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Effect of Alkalinization of Plain Lignocaine on Brachial Plexus Block

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Abstract

Background: The sensation of pain is a mechanism to protect an organism from injury. However pain is also an unpleasant experience. The conquest of pain has been considered as a path-breaking achievement in the history of medicine. Lignocaine has been considered as one of the time-tested drug used in regional anesthesia, which helped in the alleviation of pain. The duration and quality of sensory and motor blockade with lignocaine are variable. Several innovations are being tried to overcome this drawback. Therefore, there is a need to evaluate the effect of alkalinizing lignocaine in terms of, time for onset of action, degree and duration of blockade. *Methods:* This double blind, randomized controlled trial was carried out among 60 patients, aged between 18 and 60 years, of ASA Grade I and II, who underwent surgery of the upper limb over a period of six months. The participants were randomly allocated into control group who received 25 ml of 1% plain lignocaine and study group who received 25 ml of 1% alkalinized lignocaine. Onset time of analgesia and paralysis (complete motor block) were recorded. Duration and quality of sensory and motor blockade were also recorded. *Results:* The onset of sensory and motor blockade was earlier in study group than the control group ($p = 0.001$). Similarly the duration of sensory and motor block was significantly increased in the study group when compared to the control group ($p = 0.001$). The number of participants who had complete analgesia and complete paralysis was significantly higher in study group in comparison to the control group. *Conclusion:* In this modern era of anesthesia which demands higher degree of comfort, stress-free anesthetic and surgical techniques, alkalinized lignocaine solution goes a long way in advancement of anesthetic care.

Keywords: Alkalinized lignocaine; Brachial plexus; Regional anesthesia.

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Introduction

Pain is considered as a response to an inflicted stimulus. It is an alert system designed to make the body aware of a dangerous situation. The conquest of pain has been considered as a path breaking achievement in the history of medicine. Truly the central axis of anesthesia is predicated on interruption of pain. In olden times, fruit drugs like alcohol, opium, hashish and mandragora were used to reduce the pain. Trephination was practised by Incas and their tradition holds that the 'Shaman' who performed surgical procedures used to chew cocoa leaves and spat in to the wound, thereby producing the local anesthesia effect.[1]

Regional anesthesia traces its origin to Dr. Carl Koller, who in 1884, employed a solution of cocaine for topical corneal anesthesia in patients undergoing

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eye surgery. This marked the start of a new era in medicine, namely the use of regional anesthetics for prevention of pain associated with surgery. In the following year (1885), the famous surgeon Halstead demonstrated that the injection of cocaine solution around nerve tracts would completely wipe away pain and other sensation from the periphery of the region. In 1904, Einhorn synthesized procaine, an ester formed by the combination of para-amino benzoicacid and diethyl amine ethanol.

Most of the local anesthetics developed between 1900 and 1940 were basically amino ester compounds. They lost their importance due to shorter duration of action, associated allergic reaction and systemic toxicity. The next major advance was in 1930s when Erdtman, while working in Stockholm on the structure of the alkaloid gramine, tasted one of the substances that had been produced as a precursor of gramine. The significance of the numbness was appreciated immediately and the search for a clinically useful derivative was started by Erdtman. This was contributed by Nils Lofgren, who synthesized lignocaine in 1943.[2]

Perhaps almost as important as the synthesis of lignocaine was Lofgren's systematic study of a whole range of compounds (Lofgren 1948), so laying the foundation for all subsequent studies of local anesthetic drugs. From these studies have come derivatives of lignocaine such as mepivacaine, prilocaine, bupivacaine and etidocaine.

The main drawback of the long-acting drugs were, delayed onset of action, varying quality of blockade and unpredictable duration of action. To overcome these drawbacks various methods like addition of enzymes, oils, buffered carbonated solutions, alkalization, glycols and vasoconstricting agents and potentian of blockade by pain and muscular exercise were tried. Of these, only addition of carbonates, potassium and alkalinization of local anesthetics have stood the test of time. Therefore, we evaluated the effect of alkalinizing lignocaine with respect to onset time, degree and duration of blockade.

Objectives

The present study was carried out:

1. To evaluate the scope of alkalinizing plain lignocaine with sodium bicarbonate in supraclavicular brachial plexus block.
2. To compare the results with that of plain lignocaine of same concentration.

Materials and Methods

Study setting and participants

This double blind, randomized controlled trial was carried out in the Department of Anesthesia of a tertiary teaching institution for a period of six months. All the patients aged between 18 and 60 years of ASA Grade I and II, who underwent elective and emergency surgery of the upper limb, were selected for the study. Patients with progressive neurological disorders, severe kidney or liver dysfunction, history of adverse reactions to local anesthetic drugs and history of bleeding disorders were excluded. A total of 60 patients participated in the study.

Ethical approval and informed consent

Approval was obtained from Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Randomization and blinding

This study comprised of two groups –

Group I: The patients in Group I (control group) received 25 ml of 1% plain lignocaine prepared by adding 12.5 ml of distilled water to 12.5 ml of 2% plain lignocaine.

Group II: The patients in Group II (study group) received 25 ml of 1% alkalinized lignocaine (prepared by adding 3 ml of 7.5% sodium bicarbonate and 9.5 ml of distilled water to 12.5 ml of 2% plain lignocaine).

Each participant was allocated into one of the groups randomly, using computer generated random numbers. The study participants and the anesthetist performing the procedure were blinded to this allocation schedule. Each group consisted of 30 participants.

Procedure

Each patient was made to lie supine without a pillow, arms at the side, head turned slightly to the opposite side with the shoulders depressed posteriorly and downward by molding the shoulders over a roll placed between the scapulae. The supraclavicular area was aseptically prepared and draped. The anesthesiologist stood at the side of the patients to be blocked, facing the head of the patient.

An intradermal wheal was raised approximately 1 cm superior to the clavicle above the midclavicular point. The subclavian artery palpable in the supraclavicular fossa was used as landmark.[3,4] A filled 10 ml syringe with a 23 gauge, 32 mm needle was held in the right hand. The needle was inserted through the skin wheal and advanced slowly downward (caudal), rolled slightly inward (medially) and slightly backward (posteriorly), so that the shaft of the needle was almost parallel to patient's head. With the index finger and thumb of the left hand, the hub of the needle was firmly held and the movement of the needle was controlled all the time. As soon as paresthesia was elicited, the needle was fixed in position and 25 ml of respective drug was injected depending on whether the patient was allotted to Group I or Group II.

Data collection

Preliminary investigations were carried out to evaluate the general fitness of the participants. The participants were not given any premedication. The pH of plain lignocaine was 6.45 and the pH of the alkalinized lignocaine was 7.55 as tested in Biochemical Laboratory. The sensory block was recorded using pin prick in skin dermatomes C4–T2, once every 3 minutes for the first 30 minutes after injection and then once every 15 minutes till the patient regained normal sensations.

Onset time of analgesia was from time of injection of drug, to the time of loss of pain on pin prick. Onset time of paralysis (complete motor block), was from time of injection of drug to time of complete loss of movement.

Sensory block was considered complete if there was complete analgesia (Grade I), partial analgesia (Grade II) when there was dermatomal sparing and (Grade III) when there was no analgesia. The motor block was also assessed by the same observer at the same time intervals. The motor block was graded according to the movement of the upper limb by the patient.

Table 1: Grading of Motor Block Among the Study Participants

Grade	Type of movement	Interpretation
5	Normal movement of the upper limb	Total absence of block
4	Movement against resistance but less than normal power	
3	Movement present against resistance	Partial motor block
2	Movement along with gravity but not against resistance	
1	Slight flickering of movements	
0	No movement	Complete motor paralysis

Duration of sensory blockade was the time in minutes from the onset of analgesia to the recurrence of pain to pinprick. Duration of motor blockade was the time in minutes from the onset of paralysis (Grade 1) to the recurrence of motor movements. The quality of sensory and motor block was studied and graded as per whether the blocks were complete, incomplete or totally absent (Table 1).

The usage of adjuvant after block was graded according to whether the surgery was done under general anesthesia (Grade III) due to complete failure of block, whether opioids were used during intraoperative period (Grade II) or if adujvants of any kind were not used throughout the end of the surgery (Grade I). The participants were also watched for bradycardia, convulsions, drowsiness and other complications.

Data analysis

The patient data and characteristics, the onset time, duration, quality of blockade were categrorized and analyzed with students unpaired t-test, Gaussian test and chi-square test using SPSS ver.20 software. The association was considered statistically significant when the p value was <0.05.

Results

Majority of the participants in both the groups belonged to the 38–47 age group and weighed between 50 and 59 kilograms. Orthopedic surgeries were the most common surgeries performed in both the groups (70% in control group and 76.6% in the cases group) (Table 2). The detailed description of the types of surgeries performed showed that majority of the cases and controls underwent closed reduction (Figure 1).

The onset of sensory blockade was achieved in between 9 and 10 minutes in 63.3% of the controls, while the same was achieved in 3–4 minutes in the study cases. Moreover, the duration of sensory blockade was for 65–74 minutes in 50% of the controls while the same lasted for 85–94 minutes in 36.7% of the study cases (Table 3).

The onset of motor blockade was achieved in 8 and 9 minutes in 63.3% of the participants in the control group while the same was achieved in 2–3 minutes among 60% of the study group participants. Similarly, the duration of motor blockade lasted for 80–89 minutes in 46.7% of the participants in the control group, while in 40% of the participants in the study group, the duration of motor blockade lasted between 100 and 109 minutes (Table 3).

Complete analgesia was achieved in 83.3% of the cases in comparison to 30% of the controls. The association was statistically significant ($p < 0.001$) (Table 4). Majority of the participants in the study group achieved complete absence of movement (76.7%) while only 3.3% of the controls achieved complete absence of movement. The association was statistically significant ($p < 0.001$). Moreover, adjuvants were not used in 73.3% of the cases while it was not used only in 43.3% of the controls. The association was statistically significant ($p < 0.05$) (Table 5).

Table 2: Background Characteristics of the Study Participants

S. No.	Characteristics	Group	
		Control N = (30) (%)	Experiment N = (30) (%)
1	*Age (in years)*		
	18–27	5 (16.7)	6 (20.0)
	28–37	5 (16.7)	7 (23.4)
	38–47	8 (26.7)	9 (30.0)
	48–57	7 (23.2)	4 (13.3)
	≥58	5 (16.7)	4 (13.3)
2	*Weight (in kilograms)*		
	30–39	1 (3.3)	1 (3.3)
	40–49	10 (33.3)	6 (20.0)
	50–59	15 (50.0)	17 (56.7)
	≥60	4 (13.3)	6 (20.0)
3	*Surgical procedures*		
	Orthopedic procedures	21 (70)	23 (76.6)
	General surgical procedures	5 (16.7)	3 (10)
	Plastic surgery procedures	4 (13.3)	2 (6.7)
	Neurosurgical procedures	0	2 (6.7)

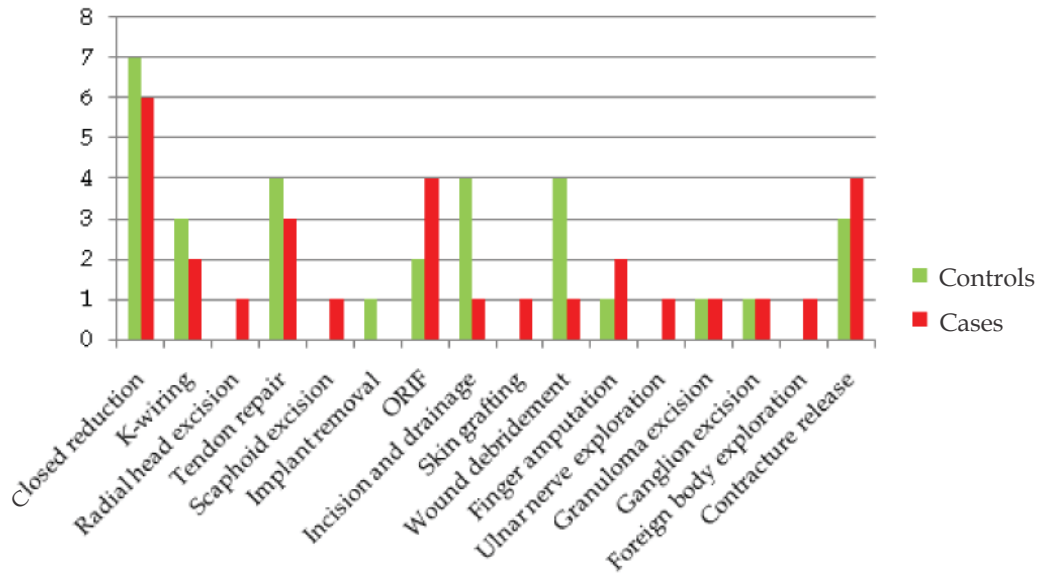

Fig. 1: Type of surgeries among the study participants

Table 3: Onset and Duration of Motor and Sensory Blockade Among the Study Participants

S. No	Characteristics	Group	
		Control N = 30 (%)	Experiment N = 30 (%)
1	Onset of sensory blockade in minutes		
	3–4	0 (0.0)	23 (76.7)
	5–6	1 (3.3)	7 (23.3)
	7–8	4 (13.3)	0
	9–10	19 (63.3)	0
	11–12	5 (16.8)	0
	13–14	0 (0.0)	0
	15–16	1 (3.3)	0
2	Onset time of motor blockade in minutes		
	2–3	0	18 (60)
	4–5	0	12 (40)
	6–7	5 (16.7)	0
	8–9	19 (63.3)	0
	10–11	5 (16.7)	0
	12–13	1 (3.3)	0
3	Duration of sensory blockade in minutes		
	65–74	15 (50.0)	0 (0.0)
	75–84	9 (30.0)	1 (3.3)
	85–94	6 (20.0)	11 (36.7)
	95–104	0	8 (26.7)
	105–114	0	6 (20.0)
	115–124	0	4 (13.3)
4	Duration of motor blockade in (min)		
	70–79	1 (3.3)	0
	80–89	14 (46.7)	0
	90–99	6 (20)	0
	100–109	9 (30)	12 (40)
	110–119	0	11 (36.7)
	120–129	0	7 (23.3)

Table 4: Comparison of Complete Analgesia Between the Groups

S. No	Characteristics	Group		Z value	*p* value
		Experiment N (30)	Control N (30)		
1	Complete analgesia	25 (83.3)	9 (30.0)	5.456	0.001

Table 5: Comparison of Effect of Analgesia Between the Groups

S. No	Characteristics	Group		Chi Sq	*p* value
		Experiment N (30)	Control N (30)		
1	Quality of motor blockade				
	No movement	23 (76.7)	1 (3.3)	34.789	0.001
	Flickering movement	5 (16.7)	13 (43.3)		
	Movement along gravity	2 (6.6)	13 (43.3)		
	Movement against gravity	0	1 (3.3)		
	Movement against resistance	0	2 (6.7)		
2	Use of Adjuvants				
	No use	22 (73.3)	13 (43.3)	6.678	0.035
	Sedation	7 (23.3)	13 (43.3)		
	Converted to GA	1 (3.4)	4 (13.4)		

Discussion

Lignocaine is a weak base with a pKa of 7.61 at 36°C.[5] As such it exists at physiological pH in two forms: a charged, protonated molecule, and an uncharged base. Lignocaine is marketed at a pH between 5.0 and 7.0 since aqueous solubility is higher at this range of pH than at more physiological pH. The lignocaine molecule is most effective at blocking the sodium channel when it is protonated but it primarily gains access to the channel by diffusion through lipid membranes.[6] The preponderance of charged lignocaine in the aqueous solution results in slow transfer of the lignocaine across lipid membranes and slows the onset of the block. Methods of improving clinical efficacy of lignocaine in nerve blockade have been studied for several decades and it was proposed that permeability of local anesthesia solutions was primarily dependent on the free base, while neural blockade was dependent on the cationic form.[7] It is known that as the pH of local anesthetic solution increases, conversion to the free base accelerates, thereby increasing neural permeability. This results in both an increased rate of penetration and a greater total mass of local anesthestic agent in the nerve fiber.[8,9]

The present study was conducted on 60 patients between 18–60 age group. The age distribution was similar in both control and study groups. This was identical to the study by Gormley W.P.[10] The mean weight of the patients in the control group was 50.63 kg and in the study group it was 53.1 kg in our study, similar to the study done by Capogna *et al.* The mean time of onset of sensory blockade was faster in the experimental group (4.13 min) compared to 9.73 minutes in control group. Gormley W.P had similar findings. Similarly Gormley, Quinlan, Bedder[10–12] showed a faster onset of sensory and motor blockade.

There have been several reasons postulated for the alkalinization controversy. Firstly the choice of local anesthetic will influence the degree to which the pH can be altered without the occurrence of precipitation. Precipitation and pH adjustment study by Peter Freund *et al.*[9] suggests that lignocaine is particularly suited for alkalinization. This is because it can be alkalinized to a pH close to the pKa value without the occurrence of precipitation. In our study the change of pH was from 6.45 in the control group to 7.55 in the study group. This change in pH after addition of sodium bicarbonate was large enough to achieve the benefits of alkalinization. Similar results were seen in studies done by Gormley, Quinlan[10,11] and Difagio, Capogna, Chow[13-15] Mary Chow had a change of pH from 6.24 to 7.15.

In our study the depth of sensory and motor blockade was significantly better in the pH adjusted group. Complete analgesia was seen in 83.3% of the patients in alkalinized group and only in 30% of the patients in control group. Similarly complete motor blockade was seen in nearly 93% of the patients in study group and in 44% of the patients in control group. Earlier studies by Nelson L. Cunningham *et al.*[16] also had similar findings. In the study by Gormley W.P. *et al.* adjuvant were used in 81.8% of patients in control group and for 50% of patients in alkalinized group.[10] The decreased requirement of adjuvant suggests greater quality of anesthesia.

The duration of sensory and motor block was significantly increased in our study group when compared with the control group (p = 0.001). Our findings corresponded with the findings of Higlier[8]. Our findings also corresponded with the findings of Gormley, and Capogna[10,14] who that showed that the quality was better in pH adjusted group and there was a significant reduction in the onset time to useful anesthesia. There was no effect on the duration of anesthesia in their studies. The difference in the duration of anesthesia could probably be due to the differences in the concentration of lignocaine.

Anatomic variations, individual patients' responses and the discrepancies in the number of patients studied should also be taken in account to explain such differences among studies. Another possible explanation for the differences among the various studies is that the lignocaine solution used may not have had a similar pH. The pH of lignocaine used in our study was 6.55. Therefore, our results suggest that alkalinization of plain lignocaine has a definitive role in improving the quality of blockade, shortening the onset time and in prolonging the duration of anesthesia.

Conclusion

The present study has demonstrated that the onset time of sensory and motor blockade is lesser with alkalinized lignocaine when compared to plain lignocaine in supraclavicular brachial plexus block. Moreover, the quality of sensory and motor blockade is better with alkalinized lignocaine. The duration of motor and blockade significantly prolonged when alkalinized lignocaine was used in supraclavicular brachial plexus block. In this modern era of anesthesia which demands greater need of comfort, stress free anesthetic and surgical

techniques, introduction of alkalinized lignocaine solution might go a long way in advancement of anesthetic care.

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Original Research Article

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Intravenous Magnesium Sulfate can be Infused in Spinal Anesthesia for Postoperative Analgesia

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Abstract

Introduction: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Spinal anesthesia using local anesthetics like hyperbaric bupivacaine is one of the most popular techniques for both elective and emergency surgical procedures. One disadvantage with spinal anesthesia is relatively short duration of action. Postoperative pain relief provides comfort to the anxious patients and improve their morale and mobility there by contributing to a rapid and complete recovery. *Aims:* Study done on IV. Magnesium Sulfate, in patients given spinal anesthesia, for postoperative analgesia. *Materials and Methods:* This prospective study was conducted on 50 adult patients of ASA physical status 1 & 2 in the 18–60 age group, of either sex, posted for elective lower limb orthopedic surgeries under spinal anesthesia over a period of 12 months. Patients were randomly divided on an alternative basis into groups of 25 each. Group-M-Patients receiving IV $MgSO_4$/infusion, Group -S-Patients receiving isotonic saline. *Results:* The mean height and mean weight in either group were identical. The type of surgeries performed were almost identical. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra-or-postoperative period. Perioperative mean arterial pressure. Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$). The cumulative requirement in 24 hrs of both tramadol and diclofenac was statistically significantly less for group M vs. S ($p = <0.05$). Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24h after surgery. *Conclusion:* IV Magnesium sulfate infusion in spinal anesthesia decreases intra-operative hemodynamic variabilities, prolongs duration of analgesia and improves the quality of analgesia in the early postoperative period with better hemodynamic stability. It also decreases the postoperative analgesic requirements, thus it can be used as a beneficial additive for prolonging spinal anesthesia.

Keywords: Magnesium Sulfate, Spinal Anesthesia, Postoperative analgesia

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Introduction

The International Association for the study of pain had described pain as unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The aim of an anesthesiologist is to render the patient pain free, during a surgical

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procedure. However the patient problem does not end with the surgical procedure, as pain following surgery is a universal problem. So pain during postoperative period is a cause of concern for both the patient and the physician.[1]

Spinal anesthesia defined as regional anesthesia obtained by blocking nerves in the subarachnoid space was introduced in clinical practice. Spinal anesthesia using local anesthetics like hyperbaric bupivacaine is one of the most popular techniques for both elective and emergency surgical procedures. One disadvantage with spinal anesthesia using hyperbaric bupivacaine alone is relatively short duration of action, which means that early analgesic intervention is needed in the postoperative period. Postoperative pain increases the morbidity and mortality and prolongs the stay in hospital. Effective postoperative analgesia results in decreased respiratory and CVS complications, early returns of GIT motility, early ambulation and discharge from hospital.[2,3]

Postoperative pain relief provides comfort to the anxious patients and improve their morale and mobility thereby contributing to a rapid and complete recovery. However, their use has been hampered by their potential to cause respiratory depression. Thus, other drugs have been tried that have the advantage of opioids, but not their drawbacks. A number of adjuvants have been used to improve postoperative analgesia, along with bupivacaine. These are epinephrine, clonidine, ketamine, neostigmine and midazolam. In this study, we have infused IV. Magnesium Sulfate, in patients given spinal anesthesia, for postoperative analgesia.

Materials and Methods

This prospective clinical study was conducted on 50 adult patients of ASA physical status 1 & 2 in the 18–60 age group, of either sex, posted for elective lower limb orthopedic surgeries under spinal anesthesia after taking informed consent at Osmania General Hospital, Hyderabad over a period of 12 months. After approval from the hospital ethical committee, a comparative study was carried out on 40 adult patients.

Patients were randomly divided on an alternative basis into groups of 25 each.

Group "M" Receiving $MgSO_4$ (50 mg/kg over 15 min-bolus)

(15 mg/kg/ltr infusion)

Group "S" Receiving isotonic saline (10 ml/kg/hr)

Inclusion criteria

ASA grade 1 and 2 patients, Age group of 18–60, patients scheduled to undergo elective orthopedic lower abdominal, lower extremity, gynecological or urological surgeries under subarachnoid block.

Exclusion criteria

With gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis or neurological involvement/diseases, Head injury, Patients with cardiac, pulmonary, hepatic or renal disorders.

Pre-anesthetic check-up was carried out preoperatively with a detailed history, general physical examination and systemic examination, Airway assessment and spinal column examination were done.

The following laboratory examinations were done in selected cases, i.e., hemoglobin, urine analysis, blood sugar, blood urea, serum creatinine, coagulation profile, blood grouping and Rh typing, ECG-for patients over 40 years of age and Chest X-ray.

Procedure

Patient was shifted to the OT table; IV access was obtained on the forearm with 18 Gauge IV cannula and Lactated Ringer's solution 10 ml/kg was infused intravenously before the block. The monitors connected to the patient included non-invasive B.P., oxygen saturation using pulse oximeter. Baseline PR, BP and RR, SpO_2 was recorded.

Under strict aseptic precautions, lumbar puncture was performed in left lateral position or sitting position by midline approach by using disposable Quincke spinal needle (23G) at L3–L4 intervertebral space. Patients were monitored continuously using Non-invasive blood pressure, pulse oximeter and electrocardiogram. After spinal anesthesia, oxygen (6 L/min) by facemask was given. Fluid therapy was maintained with lactated Ringer's solution infused according to patients hemodynamic and volume status.

After induction of spinal Anesthesia, the magnesium group (Group M), received magnesium sulphate 50 mg/kg for 15 min bolus using a burette set and then 15 mg/kg/hr by continuous IV infusion until the end of surgery. For IV bolus-$MgSO_4$ (50 mg/kg) is mixed in 30 ml NS in burette set and infused over 15 minutes (1 ml/min). Magnesium Sulfate Infusion Calculates volumes required for adult dosage of 1.5g injected into

100 ml NS infusion bottle. Drip rate is 100 drops/minute, Usual diluents—D5w, NS.

Amount of drug	1g	2g	3g	4g
Infusion volume	50 ml	100 ml	100 ml	250 ml
Infusion rate	30 min	60 min	2 hr	3 hr

The rate or I.V. injection should generally not exceed 150 mg/minute (1.5 mL of a 10% concentration or its equivalent). Solutions for iv infusion should be diluted to 20% or less.

The following parameters were observed and recorded as HR, B.P and RR, SqO_2 monitored at 1, 3, 5, 10, 15, 20, 25, 30, 45, 60, 120, 180 minutes.

Assessment of Sensory Blockade

The onset of sensory block was tested by pinprick method using a hypodermic needle. The time of onset was taken from the time of injection of drug into subarachnoid space to loss of pinprick sensation. The highest level of sensory block and time was noted. The time for two-dermatomal segment regression of sensory level was noted. The duration of sensory blockade was taken as time from onset to time of return of pinprick sensation to S1 (heel) dermatomal area.

Assessment of Motor Blockade

This was assessed by Bromage scale. The time interval between injections of drug into subarachnoid space, to the patient's inability to lift the straight extended leg was taken as onset time (Br. 3). The duration of motor block was taken from time of injection to complete regression of motor block (ability to lift the extended leg) (Br 0).

Intensity of motor block (with sensory block to s 5)

I. Complete Block	Unable to move feet or knees
II. Almost Complete	Able to move feet only
III. Partial	Just able to flex move Knees
IV. None	Full flexion of knees or Feet and hip and extend Knee

Bromage scale for assession motor block and degree of paralysis

Modified Bromage Scale

* Grade 0 — Full flexion of knees and feet.

* Grade 1 — Just able to flex knees, full flexion of feet.

* Grade 2 — Unable to flex knees, but some flexion of feet possible

* Grade 3 — Unable to move legs or feet

Assessment of analgesia

Pain was assessed by visual analogue score (VAS)

The patient simply marks the line to indicate the pain intensity and the provider then measures the length of the line to mark a point scale. All the patients were instructed about the VAS and to point out the intensity of pain on the scale 0 – no pain, 10 – worst pain.

Linear Visual Analog Scale Score

VAS Score	Intensity of pain
0–2	No pain to slight pain
2–5	Mild pain
5–7	Moderate pain
7–9	Severe pain
10	Worst possible pain

Quality of intraoperative analgesia was assessed by VAS score. Analgesics were avoided until demanded by the patient and the time taken for the first pain medication was also noted (i.e., when Vas >6) VAS was also recorded 3, 6, 12 hours postoperatively.

Postoperatively, monitoring of vital signs was continued every 30 minutes until the time of regression of sensory block to L1 dermatome. The incidence of hypotension (arterial blood pressure < 20% of baseline), and was treated with Inj.Mephentermine 6 mg intravenous increments and bradycardia as pulse rate < 60/min was treated by atropine 0.6 mg intravenous stat. Side effect like sedation, nausea, vomiting urinary retention were monitored in the recovery room and then shifted to the ward.

Neurological examination was done to rule out any neurological deficits at discharge.

After surgery, both groups M and S received Inj. diclofenac sodium 75 mg/IM/BD and Inj.Tramadol 100 mg IV/BD depending on the requirement for analgesia.

Postoperative pain score, analgesic consumption, incidence of shivering, postoperative nausea and vomiting were evaluated immediately after surgery, and at 30 min, 1 hr, 2 hr, 4 hr, 6 hr, 12 hr, 24 hr, 36 hr and 48 hr after surgery.

Serum magnesium concentrations were checked before the induction of anesthesia, immediately after surgery and at 1 and 24 hr after surgery.

Statistical Analysis

The demographic data were analyzed using either Student's t-test or chi-square test. Quantitative data were analyzed by student t-test and qualitative data was analyzed by chi-square test. All values were expressed as mean +/- standard deviation. $p < 0.05$ was considered statistically significant.

Results

Patient characteristics and anesthetic time. Values shown are mean (range) for age, mean (SD), or patient numbers (n), Group M, Mg group; Group S, Saline group. No significant differences between the two groups (Table 1).

Table 1: Demographic Data in Present Study

Patient characteristics	Group M (n=25)	Group S (n=25)
Age	36	44
Sex (M/F)	12/13	17/8
Weight (kg)	52	47.8
ASA (I/II)	15/5	16/4
Anesthetic Time (min)	298	200.6

No significant difference was found between the two groups in terms of age, weight, height, gender, or anesthetic time.

Table 2: Characteristics of Spinal Block in Present Study

Characteristics of spinal block	Group M	Group S
Height of spinal block	T5 (T3-6)	T6 (T4-8)
Time of first pain (min)	334	227
Dose of bupivacaine (mg)	13.1	13.4

No technical failure related to spinal anesthesia occurred and all surgery proceeded without difficulty. The two groups were similar in terms of height of spinal block, mean time to first pain, and administered dose of bupivacaine (Table 2).

Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24h after surgery. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia. No significant difference was observed between the two groups during the perioperative period. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intraoperative period (Fig. 1)

Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$) (Table 3).

Table 3: Duration of Analgesia in Present Study

Parameter	Group M		Group S		Mean Difference	*p** value Significance
	Mean	SD	Mean	SD		
Time of first pain medication	334	15.6	227	29.4	100.12	<0.001 HS

*Student's unpaired test

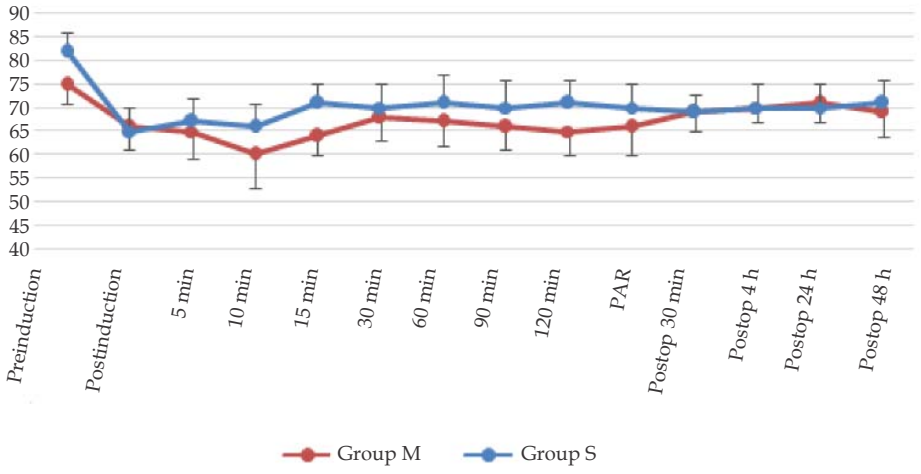

Fig. 1: Mean arterial pressure in both groups

VAS at the end of 3 hours was 0.7 in Group M whereas in Group S it was 2.4 at the end of 6 hours VAS in Group M was 1.6 whereas in Group S it was 3.4. VAS at the end of 12 hours in Group M was 4.18 whereas in Group S it was 4.2 (Fig. 2).

VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$) (Table 4).

The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for group M vs. Group S (p=<0.05) ranging from 64.42 ± 36 mg in Group M vs

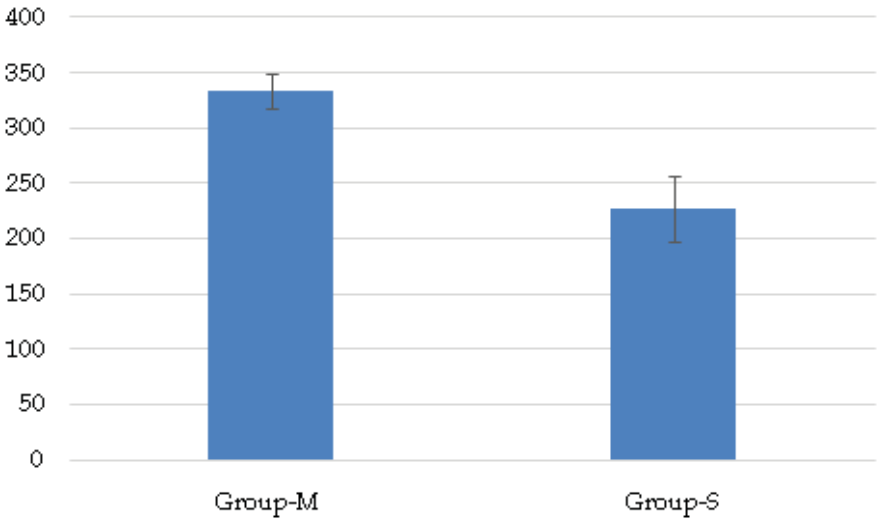

Fig. 2: Mean time of first pain in group M and group S

Table 4: Quality of Postoperative Analgesia

Quality of post of Analgesia	Group M		Group S		Mean Difference	P* value Significance
	Mean	SD	Mean	SD		
3	0.0	0.7	1.0	0.9	1.80	<0.001 HS
6	0.0	1.6	2.0	1.1	1.62	<0.001 HS
12	1.0	1.2	2.0	1.5	0.060	0.8 NS

*Mann Whitney U test

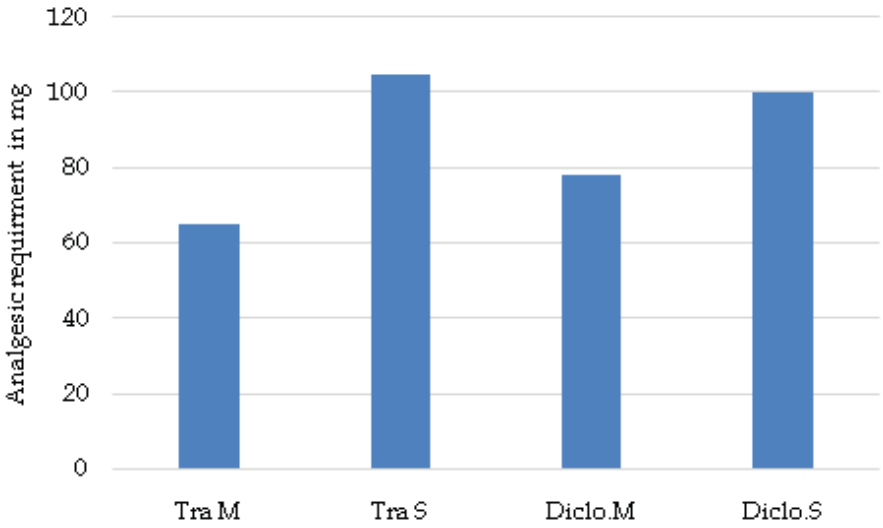

Fig. 3: Postoperative 24 hrs cumulative analgesic requirement

Tra – Tramadol; Diclo - Diclofenac; M-Magnesium Sulphate group; S-Normal Saline group

104 ± 45 mg in Group S for Tramadol and from 72 ± 35.82 mg to 100 ± 50.03 mg in Group M and Group S respectively for Diclofenac. In Group M, less patients required a single dose of Tramadol, during the first 24 hrs postoperatively, whereas in Group S, more patients required 2 or more than 2 doses of Tramadol. Similarly, fewer patients required only one dose of Diclofenac sodium during first 24 hrs postoperatively in Group M and in control group S more patients required a second dose of Diclofenac sodium to alleviate postoperative pain. No incidence of bradycardia, hypotension, hypoxia or hypoventilation was recorded during intra as well as postoperative period (Fig. 3).

Discussion

In our study majority of patients were middle aged in both groups. In group M there were 12 males and 13 females, whereas in group S there were 17 males and 8 females.

The mean height and mean weight in either group were identical. The types of surgeries performed were almost identical. These parameters were kept identical to avoid variations in intra- and post-operative outcome of patients.

Hemodynamic stability intraoperatively and postoperatively

In our study there was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra- or postoperative period. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia. In 2004, effect of IntraOperative magnesium Sulfate infusion on perioperative analgesia in open cholecystectomy study conducted by Bhatia, Kashyap, Pawar, Trikha[4] concluded that administration of intraoperative $MgSO_4$ as an adjuvant analgesic in patients undergoing open cholecystectomy, resulted in better pain relief and comfort in first postoperative hour and remitted in better sleep quality during the postoperative period without any significant side effects difference was observed between the two groups during the perioperative period.

Thus we can compare our study to above study and conclude that Group M patients were more hemodynamically stable.

Assessment of analgesia—time of first pain medication, quality of analgesia

Time of first pain medication in Group M as 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). In 2009 IV $MgSO_4$ for postoperative pain in patients undergoing lower limb orthopedic surgeries, a study concluded that IV $MgSO_4$ can serve as a supplementary analgesic therapy to suppress the acute postoperative pain, leading to less morphine requirements in first 24 hrs. The study was conducted by A. Dabbagh, H. Elyasi, S. Razavi, M. Fathi.[5] VAS at the end of 3 hours was 0.7 in Group M whereas in Group S it was 2.4 at the end of 6 hours VAS in Group M was 1.6 whereas in Group S it was 3.4. VAS at the end of 12 hours in Group M was 4.18 whereas in Group S it was 4.2. VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$).

In 2010 Hwang JY, Jean YT, Kincs[6] study done on IV infusion of $MgSO_4$ during spinal anesthesia improves postoperative analgesia, concluded IV $MgSO_4$ administration during spinal anesthesia improves postoperative pain.

In 2011, Shashi Kiran, Rachna Gupta and Deepak Verma[7] conducted a study Evaluation of Single dose of IV $MgSO_4$ for prevention of postoperative pain after inguinal surgery, concluded administration of IV $MgSO_4$ perioperatively significantly reduces, postoperative pain in patients undergoing inguinal surgery. Thus our study concluded time of first pain management was longer in Group M and also the quality of analgesia was better in Group M when compared with group S with reference to above studies.

Postoperative analgesic requirements

The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for group M vs. Group S ($p = < 0.05$), ranging from 64 ± 42.36 mg in Group M vs 104 ± 45 mg in group S for Tramadol and from 72 ± 35.82 mg to 100 ± 50.03 mg in Group M and Group S respectively for Diclofenac. In Group M, less patients required a single dose of tramadol, during the first 24 hrs postoperatively, whereas in Group S, more patients required 2 or more than 2 doses of tramadol. Similarly, fewer patients required only one dose of Diclofenac sodium during first 24 hrs postoperatively in Group M and in control Group S more patients required a second dose of Diclofenac sodium to alleviate postoperative pain. No incidence of bradycardia, hypotension, hypoxia

or hypoventilation was recorded during intra as well as postoperative period.

In 2004 McCartney, Avinash Sinha, Joel katz[8] conducted "A Qualitative systematic Review of the role of N-Methyl D-Asparate Receptor antagonist in Preventive Analgesia study conducted $MgSO_4$ as NMDA antagonist and thus reduces pain, analgesic consumption or both.

In 2006 Tauzin Fin P, Sesay M, Delort Laval S, P. Maurette[9] on IV $MgSO_4$ decreases postoperative tramadol requirement after radical prostateclary", which concluded IV $MgSO_4$ reduces tramadol consumption when used as postoperative analgesic protocol in radical prostertomy. Woolf *et al.* studied the dependence of the central sensitization on NMDA receptor activation in rats and found that NMDA receptor activation is involved in the induction and maintenance of central sensitization processes that characterize post-injury pain states.[10] Therefore, NMDA receptor antagonist may play a role in prevention and treatment of perioperative pain. Thompson *et al.* found that IV magnesium sulfate produced a dose-dependent reduction in halothane minimum alveolar anesthetic concentration (MAC), as measured by the tail-clamp technique, which could be considered as an anesthetic effect in an acute pain model.[11] Thus our result correlates with above study. We conclude that in Group M postoperative analgesic requirements were decreased.

Conclusion

On basis of our clinical study, we conclude that IV Magnesium sulfate infusion in spinal anesthesia decreases intraoperative hemodynamic variabilities, prolongs duration of analgesia and improves the quality of analgesia in the early postoperative period with better hemodynamic stability. It also decreases the postoperative analgesic requirements, thus it can be used as a beneficial additive for prolonging spinal anesthesia. Thus, the study concluded that Magnesium sulfate can be infused in spinal anesthesia for postoperative analgesia.

Summary

This study titled "Intravenous Magnesium sulfate can be infused in spinal anesthesia for postoperative analgesia" was done to evaluate the effect of Magnesium sulfate infusion for postoperative analgesia, decrease the postoperative analgesic requirements and negligible side effects.

50 patients aged 18–60 years belonging to ASA I and II undergoing elective lower limb orthopedic surgeries were randomly allocated for the study into two groups.

Group "M" – Receiving $MgSO_4$ (50 ml/kg over 15 min-bolus)

(15 mg/kg/ltr infusion)

Group "S" – Receiving isotonic saline

The mean height and mean weight in either group were identical. The types of surgeries performed were almost identical. These parameters were kept identical to avoid variations in intra- and postoperative outcome of patients. There was no significant difference in hemodynamic variables (mean arterial pressure and heart rate) during the intra-or postoperative period. Perioperative mean arterial pressure. Group M, Mg group; Group S, saline group. Values are presented as means (SD). Group M patients had a lower mean arterial pressure except immediately after the induction of spinal anesthesia.

Time of first pain medication in Group M was 334 min whereas in Group S was 227 min. This was statistically significant ($p < 0.001$). VAS was statistically significant at the end of 3 and 6 hours ($p < 0.001$), but it was insignificant at the end of 12 hours ($p > 0.05$). The cumulative requirement in 24 hrs of both tramadol and Diclofenac was statistically significantly less for Group M vs. S ($p \leq 0.05$).

Postoperative serum Mg concentrations in Group M were significantly higher than those in Group S ($p < 0.001$ immediately after surgery, and at 1 and 24 h after surgery. However, all patients in Group M had a serum Mg concentration in the normal range 24 h after surgery.

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Original Research Article

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A Comparative Study of Brachial Plexus Block Using Bupivacaine with Midazolam and Bupivacaine Alone in Upper Limb Surgeries

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Abstract

Introduction: Upper limb surgeries can be done under general anesthesia. However, using Brachial plexus block is a better alternative. This method provides good muscular relaxation and also maintains intra-operative hemodynamics at a stable level. *Aim of the study:* To study the effect of Midazolam added to brachial plexus block by supraclavicular approach. *Materials and methods:* This was a prospective, randomized, single blinded study. A total of 100ASA Grade I or II adult patients who underwent upper limb surgeries under supraclavicular brachial plexus block were studied. Patients were randomly allocated to two groups of 50 each. Patients in Group B received 30 mL of 0.375% Bupivacaine and Group BM received 30 mL of 0.375% Bupivacaine with preservative free Midazolam 0.05 mg/kg. The onset time and duration of sensory and motor blockade were noted. The patients were observed for 24 hours postoperatively for hemodynamic variables, sedation scores and rescue analgesic requirements. *Results:* Group BM showed significantly quicker onset of sensory and motor block than Group B ($p < 0.05$). Group BM also had significantly longer duration of sensory and motor block ($p < 0.05$). Group BM had significantly less requirements for rescue analgesia ($p < 0.05$). Both groups showed similar hemodynamics and sedation scores postoperatively. *Conclusion:* Midazolam (0.05 mg/kg) in combination with 30 mL of Bupivacaine (0.375%) hastened onset of sensory and motor block, and improved postoperative analgesia when used in brachial plexus block, without producing any adverse events.

Keywords: Brachial plexus block; Bupivacaine; Midazolam; Anesthesia in upper limb surgeries.

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Introduction

Upper limb surgeries can be done under general anesthesia. However, using Brachial plexus block is a better alternative. This method provides good muscular relaxation and also maintains intraoperative hemodynamics at a stable level. In addition it also provides associated sympathetic block which helps in reducing postoperative pain, vasospasm and edema caused by different local anesthetic agents. Bupivacaine is preferred frequently due to its longer duration of action which can vary from 3 to 8 hours. Bupivacaine has a few limiting factors like delayed onset, patchy or incomplete analgesia, sometimes shorter duration, etc.

For a better outcome in brachial plexus block different drugs like neostigmine, opioids,

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hyaluronidase, and clonidine have been added to local anesthetics so as to obtain quicker onset, good quality, prolonged duration and better postoperative analgesia.[1] Many of these drugs have potential for adverse systemic effects and some of them have questionable efficacy. Midazolam is a water-soluble benzodiazepine. It is used by the epidural or intrathecal route to produce antinociception and to accentuate the effect of local anesthetic. Midazolam acts on Gamma Amino Butyric Acid-A (GABA-A) receptors to give the above effects.[2] These receptors are present in the peripheral nerves also.[3]

In the present study we have attempted to compare the effect of Midazolam-Bupivacaine combination and plain Bupivacaine for brachial plexus block by using the supraclavicular route.

Materials and Methods

This was a prospective randomized single-blind study done in the department of Anesthesia at Osmania General Hospital and Osmania Medical College, Hyderabad. The study included 100 patients posted for upper limb surgeries under supraclavicular block. The patient's age ranged from 15 to 55 years. Informed written consent was obtained from all the patients and in case of minors, consent was taken from the parents. The results were noted in a pre-designed pro forma.

Inclusion criteria

- ASA CLASS I and II
- Patient age between 15 and 55 years, both males and females.
- Systolic blood pressure of 100–139 mm Hg.
- Diastolic blood pressure of 60–89 mm Hg.

Exclusion criteria

- Patients who refused to participate in the study.
- Known cases having hypersensitivity to Midazolam or Bupivacaine.
- Presence of medical complications like severe hypovolemia, septicemia, shock.
- Laboratory tests showing abnormal coagulation profile.
- Presence of local infection.

The following investigations were done in all the patients: Hemoglobin (Hb %), Total Leucocyte Count (TLC), Differential Leucocyte Count (DLC), Bleeding Time (BT), Clotting Time (CT), Random blood sugar (RBS), Blood urea and Serum Creatinine, ECG, HIV, HBs Ag.

Intravenous access with a 20-gauge intravenous (IV) cannula on the contralateral upper limb under aseptic techniques was secured.

The anesthesia machine, emergency oxygen source (E type cylinders) pipeline O_2 supply, working laryngoscopes, appropriate size endotracheal tubes with connectors and oropharyngeal airways, Working suction apparatus with suction catheter were checked.

A multiparameter monitor with pulse oximeter, ECG and Non-invasive blood pressure were used.

Procedure

The patients were randomly divided into two groups of 50 patients each.

Control group–Group-B was given 30 ml Bupivacaine (0.375%). And the Study group–Group BM was given 30 ml of mixture of Bupivacaine (0.375%) and Midazolam (0.05 mg/kg). For the brachial plexus block, a 22G, 5 cm needle, attached to a 20 ml syringe, was passed through the same point, parallel to the head and neck, in a caudal, slightly medial and posterior direction, until either paresthesia was elicited or first rib was encountered.

Anesthesia and analgesia were monitored in all the patients for a period of 24 hours post-surgery. To check the sensory block, temperature testing was done by using cotton soaked in spirit on skin dermatomes C_4 to T_2. To check the motor block, the patient was asked to adduct the shoulder and flex the forearm against gravity.

Onset of sensory block was taken as the time between injection of drug and complete loss of cold perception of the hand, and onset of motor blockade was taken as the time between the injection of drug to inability to adduct arm and flex forearm against gravity, i.e., the patient was unable to touch his/her nose.

Sedation was assessed by a score as described by Culebras *et al.*[4]

Culebras et al. sedation score

1 – awake and alert

2 – sedated, responding to verbal stimulus

3 – sedated, responding to mild physical stimulus

4 – sedated, responding to moderate or severe physical stimulus

5 – not arousable.

Heart rate, non-invasive blood pressure and oxygen saturation were monitored. Duration of sensory block and duration of motor block were also recorded. Intramuscular (IM) injection of Diclofenac sodium was given as rescue analgesia to those who complained of pain. The number of rescue analgesics used within 24 hours after surgery were also noted.

Student's '*t*' test was used to analyze quantitative data and chi-square test was used to analyze qualitative data. A *p* value of < 0.05 was considered statistically significant.

Results

A total of 100 patients were studied with patient's age ranging from 15 to 55 years.

Table 1: Age Distribution of Study Groups

Study groups	Mean ± SD (Age in years)	p value	Significance
Bupivacaine	34.3 ± 11.89	0.375	Not Sig
Bupivacaine + Midazolam	32.3 ± 10.51		

The mean age in Group BM was 32.3 ± 10.5 and in Group B was 34.3 ± 11.8 years. There was no statistically significant difference between the groups (Table 1).

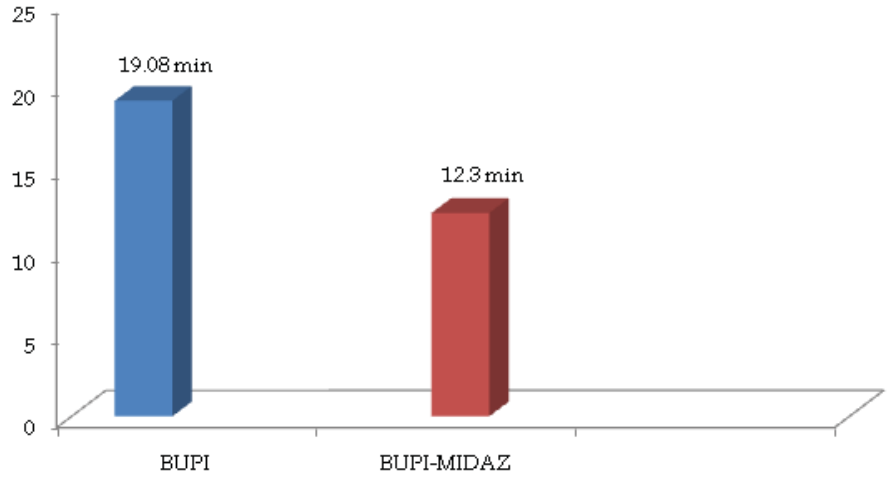

Fig. 1: Time for onset of sensory block (min)

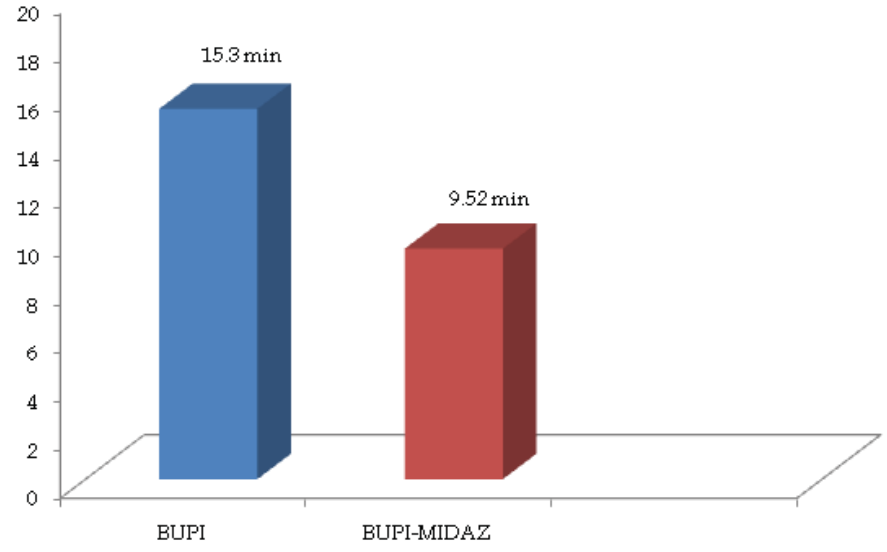

Fig. 2: Time for onset of motor block (min)

The mean time for onset of sensory block in Group BM was 12.3 ± 1.35 min and in Group B was 19.08 ± 1.7 min. The unpaired student's '*t*' test showed that Group BM had a significantly quicker time for onset of sensory block as compared to Group B ($p < 0.05$) (Fig. 1).

The mean time for onset of motor block in Group BM was 9.52 ± 1.37 min and in Group B was 15.3 ± 2.09 min. The unpaired student's '*t*' test showed that that Group BM had a significantly quicker time for onset of motor block as compared to Group B ($p < 0.05$) (Fig. 2).

All the patients were under observation for 24 hours. Time was noted when the patient complained of pain and asked for rescue analgesics. The mean duration of sensory block in group BM and in group B was 13.65 ± 2.01 hours and 6.87 ± 0.89 hours respectively. Group BM had a significantly longer sensory block as compared to Group B ($p < 0.05$) (Fig. 3).

The mean duration of motor block in Group BM and in Group B was 7.23 ± 1.01 hours and 6.17 ± 0.77 hours respectively. Group BM had a statistically significant longer motor block as compared to Group B ($p < 0.05$) (Fig. 4).

Table 2: Number of Rescue Analgesics in Post-op 24 hours

No. of RA in 24 hours post-op	Bupivacaine	Bupivacaine + Midazolam
1	0	37 (74%)
2	38 (76%)	13 (26%)
3	12 (24%)	0
$\chi 2 = 61.25$ p< 0.0001	Highly significant	

Group BM required less number of rescue analgesics as compared to Group B and it was statistically highly significant (Table 2).

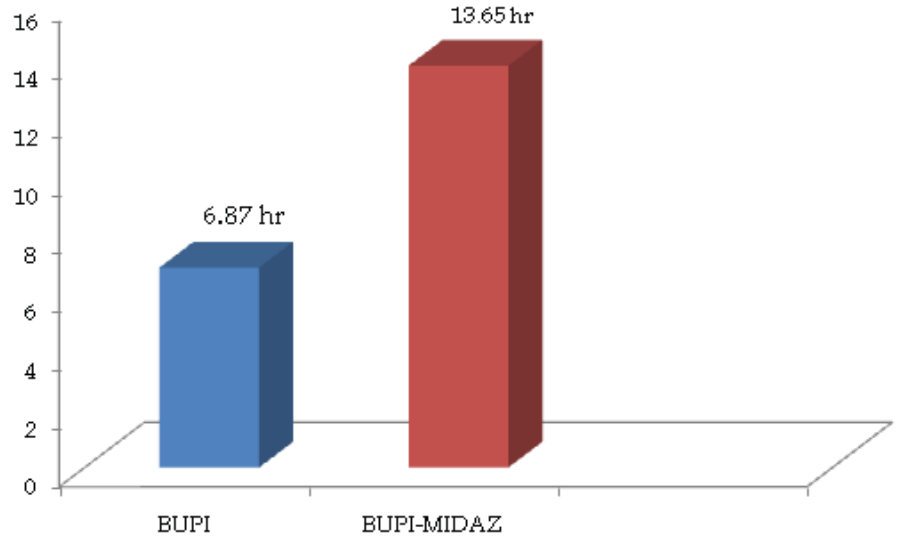

Fig. 3: Duration of sensory block

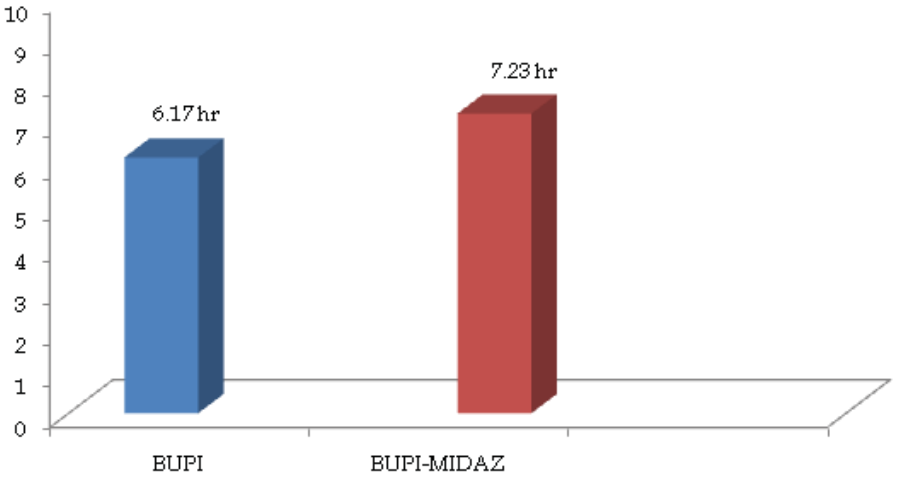

Fig. 4: Duration of motor block

Table 3: Sedation Score in Present Study

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

Sedation score*

1 – Aware and alert

2 – Sedated responding to verbal stimulus

3 – Sedated, responding to mild physical stimulus

4 – Sedated, respond to moderate to severe physical stimulus

5 – Not arousable

In Group B, all patients were awake and alert and had sedation score of 1. In Group BM, sedation corresponding to score 2 was observed in some patients between 15 min from time of injection and 60 min. None of the patients had sedation score of 3 and above during the study period. Statistical analysis of sedation score by chi-square test showed that the difference in sedation score was significant ($p < 0.05$) (Table 3).

Hemodynamic Variables

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

Table 4: Pulse Rate (beats/min)

Time of Assessment	Mean+/- SD Bupivacaine	Bupivacaine -Midazolam	*p* value	Significance
0 min	77 ± 6.8	75 ± 6.6	>0.05	NS
5 min	77 ± 6.6	76 ± 6.7	>0.05	NS
15 min	76 ± 6.5	76 ± 6.4	>0.05	NS
30 min	76 ± 6.8	76 ± 6.7	>0.05	NS
60 min	76 ± 6.6	75 ± 6.2	>0.05	NS
2 hrs	77 ± 6.5	75 ± 5.6	>0.05	NS
6 hrs	77 ± 6.4	76 ± 5.6	>0.05	NS
12 hrs	76 ± 6.2	74 ± 6.1	>0.05	NS
24 hrs	77 ± 6.5	76 ± 7.8	>0.05	NS

In Group B, the mean pulse rate ranged from 76 ± 6.2 to 77 ± 6.8 beats/min and in Group BM, it was 74 ± 6.1 to 76 ± 6.7 beats/min. The student's unpaired '*t*' test showed no statistically significant difference between the two groups ($p > 0.05$) (Table 4).

