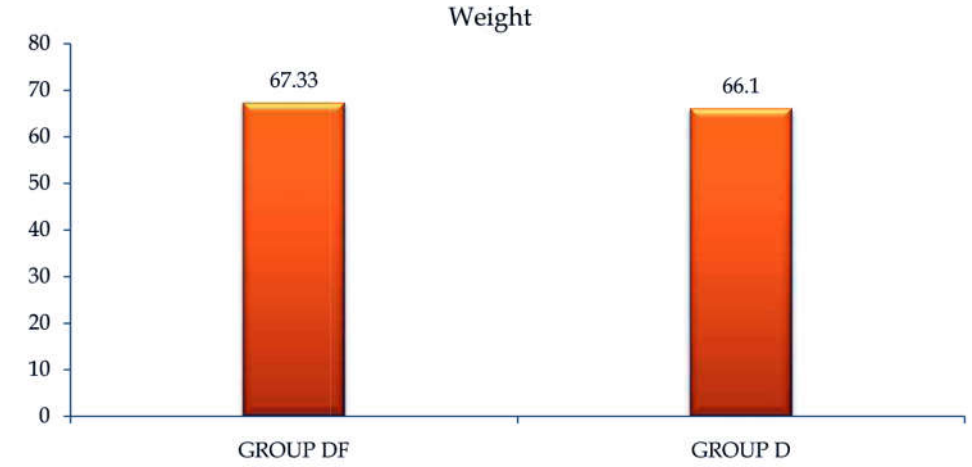
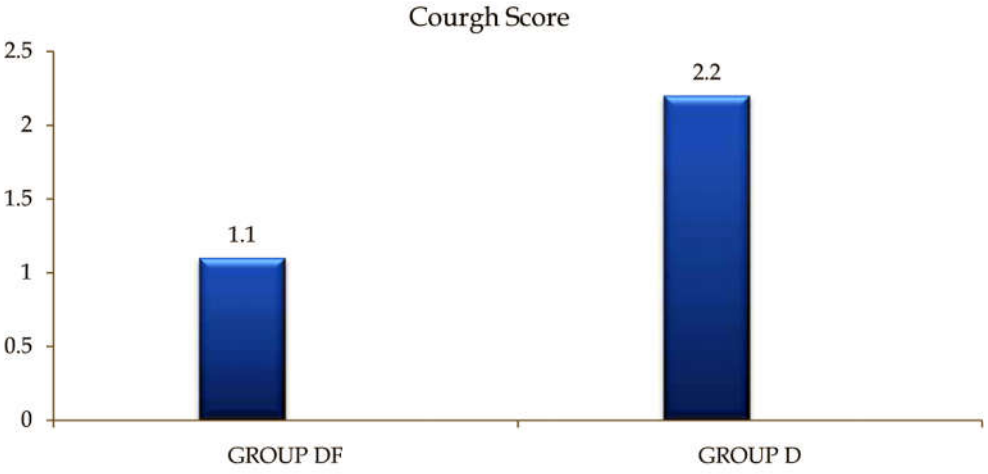


Fig. 2:



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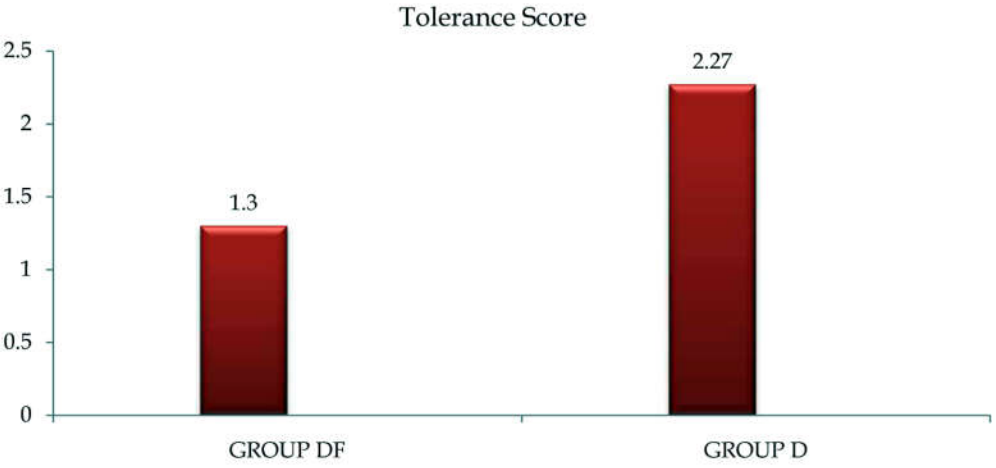

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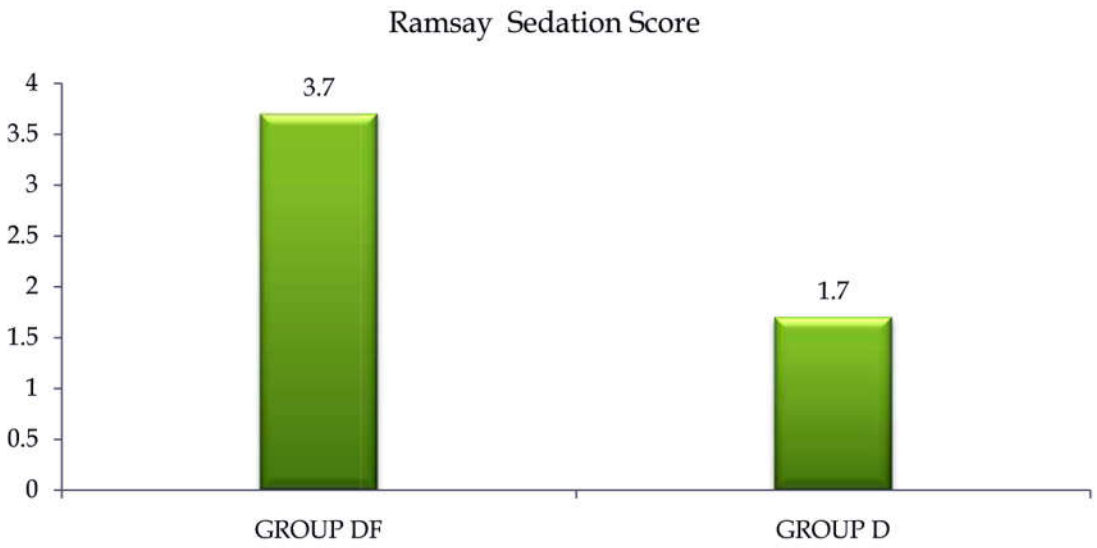

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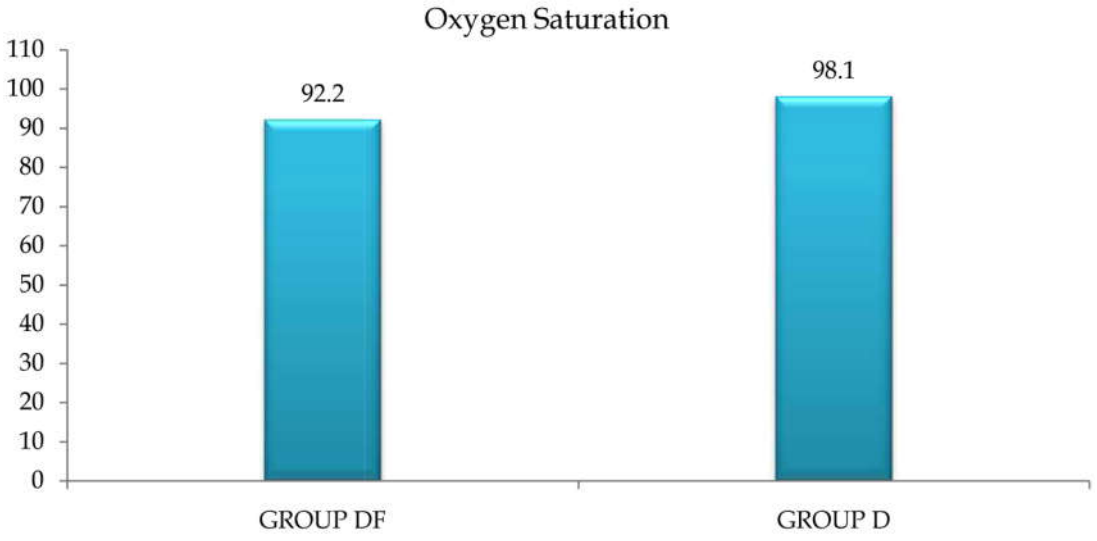