Table 5: Systolic Blood Pressure (mm Hg)

Systolic blood pressure	Mean+/- SD		p value	Significance
Time of Assessment	Bupivacaine (in mm Hg)	Bupivacaine-Midazolam		
0 min	117 ± 9.9	118 ± 9.5	>0.05	NS
5 min	118 ± 10.1	117 ± 10.5	>0.05	NS
15 min	118 ± 10.1	118 ± 10.3	>0.05	NS
30 min	118 ± 10.3	118 ± 9.9	>0.05	NS
60 min	118 ± 9.9	117 ± 9.7	>0.05	NS
2 hrs	118 ± 9.6	117 ± 9.7	>0.05	NS
6 hrs	116 ± 9.3	118 ± 9.6	>0.05	NS
12 hrs	117 ± 9.8	116 ± 10.0	>0.05	NS
24 hrs	117 ± 9.4	116 ± 9.4	>0.05	NS
Diastolic blood pressure				
0 min	76 ± 7.71	75 ± 7.11	> 0.05	NS
5 min	76 ± 7.56	76 ± 7.59	> 0.05	NS
15 min	76 ± 7.21	76 ± 7.31	> 0.05	NS
30 min	75 ± 6.59	76 ± 7.18	> 0.05	NS
60 min	77 ± 7.29	76 ± 7.42	> 0.05	NS
2 hrs	77 ± 7.40	76 ± 7.58	> 0.05	NS
6 hrs	76 ± 7.33	76 ± 7.39	> 0.05	NS
12 hrs	76 ± 7.75	76 ± 7.83	> 0.05	NS
24 hrs	76 ± 6.87	76 ± 6.93	> 0.05	NS

In Group B, the mean DBP ranged from 75 ± 6.6 to 77 ± 7.4 mm Hg and in Group BM, it was 75 ± 7.11 to 76 ± 7.59 mm Hg. The unpaired student's '*t*' test showed no significant difference between the groups ($p > 0.05$) (Table 5).

Table 6: Oxygen Saturation (%)

Time of Assessment	Mean+/- SD Bupivacaine	Bupivacaine-Midazolam	*p* Value	Significance
0 min	99.7 ± 0.57	99.7 ± 0.59	> 0.05	NS
5 min	99.8 ± 0.51	99.7 ± 0.54	> 0.05	NS
15 min	99.7 ± 0.63	99.7 ± 0.65	> 0.05	NS
30 min	99.7 ± 0.65	99.8 ± 0.53	> 0.05	NS
60 min	99.7 ± 0.58	99.8 ± 0.4	> 0.05	NS
2 hrs	99.7 ± 0.64	99.8 ± 0.48	> 0.05	NS
6 hrs	99.7 ± 0.56	99.8 ± 0.47	> 0.05	NS
12 hrs	99.7 ± 0.75	99.8 ± 0.55	> 0.05	NS
24 hrs	99.7 ± 0.53	99.8 ± 0.53	> 0.05	NS

In Group B, the mean O_2 saturation ranged from 99.7 ± 0.57% to 99.8 ± 0.51% and in Group BM it was from 98 ± 0.5%. The students unpaired '*t*' test showed no significant difference in O_2 saturation

between the two groups ($p > 0.05$) (Table 6).

Discussion

Brachial plexus block confers postoperative analgesia of short duration, even when a long-acting local anesthetic like Bupivacaine is used alone. Different adjuvant drugs like opioids, clonidine, neostigmine and hyaluronidase have been used along with local anesthetics to lengthen the period of analgesia. Many of these drugs were not efficacious or gave rise to adverse effects.

A total of 100 patients with almost an equal male to female ratio were studied. The youngest patient was 15 years and the oldest patient was 55 years. Out of which the mean age of Group B (receiving only Bupivacaine) was 34.3 ± 11.8 years and the mean age of Group BM (receiving Midazolam with Bupivacaine) was 32.3 ± 10.5 years. There was no significant difference between the groups regarding patient age.

In our study we found that the group that received a combination of Midazolam and Bupivacaine showed more rapid onset of sensory and motor blocks that was statistically significantly. Onset of sensory block (Group BM, 12.3 ± 1.5 min; group B, 19.08 ± 1.7 min). Onset of motor block (Group BM, 9.52 ± 1.37 min; Group B, 15.30 ± 2.09 min). This could be attributed to the local anesthetic property of Midazolam that exerts synergistic action when used with local anesthetics. Both the groups had faster onset of motor block than the onset of sensory block. Winnie *et al*.[5] also in their study observed similar findings and attributed it to the fact that in a nerve bundle at the level of the trunks, the motor fibers are located more peripherally than sensory fibers. Hence, when a local anesthetic is injected perineurally, it will block motor fibers first and later blocks the more centrally located sensory fibers.

In the present study, we observed that sensory block lasts longer than motor block and similar finding was noted by de Jong *et al*.[6] It is thought that larger fibers naturally require a higher concentration of local anesthetic than smaller fibers. Large motor fibres require a higher minimal effective concentration of local anesthetic than smaller sensory fibres. Thus, motor function returns before pain perception and duration of motor block is shorter than the sensory block.[6] In our study duration of motor blocks were different between the groups. (Group BM, 7.23 ± 1.01 hours; Group B, 6.17 ± 0.77 hours). In our study, the mean duration of sensory block was significantly higher ($p < 0.05$) in Group BM than in Group B. (Group BM, 13.65 ± 2.01 hours; Group B, 6.87± 0.89 hours).

A similar study was conducted by Jarbo *et al*.[7] (n = 40) where they observed the efficacy of Midazolam as an adjuvant to Bupivacaine in brachial plexus block. The mean onset of sensory block (group BM, 12 ± 2.9 min, group B, 20 ± 3.8 min) and motor block (group BM, 9.2 ± 2.38 min; group B, 17.1 ± 3.83 min) was significantly faster in group BM than in group B ($p < 0.05$). The duration of sensory block (group BM, 7 ± 4.32 hours; group B, 5.95 ± 1.4 hours) was also longer in group BM than in group B. The duration of motor block was similar between the groups (group BM, 5.65 ± 3.32 hours, group B, 5.1 ± 1.14 hours). These values are comparable with our study except for the duration of motor block which was also significantly longer in our study.

Various studies in which Midazolam was used in central neuraxial block found that Midazolam with Bupivacaine improves analgesic characteristics compared to Bupivacaine alone. Gulec *et al*.[8] observed better and prolonged postoperative analgesia with Bupivacaine-Midazolam combination as compared to a Bupivacaine-Morphine combination that was given caudally. Nishiyama *et al*.[9] reported better analgesia after adding Midazolam to a continuous epidural infusion of Bupivacaine. Jarbo *et al*.[7] used the intrathecal route for Bupivacaine with Midazolam and observed a significantly lower visual analogue score compared to use of Bupivacaine alone. Midazolam gives this enhanced effect on local anesthetics as it acts on the GABA-A receptor complexes present in the spinal cord. The addition of Midazolam in doses of 1 to 2 mg intrathecally has a positive effect on post-surgical pain and in chronic pain therapy. Intrathecally administered midazolam does not have any neurotoxic effects as demonstrated by animal studies.[9,10] More recently, Tucker and associates demonstrated that administration of 2 mg of intrathecal Midazolam accentuated the analgesic effect of intrathecal Fentanyl in patients in labor. This administration was not associated with any occurrence of neurologic or urologic symptoms.[11]

In our study, the group BM showed lesser requirement of rescue analgesia and lesser mean number of supplemental analgesic boluses. Jarbo *et al*.[7] also reported similar observations. The Group BM also had prolonged analgesia which is attributable to the action of Midazolam on GABA-A receptors of brachial plexus producing antinociception. These receptors are present in peripheral nerves as well. Brown and Marsh

have shown the presence of GABA receptors in peripheral nerve trunks in mammals.[12] Bhisitkul *et al*.[13] have demonstrated the presence of these receptors on both normal and regenerated sensory fibers in peripheral nerves in rats. These receptors are present within the temporomandibular joint and when activated, lead to reduced transmission of nociceptive signals.[14] The action of Midazolam on GABA receptors is well known.

We used Midazolam at a dose of 0.05 mg/kg, for central neuraxial block as it is safe at this dosage and does not cause any significant adverse effects. In our study, sedation scores were higher in patients in Group BM compared to Group B, 15 min after injecting the drug until 60 min after injection. This is in concurrence with the observations of Jarbo *et al*.[4] This may have been due to partial vascular uptake of Midazolam, and its transport to the central nervous system where it acts and produces sedation. Midazolam is highly lipophilic and diffuses quickly into the blood vessels. It has a rapid clearance (6–11 $mL.kg^{-1}.min^{-1}$) and short half-life (1.7–2.6 hours) which contribute to the limited sedation. Though Group BM had higher mean sedation score than Group B ($p < 0.05$) this higher sedation was not significant clinically. In our study, none of the patients experienced airway compromise or required airway assistance. This mild sedation in fact was favorable during that period.

Conclusion

The addition of Midazolam (0.05 mg/kg) as adjuvant to Bupivacaine (0.375%) in brachial plexus block, gives more rapid onset and longer duration of both sensory and motor blocks. It reduces the requirement of rescue analgesics in postoperative period. It provides comfortable sedation intraoperatively without any need for airway assistance and also does not alter the hemodynamic variables. Thus the above combination provides improved analgesia with a prolonged effect.

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Original Research Article

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Pectoral Nerve Blocks (PECS) for Postoperative Analgesia after Breast Surgeries: A Randomised Clinical Study

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Abstract

Context: Pectoral nerve blocks (PECS) is a novel technique introduced to provide analgesia for anterior and lateral chest wall surgeries. *Aims:* The present study was planned to evaluate the efficacy and safety of ultrasound-guided PECS 1 and 2 block for postoperative analgesia after breast surgeries. *Settings and Design:* Prospective, randomized, placebo controlled clinical study. *Methods and Material:* Forty female patients of ASA I/II, undergoing breast surgeries were recruited and randomly allocated into two groups. Group P patients were subjected to ultrasound-guided PECS block with 0.375% Inj. Ropivacaine (10 ml at PECS 1 and 20 ml at PECS 2) and Group C patients were injected with 0.9% saline at PECS I and II sites before reversal from anesthesia. Post operatively VAS scores, time of administration of the first rescue analgesic, number of rescue analgesics, level of blockade were recorded and rescue analgesia with Inj. Fentanyl 1 mcg/kg was given when the VAS score was 4 or more. *Statistical analysis used:* Data collected were tested for normalcy using the Shapiro Wilk test and compared using the Mann Whitney U test, Student T test and Pearson's chi-square test using the SPSS software version 23. *p*-values less than 0.05 was considered statistically significant. *Results:* The VAS scores, total Fentanyl consumption at 24 hours in Group P was less than that of Group C ($p < 0.05$). *Conclusion:* PECS provides effective postoperative analgesia for more than 12 hours from T2 to T5 dermatomal levels with opioid sparing effects after breast surgeries with no adverse effects.

Keywords: Breast surgery; PECS; Postoperative analgesia; Ultrasound.

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Introduction

Inadequate treatment of postoperative pain after surgeries is known to cause a myriad range of physiologic and psychologic consequences leading to significant morbidity and delay in recovery.[1] The traditional way to overcome postoperative pain in breast surgeries is by providing multimodal analgesia using non-steroidal anti-inflammatory drugs, paracetamol, opioids and local anesthetic infiltration at the site of surgery. Some anesthetists however prefer using the paravertebral block or thoracic epidural analgesia to tackle postoperative pain.[2] The appropriateness of these postoperative analgesic techniques become questionable when the breast surgery is performed on a day care basis.[3]

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Even relatively minor breast surgery can be associated with significant postoperative pain. A novel inter fascial plane block — PECS was described by R Blanco.[4] The pectoral nerve block is less invasive and has less complications than the other techniques.[2] In our study we evaluated the analgesic efficacy of PECS after breast surgeries in comparison with a placebo controlled group. The aim of our study was to compare the pain score, duration of analgesia, total postoperative fentanyl consumption along with the sensory and motor blockade achieved.

Materials and Methods

This prospective, randomized controlled study was conducted after obtaining institutional ethical committee approval and informed consent from all the patients participating in the study. Forty female patients belonging to American Society of Anesthesiologists (ASA) class I and II aged between eighteen and seventy, scheduled for elective breast surgeries were included in the study. Patients with history of hypersensitivity to local anesthetic drugs, bleeding disorders, receiving anti-coagulation therapy, having chest wall deformity, those who were not able to comprehend the Visual Analog Scale (VAS) and pregnant patients were excluded. They were then randomly allocated into either of the two groups using a computer generated table. The groups were PECS Group (Group P) and Control Group (Group C).

Surgery was performed under general anesthesia. All patients were premedicated with Inj. Midazolam 1 mg and Inj. Glycopyrrolate 0.2 mg intravenously. Inj. Fentanyl 2 mcg/kg, Inj. Propofol 2 mg/kg was used for induction. Inj. Vecuronium 0.1 mg/kg was used to facilitate intubation. Patients were intubated with an appropriate sized endotracheal tube and maintained with Isoflurane 1% along with 50% oxygen and nitrous oxide in 1:1 ratio. Inj. Fentanyl 25 mcg and Inj. Vecuronium 1 mg intermittent boluses were given for intraoperative analgesia and maintenance of muscle relaxation respectively. Routine ASA monitoring including non-invasive blood pressure, pulse oximetry, electrocardiography and capnography was carried out.

At the end of surgery, after closure of the skin incision and before wound dressing, the block was performed. With the patient in supine position and arm at 90 degrees abduction, painting of the skin and draping with sterile sheets was performed. The linear ultrasound (US) probe of high frequency (6–13 MHz, Sonosite, Bothell, WA, USA) after sheathing was placed along the paramedian sagittal plane in the infraclavicular region. The first rib was visualized and the caudal end of the transducer rotated laterally. The transducer in this angle was moved laterally until the second and the third ribs were visualized (Image 1). Once the pectoralis major and minor muscles were identified, color Doppler was used and the pectoral branch of the thoracoacromial artery was localized (Image 2). Skin was infiltrated with 2 ml of Inj Xylocaine 2% and the 23 Gauge needle (Spinal needle, Quincke type point, Becton Dickinson S.A, Madrid, Spain) advanced in plane to the transducer such that its tip just pierces the fascial plane between the pectoralis major and pectoralis minor muscles. Hydrodissection was done to confirm the position of the needle. In patients of Group P, 10 ml of Inj Ropivacaine 0.375% was injected. In patients of Group C, 10 ml of 0.9% saline was injected and PECS I block was completed.

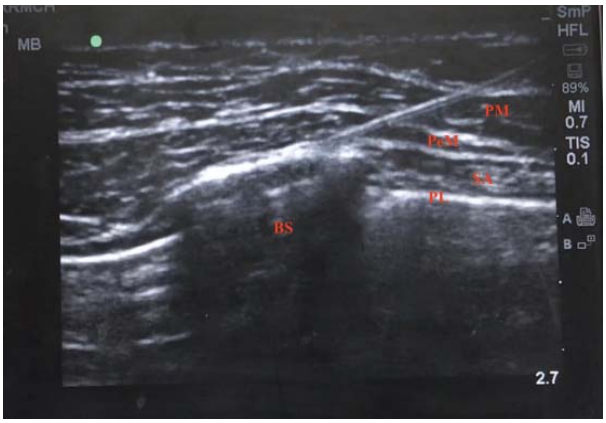


Image 1: Ultrasonographic image showing needle pathway and sonoanatomy. PM = pectoralis major, PeM = pectoralis minor, SA = serratus anterior, PL = parietal pleura, BS = bony shadow.

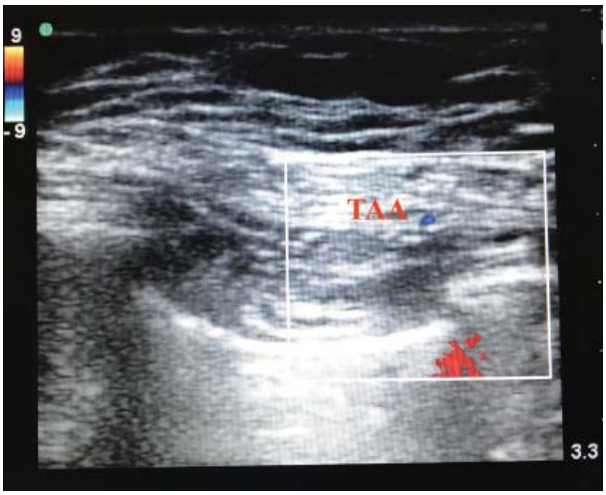


Image 2: Sonoanatomy localising the Thoraco Acromial Artery (TAA).

To perform PECS II, the transducer was moved further laterally until the pectoralis minor and the serratus anterior muscles were visualized over the second, third and fourth ribs. The needle was reinserted to hit the third rib, then it was retracted such that its tip was in the fascial plane separating the pectoralis minor and the serratus muscles. Hydrodissection was performed and position of the needle tip was confirmed. In Group P patients 20 ml of Inj Ropivacaine 0.375% was injected whereas in patients of Group C 20 ml of 0.9% saline was injected. Dressing was applied and the patients were extubated. After recovery from anesthesia, patients were shifted to the postoperative care unit (PACU) and monitored for heart rate, mean blood pressure, pain, sensory and motor blockade at 0, 2, 4, 8, 12 and 24 hours after performing the block. Pain intensity was recorded in the ipsilateral upper limb using the 10 cm VAS. Sensory levels were determined by pinprick and the dermatomal levels that were devoid of pain were recorded. Motor blockade was assessed by evaluating for any weakness of the muscles in the upper limb on the side in which the block was performed. When the VAS score was 4 or more, rescue analgesia with Inj Fentanyl 1 mcg/kg was given. The time to administration of the first rescue analgesic, the total number of rescue analgesics and complications if any (pneumothorax, nausea, vomiting, hypersensitivity reactions, sedation) were recorded. Postoperative nausea and vomiting (PONV) was assessed using a four-point numerical scale (0 = no PONV, 1 = mild nausea, 2 = severe nausea or one episode of vomiting, 3 = vomiting more than once). Sedation if present was graded using the Ramsay sedation score.[5] The primary outcome measure was the pain score (VAS) in the first 24 hours. Secondary outcome measures were the time to administration of the first rescue analgesic (duration of block), total postoperative fentanyl consumption, the sensory and motor blockade achieved and complications recorded if any.

Statistics

Based on outcome variables from previous literature for pain assessment at 24 hours, with a mean difference of 0.3 and standard deviation of 0.25, 95% statistical power and 5% level of significance, a sample size of 40 with 20 patients in each group was estimated to be adequate. Statistical analysis was done on a personal computer using the SPSS (Statistical Package for Social Sciences) version 23 software (IBM Corp., Armonk, NY). Normality of numerical data was tested using the Shapiro Wilk test. Normally distributed numerical data were presented as mean and standard deviation. Non normally distributed numerical data were presented as median and interquartile range. The intergroup differences were compared using the Student T test and the Mann Whitney U test for normally and non-normally distributed numerical data respectively. Categorical data were presented as number and percentage and differences between the two groups were compared using the Pearson chi square test. *p*-values less than 0.05 was considered statistically significant.

Results

The groups were comparable with respect to age, weight, duration of surgery and ASA physical status (p values > 0.05, as shown in Table 1).

The VAS scores in Group P was less than 4 [median (interquartile ranges)] at 0, 2, 4, 8, 12 and 24 hours and less than the VAS scores of Group C at all time durations (Table 3) which was statistically significant ($p < 0.05$) (Graph 1).

In Group P patients, the analgesia lasted for up

Table 1: Demographic data

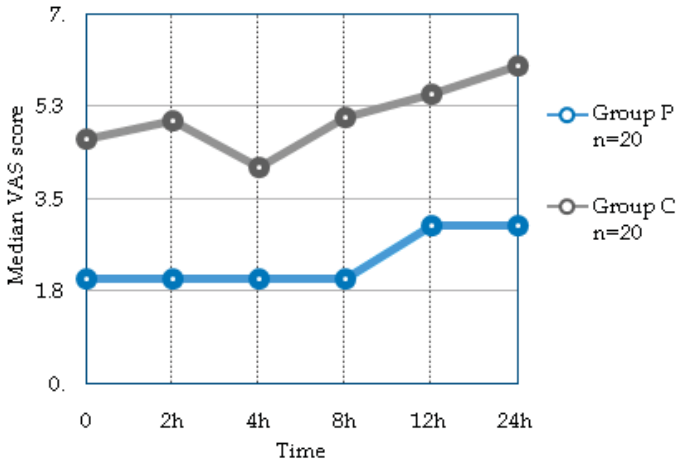
Variable	Group P n=20	Group C n=20	*p* value
Age in years	36.30 +/- 13.41	36.75 +/- 13.75	0.999
Weight in kgs	57.75 +/- 8.71	55.05 +/- 10.45	0.527
Duration of surgery in minutes	57.95 +/- 21.63	64.10 +/- 31.44	0.995
ASA grade I/II	12/8	10/10	0.613

Table 2: Type of surgery

Diagnosis	Group P	Group C
Fibroadenoma	12	10
Fibrocystic disease	2	2
Benign breast tumor	2	3
Ca breast	4	5
Total	20	20

to 12 hours after surgery [median (interquartile range)] whereas, patients in Group C required the first rescue analgesic within 2 hours after completion of surgery (Table 4). The total Fentanyl consumption at 24 hours in Group P was also significantly less when compared to that of Group C (Table 4, Graph 2).

Sensory analgesia involving the dermatomes T2 to T5, extending from the midline anteriorly up to posterior axillary line laterally was noted on the side where the block was performed in Group P patients. No sensory analgesia was noted in Group



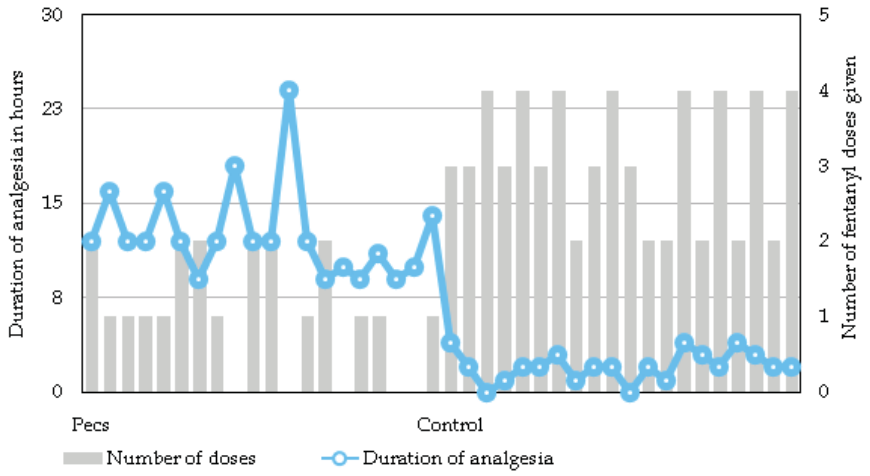
Graph 1: Depicting the difference in VAS score between the two groups.

Table 3: Comparison of VAS, expressed as median and interquartile ranges

VAS scores	0 hour	2 hour	4 hour	8 hour	12 hour	24 hour
Group P n=20	2 (2 – 3)	2 (2 – 3)	2 (2 – 3)	2 (2 – 3)	3 (2 – 3)	3 (3 – 5)
Group C n=20	4.65 (4 – 5)	5 (4 – 6)	4.1 (3 – 5)	5.05 (4.25 – 5.75)	5.5 (5 – 6)	6.05 (5 – 7)
p value	0.000	0.000	0.000	0.000	0.000	0.000

Table 4: Comparing the duration of action (median and interquartile ranges) and the number of fentanyl doses required per patient (mean ± standard deviation)

Variable	Duration of block in hours	Total number of fentanyl dose required per patient in 24 hours (Mean ± SD)
Group P	12 (10 – 13.5)	1.05 ± 0.759
Group C	2 (1.25 – 3)	3.10 ± 0.852
p value	0.004	0.000



Graph 2: Depicting the duration of analgesia achieved and the fentanyl doses given per patient in both the groups.

C. Motor blockade was not observed in either of the groups. No block related complications were noted in either of the groups.

Discussion

The anterior thoracic wall is innervated by the intercostal nerves (T2-T6) which provide segmental somatic innervation to the skin, the medial (C8–T1) and lateral (C5–C7) pectoral nerves which provide innervation to the pectoralis major and minor muscles. The axillary region is supplied by the long thoracic nerve (C5–C7) which supplies the serratus anterior muscle and the thoracodorsal nerve (C6–C8) which supplies latissimus dorsi muscle. PECS I blocks the medial pectoral nerve, the lateral pectoral nerve and the intercostal nerves. PECS II blocks the medial and lateral pectoral nerves, the long thoracic nerve and the thoracodorsal nerve.[4,6]

The present study was conducted to evaluate the analgesic efficacy of PECS I and II blocks for postoperative analgesia after various breast surgeries. In our study we found that the block was effective and provided adequate postoperative analgesia (VAS scores < 4) and reduced requirement of rescue analgesic agent. The analgesia lasted for up to 12 hours and there was an overall reduction in opioid consumption. Sensory analgesia achieved was adequate (T2–T5) and the patients were comfortable.

Bashandy and Abbas conducted a randomized clinical trial with 2 groups — general anesthesia alone and general anesthesia with PECS for postoperative pain management. PECS group showed significantly lower VAS scores and lower postoperative morphine consumption.[7] Similarly in another case report by A. Bouzinac *et al.*, patient controlled analgesia with morphine used as the rescue analgesic (dose 1 mg, lockout 7 min). The morphine consumption over the first 24 hours was zero and the pain scores were less than 2 for up to 24 hours postoperatively.[8]

In studies conducted by Eldeen *et al.* and Versyck *et al.*, where Sufentanyl and fentanyl were used respectively as rescue analgesics in the postoperative care unit, similar outcomes of reduced opioid consumption in the PECS group patients was noted.[9,10]

In several studies conducted on PECS, ropicavaine was the local anesthetic agent used. Depending on the type of surgery 0.5%, 0.375% and 0.2% ropivacaine was used to achieve the block by Kulhari *et al.*, Fujiwara *et al.*, and Bouzinac *et al.*, in their studies.[6,8,11] In our study we used 0.375% ropivacaine, 10 ml at the fascial plane between pectoralis major and minor and 20 ml at the plane between pectoralis minor and serratus anterior. In studies conducted by Blanco and Wahba *et al.*, levobupivacaine was used and analgesia for 12 hours was observed.[3,4] In the study conducted by Eldeen *et al.*, bupivacaine in combination with dexmedetomidine was injected and an increase in the duration of block compared to injection of just the local anesthetic agent alone was observed.[9]

Combipecs - The single injection technique of ultrasound-guided PECS I and II blocks was described by Arunangshu Chakraborty *et al.* They conducted a study on 21 patients where PECS I and II was performed through a single needle pass and postoperative analgesia up to 24 hours was achieved. It was equally effective and less time consuming.[12] The recent approach to increase the duration of analgesia is to place a catheter at the interfascial plane and supplement the analgesic agent as and when needed. Blanco recommends the use of 5 ml/hour infusions of Levobupivacaine 0.25% for up to 7 days if required.[4] However further studies are required to support this.

Eun-Jin Moon *et al.* reported the use of pectoral nerve block along with sedation for Breast conserving surgery without general anesthesia. In this case report after performing the PECS I and II blocks (using 4 ml of 0.375% and 10 ml of 0.375% ropivacaine respectively) at the start of the surgery when the patient was awake, they confirmed the sensory levels after 15 minutes. Once the patient was comfortable and pain free, Dexmedetomidine continuous intravenous infusion (0.4 microgram/kg/hour) was started to provide sedation and anxiolysis and the surgery was performed. They observed that when PECS was conducted in combination with monitored anesthesia care, it could suffice as primary anesthesia in patients undergoing simple breast surgeries.[2]

Thoracic epidural analgesia (TEA) is considered the gold standard technique to alleviate pain after breast surgeries.[3] It is seconded by thoracic paravertebral blocks and multimodal analgesia which may use a combination of regional anesthetic techniques and intravenous analgesic agents.

Wahba *et al.* in their study compared the analgesic efficacy of thoracic paravertebral block (PVB) with PECS for postoperative analgesia after breast surgeries. They observed that with PVB, ipsilateral dermatomal blockade was seen without contralateral sympathetic chain block (seen commonly with thoracic epidural analgesia). They

also observed that PVB does not block the medial and lateral pectoral nerves, long thoracic nerve and thoracodorsal nerves implying lack of adequate analgesia during breast surgeries involving axillary dissection.[3] With PVB 70% of the local anesthetic injected, spread to the epidural space.[13] Therefore the fact that PVB may transform into epidural block or total spinal anesthesia should be considered. Lönnqvist *et al.* reported various complications associated with PVB like hypotension (4.6%), vascular puncture (3.8%), pleural puncture (1.1%), and pneumothorax (0.5%).[14] These complications make it unsuitable for surgeries being conducted on a day care basis. PECS performed under ultrasound guidance overcomes these complications and is apt for day care surgeries.[4]

Apart from providing analgesia after breast surgeries, studies have shown that PECS I and II also provide analgesia for insertion of cardiac resynchronization devices, analgesia after rib fractures, placement of intercostal drains and analgesia for thoracotomies.[15,16]

The limitation of this study is that an ultrasound machine with a linear array probe is a must for these blocks and it cannot be performed with blind or landmark techniques. PECS is a simple new alternative for breast surgeries being conducted on a day care basis in which the overall duration of hospital stay is usually less which makes it a feasible and cost-effective mode of postoperative analgesia. The pectoral nerve blocks (PECS 1 and 2) provides effective postoperative analgesia for more than 12 hours from T2 to T5 dermatomal levels with opioid sparing effects after breast surgeries with no adverse effects.