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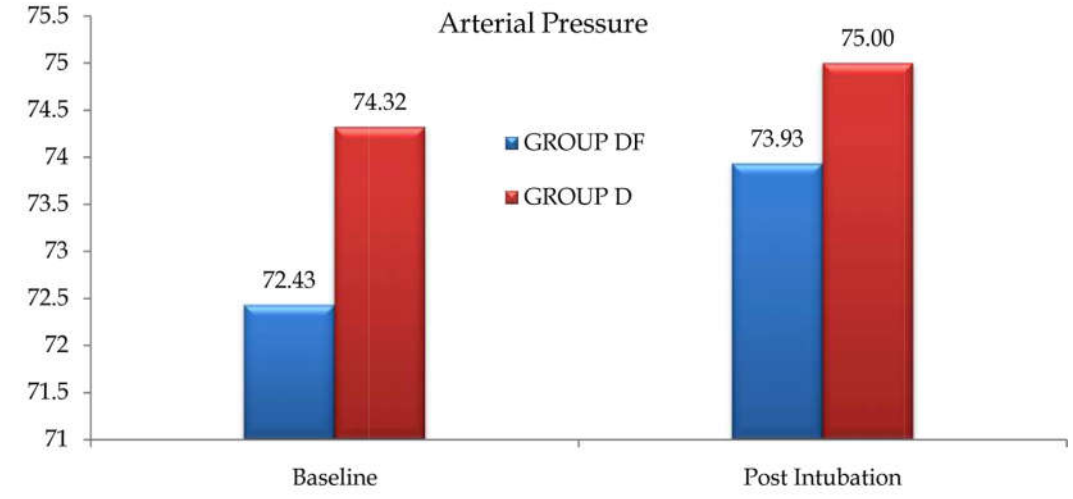

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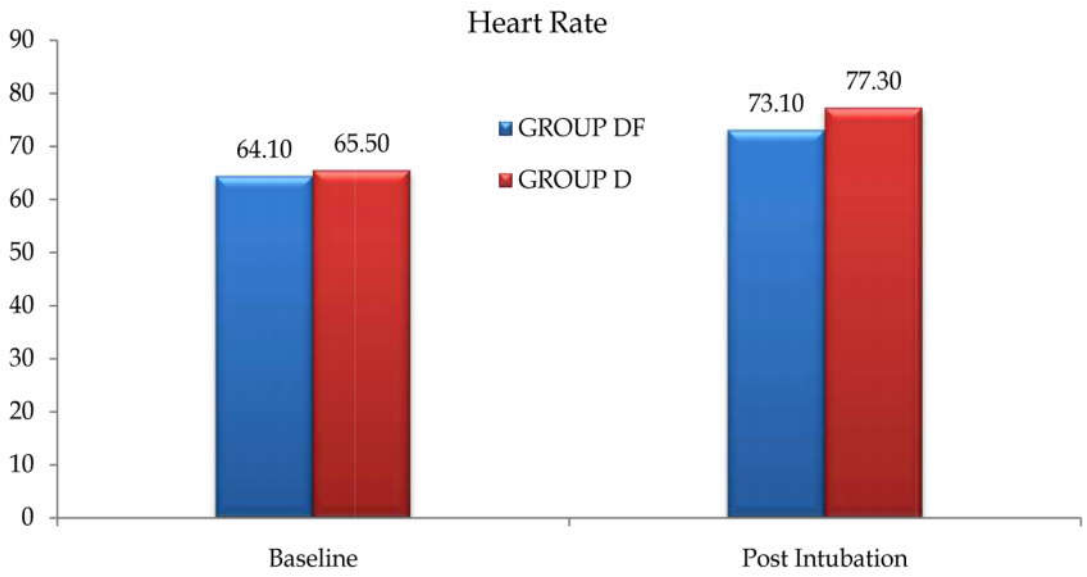

Fig. 8:

Discussion

In difficult airway scenarios, The ASA difficult airway algorithm emphasizes on awake intubation or tracheostomy as primary or alternate option [18]. Now-a-days, AFOI is the preferred method for securing a difficult airway and which requires conscious sedation during AFOI.

The aim of ideal sedation during AFOI is to achieve comfortable, cooperative patient and smooth patient tolerance of the technique through blunting of airway reflexes and attenuating the hemodynamic sympathetic response to intubation, while simultaneously achieving spontaneous breathing through a safe patent airway [19].

Dexmedetomidine is a highly selective, centrally acting α-2 agonist. It acts on presynaptic α-2 receptors to provide negative feedback causing less neurotransmitter (norepinephrine, epinephrine) available at post-synaptic α-1receptors.

Dexmedetomidine induces sedation involving activation of endogenous sleep promoting pathway through the post-synaptic α-2 receptors in the locus ceruleus, which modulates wakefulness. It produces hypnosis, amnesia, analgesia, anxiolysis, sympatholysis and antisialogogue effects all of which are desirable during AFOI [20]. The major advantages of dexmedetomidine infusion during AFOI are a unique form of sedation where patients remain sleepy, but are easily aroused, cooperative with minimum respiratory impairment. The feasibility of dexmedetomidine has been recently studied either as a sole sedative agent or as an adjuvant during AFOI [21,22].

We compared dexmedetomidine 1mcg/kg along with fentanyl 2 mcg/kg (Group DF) with dexmedetomidine 1 mcg/kg (Group D) and found that cough score was < 2 was considered as favorable intubation condition, which was achieved in 27 out of 30 patients in Group DF, but only in 5 out of 30 patients in Group D.

The difference was statistically significant ($P < 0.0001$) and Better tolerance score (Score 1) was found in 21 patients of Group DF and only 4 patients in Group D. This difference was also statistically significant ($P < 0.0001$).

Chu et al [23] observed better tolerance to intubation without respiratory depression and upper airway obstruction in dexmedetomidine group (1 mcg/kg) compared with fentanyl group (1 mcg/kg).

In our study, dexmedetomidine & fentanyl produced better intubating conditions than dexmedetomidine alone. Dexmedetomidine has also been proved as an effective agent for AFOI in certain difficult airway scenarios [24].

Bergese et al [25] noted that dexmedetomidine at 1 mcg/kg bolus was safe and beneficial for patients undergoing AFOI even without airway nerve block or topical anesthesia.

Bergese et al [25] found that dexmedetomidine in combination with low dose midazolam is more effective than midazolam alone for sedation in AFOI. However, dexmedetomidine dose in excess

of 1 mcg/kg/h with midazolam produced airway obstruction, which was managed by simple chin lift.

In our study higher RSS was achieved in Group DF (3.7±0.79)than in Group D (1.7±0.65) which provided with better cooperative condition during intubation (P < 0.0001). We observed that 8 patients of Group DF and 28 patients in Group D were able to maintain SpO 2 (≥95%) (P < 0.0001) during the procedure. 2 patients in Group D and 8 patients in Group DF suffered from significant desaturation (SpO2 ≤94%), which was managed by administration of oxygen through the port of the bronchoscope.

Ryu et al [26] compared remifentanil with dexmedetomidine for conscious sedation during bronchoscopy. They found that there were no significant difference of sedation level, MAP, HR and patient satisfaction score (P > 0.05) but cough score and incidence of desaturation was significantly lower (P < 0.01) in dexmedetomidine group than remifentanilgroup.

In our study, the baseline MAP, HR and were comparable between two groups. There was a rise of MAP compared with baseline values in both groups. The increase of MAP was minimal in Group DF as well as Group D. There was no episode of hypotension in both groups as well noticed that high bolus dose of dexmedetomidine does not cause hypertension. There was a significant increase in HR in the post-intubation period (77.30±5.98 beats/min) in comparison with the baseline value (65.50±7.25 beats/min) in Group D. The post-intubation HR (73.10±5.62 beats/min) increased in comparison with baseline value (64.39±4.31 beats/min) in Group DF .

Dexmedetomidine infusion may cause bradycardia, atrial fibrillation, hypotension or hypertension particularly in higher dose [27]. In our study there was no such untoward complications because we used dosage of 1 ìg/kg.

Bergese et al [25] compared dexmedetomidine plus midazolam versus midazolam alone, and he noticed no difference in both groups regarding systolic blood pressure. This may be because of using loading dose of 1μg/kg infused over 15 min (longer duration then our study) followed by a small infusion dose of 0.2 μg/kg/h and titrated to 0.7μg/kg/h.

Prommer [28] who compared dexmedetomidine with midazolam for sedation of 375 ICU mechanically ventilated patients and revealed that dexmedetomidine was associated with a greater incidence of bradycardia.