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Comparative Study of Hemodynamics, Postoperative Nausea and Vomiting in Middle Ear Surgeries with Desflurane and Sevoflurane

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Abstract

Introduction: Middle ear surgeries as such are associated with PONV and when inhaled anesthetics are used in these surgeries, the incidence of PONV might vary. Achieving a more effective outcome with respect to PONV will become increasingly important in the future as a result of increasing pressure to decrease discharge times. *Aims:* To compare the intra-operative hemodynamic parameters along with postoperative nausea and vomiting with Desflurane and Sevoflurane in Middle Ear Surgeries. *Materials and methods:* The present study was a prospective, randomized, comparative clinical study, was conducted in patients scheduled to undergo elective middle ear surgeries in 60 patients, planned for elective middle ear surgeries under general anesthesia. Patients between the age of 12 and 60 are selected for the study comprising of both sexes. They are divided into 2 groups randomly, Group S (Sevoflurane) and Group D (Desflurane); 30 patients in each group. *Results:* The difference in average preoperative systolic, diastolic blood pressure, heart rate was statistically not significant when compared in both groups. There was no statistically significant difference ($p > 0.05$) between the two groups with respect to PONV as Fisher's exact test statistic value is 1. *Conclusion:* No significant difference was found in terms of intra-operative hemodynamics and postoperative nausea and vomiting in patients receiving general anesthesia with sevoflurane and desflurane as inhalational agents for Middle ear surgeries.

Keywords: Middle Ear Surgeries, Desflurane and Sevoflurane

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Introduction

Middle ear surgeries are one of the most commonly performed ear procedures. Introduction of ossicular chain repairs and cochlear implantations for hearing defects has opened doors for further advances in these surgeries. The quest for an ideal anesthetic agent, which subserves the otologic goals, has now ushered us into an era whereby, sevoflurane and desflurane have gained popularity, with which, maintainence of anesthesia has become more convenient and attained more stability in terms of patients' hemodynamic profile when compared to the older inhalational agents.

Middle ear surgeries as such are associated with PONV and when inhaled anesthetics are used in

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these surgeries, the incidence of PONV might vary. Achieving a more effective outcome with respect to PONV will become increasingly important in the future as a result of increasing pressure to decrease discharge times. In this study, effects of desflurane and sevoflurane as inhalation agents on intraoperative hemodynamic profile and PONV in Middle ear surgery is comparatively investigated.

Materials and Methods

The present study, a prospective, randomized, comparative clinical study, was conducted in patients scheduled to undergo elective Middle ear surgeries at Govt ENT hospital, Koti, Hyderabad. After approval from the Departmental ethics committee and written informed consent from the patients, a randomized control study was conducted on 60 patients, planned for elective Middle ear surgeries under general anesthesia.

Patients between the age of 12 and 60 are selected for the study comprising of both sexes. They are divided into 2 groups randomly, Group S (Sevoflurane) and Group D (Desflurane); 30 patients in each group.

Inclusion Criteria

1. ASA Grade I and II
2. 12 to 60 years of age
3. Who gave informed written consent
4. Patients scheduled to undergo elective Middle ear surgeries lasting from 60 min to 2 hours.

Exclusion Criteria

1. Patients who underwent general anesthesia in the past seven days
2. Patients with history of neuropsychiatric disorders
3. Pregnant, lactating and menstruating females
4. Baseline heart rate less than 60 bpm
5. Baseline blood pressure less than 100/50 mm Hg
6. Patients with BMI > 30
7. Patients with impaired hearing.

Preoperative assessment

All patients were pre operatively evaluated for surgery. All investigations were conducted before the surgery.

Investigations conducted are as follows:

Complete blood picture with platelet count

Complete urine examination

Random blood sugar, blood urea, serum creatinine, serum electrolytes

ECG, Chest X-ray, Neck X-ray

HIV, HbSAg

CT, BT

2D Echo

Patients were informed about the procedure in detail before commencing the operation and written consent was obtained.

Preparation of operating theater

Boyle's anesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet, bougie and working suction apparatus were kept ready before the procedure. Emergency drug tray consists of atropine, adrenaline, mephenteramine, ephedrine and dopamine were kept ready.

Procedure

Patients shifted to OR table, monitors like NIBP, electrocardiogram (ECG), Pulse oximeter were applied. Base vitals were recorded, IV access was obtained on the forearm with No 20G IV cannula Ringer's lactate solution at 3 ml kg^{-1} was started.

Patients were premedicated with Glycopyrrolate 0.2 mg IV, ondansetron 4 mg IV, fentanyl 1–2 mcg/kg IV. Both the study groups received standard anesthetic technique with Propofol 2 mg/kg titrated to loss of verbal response. Endotracheal intubation was facilitated with Suxamethonium (1.5 mg/kg) and intubation done with suitable sized cuffed tube. All patients were mechanically ventilated with 33:66 O_2/N_2O mixtures. Respiratory rate (RR) and tidal volume (TV) were adjusted according to body weight to maintain normocapnia.

During the maintenance period, ventilation was controlled to maintain normocarbia using a closed circle system with a total fresh gas flow rate of 5 L/min with 66% N_2O and 33% O_2. Vecuronium was used during maintenance of anesthesia. Group S received Sevoflurane of 1–2% and Group D received Desflurane of 4–6% for maintainence of anesthesia.

The inhalational anesthetic was discontinued at the end of the procedure and N_2O was discontinued after the last skin suture was placed. After completion of surgery, oral suctioning was done. At the end of anesthesia, residual neuromuscular blockade was reversed using glycopyrrolate, 0.01 mg/kg IV, and neostigmine, 0.06 mg/kg IV. Intraoperative monitoring of hemodynamics was done.

The durations of anesthesia (from the start of induction to discontinuation of N_2O) and surgery (from surgical incision to skin closure) were also recorded. Monitoring included non-invasive blood pressure measurement, heart rate, and oxygen saturation. Hemodynamics were recorded preoperatively (baseline), intraoperatively (at intubation time, 5 min, 10 min, 15 min, 30 min and for every 30 min thereafter), until the completion of surgery. After extubation and full recovery, patients were transferred to the postanesthesia care unit (PACU).

In the postoperative period, the incidences of PONV were recorded within the first 24 hours after surgery. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. No distinction between nausea, vomiting and retching.

Statistical analysis

The data collected was entered into an Excel sheet. It was subjected to statistical analysis in MS Excel and SPSS v.16. Data was expressed in frequencies and percentages when qualitative and in Mean ± SD when quantitative. Unpaired Student *t*-test was used for comparing the trends for all parameters in the two groups. A '*p*' value of < 0.05 was considered significant.

Results

Sixty patients, undergoing Middle ear surgery, were selected for the study. The patients were randomly divided into two groups of 30 patients each.

The average age of Group S was 40.03 ± 12.04 and that of Group D was 37.36 ± 11.74. The youngest patient in the study group was 17 years and the oldest was 60 years. There was no statistically significant difference in age between the 2 groups. Total number of males in Group S are 18 whereas Group D has 16 males. Total number of females in Group S are 12 whereas Group D has 14 females. Total number of ASA-1 patients in Group S are 17 whereas Group D has 20 patients. Total number of ASA-2 patients in Group S are 13 whereas Group D has 10 patients (Table 1).

There was no statistically significant difference between the two groups in mean duration of surgery and mean duration of anesthesia (Fig. 1).

There was no statistically significant difference ($p > 0.05$) between the two groups in mean systolic BP (Fig. 2).

There was no statistically significant difference ($p > 0.05$) between the two groups in mean diastolic BP (Fig. 3).

Table 1: Demographic Distribution between Groups

	Group S		Group D	
	Number of patients	**Percentage**	**Number of patients**	**Percentage**
Age in Years				
12–20	2	6.66	2	6.66
21–30	5	16.66	7	23.33
31–40	6	20	9	30
41–50	11	36.66	8	26.66
51–60	6	20	4	13.33
Total	30	100	30	
Mean	40.03		37.36	
Sd	12.04		11.74	
p value = 0.388				
Sex				
Male	18	60	16	53.34
Female	12	40	14	46.66
Total	30	100	30	100
ASA				
I	17	56.66	20	66.66
II	13	43.34	10	33.34
Total	30	100	30	100

There was no statistically significant difference ($p > 0.05$) between the two groups in mean heart rate (Fig. 4).

There was no statistically significant difference ($p > 0.05$) between the two groups with respect to PONV as Fisher's exact test statistic value is 1 (Table 2).

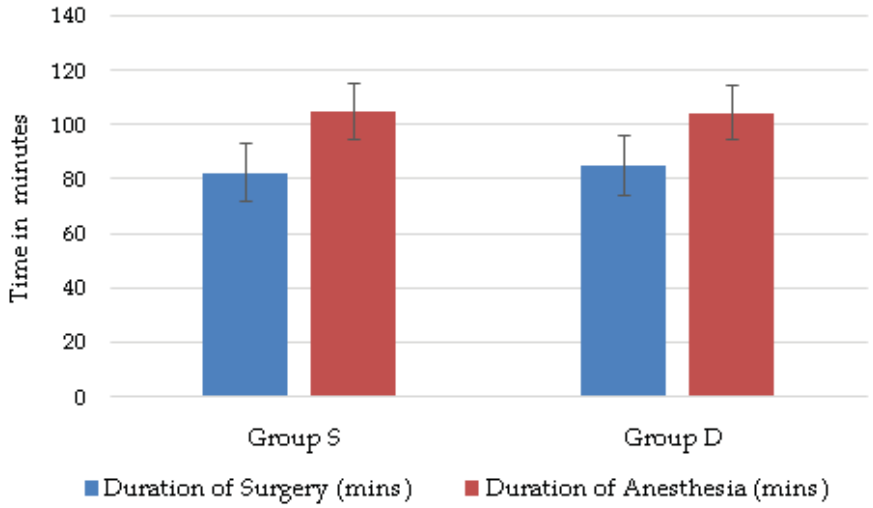

Fig. 1: Comparison of mean duration of Anesthesia and mean duration of Surgery of groups

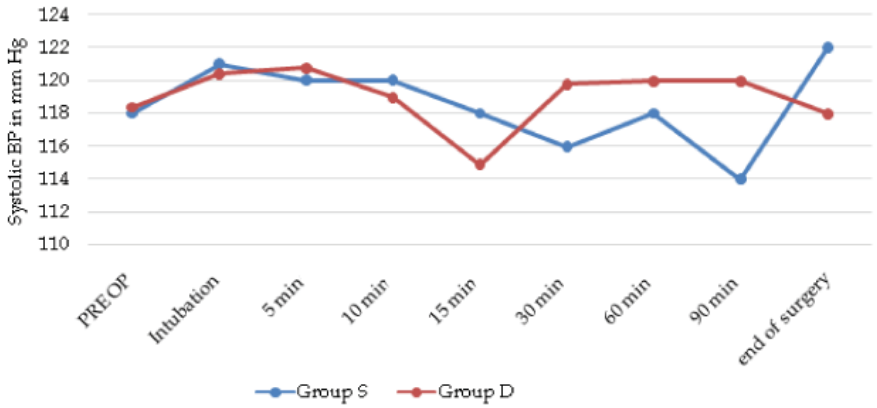

Fig. 2: Comparison of Systolic BP of groups

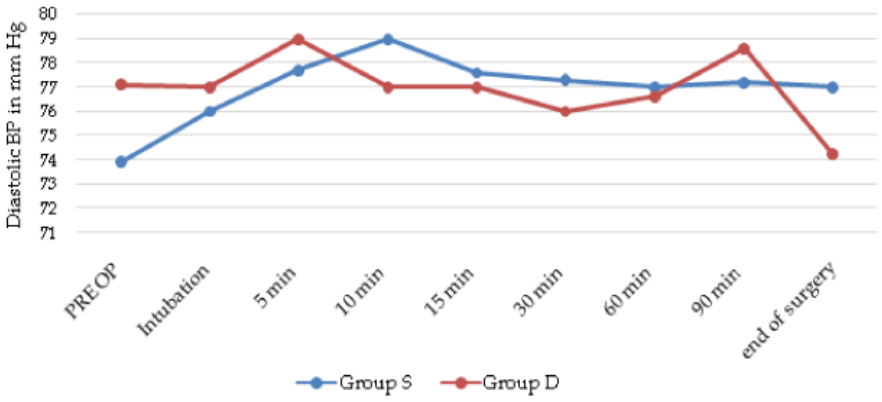

Fig. 3: Comparison of Diastolic BP between groups

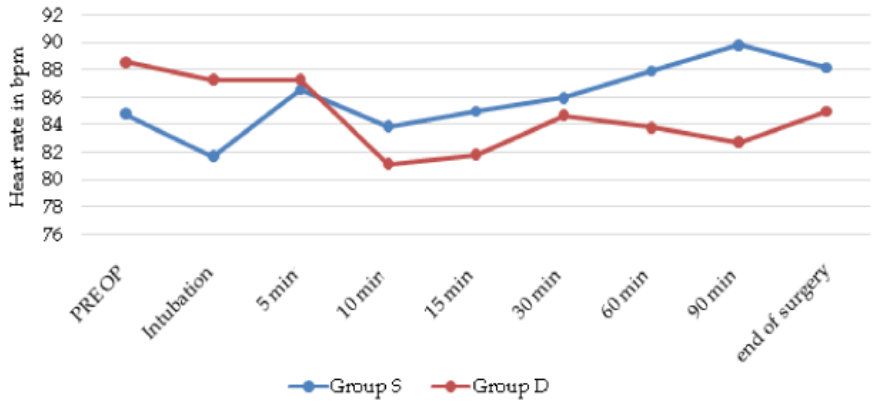

Fig. 4: Comparison of mean Heart rate between groups

Table 2: Comparison of PONV in first 24 Hrs in Groups

PONV	Group S		Group D	
	Number of cases	Percentages	Number of cases	Percentages
Yes	7	23.33	8	26.66
No	23	76.66	22	73.33
Total	30	100	30	100

Discussion

Middle ear surgeries requires a bloodless, motionless operative field, non-fluctuant hemodynamics, and a reduced incidence of postoperative morbidities especially nausea and vomiting (PONV). This study assesses intraoperative and perioperative outcomes (PONV) using Desflurane or Sevoflurane anesthesia for middle ear surgery. The quest for an ideal anesthetic agent, which subserves the otologic goals has now ushered us into an era whereby, sevoflurane and desflurane have gained popularity. The two anesthetic agents in our study appear to subserve the objectives of maintaining hemodynamic stability, providing adequate conditions.

Patients were selected between the age of 12 and 60. The Mean age was (Mean ± SD) 40.03 ± 12.04 in Group S and Mean age was 37.36 ± 11.74 in Group D. The difference was statistically insignificant ($p > 0.05$) i.e ($p = 0.38$). The difference in average preoperative heart rate was statistically not significant ($p = 0.27$). Preoperative mean pulse rate in Group S 84.8 ± 13.39 and in Group D 88.66 ± 13.55. The preoperative Systolic BP (SBP) in Group S 118.33 ± 11.13 and in Group D 118.4 ± 9.84 and differences were observed that there are statistically insignificant ($p > 0.05$) i.e. ($p = 0.98$).

The Preoperative Diastolic BP (DBP) in Group S 73.93 ± 6.79 and in Group D 77.13 ± 6.14 and differences were observed that there are statistically insignificant ($p > 0.05$) i.e. ($p = 0.06$).

All patients were followed in the intraoperative period for hemodynamics (heart rate, SBP and DBP). Recordings were done during intubation, at the intervals of 5, 10, 15, 30 min and every 30 min thereafter intraoperatively.

Mayur Patel *et al.*[1] compared intraoperative hemodynamic profile of desflurane and sevoflurane as maintenance anesthetic in patients undergoing day care gynecological laparoscopic surgery. A prospective randomized single-blind study was conducted in 100 female patients belonging to the American Society of Anesthesiologists grade I or II. Patients were randomized into two groups to receive either desflurane (Group D; $n = 50$) or sevoflurane (Group S; $n = 50$) for maintenance of anesthesia.

Mayur Patel *et al.*[1] based on the above parameters, reported that intraoperative hemodynamic parameters are similar in both desflurane and sevoflurane anesthesia which is in concordance with our study.

Fraga *et al.*[2] compared the MAP, ICP, and cerebral perfusion pressure (CPP) using 1 MAC of either isoflurane or desflurane (with 60% N_2O) in normocapneic patients undergoing craniotomy for supratentorial brain tumors. The ICP measurements throughout the study did not change within each group compared with baseline values and they did not find any significant difference of MAP, ICP, and CPP between the two groups. Our study results have shown that the hemodynamic parameters in both the groups were comparable similar to the

results of the above study and we did not include measurement of ICP in this study.

Sponheim *et al.*[3] reported a dose-dependent and clinically similar increase ICP and reduced MAP with $p < 0.001$ and CPP at 0.5 and 1.0 MAC of isoflurane, sevoflurane and desflurane in N_2O (60%) in hypocapneic children of study population of 36 divided into 3 groups of 12 each. They concluded that 0.5 and 1.0 MAC of isoflurane, sevoflurane and desflurane in N_2O all increased ICP and reduced MAP and CPP in a dose dependant manner. In our study, SBP and DBP values (indicating MAP) between the two groups were not statistically significant and we did not compare the effect on ICP.

White *et al.*[4] studied the hemodynamics, emergence, and recovery characteristics of sevoflurane with those of desflurane in nitrous oxide anesthesia and concluded that the groups did not differ in these hemodynamic measures. Findings in our study are consistent with the above study.

The current findings are consistent with previously published comparative study conducted by Heavner *et al.*[5] demonstrating that sevoflurane and desflurane provided similar intraoperative conditions during the maintenance period. The study by Nathanson *et al.*[6] suggested that sevoflurane and desflurane provided similar intraoperative conditions during the maintenance period. Although early recovery was faster with desflurane, there was no difference in the intermediate recovery end points. Gergin *et al.*[7] concluded intraoperative cardiovascular stability was easily achieved with both sevoflurane and desflurane, with MAP and HR maintained at ± 20% baseline values during the maintenance period. Although HR reduced below baseline values, reduction was less in desflurane group.

In conclusion, desflurane like sevoflurane maintains hemodynamic stability during intraop period. Although duration of anesthesia was longer early recovery profile was rapid in desflurane group. In our study, though a fall in heart rate with desflurane was not much appreciable, heart rate between Group S and Group D remained comparable. SBP and DBP (indicating MAP) values along with HR showed no statistical significance.

All patients were followed postoperatively for PONV during the first 24 hours. There was no statistically significant difference ($p > 0.05$) between the two groups with respect to PONV as Fisher's exact test statistic value is 1. Gupta *et al.*[8] did systemic analysis of recovery after ambulatory surgery comparing isoflurane, sevoflurane, and desflurane with a conclusion that early recovery and time to obey was significantly less with desflurane when compared to sevoflurane and isoflurane. They also observed that time to home readiness was 5 min earlier with sevoflurane as compared to isoflurane and other parameters such as pain, N/V were comparable.

Our study showed similar results, except that we did not compare recovery parameters.

The incidence of postoperative nausea and vomiting was similar in both the groups, consistent with the study by Kim *et al.*[9] who also found that late recovery profiles and incidences of postoperative side effects were similar after desflurane and sevoflurane. Our study was in concordance with this study.

Conclusion

This study was conducted to compare the intraoperative hemodynamics and postoperative nausea and vomiting in patients undergoing Middle ear surgeries in general anesthesia with a sevoflurane/desflurane based technique.

Intraoperative hemodynamics in these patients was studied in relation to variables like Heart rate, Systolic blood pressure and Diastolic blood pressure along with presence/absence of postoperative nausea and vomiting in 24 hrs. Concluded no significant difference was found in terms of intraoperative hemodynamics and postoperative nausea and vomiting in patients receiving general anesthesia with sevoflurane and desflurane as inhalational agents for Middle ear surgeries.

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Original Research Article

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Comparison of Hemodynamic Response Among IV Butorphanol and Dexmedetomidine as a Premedication in Laparoscopic Cholecystectomy

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Abstract

Background: In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation due to noxious stimuli of the upper airway. To minimize this various drugs have been used. Newer opioids like butorphanol, and dexmedetomidine have significant role to suppress hemodynamic changes during laryngoscopy, intubation and pneumoperitoneum. So we have compared the intravenous butorphanol and dexmedetomidine to reduce stress response during laryngoscopy in laparoscopic cholecystectomy. *Materials and Methods:* The study was carried on 100 patients of both sex with comparable characteristics and of ASA Grade I and II physical status. Patients were allocated into two groups: Group B inj. Butorphanol 30 µg/kg was given 5 minutes before induction and Group D inj. Dexmedetomidine 1 µg/kg diluted in 10 ml normal saline, was given in 10 minutes by infusion pump. *Results:* The rise in heart rate and blood pressure was less in Dexmedetomidine group as compared to Butorphanol. *Conclusions:* Dexmedetomidine is better in attenuating the stress response during laryngoscopy, intubation and pneumoperitoneum as compared to butorphanol.

Keywords: Dexmedetomidine; Butorphanol; Laparoscopic Cholecystectomy; hemodynamic response; pneumoperitoneum; laryngoscopy.

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Introduction

In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation due to noxious stimuli of the upper airway.[1] The rise in Blood pressure and heart rate is usually transient occurring 30 seconds after intubation and lasting for less than 10 minutes.[2] To minimize these adverse effects various drugs have been used as premedicant. Benzodiazepines as anxiolytic, anticholinergic to counteract vagal reflexes and opioids for analgesia are in common practice. The basic physiological or hemodynamic changes occurring during pneumoperitoneum in laparoscopy due to systemic absorption of carbon dioxide (CO_2) and reverse Trendelenburg position. To avoid these hemodynamic changes, different techniques and drugs like opioids, sedatives, beta blockers, iv lignocaine and others have been used with their merits and demerits.[3] Newer opioids like butorphanol, and other drugs like dexmedetomidine have significant role to suppress hemodynamic changes during laryngoscopy and pneumoperitoneum. Butorphanol is a lipid-soluble

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narcotic agent with strong κ-receptor agonist and weak μ-receptor agonist/antagonist activity. The above-mentioned narcotic analgesics have been used frequently for postoperative analgesia.[4] The analgesic effect of Butorphanol is influenced by the route of administration. Onset of analgesia is within a few minutes for intravenous administration and within 15 minutes for intramuscular injection. Peak analgesic activity occurs within 30 to 60 minutes following intravenous administration. Dexmedetomidine Is a highly selective α_2 adrenergic receptor agonist with sedative, analgesic, and antianxiety activity.[5,6] Introduced in clinical practice in United States in 1999 and approved by FDA. α_2 adrenergic agonists are used for sedation and premedication prior to general anesthesia in several patients. Racemic medetomidine has a binding ratio of 1620:1 (α_2:α_1) 10 and its d-enantiomer, dexmedetomidine is even more selective. Advantages of α_2-agonists include potent, predictable sedation[7], analgesia, reduced anesthetic requirement, and reversibility.[8] Dexmedetomidine also causes dose-dependent hypotension, bradycardia, and sedation. Dexmedetomidine decreases the heart rate and blood pressure by decreasing plasma levels of norepinephrine and epinephrine.[9] Dexmedetomidine and butorphanol can be used safely and effectively for postoperative analgesia in patients undergoing laparoscopy. The use of Dexmedetomidine 1 μg/kg and butorphanol 30 μg/kg is particularly beneficial in these patients.[10] So in this study we have compared the intravenous butorphanol and dexmedetomidine to reduce the hemodynamic stress response during laryngoscopy, intubation and pneumoperitoneum.

Aims and Objectives

To compare the effect of intravenous butorphanol and dexmedetomidine on the hemodynamic cardiovascular responses as premedication in laparoscopic cholecystectomy.

Following parameters were assessed

Heart rate and Non-Invasive Blood Pressure, SpO_2, $EtCO_2$.

Baseline vitals

Pre-intubation vitals

Post-intubation vitals till the end of surgery at specified intervals

Post-extubation vitals till 10 min after extubation at specified intervals

Materials and Methods

After obtaining ethical committee approval and informed consent from patient, the study entitled "*Comparison of Hemodynamic Response Among Intravenous Butorphanol and Dexmedetomidine as Premedication in Laparoscopic Cholecystectomy*" was carried on 100 patients of both sex with comparable characteristics and group of ASA Grade I and II physical status.

Following patients were excluded from the study

Patients of ASA Class III and above, Age <18 yrs and >60 yrs, Patients with cardiac illness, Patients with pulmonary illness, Patient with nervous system disorders, Pregnant or nursing women, Known hypersensitive to any of the study medication, Patients with anticipated difficult intubation, Duration of laryngoscopy and endotracheal intubation >30 seconds, Chronic narcotic user, Patient refusal.

Anesthesia protocol

All the patients scheduled for laparoscopic cholecystectomy visited a day prior to surgery and a thorough pre-anesthetic examination was done. All routine investigations were done and reviewed. Patients were kept fasting for 8 hrs prior to the surgery. A written and informed consent was obtained from the patients. All patients were premedicated with tab ranitidine 150 mg and tab alprazolam 0.25 mg night before the surgery. The patients were assigned to one of the two groups using a "slips of paper in a box" technique. The grouping is as follows: Group (B) – i.v. Butorphanol (30 μg/kg) Group (D) – i.v. Dexmedetomidine (1 μg/kg) A large bore (18) intravenous canula was inserted for drug and fluid administration. All the patients were premedicated using inj midazolam 1 mg iv, Inj. Ondansetron 0.08 mg/kg IV inj. glycopyrrolate 0.2 mg iv prior to induction of anesthesia. Baseline parameters of hemodynamic and pulmonary status were measured 5 minutes after arrival of patient in the operating room. In Group B inj. Butorphanol 30 μg/kg was given 5 minutes before induction. In Group D inj. Dexmedetomidine 1 μg/kg diluted in 10 ml normal saline, was given in 10 minutes by infusion pump. Patients were induced with inj. propofol 2 mg/kg iv. and inj. succinylcholine 1.5 mg/kg i.v. There after laryngoscopy and tracheal intubation was performed with cuffed endotracheal tube of appropriate size. Anesthesia was maintained with

66:33 (N_2O:O_2) ventilation and isoflurane was used in 0.5–1% concentration. Adequate skeletal muscle relaxation was maintained with loading dose of vecuronium (0.08 mg/kg) followed by intermittent i.v boluses of 0.02 mg/kg. Isoflurane was stopped 10 minutes prior to the end of surgery and N_2O was discontinued after skin closure. At the end of anesthesia, the neuromuscular blockade was antagonized with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01 mg/kg intravenously.

Following parameters were monitored at specific intervals

1. Heart rate
2. Systolic blood pressure
3. Diastolic blood pressure
4. SpO_2
5. $EtCO_2$ (after intubation till extubation)

At baseline, Preintubation, 1 min after intubation, 3 min after intubation 5 min after intubation, Every 5 min till 10 min after extubation patients were observed for 1 hour after extubation complications like, bradycardia, hypotension, abnormal ECG, nausea and vomiting were recorded during the study. The results were compared and statistically analyzed.

Statistical Analysis: The results obtained in the study were presented in a tabulated manner as Mean ± SD and were analyzed using with Statistical Package for Social Sciences (SPSS 23.0). The demographic data for categorical variables were done by Independent samples t-test, paired t-test, chi-square test, or suitable stats was used for the purpose of analysis of data. *p* value of <0.05 was considered statistically significant.

Results

Table 1: Distribution of Patients according to their Age and Gender

	Group B (N = 50)	Group D (N = 50)	*p* value
Age (year)	47.64 ± 9.1	46.16 ± 9.3	0.423
Male	22 (44.0)	29 (58.0)	0.161
Female	28 (56.0)	21 (42.0)	

The distribution of patients on the basis of their age and gender in both the groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 1).

Table 2: ASA Grade between Two Groups

ASA Grade	Group B (N=50) (%)	Group D (N=50) (%)	*p* value
I	34 (68%)	31 (62%)	0.529
II	16 (32%)	19 (38%)	

The distribution of patients on the basis of ASA grade in both the groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 2).

Table 3: Comparison of Mean duration of Surgery in both Groups

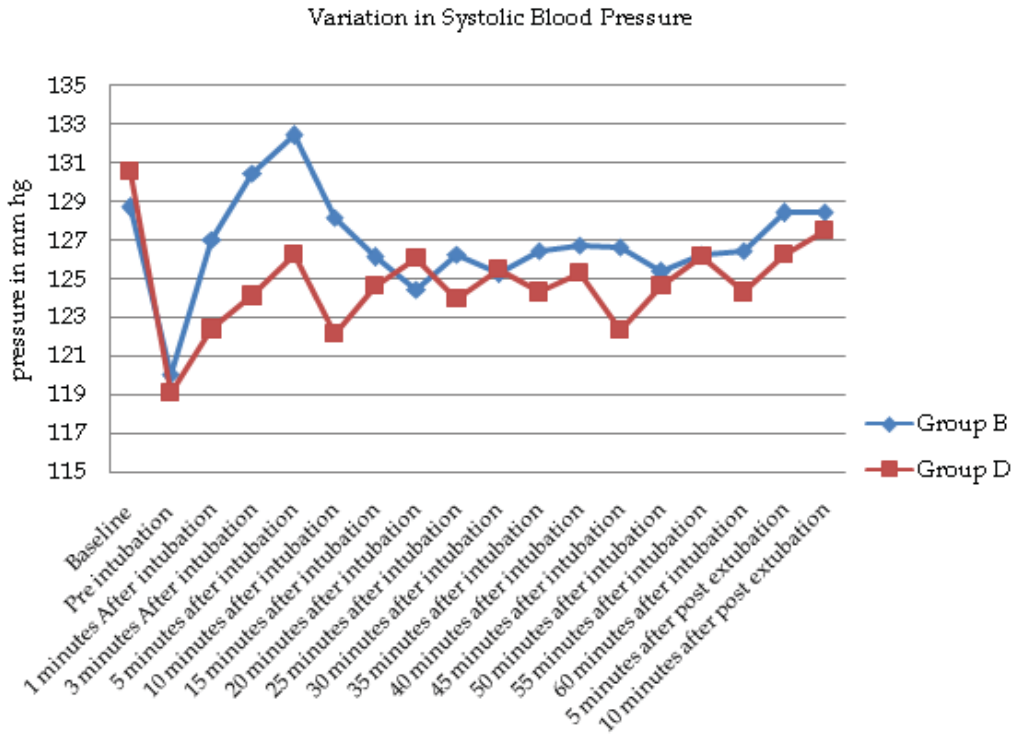
	Group B	Group D	
Duration of surgery (min)	Mean ± SD	Mean ± SD	*p* value
	54.26 ± 4.2	53.02 ± 4.37	0.151

The mean duration of surgery in both groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 3).

Table 4: Variation of Systolic (SBP) and Diastolic (DBP) Blood Pressure

		Systolic blood pressure			Diastolic blood pressure		
Time	T	Group B	Group D	*p*-value	Group B	Group D	*p*-value
Baseline	T0	128.70 ± 14.60	130.56 ± 13.03	0.503	82.06 ± 8.18	80.28 ± 7.74	0.266
Pre-intubation		120.08 ± 6.34	119.08 ± 10.59	0.254	74.58 ± 3.68	72.40 ± 5.74	0.326
1 minute after intubation	T1	127.02 ± 14.45	122.40 ± 15.04	0.120	78.30 ± 7.78	79.80 ± 7.61	0.332
3 minutes after intubation	T3	130.44 ± 9.12	124.12 ± 13.71	0.008	82.16 ± 7.91	81.12 ± 8.10	0.017
5 minutes after intubation	T5	132.42 ± 10.00	126.28 ± 17.28	0.032	83.44 ± 8.30	82.16 ± 7.91	0.043
10 minutes after intubation	T10	128.18 ± 14.22	122.18 ± 15.21	0.044	81.32 ± 8.10	80.12 ± 7.98	0.457
15 minutes after intubation	T15	126.12 ± 14.85	124.64 ± 14.31	0.013	81.56 ± 8.83	79.56 ± 6.62	0.023
20 minutes after intubation	T20	124.46 ± 13.29	126.10 ± 16.17	0.058	80.56 ± 7.84	78.20 ± 6.00	0.094
25 minutes after intubation	T25	126.26 ± 13.24	124.0 ± 17.81	0.047	80.12 ± 7.98	78.08 ± 6.41	0.016
30 minutes after intubation	T30	125.26 ± 11.09	125.48 ± 15.73	0.035	79.28 ± 8.86	76.30 ± 6.11	0.043
35 minutes after intubation	T35	126.46 ± 10.48	124.30 ± 14.57	0.039	79.70 ± 9.08	75.22 ± 5.80	0.004
40 minutes after intubation	T40	126.76 ± 10.65	125.34 ± 13.78	0.055	79.22 ± 9.07	76.44 ± 6.32	0.078
45 minutes after intubation	T45	126.66 ± 13.65	122.36 ± 13.73	0.019	78.08 ± 6.41	77.42 ± 5.66	0.586
50 minutes after intubation	T50	125.36 ± 9.96	124.64 ± 14.31	0.770	78.12 ± 6.96	77.18 ± 5.74	0.463

Time	T	Systolic blood pressure			Diastolic blood pressure		
		Group B	Group D	*p*-value	Group B	Group D	*p*-value
55 minutes after intubation	T55	126.24 ± 11.83	126.14 ± 14.18	0.969	77.32 ± 7.83	79.42 ± 6.91	0.158
60 minutes after intubation	T60	126.46 ± 11.70	124.30 ± 11.12	0.046	78.48 ± 7.34	80.06 ± 7.30	0.283
5 minutes after post-extubation		128.40 ± 13.74	126.28 ± 17.28	0.049	80.12 ± 7.98	81.18 ± 7.59	0.001
10 minutes after post-extubation		128.44 ± 14.00	127.48 ± 18.55	0.770	81.32 ± 8.00	80.14 ± 7.76	0.001



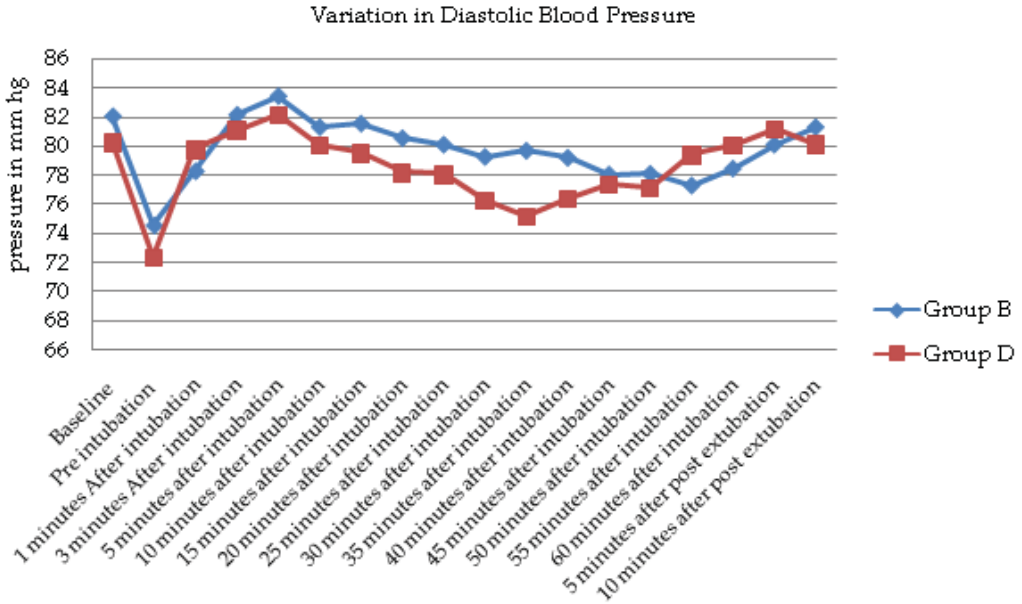


Table 5: Showing Variation in Heart Rate (HR)

Time	T	Group B Mean ± S.D	Group D Mean ± S.D	*p*-value
Baseline	T0	77.34 ± 7.26	77.58 ± 4.12	0.839
Pre-intubation		71.22 ± 13.26	68.76 ± 11.27	0.028
1 minute after intubation	T1	77.42 ± 7.25	69.34 ± 10.25	0.001
3 minutes after intubation	T3	78.56 ± 6.16	73.74 ± 6.65	0.003
5 minutes after intubation	T5	82.84 ± 5.83	75.48 ± 7.41	0.001
10 minutes after intubation	T10	80.34 ± 15.29	73.78 ± 6.64	0.006
15 minutes after intubation	T15	82.24 ± 14.74	74.54 ± 7.09	0.001
20 minutes after intubation	T20	80.56 ± 11.60	75.22 ± 6.32	0.005
25 minutes after intubation	T25	77.42 ± 7.25	75.32 ± 6.32	0.125
30 minutes after intubation	T30	78.54 ± 7.39	74.48 ± 6.78	0.005
35 minutes after intubation	T35	77.42 ± 7.25	75.08 ± 7.41	0.113
40 minutes after intubation	T40	78.20 ± 7.39	73.78 ± 6.64	0.001
45 minutes after intubation	T45	77.10 ± 6.90	74.54 ± 7.09	0.070
50 minutes after intubation	T50	78.32 ± 7.00	75.14 ± 7.87	0.035
55 minutes after intubation	T55	77.42 ± 7.25	77.58 ± 4.12	0.892
60 minutes after intubation	T60	77.88 ± 17.89	76.36 ± 8.12	0.585
5 minutes after post-extubation		78.16 ± 6.87	76.24 ± 7.83	0.015
10 minutes after post-extubation		77.38 ± 7.22	77.22 ± 6.16	0.905

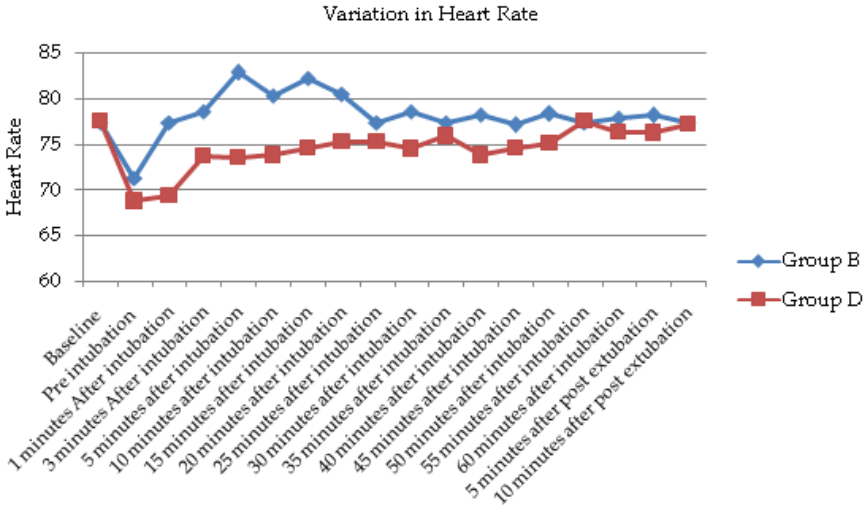


Table 6: Showing Variation in $EtCO_2$ and SpO_2

Time	T	$EtCO_2$			SpO_2		
		Group B Mean ± S.D	Group D Mean ± S.D	*p*-value	Group B Mean ± S.D	Group D Mean ± S.D	*p*-value
Baseline	T0				99.40 ± 0.60	99.46 ± 0.81	0.674
Pre intubation					99.12 ± 0.71	98.86 ± 1.06	0.152
1 minute after intubation	T1	28.08 ± 3.02	28.08 ± 3.67	1.000	99.14 ± 0.78	98.80 ± 1.27	0.109
3 minutes after intubation	T3	29.78 ± 4.40	29.24 ± 3.37	0.492	98.66 ± 1.20	98.44 ± 1.24	0.369
5 minutes after intubation	T5	30.06 ± 2.28	29.58 ± 3.45	0.413	98.58 ± 1.24	98.10 ± 1.31	0.062
10 minutes after intubation	T10	30.74 ± 2.35	29.96 ± 3.03	0.153	98.60 ± 1.24	98.05 ± 1.64	0.061
15 minutes after intubation	T15	31.14 ± 4.14	30.08 ± 3.07	0.149	98.68 ± 1.06	98.34 ± 1.36	0.166
20 minutes after intubation	T20	31.64 ± 5.37	29.88 ± 6.04	0.126	98.66 ± 1.22	98.46 ± 1.40	0.448
25 minutes after intubation	T25	31.90 ± 5.53	29.64 ± 6.86	0.072	98.12 ± 0.98	97.90 ± 1.58	0.404
30 minutes after intubation	T30	32.04 ± 5.30	30.04 ± 7.13	0.059	98.18 ± 0.85	97.88 ± 1.42	0.202
35 minutes after intubation	T35	32.44 ± 6.41	30.04 ± 7.13	0.078	98.28 ± 0.87	97.84 ± 1.54	0.081
40 minutes after intubation	T40	32.52 ± 6.50	31.22 ± 7.22	0.346	98.18 ± 0.87	98.10 ± 1.12	0.690
45 minutes after intubation	T45	32.12 ± 6.24	32.18 ± 7.62	0.965	98.38 ± 0.63	98.78 ± 1.48	0.081
50 minutes after intubation	T50	33.48 ± 3.18	33.26 ± 7.49	0.848	98.08 ± 1.17	98.34 ± 1.35	0.306
55 minutes after intubation	T55	34.52 ± 3.98	34.22 ± 7.41	0.801	98.76 ± 1.29	98.44 ± 1.44	0.244
60 minutes after intubation	T60	35.24 ± 2.79	35.08 ± 6.57	0.874	98.74 ± 1.07	98.52 ± 1.69	0.438
5 minutes after extubation					98.52 ± 1.96	98.30 ± 1.52	0.389
10 minutes after extubation					97.88 ± 1.02	97.50 ± 1.47	0.136

Table 7: Side Effects

Side effects	Group B (%)	Group D (%)	*p* value
Nausea	17 (34)	9 (18)	0.068
Vomiting	12 (24)	3 (6)	0.011
Hypotension	2 (4)	6 (12)	0.398
Bradycardia	3 (6)	5 (10)	0.461

Discussion

Demographic data showed that Group B (butorphanol) and Group D (dexmedetomidine) were comparable in terms of number of patients, age, sex, weight, ASA status, types and duration of laparoscopic surgeries ($p > 0.05$).

Baseline parameters: Present study shows, baseline parameters of hemodynamic like HR, SBP, DBP and SpO_2 were comparable between both groups ($p > 0.05$)

Variation of systolic (SBP) and diastolic (DBP) blood pressure

As shown in table 4 baseline SBP and DBP were comparable between both groups. The blood pressure start to rise during laryngoscopy and intubation. The rise in blood pressure was more in Group (B) as compared to Group (D). Then blood pressure starts declining and at around 10 min come back to baseline value in Group (B) but remain below baseline in Group (D) and below base line during preoperative period. Our result is comparable with Vaswani JP *et al.*[11] they found that there is significantly less increase in blood pressure of dexmedetomidine group after laryngoscopy, intubation, pneumoperitoneum, and in intraoperative period and after extubation. Patel CR *et al.*[12] found lesser increase in SBP, DBP after intubation with dexmedetomidine 1 µg/kg given as loading dose prior to induction. Pandit and Kothary *et al.*[13] compared fentanyl with butorphanol for outpatient laparoscopic procedures. They concluded that butorphanol gives better protection against sympathetic stimulation to tracheal intubation. Rao MH *et al.*[14] observed very minimal changes in pulse rate in both the butorphanol and fentanyl groups. Fall in pulse rate in group butorphanol was more in comparison to fentanyl throughout peri-operative period.

Variation in Heart Rate (HR)

As shown in Table 5 baseline HR was comparable between both groups. The heart rate start to rise during laryngoscopy and intubation. The rise in heart rate was more in Group (B) as compare to Group (D). Then heart rate starts declining and at arround 10 min come back to baseline value in Group (B) but below baseline in Group (D) and remain below baseline during preoperative period. Our result is comparable with Vaswani JP *et al.*[11] in their observation found that there is significantly less increase in heart rate of dexmedetomidine group after intubation, after pneumoperitoneum, in intraoperative period and after extubation. Patel CR *et al.*[12] found lesser increase in heart rate after intubation with dexmedetomidine 1 µg/kg given as loading dose prior to induction. Pandit and Kothary *et al.*[13] compared fentanyl with butorphanol for outpatient laparoscopic procedures. They concluded that butorphanol gives better protection against sympathetic stimulation to tracheal intubation. Rao MH *et al.*[14] observed very minimal changes in pulse rate in both the butorphanol and fentanyl groups. Fall in pulse rate in group butorphanol was more in comparison to Group fentanyl throughout perioperative period.

Variation in $EtCO_2$ and SpO_2

As shown in Table 6 there were no significant changes in $EtCO_2$ and SpO_2 in both the groups in intra and intergroup study. These findings were similar to study was conducted by Rao MH *et al.*[14] where no significant changes were observed in $EtCO_2$ and SpO_2 in butorphanol group. Vaswani JP *et al.*[11] observed that there was no significant difference in pre- and intraoperative SpO_2 and $EtCO_2$ values.

Side Effects

As shown in Table 7 in nausea and vomiting was more in Group (B) as compare to Group (D). But hypotension and bradycardia was more in Group (D). as compare to group (B). Vaswani JP *et al.*[11] used IV dexmedetomidine they found intraoperative hypertension and bradycardia.

Conclusion

We found that butorphanol and dexmedetomidine both provide adequate sedation and analgesia. But patients who received dexmedetomidine as premedication the rise in heart rate and blood pressure after laryngoscopy and intubation was less as compared to the patients who received butorphanol, in which the rise in heart rate and blood pressure after laryngoscopy and intubation was more. So we found that dexmedetomidine is

better in attenuating the stress response during laryngoscopy, intubation and pneumoperitoneum as compared to butorphanol.

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Comparative Study of the Effects of Intravenous Etomidate and Propofol Used for Induction of General Anesthesia

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Abstract

Aims and objectives: To compare hemodynamic responses and side effects while induction and intubation with intravenous etomidate and propofol. *Material and Methods:* We conducted a prospective, randomized, double-blind study, in which 100 patients undergoing elective surgery under general anesthesia were enrolled for the study. Patients were randomly distributed in two groups (50 in each group). Group P received propofol at 2 mg/kg and Group E received etomidate at 0.2 mg/kg. *Results:* When both the groups were compared it was found out there was statistically significant difference in Group P as compared to Group E in terms of decrease in HR , SBP , DBP, MAP, incidence of myoclonic movements and incidence of pain on injection. There was no overall complication in both groups. *Conclusion:* Induction of anesthesia with etomidate had more stable hemodynamic conditions as compared to propofol. There was significant reduction in heart rate and blood pressure leading to hypotension in propofol group while etomidate group had stable hemodynamics. Incidence and severity of pain on injection was more with propofol while incidence of myoclonus was more with etomidate. Overall, it was concluded that etomidate was a better choice for induction of anesthesia, only drawback being higher incidence of myoclonus.

Keywords: Hemodynamic responses; Etomidate; Propofol.

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Introduction

For general anesthesia, an idyllic inducing agent must have hemodynamic stability, negligible respiratory side effects and rapid clearance. Currently etomidate and propofol are most common rapid acting inducing agents.[1–3] Propofol is one of the regularly used drugs for induction of general anesthesia. Due to its satisfactory recovery, short half-life and quick elimination from the blood circulation causing less sedative effects and vomiting, this agent is used more commonly.[4] The most significant side effects of this drug are unstable hemodynamics and cardiovascular complications. Propofol can lead to profound reduction in heart rate.[5–7] In an analysis done on 25000 patients, 4.2% of patients had fall in heart rate after administration of propofol.[8] Induction of anesthesia with propofol could drop arterial pressures as much as 25 to 40% in all patients irrespective of any underlying conditions.[9,10] Reduction of preload and after load of heart is the cause behind propofol induced hypotension. This is not harmonized with heart's compensatory mechanism and were intensified

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when high dose is given or when the drug is infused fastly.[11,12] Etomidate is also a short-acting drug, used for induction and maintenance of anesthesia.[13] Nausea and vomiting, myoclonic movements and hiccups are common side effects of etomidate.[14–16] One of the most important side effects of this drug is the adrenocortical suppression by reversible inhibition of 11 beta hydroxylase enzyme but this effect is not so common. Administration of etomidate leads to a stable hemodynamic status.[14–19] This study was performed to explore the cardiovascular response during the induction of anesthesia with etomidate and propofol and to assess pain on injection and myoclonic movements after injecting respective drugs in elective surgeries under general anesthesia due to varied range of consequences and controversies in other studies.

Aims and Objectives

1. To compare hemodynamic responses while induction and intubation with intravenous etomidate and propofol.
2. To compare the myoclonus, pain on injection or any other side effects during induction with both the drugs.

Materials and Methods

After having approval from the institutional scientific and ethics committee, a prospective randomized comparative study on 100 patients was undertaken in the Department of Anesthesiology, M.G.M. Medical College, Kamothe, Navi Mumbai. This included history of any systemic diseases like hypertension, bronchial asthma, cardiac and/or pulmonary disorder, psychiatric disorder, substance abuse and allergy to any drugs. Additionally a thorough general and systemic examination was carried out for each patient enrolled. The study was conducted as a double-blind trial from May, 2016 to May, 2017 at Mahatma Gandhi Mission Institute of Medical Sciences, Kamothe, Navi Mumbai. Sixty patients scheduled for elective surgery under general anesthesia were randomized into two groups.

Sample size: Sixty patients were enrolled for the study (randomly distributed in two Groups D and C [n = 30 in each group]. Group D dexmedetomidine group and Group C control group).

Patients age 18 to 50 years of both sexes with ASA grade I and II and hemodynamically stable were included in the study.

Patients with vascular diseases, habituation to analgesics (cardiac, pulmonary, neurological disease), allergy to the drug to be used were excluded.

In this study a total of 100 patients undergoing elective surgery under general anesthesia were randomized in two groups comprising 50 patients each. In order randomize computer generated randomization table was used. Among the two groups, the first group (Group P) underwent general anesthesia by Propofol and the second group (Group E) by Etomidate. All the patients underwent a thorough pre-anesthetic check up and were investigated for all the routine and special investigations. Study was carried out after taking the written informed consent from the patient.

Methodology: A detailed pre-anesthetic check-up of all patients were done including airway assessment, clinical history, general and systemic examination, routine biochemical investigations, chest X-ray and electrocardiography. All patients were kept fasting overnight. Patients were given Tablet Pantoprazole 40 mg and Tablet Alprazolam 0.5 mg on the day before surgery during pre-anesthetic evaluation. On entering the operation theater, IV line were secured. Monitors like Electrocardiogram (ECG), Non-invasive blood pressure monitor (NIBP) and pulse oximeter was connected and baseline parameters were recorded.

Patients were randomly assigned to propofol (P) group and etomidate (E) group. Baseline hemodynamic parameters were measured. Fentanyl 2 microgm/kg and Midazolam 0.02 mg/kg were given IV. Patients were preoxygenated with 100% oxygen for 3 minutes. Two minutes after fentanyl administration; anesthetic agents were injected. Propofol group was receive propofol at 2 mg/kg and etomidate group was receive etomidate at 0.2 mg/kg. Pain on injection and myoclonic movements were recorded, if any at induction. As soon as the onset of unconsciousness occurs consumed dose of anesthetic were recorded individually.

Endotracheal intubation was done using vecuronium 0.1 mg/kg and anesthesia were maintained as per institutional protocol. The cases in which tracheal intubation could be performed successfully within 30 seconds in a single attempt were included in the study. Reversal of residual neuromuscular blockade was done with neostigmine 0.05 mg/kg and glycopyrolate 0.008 mg/kg. Trachea was extubated after adequate recovery of muscle power and patients were

monitored postoperatively.

The patient's hemodynamic and cardiovascular indicators such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (O_2 sat) were recorded before induction (T1), before intubation (T2) and at 1 (T3), 3 (T4), 5 (T5), and 10 (T6) minutes afterward. The hemodynamic parameters before induction, i.e. T1 were taken as baseline. Hypertension was defined as increase in baseline SBP > 20% while hypotension as <20% of baseline, Tachycardia as HR > 20% of baseline and bradycardia were defined as <60 heart rate. Patient whose oxygen saturation was fall below 90% were considered to be desaturating.

Adverse effects such as pain on injection and myoclonus if any were recorded. Pain on injection was measured using four graded scale (0: no pain, 1: verbal complaint of pain, 2: withdrawal of the arm, 3: both verbal complaint and withdrawal of arm. Patients were observed visually for myoclonus and when present, myoclonus severity were graded. Degree of such muscular activity were scored as follows – 0: no myoclonus, 1: minor myoclonus, 2: moderate myoclonus, 3: severe myoclonus. The rescue drugs – IV Mephentramine 6 mg bolus was given if the mean arterial pressure (MAP) was drop by > 20% from baseline, IV Diltiazem 2.5 mg were used if MAP was increase by > 20% from the baseline and IV Esmolol 20 mg were employed in case the heart rate was rise above 100 beat per minute.

Results

The mean age among group P and E was 32.06 + 9.69 and 32.51 + respectively. Statistically, there was no noteworthy difference between the two groups (p = 0.82). The male : female ratio in Group P was 19 : 29 and in Group E was 29 : 18 which was comparable. The mean weight of patients in Group P was 57.98 + 5.76 and 56.77 + 6.29 which was statistically insignificant (p = 0.37).

The baseline SBP was comparable in both groups and had no statistically significant difference (p = 0.42). There was significant difference in SBP in both groups measured before intubation and after intubation at 1, 3, 5 and 10 minutes with p < 0.001 at all stages (Fig 1).

The baseline DBP was comparable and had no statistically noteworthy difference in both groups (p = 0.072). There was significant difference before intubation (p=0.032) and after intubation at 1 minute (p < 0.001), 3 minutes (p < 0.001), 5 minutes (p = 0.001) and 10 minutes (p = 0.003) in Group P and E (Fig 2).

The baseline MAP showed no statistically significant difference (p = 0.18) in baseline values amongst both groups. There was statistically substantial difference before intubation (p < 0.001) and after intubation at 1 minute (p < 0.001), 3 minutes (p < 0.001), 5 minutes (p = 0.017) and 10 minutes (p < 0.001) in Group P and E (Fig. 3).

Heart rate was comparable in both the groups and had no statistically significant difference in baseline values (p = 0.72). There was difference before intubation and after intubation but the difference was not statistically significant (p = 0.11 and p = 0.29 respectively). Heart rate at 3, 5 and 10 minutes showed significant difference amongst two groups (p = 0.008, p = 0.04 and p = 0.03 respectively) (Fig. 4).

Mean saturation for Group P was 98.9 + 0.7 and for Group E was 98.6 + 0.6 and showed no statistically noteworthy difference (p = 0.13). Mean time for laryngoscopy for Group P was 17.13 + 2.92 and for Droup E was 17.40 + 3.2 and was comparable. It showed no statistically significant difference (p = 0.66).

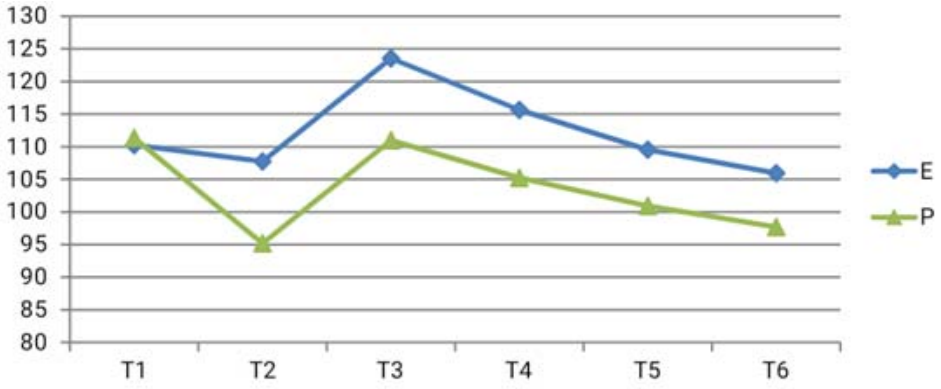

Fig. 1: Systolic Blood Pressure (SBP)

Incidence of myoclonic movements in Group P and E showed statistically substantial difference ($p < 0.05$). Incidence of pain on injection after administering the drug in Group P and E showed statistically significant difference ($p < 0.05$).