Gupta et al [29] compared dexmedetomidine versus propofol premedication for fiberoptic intubation in patients with temporomandibular joint ankylosis and found that the HR decreased significantly in the dexmedetomidine group at the end of drug infusion.

Conclusion

Dexmedetomidine with fentanyl provided better patient tolerance, less cough score,good sedation, and reduced hemodynamic responses&provided favourable intubating conditions but desaturation was more when compared with dexmeditomidine alone which was manageable by providing oxygen supplementation.

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Original Research Article

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A Comparative Study between Dexmedetomidine 1 µg/kg and and 25mg/kg of 50% Magnesium Sulphate as Adjuvants with 0.5% Lidocaine for Intravenous Regional Anaesthesia

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Abstract

Introduction: Intravenous regional anaesthesia (IVRA) also called as Bier's block is a commonly used anaesthetic technique for surgical procedures on the upper extremities. Many adjuvants have been used to improve the quality of intravenous regional anaesthesia (IVRA). *Aims and objectives*: The aim of this study was to compare the use of dexmedetomidine and magnesium sulphate as adjuvants lidocaine for IVRA as regards to onset and duration of sensory and motor blocks, hemodynamic variables. *Materials and Methods:* This prospective, randomized, double-blinded trial was conducted in 60 ASA I and II patients scheduled for upper hand and forearm surgeries who were randomly divided into two groups, comprising 30 patients each. Group D received dexmedetomidine 1mic/kg and 0.5% lidocaine to a total volume of 40 ml, whereas group M received 25mg/kg of 50% magnesium sulphate and 0.5% lidocaine to a total volume of 40 ml. Onset and duration of sensory and motor block, hemodynamic variables were recorded and compared between the two groups. *Results:* There was statistically significant difference between both the groups as group D achieved rapid onset and prolonged duration of sensory and motor block compared to group M ($p<0.0001$). Group D showed significant difference in heart rate and mean arterial pressure compared to group M after the tourniquet deflation. ($p<0.0001$). *Conclusion:* Our study shows that Dexmedetomidine provides rapid onset and prolonged duration of sensory and motor block in Intravenous regional anaesthesia compared to magnesium sulphate.

Keywords: Intravenous Regional Anaesthesia**;** Dexmedetomidine; Lidocaine; Magnesium Sulphate.

Introduction

Augustus Bier first described Intravenous regional anaesthesia (IRVA) [1] in1908 which was re-popularised by Holmes in 1963 [2]. The administration of intravenous local anaesthetic in an isolated limb by applying a tourniquet to the limb is a simple and effective technique, with a low incidence of failure and high degree of safety. IVRA or Bier's block is an ideal choice for short surgical procedures on extremities, performed on day care basis. The advantages of IVRA are rapid onset of analgesia and good muscular relaxation. The disadvantages are application of a pneumatic tourniquet throughout the procedure which may produce pain, limited duration of action. Over the years numerous adjuvants have been tried in an effort to overcome these problems, like opioids, ketamine, nonsteroidal anti-inflammatory drugs, alpha2 agonist, magnesium sulphate etc [3,4,5]. In our study we compared Dexmedetomidine and Magnesium sulphate as adjuvants to 0.5% lidocaine for IVRA.

Materials and Methods

This prospective, randomized, double-blinded study was conducted in Narayana Medical College, Nellore from April 2016 to January 2017 with

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institutional ethical committee approval. After obtaining written informed consent, 60 patients aged 20–60 years with American Society of Anesthesiologists (ASA) Physical Status class I–II who were scheduled for hand and forearm surgeries of duration less than 90 mins (i.e. facture both bones forearm, carpal tunnel release and tendon release) were divided into two groups Group D and Group M of 30 each. Exclusion criteria were history of allergy to study drugs, sickle cell anemia, Reynaud's disease, scleroderma, myasthenia gravis, cardiac disease, liver or renal insufficiency and history of convulsions were excluded from the study.

All patients were kept fasting for 6 hours before surgery. Lidocaine intradermal sensitivity testing was done for all patients. All patents were pre medicated with 1mg midazolam. In the Operation theatre, all the patients were monitored for non-invasive arterial blood pressure, electrocardiogram and oxygen saturation. A 22g i.v cannula was placed in a distal vein on the dorsum of the hand to be operated and a wide bore cannula in the opposite hand. A pneumatic double tourniquet was applied on the upper arm of the hand to be operated. Arm was exsanguinated for 2 mins with esmarch bandage. The esmarch bandage was removed after the proximal tourniquet was inflated to a pressure of 100 mmHg above the systolic blood pressure of the patient The anaesthetic solution was prepared by an observer unaware of the study and was given over a period of 90 seconds.

- Group D received 1mic/kg of Dexmedetomidine and 0.5% Lidocaine to a total volume of 40 ml.
- Group M received 25mg/kg of 50% Magnesium sulphate and 0.5% Lidocaine to a total volume of 40 ml.

When patient complains of discomfort at the proximal tourniquet site, the distal tourniquet was inflated to the same pressure and proximal one was deflated. Sensory block onset time was noted as time elapsed from injection of drug to sensory block achieved in all dermatomes. Onset of motor block was assessed by asking the patient to flex and extend his/her wrist and fingers. Complete motor block was noted when no voluntary movement was possible. Sensory block duration was noted as the time elapsed from release of tourniquet to sensory block recovery in all dermatomes. Motor block duration was noted as the time elapsed from release of tourniquet to complete motor block recovery. The tourniquet was not deflated before 30 min and was not kept inflated for more than 90 mins. The tourniquet was deflated by a cyclic deflation technique at the end of surgery. Heart rate, mean arterial pressure were recorded during the procedure.

Statistical Analysis

All recorded data were entered using MS Excel software and analysed using SPSS 20 version software for determining the statistical significance. Results were presented as mean+standard deviation. Proportions were compared using Chi-square test. Statistical difference between both the study groups was determined by student 't' test. $p < 0.005$ was taken as statistically significant, p value of <0.001 has high statistical significance and p value of <0.0001 was considered as extremely statistically significant.

Results

Sixty patients scheduled for elective hand and forearm surgeries expected to last for no more than 90 min participated in this study. Age, sex, height & weight were similar in both the groups. The difference was not statistically significant ($p > 0.05$). (Table 1). There was no statistically significant difference in Tourniquet time and duration of surgery. Onset of sensory block was achieved earliest in group D (mean of 2.49 min) compared to Group M (mean of 3.22mins) which was statistically highly significant ($p < 0.0001$). Onset of motor block in group D (5.5mins) was also achieved earlier than in Group M (7.89) ($p<0.0001$). Duration of sensory block was also achieved earlier in Group D (7.37hrs) compared to group M (5.868hrs) ($p<0.0001$). Duration of Motor block was also significantly prolonged in Group D (3.47) compared to Group M (2.84) ($p<0.0001$) (Table 2 and Figure 1).

Table 1: Demographic data

Demographic Variables among the groups	Group D	Group M	P Value
Age in years (mean ± SD)	34.1812.13	34.87±10.12	0.964
Height in CMS (mean ± SD)	168.88±66	164.32±2.10	0.53
Weight in KGS (mean ± SD)	60.45±3.26	63.32±7.22	0.43
Gender (M/F)	16/14	17/13	0.34

Table 2: Average differences in Tourniquet time, sensory and motor block onset, Sensory and motor block Duration

S. No	Variables	Group D		Group M		T value	P value
		Mean	SD	Mean	SD		
1.	Tourniquet time	63	15.36	60.2	12.61	0.5457	0.58
2.	Sensory block onset (mins)	2.49	0.33	3.22	0.15	7.799	0.0001**
3.	Motor block onset(mins)	5.5	0.61	7.89	0.89	8.578	0.0001**
4.	Sensory block Duration(hrs)	7.37	0.49	5.868	0.354	9.623	0.0001**
5.	Motor block Duration(hrs)	3.47	0.32	2.84	0.41	4.6914	0.0001**

Table 3: Average differences in Heart rate after tourniquet release

S. No	Time	Group D		Group M		T value	P value	S/NS
		Mean	SD	Mean	SD			
1.	0 mins	72.3	9.16	86.8	7.7	4.69	0.0001**	Highly significant
2.	30 mins	73.9	7.7	90.2	7.7	5.79	0.001**	Highly significant
3.	60 mins	75.7	7.3	91.8	8.13	5.706	0.001**	Highly significant
4.	90 mins	77.8	6.78	93	7.5	5.827	0.001**	Highly significant