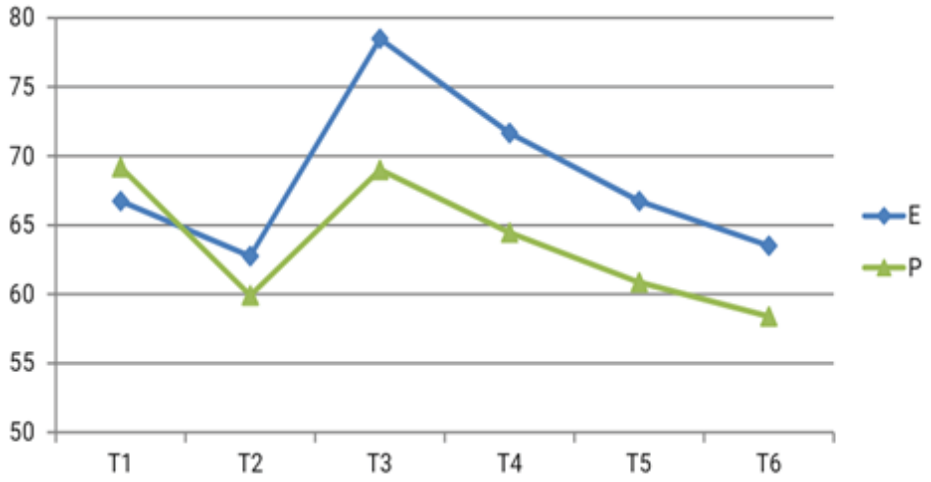

Fig. 2: Diastolic Blood Pressur (DBP)

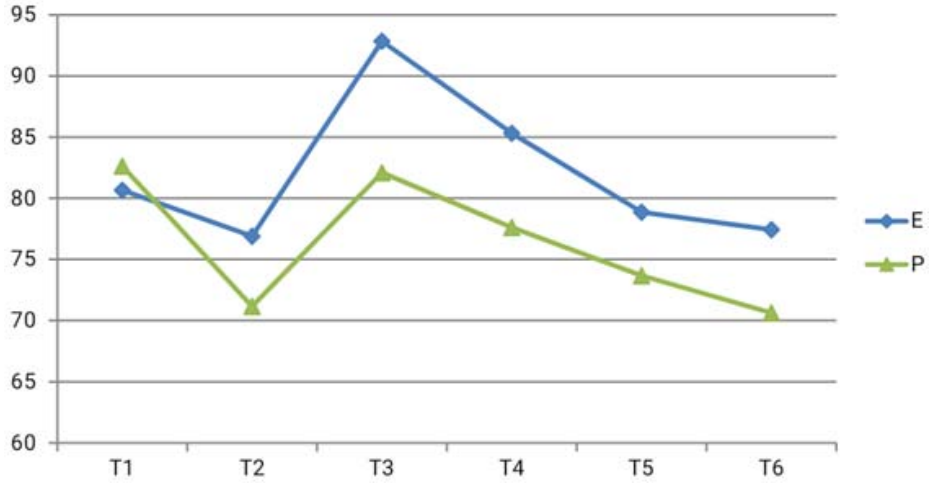

Fig. 3: Mean Arterial Pressure (MAP)

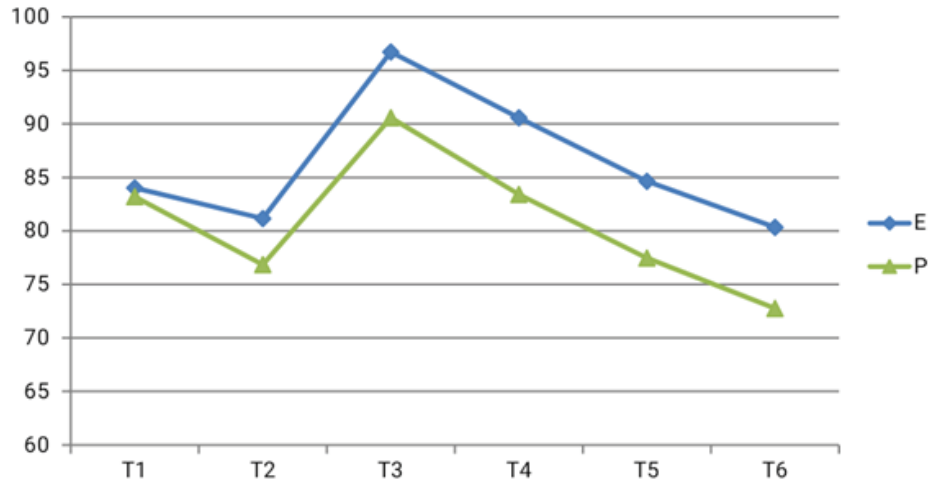

Fig. 4: Heart rate

Discussion

Demographic Profile

The mean age of patients in Groups P and E was 32.06 ± 9.69 years and 32.51 ± 9.13 years respectively. Statistically, there was no significant difference between the groups (p = 0.82). The mean weight of patients in Group 1 and Group 2 was 59.17 ± 9 and 60.43 ± 9.4 kilograms respectively. Statistically, there was no significant difference between the groups (p = 0.599). The mean weight of patients in Groups P and E was 57.98 ± 5.76 kg and 56.77 ± 6.29 kg respectively. Statistically, there was no significant difference between the groups (p = 0.37). The gender ratio (Male : Female) in patients of Group P was 29 : 19 and in patients of Group E was 18:29 and were comparable.

This was in settlement with study done by Ebert TJ, Muzi M where both groups were demographically similar and had no significant difference in age, height and weight.[20] A. Pandey (70) in his study also showed that demographic characteristics namely age, weight and sex distribution were similar in etomidate and propofol group.[21]

Arterial Blood Pressure:

In our study, arterial blood pressure was recorded before induction (T1), before intubation (T2) and at 1 (T3), 3 (T4), 5 (T5), and 10 (T6) minutes after intubation. Baseline systolic, diastolic blood pressures and mean arterial pressures in both the groups were comparable and variations were statistically insignificant. We observed that both systolic and diastolic BP reduced from the baseline values, mean SBP being 107.4 + 11.6 and 95.1 + 7.8 while mean DBP being 62.7 + 6.9 and 59.9 + 5.6 respectively after induction with etomidate and propofol. MAP also dropped from baseline values with mean value being 76.8 + 7.8 and 71 + 5.8 respectively with etomidate and propofol. We observed that there was marked reduction in all 3 parameters after induction with propofol as compared to that of etomidate which was statistically significantly (p values being <0.001, 0.032 and <0.001 for SBP, DBP and MAP respectively.

This is in agreement with study done by Ebert TJ, Muzi M, Berens R *et al.* in which both systolic and diastolic blood pressures were well maintained with etomidate but were decreased after induction with propofol.[20]

After intubation, blood pressure recordings were done at 1, 3, 5 and 10 minutes'. There was significant increase in all 3 parameters namely SBP, DBP and MAP (p values being < 0.001 at 1 and 3 minutes for all three parameters, < 0.001, 0.001 and 0.017 at 5 minutes and < 0.001, 0.003 and < 0.001 at 10 minutes of SBP, DBP and MAP respectively), as compared to before intubation values but in case of propofol, the arterial pressures did not increase more than the baseline values.

This is in settlement with the study done by Harris CE, Murray AM *et al.* on 303 patients in which it was observed that there was significant decrease in arterial pressures after induction with propofol and just prior to intubation was highly significantly lower than the baseline values as compared to etomidate.[22] Aggarwal Supriya *et al.* also concluded in their study on 100 patients that etomidate is better for its hemodynamic stability as compared to propofol.[23]

Pandey, N. Makhija *et al.* studied hemodynamic response on 100 patients and stated that SBP and DBP were significantly lower post induction in propofol group as compared to etomidate group suggesting that etomidate was associated with more hemodynamic stability on induction of anesthesia than propofol.[21] Study done by Fatma S, Sennur U *et al.* also recorded that etomidate is associated with hemodynamic stability of very high degree as compared to propofol.[24] Our result is also in agreement with the results stated by Miner J.R. *et al.* which concluded that there was a larger percentage of decrease in SBP in patients who received propofol than who received etomidate.[25]

In our study and in agreement with previous literatures, in spite of stimulus provided by intubation, arterial pressures remained lower than baseline values in propofol group as compared to etomidate. Hypotension occurring due to propofol is mainly because of decrease in sympathetic activity which leads to vasodilatation or direct effect of propofol on vascular smooth muscle while hemodynamic stability observed with etomidate can be because of its unique lack of effect on sympathetic nervous system and baroreceptor function.[22]

Heart Rate

In present study baseline heart rate was comparable between the two groups. We observed that heart rate decreased after induction in both the groups from the baseline values but the changes were not statistically significant (p = 0.11). After intubation there was rise in heart rate in both the groups at 1 and 3 minutes, significantly more rise in etomidate group than propofol group at 3 minutes (p = 0.008).

After 5 and 10 minutes of intubation heart rate fell back near the baseline values with etomidate group but showed statistically significant decrease in patients induced with propofol (p = 0.04 and p = 0.03 respectively at 5 and 10 minutes).

Gooding JM, Corssen G *et al.* in their study showed there was 10% rise in heart rate after induction with etomidate.[26] This is also in settlement with randomized controlled trial done on 60 adults by Shah SB, Chowdhury I *et al.* where post induction there was rise in patients allocated in etomidate group.[27] Harris CE, Murray AM observed that there were significant increases in heart rate in both groups (p < 0.01) but there was greater increase in those who received etomidate.[22] Ko YK *et al.* in his study on 46 patients observed that patients induced with propofol had significant decrease in heart rate and concluded that propofol precipitates vascular dilatation, decreases preload and afterload, and impairs myocardial contractility.[28]

Kaushal RP *et al.* also stated that there was significant decrease in cardiac output and cardiac index in patients induced with propofol than in those induced with etomidate.[29] Tachycardia and increase in arterial blood pressure are the two commonest cardiovascular response to intubation because of increased sympathetic activity.[22] Cardiovascular hemostasis is mediated by sympathetic nervous system which helps in modulating heart rate, myocardial contractility, arterial resistance and venous capacitance. Propofol seems to attenuate greatly the baroreflex changes in sympathetic activity that occurs in response to BP perturbations while during administration of etomidate there is preservation of both tonic and baroreflex regulation of sympathetic activity.

Oxygen Saturation

In current study the saturation was recorded before induction (T1), before intubation (T2) and at 1(T3), 3(T4), 5(T5), and 10 (T6) minutes post intubation. The mean saturation for Group P was 98.8 + 0.7 and for Group E it was 98.6 + 0.6 which showed statistically insignificant difference (p = 0.13).

Time for Laryngoscopy

The mean time taken for laryngoscopy for group E was 17.4 ± 3.23 seconds and for group P it was 17.13 ± 2.92 seconds showing no statistically significant difference (p = 0.66). Laryngoscopy is part and parcel of anesthesia. To secure and protect the airway is of prime importance while inducing anesthesia. Prolonged laryngoscopy can lead to sympathetic stimulation leading to increase in heart rate and blood pressure. Hence, in our study only those patients were included in whom time for laryngoscopy was < 30 seconds. 5 patients were excluded since the time for laryngoscopy exceeded 30 seconds.

Myoclonus

In present study incidence of myoclonic movements observed among two groups and severity of myoclonus was graded as follows: 0: no myoclonus, 1: minor myoclonus, 2: moderate myoclonus, 3: severe myoclonus. Out of all the patients induced with etomidate 31.2% showed myoclonic movements of grade 1 (20.8%) 2 and 3 (10.4%) while none of the patients in propofol group showed myoclonic movements. This difference was statistically significant (p < 0.05).

In study done by Miner J.R., Danahy M *et al.* they found that out of 110 patients randomized in etomidate group 20% had myoclonic movements depicting that myoclonus was observed much more frequently in patients receiving etomidate.[25] Our results are also in correlation with study done by Fatma S, Sennur U *et al.* which suggested that a higher incidence of myoclonic activity was seen in etomidate group (93.4%) as compared with propofol group.[24] Study done by Aggarwal Supriya *et al.* also showed that myoclonic movements were only seen in etomidate group and patients induced with propofol did not show any sign of myoclonus.[23]

The neurologic mechanism of myoclonus is unclear. There are few theories suggesting that it represents some kind of seizure activity while other theories suggest that it's a disinhibition phenomenon, apparently because large doses of etomidate depresses cortical activity before the depression of subcortical activity.[30]

Pain on Injection

In our study we measured pain on injection using four graded scale (0: no pain, 1: verbal complaint of pain, 2: withdrawal of the arm, 3: both verbal complaint and withdrawal of arm). We observed that out of all the patients receiving propofol 48% experienced pain on injection while administration of drug of Grade 1 (31.3%) and 2 (16.7%) while only 6.3% patients in etomidate group experienced pain of Grade 1 on injection.

In the study done by Fatma S, Sennur U *et al.*, they observed that there was a very high incidence of pain on injection after administering propofol and was statistically significant as compared to

etomidate group.[24] Aggarwal Supriya *et al.* observed that 50% of patients receiving propofol complained of pain while only 4% of patients experienced pain in etomidate group concluding that patients receiving propofol had higher incidence as well as severity of pain on injection.[23]

Pain on injection post-administration of propofol is common and can be a bad experience to the patients. Many factors appear to affect the incidence of pain on administration of propofol, few being size of vein, site of injection, speed of injecting drug, propofol concentration in aqueous phase and the buffering effect of blood. Degree of pain also depends upon the volume injected and the flow of blood through the vein.[31]

Conclusion

Etomidate was having more stable hemodynamic conditions as compared to propofol induced anesthesia. There was significant reduction in heart rate and blood pressure leading to hypotension in propofol group while etomidate group had stable hemodynamics. Incidence and severity of pain on injection was more with propofol while incidence of myoclonus was more with etomidate. Thus, we can conclude that etomidate can be a better choice of induction for general anesthesia as compared to propofol, only drawback being higher incidence of myoclonic movements.

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Original Research Article

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Magnesium Sulphate with and without Clonidine as Adjuvant to Bupivacaine for Lower Abdominal Surgeries: A Randomized Clinical Trial

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Abstract

Background: Postoperative pain relief is a growing concern for an anesthesiologist as an uneventful postoperative period makes surgery a comfortable proposition for surgical patients. *Objectives:* To assess the duration of effective analgesia. To assess hemodynamic parameters during the surgery and to determine any adverse effects if any. *Methods:* A prospective randomized controlled trial was done in patients posted for elective lower abdominal and lower limb surgeries for 2 years. Two groups were decided Group M (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulfate 50%, 0.1 ml (50 mg) and preservative free normal saline 0.5 ml. Group CM (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulfate 50%, 0.1 ml (50 mg) and clonidine 0.5 ml (75 µg). SPSS (version 22.0) was used for analysis. *Results:* Most of the patients belonged to age group between 41–50 years in both the groups. The duration (minutes) of analgesia was prolonged in Group CM compared to group M. By using unpaired *t*-tests, *p*-value was < 0.0001. The total dose of diclofenac given was less in Group CM compared to Group M. Pulse rate and Mean arterial pressure were not significant. No significant difference with respect to hypotension and bradycardia (*p*-value > 0.05). *Conclusion:* The duration of postoperative analgesia seems to be augmented by the combination since these are more prolonged than what is expected with either of the drugs used alone as adjuvants.

Keywords: Spinal Anesthesia; Intrathecal Bupivacaine; Randomization; Visual analog scale; hypotension; postoperative analgesia.

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Introduction

The task of medicine is to preserve, to restore health and to relieve pain. Understanding pain is essential to both these goals.[1] Pain is derived from the Latin word *poena* which means 'penalty or punishment'.[2] Postoperative pain relief is a growing concern for an anesthesiologist as an uneventful postoperative period makes surgery a comfortable proposition for surgical patients.[3] Perkins and co-workers provided an insight into the reality that poorly managed acute pain like postoperative pain can lead to the occurrence of chronic pain.[4] Spinal anesthesia, defined, as the regional anesthesia obtained by blocking the conduction of nerve impulses is a popular and common technique used worldwide. The advantages of an awake patient,

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simple to perform, offers rapid on set of action, minimal drug cost, relatively less side effects and rapid patient turnover has made this the choice of many surgical procedures. Intrathecal clonidine is being extensively evaluated as an alternative to neuraxial opoids for control of pain and has proven to be a potent analgesic, free of at least some of the opoid related side effects.[5] It prolongs the necessary blockade and reduces the amount or concentration of local anesthetic required to produce postoperative analgesia.[6] Adding magnesium sulfate, on other hand, may improve the quality and increase the duration of spinal anesthesia.[7] Magnesium sulfate ($MgSO_4$), which is the fourth most plentiful cation in the body, proved to have antinociceptive effects in animal and human model of pain. This present study was designed to evaluate the efficacy and to know the duration of intraoperative and postoperative analgesia when clonidine with $MgSO_4$ was added as an adjunct to bupivacaine in comparison with $MgSO_4$ alone added as an adjunct to bupivacaine.

Materials and Methods

Study Design: Prospective, Randomized double blind, controlled trial

Study Settings: Krishna institute of medical sciences and hospital, Karad

Study Duration: 2 years between 2012 and 2014

Study Population: Those patients posted for elective lower abdominal and lower limb surgeries.

Sampling Technique: Purposive sampling technique

Inclusion criteria:

1. ASA physical status I and II
2. Valid informed consent

Exclusion criteria:

1. ASA III and IV
2. Contraindication to regional anesthesia.
3. Significant coexisting systemic disorders like neuromuscular diseases, neuronal degenerative disorders, bleeding and hematological disorders, cardiac disorders or gestational diabetes.
4. History of allergy to bupivacaine or clonidine.
5. History of opioid, clonidine medication or magnesium treatment prior to surgery
6. Parturients
7. Patient refusal
8. History of seizures

Sample Size: Sample size was calculated based on onset of sensory block to detect that onset will be earlier by 3.1 min (SD ± 0.6) and duration of analgesia will be prolonged by at least 50 min (SD ± 35) more, with α value of 0.05, power >95%

Ethical Consideration: The study was approved by Institutional ethics committee.

Consent type: Written informed consent.

Methodology:

Seventy adult patients of each gender, randomly divided into two groups of 35 each were included in the study:

Group M (n=35) received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulphate 50%, 0.1 ml (50 mg) and preservative free normal saline 0.5 ml.

Group CM (n=35) received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulfate 50%, 0.1 ml (50 mg) and clonidine 0.5 ml (75 μg).

The procedure of double blinding was done by 2 separate anesthetist and patient underwent thorough preoperative evaluation which includes history taking, general physical examination and investigation.

Patient was shifted to the operation table; intravenous access was obtained on the forearm with 20 Gauge intravenous cannula and Lactated Ringer's solution 500 mL was infused intravenously before the block. The monitors connected to the patient included noninvasive blood pressure, oxygen saturation using pulse oximeter and electrocardiogram. Baseline PR and MAP was recorded.

A lumbar subarachnoid block was performed under strict aseptic precautions with the patients in the left lateral position with a 25-gauge Quincke needle at L 2-3 or L 3-4 using a midline approach. After free flow of cerebrospinal fluid (CSF), the

premixed solution was injected over 10 sec with the needle orifice directed cephalad, making sure of negative aspiration for blood. Patients were made to lie supine immediately after the completion of injection. The time of injection of the drug was recorded as 0 minute. Vital parameters such as PR and MAP were monitored at baseline, after drug injection and every 5 min for first 20 min and 15 min thereafter till end of the surgery were studied and duration of effective analgesia was also studied. Duration of analgesia was defined as the time from the intrathecal injection to VAS > 4. VAS was also recorded 3, 6, 12 and 24 hours postoperatively. Intramuscular injection Diclofenac 75 mg was given for rescue analgesia whenever the pain score was > 4.

Statistical Analysis: Patients were allocated to the two insertion techniques randomly by computer generated random numbers. Parametric data were expressed as mean and standard deviation (S.D) and analyzed using the independent t test using SPSS (version 22.0). $p < 0.05$ is considered statistically significant.

Results

As per Table 1 most of the patients belonged to the age group between 41 and 50 years in both the groups. By using independent sample t-test, *p*-value was 0.10. Since the *p*-value is > 0.05 therefore there is no significant difference between age (years) in

Table 1: Agewise Distribution of Patients in Both the Groups

Age (Year)	Group M		Group CM	
	No. of Patients	Percentege (%)	No. of Patients	Percentege (%)
≤20	00	00	03	8.57
21–30	02	5.71	06	17.14
31–40	09	25.71	08	22.86
41–50	11	31.43	08	22.86
51–60	07	20	05	14.28
61–70	05	14.29	05	14.28
>70	01	2.86	00	00
Total	35	100	35	100
Mean age ± SD	48.28 ± 12.9		42.6 ± 15.5	
p-Value	0.101			

Table 2: Comparison of Distribution of Patients in Group M and Group CM with Respect to the Type of Surgeries

Type of Surgery	Group M		Group CM	
	No. of Patients	Parcentege (%)	No. of Patients	Percentege (%)
Vaginal Hysterectomy (VH)	5	14.3	5	14.3
Abdominal Hysterectomy (AH)	5	14.3	6	17.2
Heranioplasty	6	17.2	5	14.3
Open appendicectomy (OA)	3	8.6	3	8.6
Exploratory Laparotory (Exp lap)	2	5.7	2	5.7
Jaboulay's Procedure	2	5.7	2	5.7
CRIF with tibia nailing (TN)	2	5.7	3	8.6
ORIF with tibia plating (TP)	3	8.5	3	8.6
Debridement	3	8.5	1	2.8
STSG	4	11.5	5	14.3
Total	35	100	35	100

Table 3: Comparison of Duration of Analgesia (Minutes) in Group M and Group CM

Time in Minutes	Group M	Group CM
Minimum	160	360
Maximum	260	480
Mean ± SD	218.42 ± 23.88	430.85 ± 32.39
p-value	<0.0001	

both the groups. While distribution of gender was almost equal in both.

As per Table 2 distribution of patients according to the type of surgeries in Group M and Group CM. Both the groups are comparable with respect to the type of surgery.

As per Table 3 the duration (minutes) of analgesia was prolonged in Group CM compared to Group M. By using unpaired *t*-tests, *p*-value was <0.0001. Since the *p*-value is <0.05, hence the difference between duration (minutes) of analgesia in Groups M and CM is statistically significant. 95% confidence interval of the difference: 198.86 to 226.00.

According to Figure 1 shows comparison of mean pulse rate in Group M and Group CM Statistical evaluation done between the two groups showed no significant difference in mean pulse rate at any interval, (*p*-value = 0.676).

Figure 2 shows comparison of mean arterial pressure in Group M and Group CM. Statistical evaluation done between the two groups did not show a significant difference in mean arterial pressure at any interval, (*p*-value = 0.25).

As per Table 4 shows comparison of total dose of diclofenac given in the postoperative period in Group M and Group CM. The total dose of diclofenac given was less in Group CM compared to Group M. By using unpaired *t*-tests, *p*-value was <0.0001. Since the *p*-value is <0.05, hence there is a statistically significant difference between total

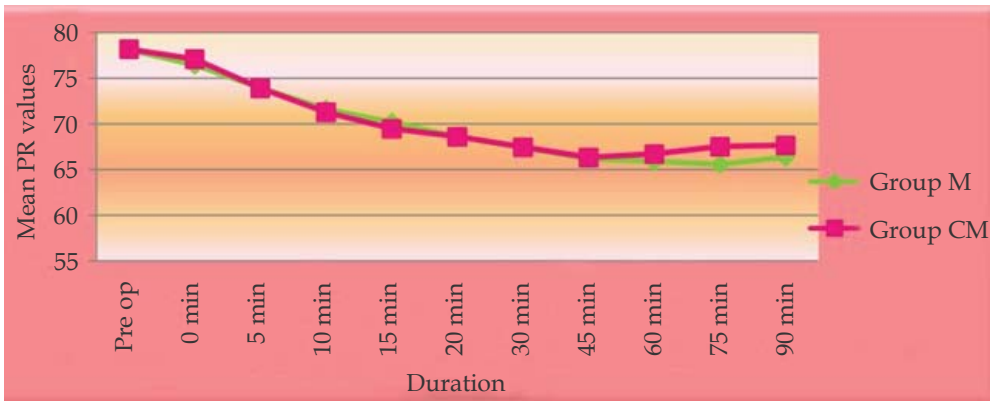

Fig. 1: Mean pulse rate in both the groups at different time intervals.

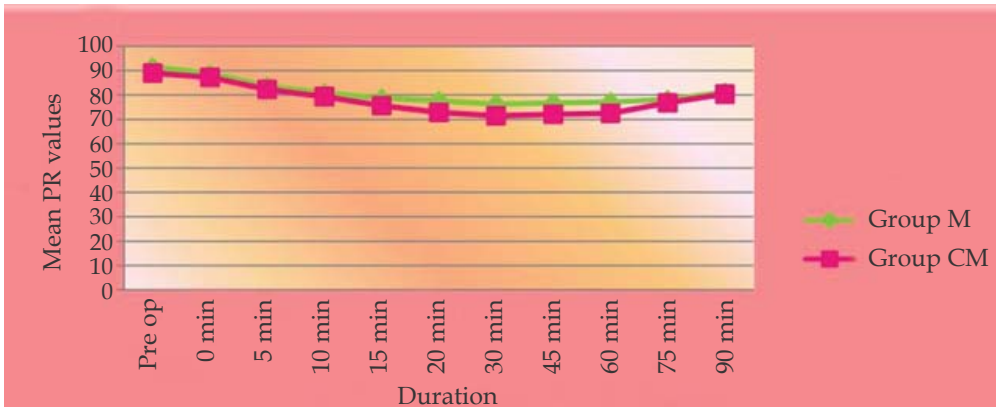

Fig. 2: Mean arterial pressure in both the groups at different time intervals.

Table 4: Comparison of Total Dose of Diclofenac (mg) Given in the Postoperative Period in Group M and Group CM

Total dose (mg)	Group M	Group CM
Minimum	150	75
Maximum	300	150
Mean ± SD	216.42 ± 43.70	98.57 ± 35.32
p-value	<0.0001	

Table 5: Comparison of Distribution of Patients in Group M and Group CM with Respect to their Adverse Effects

Adverse Effect	Group M		Group CM		*p*-value
	No. of Patients	Percentage (%)	No. of Patients	Parcentege (%)	
Hypotension	02	5.7	05	14.2	0.428
Bradycardia	02	5.7	03	8.5	1.000
PONV	00	00	00	00	
Sedation	09	25.7	22	62.8	0.003
Urinary Retention	00	00	00	00	
Pruritis	00	00	00	00	

dose of diclofenac given in the postoperative period in Groups M and CM. 95% confidence interval of the difference: –136.81 to –98.904.

As per Table 5 Statistical evaluation done by using Fischer's exact test between the two groups showed no significant difference with respect to hypotension and bradycardia (p-value > 0.05) but showed a statistical significant difference with respect to sedation (p-value < 0.05).

Discussion

The gate control theory of pain has had considerable influence on the anesthesiologists management of pain focusing attention on the unique pharmacology of the dorsal horn of the spinal cord. The technique has implications in acute and chronic pain therapy. A typically modern view of perioperative pain is to view it as an impediment to recovery. Aggressive methods are often used to minimize pain to facilitate hospital discharge and a rapid return to normal functional activity.[8] Our study design consisted of 70 patients, ASA physical status I, II undergoing elective lower abdominal and lower limb surgeries under spinal anesthesia were randomly divided into two groups after taking informed consent. In a study conducted by Stephen Strebel, *et al.*[9] intrathecal clonidine in dose of 37.5 µg, 75 µg and 150 µg used showed no intergroup differences in mean arterial BP decrease ≥30% (21% ± 13%, 25% ± 14%, 26% ± 12%, and 25% ± 13%) and also showed duration of analgesia was prolonged with higher doses (295 ± 80 min, 343 ± 75 min, 381 ± 117 min, and 445 ± 136 min). In our study, the time for first rescue analgesic required was prolonged ingroup CM with 430.85 ± 32.39 min and in Group M it was 218.42 ± 23.88 min which was statistically significant (p < 0.0001). Stephen S, *et al.*[9] conducted a study to evaluate dose response relationship of intrathecal clonidine at small doses (<150 µg) with respect to prolonging bupivacaine spinal anesthesia in 80 orthopedic patients. The duration of analgesia was prolonged in group receiving bupivacaine andclonidine (381 ± 117 min vs 295 ± 80 min) compared to group receiving bupivacaine alone. Shashni, *et al.*[10] in her study conducted on 124 patients showed duration of analgesia was prolonged in group receiving bupivacaine and magnesium (206.452 ± 26.246 min vs 185.323 ± 12.89 min) compared to group receiving bupivacaine and midazolam. Our study results show that the duration of analgesia is prolonged by combination of clonidine and magnesium sulfate with bupivacaine than magnesium sulfate alone or what is known to occur with clonidine alone. Clonidine augments the action of magnesium sulfate when given as a combination compared to what is documented with either drug. Also in a study conducted by I. Dobrydnjov *et al.*[11] on 45 patients showed the duration of analgesia in clonidine group (30 µg) (253 ± 71 min vs 171 ± 65 min) in control group. Duration of analgesia was higher in our study which is as expected considering the different doses of clonidine and bupivacaine used. This suggests that the prolongation of duration of analgesia is dose dependant. In our study the total dose of diclofenac given in the postoperative period was higher in Group M 216.42 ± 43.70 mg when compared to Group CM 98.57 ± 35.32 mg which was statistically significant (p < 0.0001). In our study also there was significant reduction in the VAS scores of the patients receiving clonidine in comparison with higher VAS scores in control group patients in the first twenty-four hours postoperatively. The requirement of diclofenac in the first 12 hours postoperatively was reduced in clonidine group compared to the control group. These results are comparable with the results in a study conducted by Gurudutta CL *et al.*[12] on 50 patients showing the 6-hour postoperative requirement of diclofenac injection was less in group receiving clonidine and bupivacaine. Also Sethi *et al.*[13] in his study showed that the number of injections of diclofenac required in 24 hours was also significantly higher for bupivacaine group (mean – 2.66) than the clonidine and bupivacaine group (mean – 1.16) [p < 0.05]. Our study results

concur with these studies and imply better quality and prolongation of analgesia postoperatively, and reduced need of analgesics with the use of intrathecal clonidine in our study, hypotension was 14% and bradycardia 9% in Group CM compared to 6% hypotension and 6% bradycardia in Group M which was statistically insignificant. Also, in our study 64% of patients in Group CM had sedation compared to 26% of the patients in Group M which was statistically significant ($p < 0.05$). Our study results are comparable with a study conducted by Dobrydnjov *et al.*[11] showing there is no incidence of hypotension and bradycardia with small dose of clonidine. Kothari *et al.*[14] in his study showed incidence of sedation in clonidine with bupivacaine group was 64.28% which was statistically significant ($p < 0.05$).

Conclusion

Based on the present study combination of clonidine (75 µg) and magnesium sulfate (50 mg) as adjuvants with hyperbaric bupivacaine 0.5% (15 mg) for subarachnoid blockade results in earlier onset of action and extended postoperative analgesia. The duration of postoperative analgesia seems to be augmented by the combination since these are more prolonged than what is expected with either of the drugs used alone as adjuvants. This approach to pain therapy may hold promise, that favourable outcomes such as successful analgesia may be achieved.