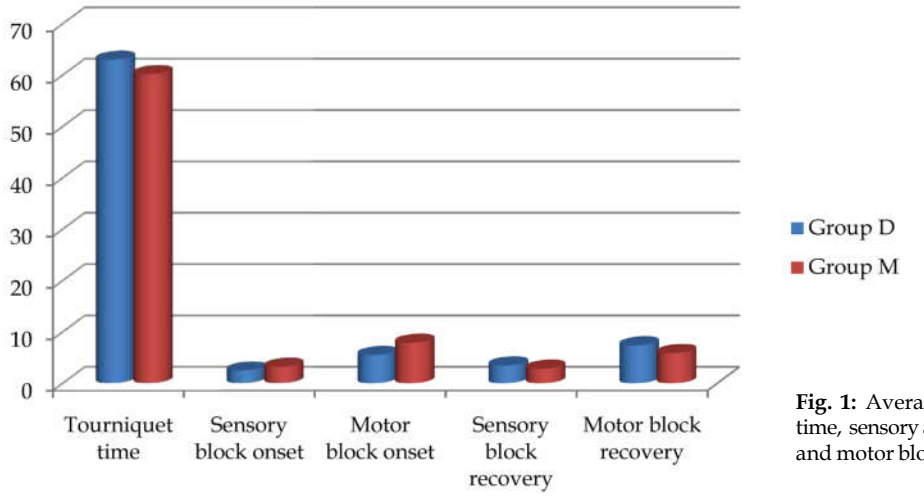

Fig. 1: Average differences in Tourniquet time, sensory and motor block onset, Sensory and motor block recovery

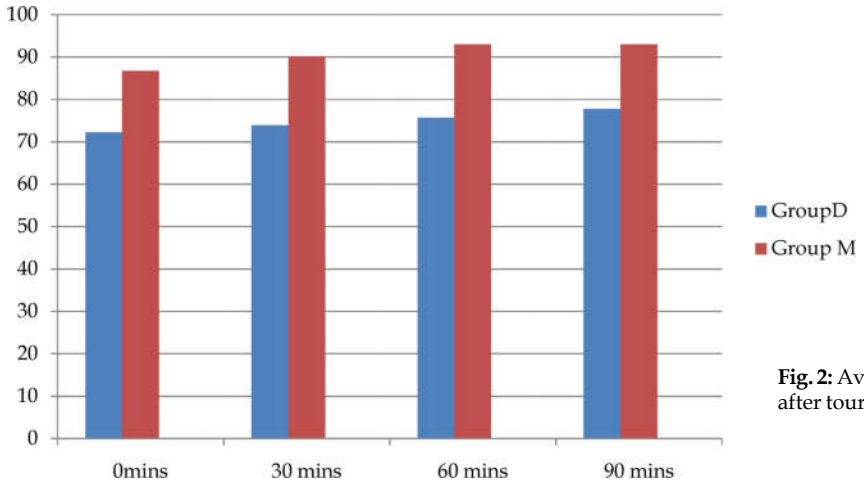

Fig. 2: Average differences in Heart rate after tourniquet release

Table 4: Average differences in MAP after tourniquet release

S. No	Time	Group D		Group M		t value	p value	S/NS
		Mean	SD	Mean	SD			
1.	0 mins	78.06	5.9	85.6	9.17	2.67	0.01**	Highly significant
2.	30 mins	75.2	6.3	86.06	8.55	3.96	0.0005**	Highly significant
3.	60 mins	74.3	5.5	90.4	9.03	5.897	0.0001**	Highly significant
4.	90 mins	74.4	5.74	93.4	8.166	7.371	0.0001**	Highly significant

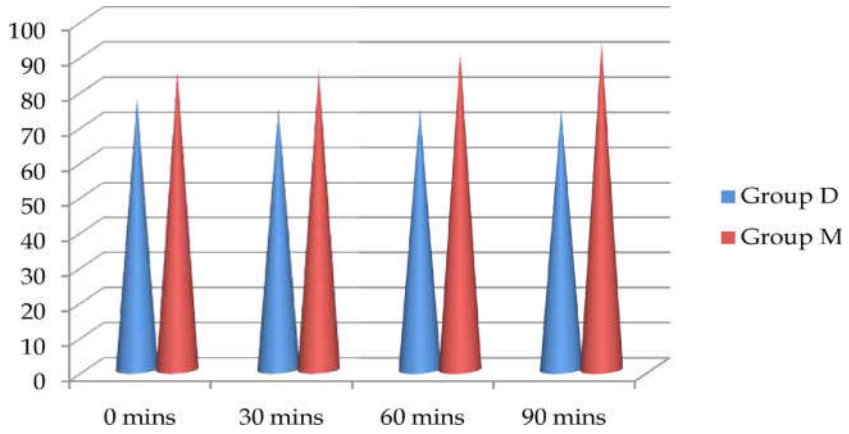

Fig. 3: Average differences in MAP after tourniquet release

Heart rate and Mean arterial pressure were comparable in both the groups after the tourniquet is inflated. The mean differences in heart rate and mean arterial blood pressure were found to be statistically highly significant after deflation of tourniquet which were measured up to 90mins (Table 3,4 and Figure 2,3). None of the patients had significant side effects such as Bradycardia, hypotension, intraoperative bleeding, nausea, or vomiting.

Discussion

Intravenous regional anaesthesia involves the intravenous administration of a local anaesthetic into the limb occluded by a tourniquet (i.e., Bier block) [6].

The local anaesthetic diffuses from the peripheral vascular bed to nonvascular tissue such as axons and nerve endings. Both the safety and the efficacy of this regional anaesthetic procedure depend on interruption of blood flow to the involved limb and gradual release of the tourniquet to prevent the sudden release of local anaesthetic into the circulation which may cause complications. Intravenous regional anaesthesia has been used primarily for surgical procedures on the upper limbs. Shorter procedures on the foot can also be successfully performed under intravenous regional anaesthesia [7].

Though various local anaesthetics have been used, Lidocaine has remained the main stay for intravenous regional anaesthesia in view of its short duration of action and less cardiovascular effects. Use of Bupivacaine has been discouraged due to sudden cardiovascular collapse which may occur after the release of tourniquet [8]. Preservative –free Lidocaine can be used up to a dose of 3 mg/kg diluted to 0.5% solution to a volume of 40ml for upper extremity procedures. For surgical procedures on the lower limbs, 50 to 100 mL of a 0.5% lidocaine solution has been used.

Over the years various adjuvants were used as additives to lidocaine for IVRA, including ketamine, diclofenac, opioids, neostigmine, alpha2 agonists and magnesium sulphate [9,10].

In our study, we compared the efficacy of two adjuvants to lidocaine in IVRA, dexmedetomidine and magnesium sulphate. alpha2 agonists provide sedation, analgesia, anxiolysis, sympatholysis, cardiovascular stabilising effects, reduced anaesthetic requirements and preservation of respiratory function.

These properties have been extensively studied and clinically employed in regional anaesthesia [11,12]. Dexmedetomidine has side effects such as Bradycardia, hypotension, and sedation. Dexmedetomidine is 8–10 times more selective toward alpha2 adrenergic receptors and is 3.5 times more lipophilic than clonidine. It thus prolongs the duration of both sensory and motor blockade induced by local anaesthetics, irrespective of the route of administration [13-15].

Very few authors have studied the role of Magnesium sulphate as an adjuvant for IVRA who showed it as a suitable adjuvant to lidocaine for IVRA. This could be attributed to the antagonistic properties of magnesium on the NMDA receptor and its inhibitory properties for calcium channels. NMDA receptor antagonists can inhibit the induction of central sensitization owing to peripheral nociceptive stimulation and can eliminate hypersensitivity [16].

Kol et al [17] conducted a prospective, randomized, double-blinded study on 75 patients scheduled for hand and forearm surgery found that addition of dexmedetomidine (0.5 µg/kg) to prilocaine improved the quality of anesthesia, decreased tourniquet pain, and decreased analgesic requirements as determined by hemodynamic variables and pain scores. Tramer and Glynn [14] used magnesium for the treatment of chronic limb pain in IVRA and showed that the addition of magnesium to lidocaine increases the quality of the block and decreases overall failure rate.

Our study showed that Dexmedetomidine provides rapid onset of sensory and motor block and also prolonged duration of sensory and motor block. Tourniquet pain was not experienced in both the groups. Hemodynamic changes were significant in Dexmedetomidine group after deflation of tourniquet which did not require any intervention.

Conclusion

We conclude that Dexmedetomidine is superior to Magnesium sulphate in providing rapid onset and prolonged duration of sensory and motor block.

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