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Original Research Article

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A Comparative Study of Intrathecal Midazolam vs Fentanyl Along with Hyperbaric Bupivacaine in Below Umbilicus Surgeries

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Abstract

Context: The addition of adjuvant like midazolam or fentanyl has further expanded the advantage of spinal anesthesia. *Aims:* The aim of the present study is to compare the efficacy of intrathecally administered midazolam and fentanyl in combination with hyperbaric bupivacaine with respect to the time of onset of sensory block; Duration of sensory block; Quality of intraoperative anesthesia; Duration of effective postoperative analgesia; Incidence of side effects. *Settings and design:* A comparative study. *Methods and materials:* The study was conducted in 120 ASA Grade I-II patients between age group 20–55 years posted for elective lower abdominal surgeries and gynecological surgeries. We have divided these patients into three groups. Group B — 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and 0.5 ml of 0.9% normal saline. Group M — 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and preservative free midazolam 1 mg (0.2 ml) and 0.3 ml of 0.9% normal saline. Group F - 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and fentanyl 25 micrograms (0.5 ml). *Statistical analysis used: t*-test. *Results:* The patients studied across the groups did not vary much with respect to age, sex. The onset of sensory block was shortened in Group F (4.02 min)when compared to Group M (4.55 min) the two segment regression time was delayed in Group F (190.75 min) when compared to Group M (141.63 min). The addition of fentanyl 25 micrograms and midazolam 1 mg to hyperbaric bupivacaine gives better intraoperative comfort and postoperative analgesia than bupivacaine alone. The Group F (253.63 min) has more comfort and prolonged duration of analgesia than Group M (195.08 min). The Group M has more hemodynamic stability than Group F by fewer incidences of side effects like respiratory depression, hypotension, and bradycardia. The intraoperative comfort without significant hemodynamic changes is a welcome effect in immediate postoperative period in Group M. *Conclusions:* The addition of fentanyl and midazolam to bupivacaine gives better intraoperative comfort and postoperative analgesia than local anesthetic bupivacaine alone.

Keywords: Spinal anaesthesia; Midazolam; Fentany; Bupivacaine.

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Introduction

Spinal anesthesia consists of temporary interruption of nerve transmission within the subarachnoid space produced by injection of a local anesthetic solution into cerebrospinal fluid. Used widely, safely and successfully for almost 100 years spinal anesthesia has many potential advantages over general anesthesia, especially for operations involving the lower abdomen, the perineum and the lower abdominal surgeries.

The main reasons for the popularity of spinal block are that the block has well-defined end points and the anesthesiologist can produce the blocks reliably with single injection.[1]

Local anesthetic agents have been widely used in spinal anesthesia. One of the main disadvantages is the limited duration of block achieved with local anesthetics. To overcome this, various adjuvants have been tried and used successfully. This addition of adjuvant has further expanded the advantage of regional anesthesia over general anesthesia. These may be opioids like morphine, fentanyl, sufentanil or buprenorphine. It may be benzodiazepines alpha-2 agonist clonidine, acetylcholine esterase inhibitors like neostigmine, NMDA receptor antagonist ketamine or nonsteroidal anti-inflammatory agents.

The aim of the present study is to compare the efficacy of intrathecally administered midazolam and fentanyl in combination with hyperbaric bupivacaine with respect to the time of onset of sensory block, duration of sensory block, quality of intraoperative anesthesia, duration of effective postoperative analgesia and side effects.

Subjects and Methods

The study was conducted in 120 patients posted for elective surgeries under spinal anesthesia for lower abdominal and gynaecological surgeries after getting approval of ethical committee of department of Anesthesiology, MGM and CKM, GMH Hospitals and Kakatiya Medical College, Warangal during the period 2011–2013. Adult patients aged 20–55 yrs. ASA physical status I and II, Cases like lower abdominal surgeries and gynecological surgeries were included in this study. ASA physical status III and IV, Allergy to local anesthetics. Pregnancy patients who severe systemic diseases, metabolic disorders, and neurological, congenital and cardiovascular diseases were excluded from this study. On the eve of the surgery all the patients were visited and detailed preanesthetic examination including history and clinical examination.

Once the patient was shifted to the operating room, the patient was connected to the routine monitors which include non-invasive sphygmomanometer, pulse oximeter and electrocardiogram. All the emergency equipment like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephenteramine, adrenaline and other emergency drugs were kept ready. The Boyles anesthetic machine along with oxygen cylinders was also checked. Base line pulse rate, blood pressure and respiratory rate were recorded. Intravenous line was secured with 18G cannula. Preloading was done with 15–20 ml/kg of crystalloid solution.

Patients were put on right lateral position under strict aseptic precaution, subarachnoid block was performed using 25G Quinke Babcock`s needle in L3–L4 intervertebral space. After ensuring free flow of CSF the drug was injected as per the group assigned. After injecting the drug patients were turned supine.

The following parameters were recorded:

1. Time of institution of subarachnoid block.
2. Maximum level of sensory block achieved (which is tested by pinprick).
3. Time of onset of the maximum level of sensory block.
4. Time of onset of the surgery.
5. Pulse rate, blood pressure, respiratory rate and oxygen saturation were monitored every 5 minutes for the first 15 minutes, thereafter every 10 minutes for rest of the surgery and every half an hour in the postoperative period.
6. Analgesia.

Pain in the post operative period was evaluated using word category scale.

Constant worst pain	4
Severe pain	3
Moderate pain	2
Mild pain	1
No pain	0

Supplementary analgesia was given if the patient developed moderate pain during the postoperative period. The duration of analgesia was taken as the time between the institution of subarachnoid block and analgesic requirement.

Results

The three study groups each consist of 40 members were compared with respect to age, sex, baseline, vital parameters and duration of surgery (Tables 1-3).

Table 1: Distribution of Age

Age in Years	B	M	F
20–30	4	8	11
31–40	11	8	13
41–55	25	24	16

Table 2: Distribution of Sex

Sex	B	M	F
Male	19	20	22
Female	21	20	18

Table 3: Base Line Hemodynamic Vitals

Groups	Age (in years)	Baseline vitals	
		PR (pulse rate/min)	BP (blood pressure mm Hg)
B	42.95 ± 8.86	87 ± 4.89	118.25/75.75 ± 18.23/5.04
M	41.48 ± 9.77	87.58 ± 5.44	119.5/75.5 ± 7.68/5.06
F	38.01 ± 10.2	93.00 ± 5.4	118.3/78.7 ± 8.39/5.05

The maximum level of sensory block achieved was elicited with pinprick (Table 4).

Table 4: The Maximum Level Achieved in Each Group

	B	M	
up to T_4	0	2 (5%)	12 (30%)
up to T_5	0	4 (10%)	10 (25%)
block up to T_6	4 (10%)	12 (30%)	10 (25%)
block up to T_7	8 (20 %)	10 (25%)	4 (10%)
block up to T_8	10 (25 %)	8 (20%)	4 (10%)
block up to T_9	16 (40 %)	2 (5%)	0
block up to T_{10}	0	2 (5%)	0

Table 5: Anesthesia Parameters in All Groups

	B	M	F
Average time for maximum sensory blockade (min)	7.35	4.55	4.02
Average two segment dermatomal regression of sensory level in min	96.28	141.63	190.75
Average duration of analgesia	145.55	195.08	253.63

The time taken for maximum sensory blockade when compared in all, both the study groups was less for fentanyl and Bupivacaine combination. When the difference in time taken for maximum sensory blockade was analysed statistically, the *p* value was which is <0.05 that is statistically significant. Fentanyl—Bupivacaine combination had more effective time of anesthesia when compared to the other group. It is statistically significant (Table 5).

Table 6: Sedation Scale

Score	Group B	Group M	Group F
1	4 (10%)	0	
2	30 (75%)	8 (20%)	2 (5%)
3	6 (15%)	16 (40%)	16 (40%)
4	0	16 (40%)	21 (52.5%)
5	0	0	1 (2.5%)

Table 7: Side Effects

Group	Bradycardia	Hypotension	Respiratory depression	Others
B	2	4	0	0
M	1	4	0	0
F	4	8	1	0

The incidence of bradycardia, hypotension and respiratory depression was more in Fentanyl—Bupivacaine group compared to the other group and this when analyzed statistically showed a *p* value <0.05 which is statistically significant indicating the higher incidence of side-effects with Fentanyl—Bupivacaine combination compared to Midazolam—Bupivacaine (Table 6 and 7).

Discussion

In this present study the two segment dermatomal regression time is prolonged in both groups compared with the control group in a statistically significant manner.

Lyman A Rust *et al.*[2] conducted a study to examine whether intrathecal opioids like Fentanyl, morphine for labour analgesia offer adequate and cost-effective alternative to epidural analgesia with minimal side effects. They found this technique offered an excellent and cost-effective alternative to epidural analgesia.

Sibel Baris *et al.*[3] conducted study was to evaluate the intensity and effectiveness of 0.75 ml·kg^{-1} bupivacaine 0.25% with the addition of fentanyl or midazolam for caudal block in children undergoing inguinal herniorrhaphy. Seventy-five children were allocated randomly to three groups to receive a caudal block with either 0.25% bupivacaine with fentanyl 1 μg·kg^{-1} (Group BF)

or with midazolam 50 μg·kg^{-1} (Group BM) or bupivacaine alone (Group B) after induction of anesthesia. Hemodynamic parameters, degree of pain, additional analgesic requirements and side-effects were evaluated. There was no difference in additional analgesic requirements between the groups in the first 24h. Sedation score was higher in the midazolam group at 60 and 90 min postoperatively than the other groups.

Intrathecal midazolam causes antinociception by combining with spinal cord benzodiazepine receptors. This effect is reversible with doses of naloxone, suggesting involvement of spinal kappa or delta but not mu opioid receptors. The antinociceptive effects of intrathecally administered drugs in the spinal cord were demonstrated by measurements of the electrical current threshold for avoidance behavior in rats with chronically implanted lumbar intrathecal catheters. A comparision was made of suppression by two opioid selective antagonists (nor-binaltorphimine (kappa selective) and naltrindole (delta selective)) of spinal antinociception caused by equipotent doses of opioids selective for different receptor subtypes [u-50488h (kappa), dslet and dsbulet (delta), fentanyl (mu)] and the benzodiazepine midazolam. Nor-binaltorphimine selectively suppressed the effects of u-50488h but not midazolam or fentanyl. However, the delta selective antagonist, naltrindole, caused dose-related suppression of antinociception produced by both delta opioid agonists and midazolam with the same ed 50 (0.5 nmol). We conclude that intrathecal midazolam caused spinally mediated antinociception.[4–6]

In this present study Duration of analgesia has been shown to be prolonged with the addition of the midazolam and fentanyl. Fentanyl scores over midazolam in duration of analgesia in a statistically significant manner.

Kararmaz A. *et al.*[7], evaluated the effects of low dose Bupivacaine plus Fentanyl administered intrathecally in elderly patients undergoing transurethral prostatectomy. This study showed addition of Fentanyl to local anesthetic provides adequate analgesia with few side effects. Motor block was higher and duration was prolonged.

H. Singh, J Yang *et al.* investigated the effect of intrathecal Fentanyl 25 μg on the onset and duration of Bupivacaine 13.5 mg induced spinal block in adult male patients who underwent urological procedures. Addition of Fentanyl to local anesthetic prolongs the duration of sensory block and reduces the analgesic requirement in the early postoperative period.[8]

Bruce Ben David *et al.* studied 50 patients undergoing ambulatory surgical arthroscopy and found that although small dose Bupivacaine alone is inadequate for this procedure the addition of Fentanyl makes it reliable.[9]

Gulec *et al.*[10] In their study of Comparison of caudal bupivacaine, bupivacaine-morphine and bupivacaine-midazolam mixtures for postoperative analgesia in children included sixty children undergoing inguinal or urogenital surgery were allocated randomly to three groups to receive a caudal injection of either 0.125% bupivacaine 0.75 mol kg^{-1} with 0.5% midazolam 50 μg kg^{-1} (n=20) or with 1% morphine chlorhydrate 0.05 mg kg^{-1} (n=20), or bupivacaine alone (n=20) after surgery under general anesthesia. It is suggested that caudal administration of a bupivacaine-midazolam mixture produces a longer duration of postoperative analgesia than a bupivacaine-morphine mixture and bupivacaine alone with sedation for 8–12h postoperatively.

In this present study on comparing sedation level intraoperatively with midazolam and fentanyl, they are statistically significant. This shows that patients who received fentanyl were more comfortable than those of midazolam group.

Conclude that the use of intrathecal midazolam combined with intrathecal bupivacaine produces a more effective and longer analgesia with a mild sedative effect in perianal surgery.[11,12]

In this study the incidence of bradycardia, hypotension and respiratory depression was more in Fentanyl-Bupivacaine group compared to the other group and this when analyzed statistically showed a p value <0.05 which is statistically significant indicating the higher incidence of side-effects with Fentanyl-Bupivacaine combination compared to Midazolam-Bupivacaine.

In a study administered intrathecal Fentanyl 25 μg with Bupivacaine 2.5 mg in labouring parturients. They found that addition Bupivacaine 2.5 mg to intrathecal fentanyl attenuates the frequency of pruritus on all parts of body except the face. This combination also resulted in rapid and prolonged duration of labor analgesia compared with either drug alone.[13]

Administration of epidural and intraspinal opioids may provide excellent postoperative analgesia, but a minority of patients will suffer from respiratory depression. Etches *et al.* study shows effects of respiratory depression following intrathecal opioid administration.[14]

Rudra Pallab *et al.* in their study the Compared Intrathecal Fentanyl and Midazolam for prevention of Nausea and Vomiting during caesarean delivery under Spinal Anesthesia—Incidence of intraoperative and early postoperative nausea-vomiting was 75% with placebo, 40% with midazolam and 25% with fentanyl (*p* values with placebo <0.05, while that between midazolam and fentanyl >0.05). Adverse events caused by the study agents did not differ significantly. Intrathecal co-administration of midazolam or fentanyl significantly minimize the incidence of nausea-vomiting during intraoperative and early postoperative.[15]

Conclusion

The addition of Fentanyl and Midazolam to Bupivacaine gives better intraoperative comfort and postoperative analgesia than local anesthetic bupivacaine alone. But the Fentanyl gives more comfort and prolonged duration of analgesia compared to Midazolam. The hemodynamic stability was better with Midazolam than that of Fentanyl, with fewer incidences of hypotension, bradycardia and respiratory depression. Though Fentanyl-Bupivacaine combination provided better intraoperative comfort and prolonged analgesia and sedation, Midazolam-Bupivacaine combination has been considered better as it provided good sedation, analgesia and intraoperative comfort though less compared to Fentanyl group but without any side effects.

Conflicting Interest (If present, give more details): Nil

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Effect of Dexmedetomidine as an Adjuvant to Neuraxial Block with Bupivacaine in Lower Abdominal and Lower Limb Surgeries

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Abstract

Background: The local anesthetics are associated with relatively short duration of action which limit the technique for comparatively long duration surgery and also analgesic intervention is needed in postoperative period. Dexmedetomidine, the new highly selective α2-agonist drug, is now being used as a neuraxial adjuvant. The aim of this study was to evaluate the onset and duration of sensory and motor block hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine given intrathecally with hyperbaric 0.5% bupivacaine. *Materials and Methods:* The study was carried out on 60 patients of both the sexes of ASA Grade I and II physical status scheduled for lower abdominal and lower limb surgeries. Patients were allocated into two groups. Group I (Control): 15 mg hyperbaric bupivacaine + 0.5 ml saline (preservative free). Group II (Dexmedetomidine): 15 mg hyperbaric bupivacaine + 10 µg Dexmedetomidine. *Results:* Patients in dexmedetomidine group (II) had a significantly longer sensory and motor block time than patients in control Group (I). The mean time of sensory regression to S1 was 367 ± 32 min in group II and 204 ± 21 min in Group I. The regression time of motor block to reach modified Bromage 0 was 325 ± 21 min in group II and 138 ± 15 min in Group I. *Conclusions:* Intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics.

Keywords: Dexmedetomidine; Neuraxial Block; Bupivacaine; Intrathecal; VAS (visual analogue score).

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Introduction

It is the neuraxial block which makes the surgeries possible below umbilicus in low risk and highly compromised patient with safety of patient. First planned spinal anesthesia in man was given by Bier August[1] on 16th August 1898. In Kiel when he injected 3 ml of 0.5% cocaine solution into 34 years old laborer.

Since the local anesthetics are associated with relatively short duration of action which limit the technique for comparatively long duration surgery and also analgesic intervention is needed in postoperative period. Over the last decade, there has been considerable revival of interest in the use of adjuncts to local anesthetic agents in central neuraxial blocks.[2] Newer adjuvants are therefore being investigated. Many drugs are used as an adjuvant like: Vasoconstrictor–

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adrenaline, Opioids–fentanyl, morphine, α_2 adr. agonist–dexmedetomidine, clonidine NMDA receptor antagonist–ketamine, magnesium, Ach esterase inhibitor–neostigmine, Benzodiazepines–midazolam, etc. to prolong the duration of neuraxial block and reduce the postoperative analgesic requirement.

Dexmedetomidine is an α_2 adrenergic agonist that provides sedation, and anxiolysis, It is more selective α_2 agonist. $\alpha_2 : \alpha_1$ ratio is 1600 : 1 making it complete α2 agonist[3] It was introduced in clinical practice in united states in 1999 and approved by FDA. The sedative and hypnotic effect is produced by action on α_2 receptor in locus ceruleus. The analgesic effect is produced by action on α_2 receptor in locus ceruleus and within spinal cord.[4] Despite sound level of sedation with dexmedetomidine there is limited respiratory depression providing wide safety margin. It has also been noted that α_2 agonists have analgesic effect when injected via intrathecal or epidural route.[5] Dexmedetomidine is rapidly and extensively metabolized in liver and excreted in urine and feces Dr. Rachana Joshi Dr. Jignesh Mori *et al.*[2] 2013: Concluded that 5 µg dexmedetomidine is an attractive alternative as adjuvant to spinal bupivacaine in surgical procedures especially in those that need quite long time with minimal side effects and excellent quality of spinal analgesia. Sukhminder Jit Singh Bajwa, *et al.*[6] (2011) compared the efficacy and clinical profile of dexmedetomidine and clonidine, Deepika shukla, Anil Verma, *et al.*[7] (2011) in a Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate found that onset of anesthesia was rapid and of prolonged duration in the dexmedetomidine group B. Maharani *et al.*[8] (2013) Compared the dexmedetomidine and buprenorphine as adjuvants to spinal anesthesia. They concluded that 10 µg of DXM seems to be a better alternative.

Aims and Objectives

To evaluate the efficacy of intrathecal dexmedetomidine 10 µg as an adjuvant to 0.5% hyperbaric bupivacaine in neuraxial block. With respect to:

- Onset and duration of sensory and motor block
- Duration of analgesia
- Hemodynamic changes
- Adverse effect of drugs
- Sedation

On the basis of above parameters overall efficacy of dexmedetomidine as adjuvant was assessed.

Materials and Methods

After obtaining ethical committee approval and informed consent from patient. the study entitled "*Effect of Dexmedetomidine as an Adjuvant to Neuraxial Block with Bupivacaine in Lower Abdominal And Lower Limb Surgeries*" was carried out on 60 patients of both the sexes between the age of 18 to 65 and of ASA Grade I & II physical status. scheduled for lower abdominal and lower limb surgeries. Patient with the history of uncontrolled labile hypertension, heart block, dys arrhythmia, on therapy with adrenergic receptor antagonist, calcium channel blocker or ACE inhibitor, addiction to narcotic, sedation, LSCS and contraindication to spinal anesthesia were not included in the study. All the patients were thoroughly examined and investigated before the surgery. These patient were premedicated with injection atropine 0.60 mg IM. 45 mints before surgery. After premedication patients were allocated into two groups. Each group consisted of 30 patients.

Group I (Control): 15 mg hyperbaric bupivacaine + 0.5 ml saline (preservative free). *Group II (Dexmedetomidine):* 15 mg hyperbaric bupivacaine + 10 µg Dexmedetomidine.

In each group equal volume was injected, i.e 3.5 ml by dilution with normal saline [preservative free]. In the operation theater pulse oxymetry (SpO_2), noninvasive blood pressure (NIBP) and ECG was monitored. Following infusion of 15 ml/kg of Ringer lactate and with sitting posture lumbar puncture was performed under strict aseptic condition at L3–L4 level, using quinckes needle of 25 gauge. After intrathecal injection patient was placed in supine and oxygen @ 3 litre/min was given via face mask.

The following parameters were observed.

1. Onset, duration and quality of anesthesia.
2. Sensory block was assessed by short hypodermic needle in midclavicular line.
3. Motor block was assessed by modified bromage scale.
4. Sedation and pain was assess by modified Ramsay scale and visual analog scale.
5. Hemodynamic changes, viz. Pulse rate, and rhythm, B.P., ECG were recorded at regular interval per op and then in post op.

6. Any other untoward incidence of nausea, vomiting, shivering, pruritis, respiratory depression and sedation were assessed.

Statistical analysis was done using the Statistical Package (SPSS15.0 Evaluation version). Data were expressed as either mean and standard deviation or numbers and percentages. Continuous covariates were compared using analysis of variance (ANOVA). The comparison was studied using the chi-square test. The *p* value reported at the 95% confidence interval. $p < 0.05$ was considered statistically significant. $p > 0.05$ was considered statistically non significant.

Results

The distribution of the patients according to their age and gender in both groups remain comparable and statistically insignificant. having *p* value >0.05 (Table 1).

The distribution according to surgery remain comparable in both groups and statistically insignificant in both groups having *p* value >0.05 (Table 2).

It is evident from the table that sedation score was more (mean 2.3–2.13) in Group II (dxm) between 60–120 min (Table 4).

Table 1: Distribution of Patients according to their Age and Gender

	Group I (Contr)	Group II (Dxm)	*p* value	
Age (Mean ± SD)	41.366 ± 6.462	40.933 ± 7.210	> 0.05	
Male	16	15	>0.05	Chi square .368
Female	14	15		

Table 2: Distribution according to Their Type of Surgery

Surgery	Group I (Control)	Group II (Dxm)	Total	chi squar	*p* value
Appendicectomy	5	6	11	2.135	(>0.05)
Hernioplasty	7	7	14		
T.A.H.	7	6	13		
V.H.	7	8	15		
Lower limb	4	3	07		

Table 3: Showing Onset and Regression of Block with duration of Analgesia

	Group I (Contr)	Group II (Dxm)	*p* value
Sensory onset up to T-10 (in seconds)	297.866 ± 35.411	164.033 ± 25.557	<0.05
Motor block to Bromage-3 (in seconds)	353.766 ± 37.414	249.866 ± 24.639	<0.05
Regression to Bromage-0 (in minutes)	138.833 ± 15.572	325.133 ± 21.013	<0.05
Sensory regression to S-1 (in minutes)	204.133 ± 21.421	367.700 ± 32.161	<0.05
Duration of analgesia (in minutes)	139 ± 14.70	299 ± 20.06	<.001

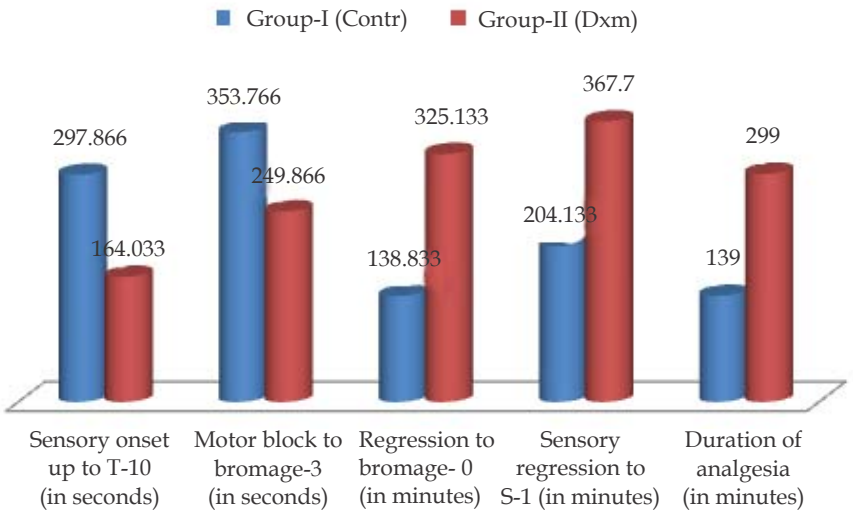

Fig. 1: Graph showing onset and regression of block with duration of analgesia

Table 4: Variation in Ramsay Sedation Score (RSS)

	Group I (Contr)	Group II (Dxm)
0 min	1 ± 0	1 ± 0
30 min	1.36 ± 0.49	1.86 ± 0.34
60 min	1.40 ± 0.49	2.30 ± 0.46
90 min	1.46 ± 0.50	2.30 ± 0.43
120 min	1.30 ± 0.40	2.13 ± 0.34
150 min	1.08 ± 0.28	1.83 ± 0.53
180 min		1.80 ± 0.50
210 min		1.66 ± 0.49
240 min		1.56 ± 0.50
270 min		1.36 ± 0.49
300 min		1.04 ± 0.20
330 min		1.0 ± 0

Table 5: Showing Variation of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP)

Time	Systolic blood pressure (SBP)			Diastolic blood pressure (DBP)		
	Group-I (Contr)	Group-II (Dxm)	*p* values	Group-I (Contr)	Group-II (Dxm)	*p* values
0 min	129.7 ± 7.03	130.63 ± 4.89	> .05	79.56 ± 5.34	79.80 ± 5.14	> .05
5 min	120.36 ± 7.59	112.80 ± 9.05	< .05	77.26 ± 4.79	73.53 ± 3.33	< .05
10 min	114.06 ± 6.12	108.00 ± 8.40	< .05	74.03 ± 5.05	72.03 ± 2.09	> .05
15 min	115.53 ± 5.32	108.20 ± 8.26	< .05	74.53 ± 3.62	72.03 ± 2.12	> .05
30 min	118.23 ± 5.41	110.63 ± 7.73	< .05	75.46 ± 3.41	73.16 ± 2.69	> .05
60 min	120.03 ± 5.30	112.83 ± 5,91	< .05	75.93 ± 3.38	73.03 ± 2.05	> .05
90 min	122.10 ± 4.50	116.10 ± 4.46	< .05	77.66 ± 4.09	74.03 ± 1.47	> .05
120 min	125.00 ± 5.72	122.20 ± 2.00	> .05	77.70 ± 3.86	74.13 ± 1.33	> .05
150 min	126.50 ± 5.73	124.10 ± 4.37	> .05	77.80 ± 5.43	75.00 ± 2.13	> .05
180 min	127.97 ± 7.34	130.30 ± 7.34	> .05	77.36 ± 4.61	76.16 ± 2.70	> .05
210 min	128.37 ± 7.22	130.16 ± 7.50	> .05	78.07 ± 4.20	76.86 ± 5.55	> .05
240 min	129.66 ± 5.24	131.30 ± 7.60	> .05	78.33 ± 5.08	76.20 ± 5.68	> .05
270 min	128	131.10 ± 7.27		77.00	76.63 ± 5.91	
300 min		130.93 ± 7.51			76.63 ± 5.22	
330 min		131.70 ± 7.58			76.77 ± 5.12	
360 min		131.20 ± 8.09			76.20 ± 4.39	
390 min		129.36 ± 9.27			76.18 ± 3.91	
420 min		132.20 ± 6.30			76.80 ± 3.56	

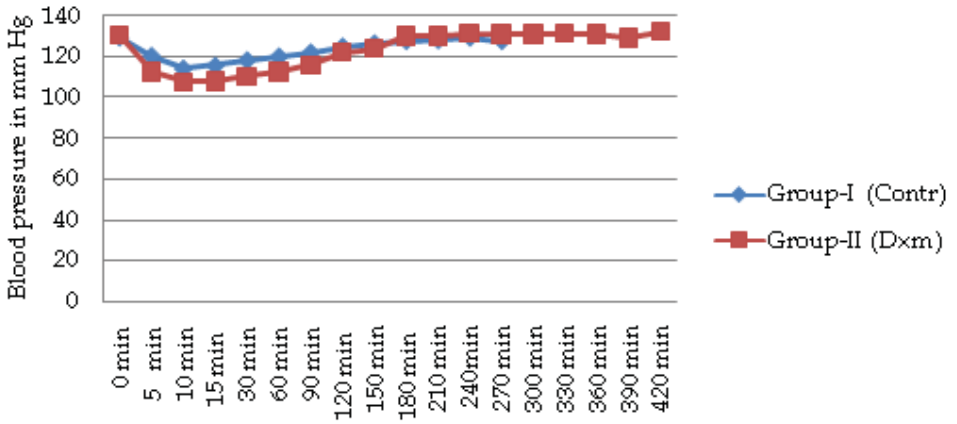

Fig. 2: Systolic blood pressure variation

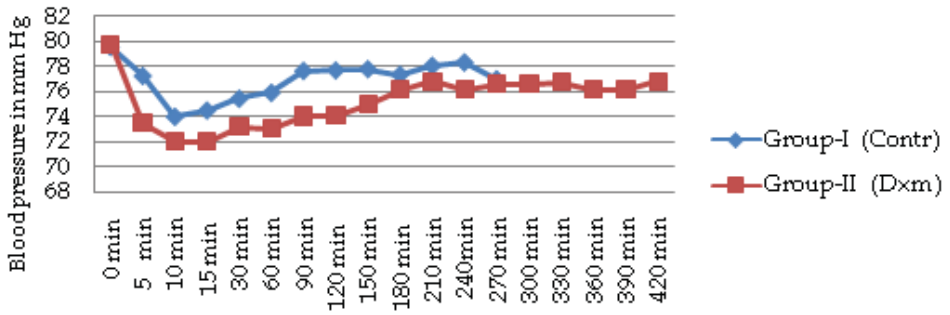

Fig. 3: Diastolic blood pressure variation

Table 6: Showing Variation in Heart Rate (HR)

Time	Heart rate (HR)		
	Group-I (Contr)	Group-II (Dxm)	P values
0 min	81.13 ± 10.48	83.73 ± 9.11	> .05
5 min	80.13 ± 10.07	82.10 ± 7.71	> .05
10 min	76.43 ± 13.30	73.96 ± 2.73	> .05
15 min	75.00 ± 8.91	73.00 ± 2.93	> .05
30 min	75.50 ± 9.27	73.10 ± 2.64	> .05
60 min	77.33 ± 8.65	75.06 ± 2.19	> .05
90 min	79.70 ± 9.47	77.03 ± 4.11	> .05
120 min	83.06 ± 9.21	80.06 ± 6.65	> .05
150 min	83.16 ± 7.87	82.00 ± 6.92	> .05
180 min	84.33 ± 9.12	82.50 ± 8.25	> .05
210 min	84.11 ± 9.85	82.96 ± 7.86	> .05
240 min	84.28 ± 7.38	82.60 ± 7.46	> .05
270 min	84.00	83.96 ± 9.08	> .05
300 min		84.00 ± 8.93	
330 min		84.00 ± 7.40	
360 min		83.55 ± 9.43	
390 min		83.45 ± 6.90	
420 min		84.20 ± 6.05	

Table 7: Side Effects

	Group I (cont)	%	Group II (dex)	%
No side effect	21	70%	24	80%
Hypotention	1	3.3%	3	10%
Nausea/Vomitting	3	10%	1	3.3%
Pruritis	1	3.3%	–	0%
Shivering	3	10%	1	3.3%
Urinary retention	1	3.3%	1	3.3%

Discussion

Base line comparison of groups according to gender was comparable among the total 60 patients.

Time of sensory onset up to T-10 (in seconds) In our study time of sensory onset up to T-10 in Group I (Contr.) was 297.88 ± 35.411 sec, in Group II (Dxm) 164.03 ± 25.55 sec. Wafiya Ramadan Mahdy, *et al.*[9] (2011) studied the effect of dexmedetomidine as adjuvant in spinal anesthesia. Their time of sensory onset was 2 ± .74 min perhaps this time is comparable with our time. That is dexmedetomidine as an adjuvant shorten the time of sensory onset.

Time of motor block onset to Bromage-3 (in seconds) In our study time of motor block onset to Bromage-3 in Group I (Contr.) was 353.766 ± 37.41 sec in

Group II (dxm) 249.86 ± 24.63 sec. Deepika Shukla, *et al.*[7] (2011) studied the effect of Dexmedetomidine as adjuvant in spinal anesthesia. Their time of motor block onset was comparable with the time of motor block onset in present study. That is dexmedetomidine as an adjuvant shorten the time of motor block onset.

Time of motor block regression to Bromage -0 (in minutes). In our study time of motor block regression to Bromage-0 in Group I (Contr.) was 138.83 ± 15.57 min and in Group II (Dxm) 325.13 ± 21.01 min. Hala EA Eid, *et al.*[10] (2011) used Dexmedetomidine as adjuvant in spinal anesthesia. Their time of motor regression was comparable with our time of motor regression. The time of motor block regression was longer in Group II (Dxm) as compared to control That is dexmed prolonged the time of motor block regression.

Time of sensory regression to S-1 (in minutes). In our study time of sensory regression to S-1 in Group I (Contr.) was 204.13 ± 21.42 min and in Group II (dxm) 367.70 ± 32.161 min. Maharani, *et al.*[8] (2013) used dexmedetomidine as adjuvant in spinal anesthesia. Their time of sensory regression was comparable with our time of sensory regression. That is dexmed prolonged the time of sensory regression.

Duration of analgesia In our study duration of analgesia in Group I (Contr.) was 139 ± 14.70 min in and Group II (dxm) 299 ± 20.06 min Maharani *et al.*[8] (2013) used dexmed with bupivacine their duration of analgesia was comparable with our time of analgesia. The analgesia was longer in group II (dxm) as compared to control group.

Hemodynamic changes Base line systolic blood pressure, diastolic pressure, heart rate, oxygen saturation were comparable. After spinal anesthesia systolic, diastolic blood pressure and heart rate, fall in each group but fall in Group II (dxm) was more as compared to Group I (cont), But after 30 min they start returning to baseline values. Though fall in blood pressure was more in Group II (dxm). Oxygen saturation was similar in both the groups. There was no statistically significant difference. Similar results were also found by G.E. Kanazi, MT. Aouad, *et al.*[11] (2006).

Sedation (Ramsay Sedation Score) Sedation score was more (mean 2.3–2.13) in Group II (dxm) between 60–120 min than Group I (mean 1.4–1.3) in between 60–120 min. Hala EA Eid, *et al.*[10] (2011) found that sedation score was more in dexmedetomidine group Rajni Gupta *et al.*[12] (2011) also found that sedation score was more in dexmedetomidine group.

VAS score The progression of VAS score was slower in Group II (dxm) than Group I (cont). Rajni Gupta, *et al.*[12] (2011) found that progression of VAS score was slow in dexmedetomidine group.

Among side effects hypotension was more common in Group II (dxm). Whereas nausea vomiting and shivering was more in Group I (cont).

Conclusion

Dexmedetomidine seems to be an attractive alternative as an adjuvant to spinal bupivacaine for long duration surgical procedures due to its profound anesthetic and analgesic properties combined with minimal side effects.

Source(s) of support: Nil

Conflicting Interest: Nil

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Ultrasonography: A Novel and Noninvasive Tool for Airway Assessment

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Abstract

Context: Securing the airway to ensure alveolar ventilation and prevent pulmonary aspiration constitutes a crucial component in the practice of clinical anesthesia. Unanticipated difficult intubation still occur despite adoption of various clinical predictors. Ultrasound imagimg technique has emerged as new tool for various aspects in anesthesia practice. *Aims:* We have evaluated the feasibility of ultrasonography as an imaging tool in identifying important airway anatomical structures on the anterior aspect of the neck and correlated the ultrasound-guided measurements of the airway parameters with the modified Cormack-Lehane grading of the direct laryngoscopy for prediction of the difficult airway. *Settings and Design:* For this prospective observational study, 100 patients above the age of 18, ASA I to III grades, scheduled for elective surgery, requiring general anesthesia and endotracheal intubation were included. *Methods and Materials:* Modified Mallampati score, Body Mass Index, distance between the anterior commissure to epiglottis (DACE) and distance from epiglottis to midpoint of maximum distance between vocal cords (DEM) using the USG machine followed by MCLS grade on laryngoscopy were noted. *Statistical analysis used:* Software named Statistical package for the social sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows. *Results:* On data analysis mean of DACE in Easy MCLS group was 0.46 ± 0.19 while in Difficult MCLS group was 0.91 ± 0.23 and the difference was statistically significant. Similarly mean of DEM in Easy MCLS group was 0.66 ± 0.21 while in Difficult MCLS group was 0.59 ± 0.23. The Mean of Ratio of DACE to DEM in Easy MCLS group was 0.71 ± 0.19 while in Difficult MCLS group was 1.67 ± 0.23 and this difference was also statistically significant. From Receiver operating characteristic (ROC) analyses distribution of area under the curve for DACE/DEM ratio was 0.96 which was significantly higher for prediction of difficult laryngoscopy. *Conclusions:* We as anesthesiologists can use USG as a clinical tool for assessing airway in order to rule out difficult airway and prepare the anesthesia workstation for the benefit of the patient.

Keywords: Difficult airway; Ultrasonography; Distance from the anterior commissure to epiglottis; Distance from epiglottis to midpoint of maximum distance between vocal cords; Laryngoscopy, Modified Cormack-Lehane grading.

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Introduction

Securing the airway to ensure alveolar ventilation and prevent pulmonary aspiration constitutes a crucial component in the practice of clinical Anesthesia. Unanticipated difficult intubation still occur despite adoption of various clinical predictors like demographic variables, body mass index, ability to move the lower teeth in front of the upper teeth, interincisor gap, modified Mallampati score,

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thyromental distance, neck flexibility, etc.[1] These bedside physical Airway assessment tools have high inter observer variability, and may be difficult to apply in emergency and critical care settings.

The Cormack-Lehane classification is frequently used to describe the best view of the larynx seen during laryngoscopy. Being too invasive, the major drawback is, it cannot be applied comfortably in awake patient on OPD basis regularly for predicting difficult airway.

Ultrasound imaging technique has recently emerged as a novel, simple, portable, noninvasive tool helpful for airway assessment and management. The ready availability of ultrasound machines along with better probes, high resolution, imaging real-time picture and clinical experience, this has become the potential first line noninvasive airway assessment tool in anesthesia and intensive care practice. Accurate interpretation of ultrasound images requires a basic understanding of the physical principles involved in image generation. Vocal cords are seen forming an isosceles triangle with a central tracheal shadow. During phonation, the vocal cords oscillate and move towards the midline when compared to the false vocal cords which remain relatively immobile.[2,3]

The purpose of our study is to evaluate the feasibility of sonography as an imaging tool in identifying important airway and anatomic structures on the anterior aspect of the neck and to compare and correlate the ultrasound view of the airway with the Cormack-Lehane classification of the direct laryngoscopy.

Materials and Methods

After institutional ethical committee approval and obtaining the written informed consent for the study, hundred patients undergoing elective surgery under general anesthesia with direct laryngoscopy and endotracheal intubation were enrolled. The study was a prospective observational study conducted in department of anesthesia of a tertiary care center. Patients above the age of 18, without any known airway pathology were included in the study. Those patients with restricted mouth opening, edentulous, cervical spine pathology, high risk of aspiration and patient who are difficult to assess by ultrasonography due to facial and neck abnormality were excluded.

In the preoperative holding area, the Mallampati classification of Pre anesthetic Airway assessment was documented as follows:

Class 1: Full visibility of tonsils uvula and soft palate

Class 2: Visibility of hard palate and soft palate upper portion of tonsil and uvula

Class 3: Soft and hard palate base of the term

Class 4: Only hard palate visible

Subsequently, the ultrasound view of the Airway of study patients was carried out by the same principal investigator with a high frequency linear probe (sonosite, EDGE II). The patient was asked to lie down supine with maximum head tilt chin lift. The probe was then placed transversely in the submandibular area in the midline and was rotated in transverse plane from cranial to caudal without changing the position of the probe till an oblique transverse view that bisects the epiglottis and posterior part of the vocal cord with arytenoids was visualized.

In this plane, the epiglottis is visible as a hypoechoic curvilinear structure. Its anterior border is demarcated by the hyperechoic PES and its posterior border by a bright linear air mucosal interface. The posterior most part of the two vocal folds with arytenoids appears as hyperechoic lateral V-shaped structures facing away from each other (Figure 1). Protrusion of the tongue or swallowing helps to identify the epiglottis. Identification of the vocal folds is facilitated by observing their linear movement during quiet breathing or phonation.

The following study measurements were obtained with the transverse ultrasound view:

a. The distance between anterior commissure to epiglottis (DACE)

b. The distance between epiglottis to the midpoint of the cords (DEM)

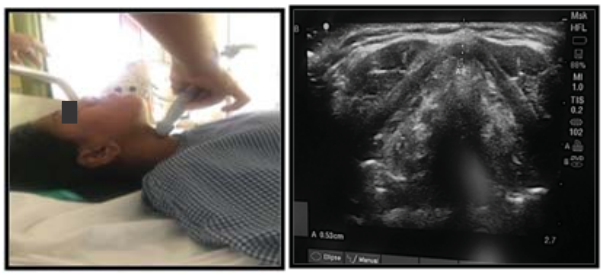


Fig. 1: Probe placement and ultrasound image.

The patients were then taken to the operating room and standard general anesthesia procedure was performed as per the discretion of the attending senior anesthesiologist in accordance with good clinical practice and standard of care. Direct laryngoscopy was performed using a Macintosh blade size number 3 or size 4 as per the built of the

patient. During the intubation the anesthesiologist was asked to note down the Cormack-Lehane grading of the laryngoscopy view. Intubation was classified as easy for Cormack-Lehane grade 1 and 2 or difficult for grade 3 and 4 Cormack-Lehane grading was done as per following scale:

Grade I: Visualization of entire laryngeal aperture

Grade II: IIa: Visualization of parts of the laryngeal aperture or arytenoids

IIb: Only the posterior tip of arytenoids is seen

Grade III: IIIa: Visualization of epiglottis only and it can be lifted

IIIb: Visualization of epiglottis only but cannot be lifted visualization

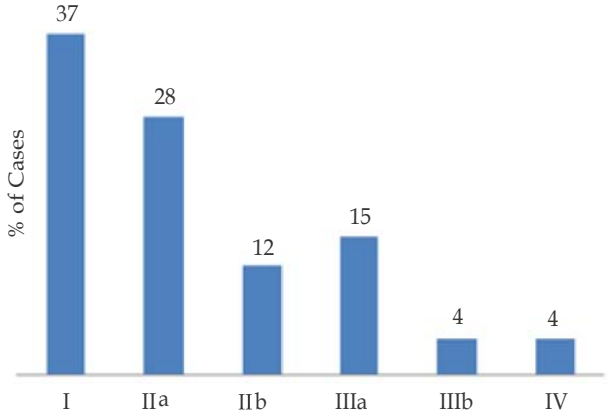
Grade IV: No laryngeal structures are visualized

Appropriate sized endotracheal tube was inserted and anesthesia was maintained. At the end of the surgical procedure anesthesia was reversed and patient extubated.

Results

Hundred patients scheduled for elective surgery and requiring general anesthesia with endotracheal intubation were included in this study.

Of 100 cases studied, 37 (37.0%) had Grade I MCLS, 28 (28.0%) had Grade IIa MCLS, 12 (12.0%) had Grade IIb MCLS, 15 (15.0%) had Grade IIIa MCLS, 4 (4.0%) had Grade IIIb MCLS and 4 (4.0%) had Grade IV MCLS (Graph 1).



Graph 1: Distribution of Cormack Lehane grades

Depending upon the MCLS, direct laryngoscopy was classified as easy (MCLS Grade I to IIb) or difficult (Grade IIIa to IV) (Table 1).

Table 1: Distribution of Cormack Lehane

Grades	Status	No. of cases	% of cases
I to IIb	Easy	77	77.0
IIIa to IV	Difficult	23	23.0
Total	–	100	100.0

The distribution of mean age and sex did not differ significantly between groups of cases with easy and difficulty laryngoscopy (p value >0.05) (Table 2)

Table 2: Demographic Data

Parameter	Cormack-Lehane Grades				p-value
	Easy (n=77)		Difficult (n=23)		
	Mean	SD	Mean	SD	
Age (years)	44.06	± 17.97	44.13	± 16.88	0.988 NS
Sex –Male/Female (no)	37/40		11/12		0.985 NS

p-value by independent sample t-test. p-value <0.05 is considered to be statistically significant. NS-Statistically non-significant.

Distribution of means of distance between anterior commissure to epiglottis (DACE), distance from epiglottis to midpoint of cords (DEM) and DACE/DEM ratio according to Cormack-Lehane grades (MCLS).

The distribution of mean DACE is significantly higher in difficult laryngoscopy group compared to mean DACE in easy laryngoscopy group (p-value <0.001).

The distribution of mean DEM did not differ significantly between groups of cases with easy and difficult laryngoscopy (p-value >0.05).

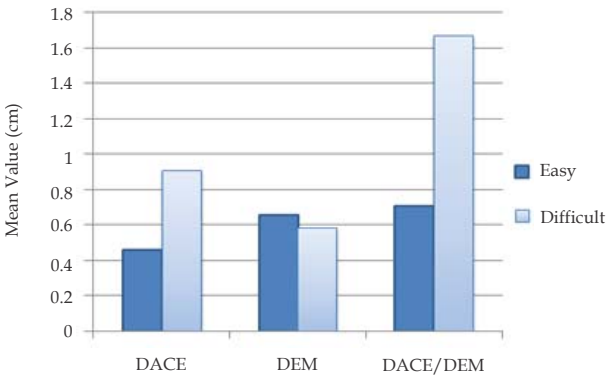
The distribution of mean DACE/DEM ratio is significantly higher in difficult laryngoscopy group compared to mean DACE in easy laryngoscopy group (p-value <0.001). (Table 3) (Graph 2)

Table 3: USG Measurements

Parameters		Cormack Lehane Grades		p-value
		Easy (n=77)	Difficult (n=23)	
DACE (cm)	Mean ± SD	0.46 ± 0.19	0.91 ± 0.23	0.001***
	Minimum – Maximum	0.13 – 0.99	0.57 – 1.59	
DEM (cm)	Mean ± SD	0.66 ± 0.21	0.59 ± 0.23	0.218 NS
	Minimum – Maximum	0.30 – 1.15	0.30 – 1.01	
DACE/DEM Ratio	Mean ± SD	0.71 ± 0.19	1.67 ± 0.46	0.001***
	Minimum – Maximum	0.29 – 1.40	1.02 – 2.96	

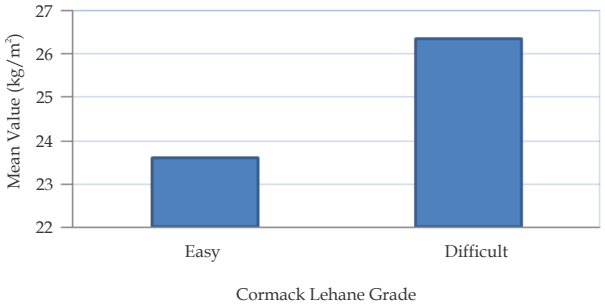
p-values by independent sample t test. p-value <0.05 is considered to be statistically significant.

*** p-value < 0.001, NS-Statistically non-significant.



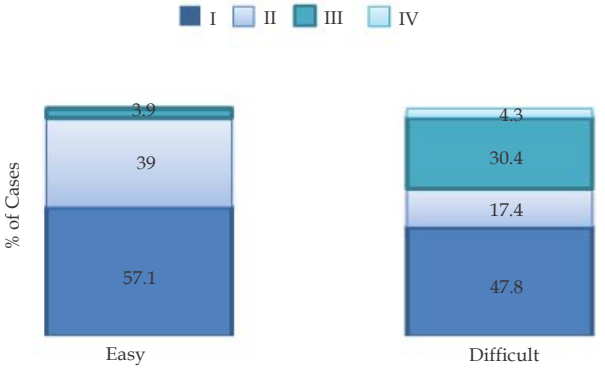
Graph 2: USG measurements

The distribution of mean BMI is significantly higher among the group of cases with difficult laryngoscopy compared to the group of cases with easy laryngoscopy (p-value < 0.05) (Graph 3).



Graph 3: Distribution of mean BMI by Cormack Lehane

The distribution of Mallampati grades of cases studied differs significantly between groups of cases with easy and difficult laryngoscopy (p-value < 0.001) (Graph 4).



Graph 4: Distribution of Mallampati

The distribution of area under the curve (AUC) is significantly higher for DACE/DEM ratio for the prediction of difficult Laryngoscopy (p-value < 0.001).

The distribution of area under the curve (AUC) did not differ significantly for Mallampati Grades for the prediction of difficult laryngoscopy (p-value > 0.05).

Based on the ROC analysis, the optimal cut-off of DACE/DEM ratio measurement for the prediction of difficult laryngoscopy is 0.96 with area under the curve being 0.993.

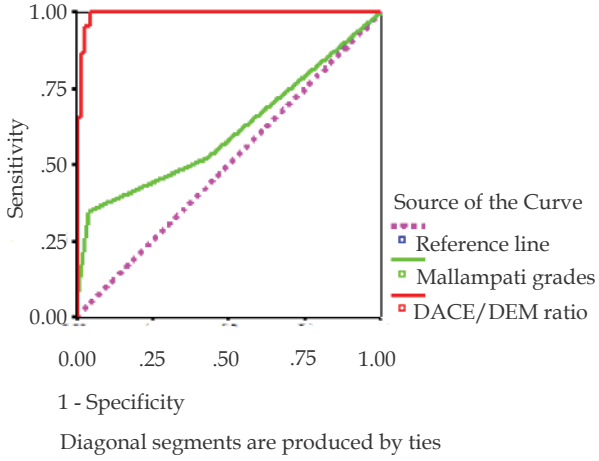
Based on the ROC analysis, the optimal cut-off Mallampati grades for the prediction of difficult laryngoscopy is Grade II and above with area under the curves being 0.612 (Table 4).

Table 4: Distribution of area under the ROC curves (AUC) for DACE/DEM ratio and Mallampati grades for the prediction of difficult laryngoscopy

Parameter	Optimal Cut-Off Based on ROC	AUC ± SE	95% CI of AUC	p-value
DACE/DEM Ratio	0.96	0.993 ± 0.006	0.982 – 0.999	0.001***
Mallampati grades	Grade II	0.612 ± 0.105	0.463 – 0.760	0.105NS

***p-value < 0.001, NS-Statistically non-significant, Reference value = 0.500; SE – Standard Error.

Receiver operating characteristic (ROC) analyses for DACE/DEM ratio (red line), Mallampati grades (green line). Cormack-Lehane grading of glottis exposure over II was considered the threshold of difficult laryngoscopy during the study. Pink dotted line=reference line. (Graph 5)



Graph 5: ROC curve

Discussion

The major responsibility of anesthesiologist is to provide adequate ventilation to the patient. Recognizing before anesthesia the potential for difficult airway allows time for optimal preparation and proper selection of equipment and technique in difficult airway management. With available noninvasive model airway assessment modality like Mallampati classification, thyromental distance assessment,

neck extension the anesthesiologist usually comes to a conclusion of prediction of airway, as difficult or easy along with other external observations like mouth opening, head and neck pathology, Lemon score. However, as observed, intraoperative laryngoscopy grade, Cormack -Lehane classification may not always correlate adequately well with the preoperative predictors of airway assessment. Also, it is not always viable to do a complete airway assessment in emergency clinical scenarios especially in non-cooperative and unconscious patient. Also, none of them are 100% sensitive and specific.

With latest advancement of ultrasonography, attempts have been made to widen its horizon of utility because of its accuracy and patient friendly noninvasive technique. Airway assessment by ultrasonography can be a good supplementary tool in the busy anesthesiologist armamentarium.

Multiple studies investigating the use of ultrasonography in the evaluation of difficult laryngoscopy by measuring the soft tissue thickness at the level of base floor of the mouth, thyroid bone, epiglottis, thyroid membrane has been undertaken with conflicting results.[4-7]

The present study was designed to establish a correlation between preoperatively measured USG parameters and the grade of difficulty of visualisation of cords (Cormack Lehane) at direct laryngoscopy.

The parameters assessed by ultrasound in a study were:

A. The distance between anterior commissure to epiglottis (DACE)

B. The distance between epiglottis to the midpoint of the vocal cords (DEM)

Before collecting data for the study group proficiency in assessing the ultrasound imaging for airway assessment was achieved by scanning multiple patients with ultrasonography in pre anesthesia holding area.

Out of 100 cases studied, 77 patients belong to easy laryngoscopy group with CL grade I to IIb where as 23 belong to difficult laryngoscopy group, the patients with CL of grade IIIa–IV. Demographic profile was analyzed for any statistical difference. The age and sex distribution of cases studied did not differ significantly between group of cases with easy and difficult laryngoscopy.

In our study, we observed strong correlation of the mean distance from anterior commissure to epiglottis (DACE) with difficult laryngoscopy group (p-value 0.001). On the other hand, mean distance between epiglottizes to the midpoint of vocal cords (DEM) did not differ much with easy and difficult laryngoscope.

Also, DACE to DEM ratio was significantly higher in difficult laryngoscope group compared to easy one. (p value 0.001).

We also compared prediction of difficult Airway with Mallampati grading by plotting distribution of area under the ROC. We observed distribution area under the curve is significantly higher for DACE/DEM ratio for the prediction of difficult laryngoscopy (p value <0.001) with the optimal cut-off value of 0.96 with area under the curve being 0.993. While distribution of area under the curve did not differ significantly for Mallampati grades for prediction of difficult Airway with optimal cut-off for prediction of difficult laryngoscopy is Grade 2 and above with area under the curve being 0.612.

Similar study conducted at Wayne University by Gupta *et al.* attempted to predict CL grading with ultrasound.[8] They observed positive correlation with pre-epiglottic thickness and negative correlation with epiglottis to vocal cord distance and the ratio of pre- E to E-VC strongest positive correlation with CL grading. They concluded that CL grades could be adequately made by ratios of Pre-E to E-VC distance with 67%–68% sensitivity. Similar findings were found by Preeti Reddy *et al*. where along with the ratio they compared anterior neck soft tissue at the level of hyoid and vocal cords.[9] They observed prediction of difficult laryngoscopy view using the ratio had a high specificity (86.7%) but very low sensitivity.

The noninvasive prediction of difficult airway can be done by pre-E/EVC ratio (range: 0.29–1.40 corresponds to easy CL grading, 1.02–2.96 corresponding to difficult CL grading. This predictability was similar in the study observed by Rana S *et al.* in their study.[10] They also observed strong positive correlation with AUC of 0.868 with cut-off value 1.77 with sensitivity of 82% and specificity of 80%.

We acknowledge the limitations of our study that the number of the patients was small.

Key Messages: USG guided measurements are better predictors of difficult airway as compared to Mallampati.

Acknowledgement: Nil

Conflict of Interest: Nil

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Original Research Article

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Comparison of Levosimendan vs. Milrinone in Pediatric Cardiac Surgery

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Abstract

Background: Conventional cardiac surgery involving cardiac arrest and cardiopulmonary bypass (CPB) is well known to be associated with postoperative myocardial dysfunction and low cardiac output syndrome (LCOS). The aim of this study is to compare the effect of prophylactically administered levosimendan and milrinone on postoperative parameters and outcomes in neonates and infants after corrective open-heart surgery and comparing postoperative parameters like heart rate, mean arterial pressure, arterial and venous blood gasses at certain particular points of time. *Method:* We performed a prospective observational study at our institute. Total 100 pediatric patients undergoing complex congenital cardiac surgeries to evaluate the efficacy of milrinone and levosimendan on intraoperative and postoperative outcomes. *Result:* In the postoperative period heart rate and mean arterial pressure at three different time periods (T1, T2 and T3) did not show any statistically significant difference in both the groups. The VIS score after 48 hours was less in Group L (p = 0.0005). Serum creatinine estimated at T2 and T3 showed a statistically significant difference. (p value at T2 = <0.001, p value at T3 = 0.002). Duration of ventilation was less in Group L (p = 0.0297). *Conclusion:* In our prospective observational study of 100 infants undergoing surgery for complex congenital cardiac conditions, postoperative hemodynamic parameters and markers of tissue perfusion overtime were similar in infants with administration of either levosimendan or milrinone. Our results might be the basis of future controlled trials of levosimendan in children with a special focus on duration of mechanical ventilation and the incidence of renal complications.

Keywords: Levosimendan; Milrinone; Cardiopulmonary bypass (CPB); Low cardiac output syndrome (LCOS).

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Introduction

Conventional cardiac surgery involving cardiac arrest and cardiopulmonary bypass (CPB) is well known to be associated with postoperative myocardial dysfunction and low cardiac output syndrome (LCOS). A multitude of intraoperative factors are thought to be related to myocardial damage including: (1) type of pump priming solution (2) persistent arrhythmias, especially ventricular fibrillation (3) inadequate myocardial perfusion or protection (4) ventricular distension (5) coronary artery embolism (6) use of catecholamine (7) aortic cross- clamp time, (8) complex surgical repairs (*e.g.*, ventriculotomies) (9) reperfusion following ischemia (10) cardiopulmonary bypass time and

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(11) subsequent systemic inflammatory response.[1] In addition, some patient-specific factors such as the neonatal myocardium, ventricular hypertrophy, severe cyanosis and pre-existing heart failure ("starving myocardium") affect the susceptibility of the myocardium and propensity for LCOS.[2-4]

The LCOS occurs in up to 25% of young children, even if there are no residual cardiac lesions after surgery[5] and typically occurs between 6 and 18 hours after surgery in a setting of elevated systemic and pulmonary vascular resistances, impaired myocardial function, and arrhythmias.

The LCOS is detected invasively or by signs of inadequate oxygen delivery to the organ systems, e.g. tachycardia, poor systemic perfusion, decreased urine output, elevated lactate, and reduced mixed venous oxygen saturation.[6] If left untreated, LCOS can lead to cardiac arrest, the need for cardiopulmonary resuscitation or extracorporeal life support[7] prolonged mechanical ventilation,[8] a prolonged intensive care stay and increased mortality.[9] Therefore, prevention, early detection, and treatment of postoperative LCOS are paramount. In the adult intensive care setting, cardia output can be measured directly by indicator dilution techniques like thermodilution,[10] by Doppler echocardiography[11] or by arterial pulse contour analysis.[12,13] A cardiac index of <2.2 L/min/m^2 is considered low.[14,15] In children, especially in neonates and infants, it is usually not feasible to employ these techniques due to device sizes, shunts, and other characteristics of cardiovascular physiology[16] as well as poor correlation with tissue oxygen delivery.[17]

With lack of a clear definition, different authors describe various parameters, which are often used as a compound measure. Such a composite parameter for LCOS may consist of several of the following findings:

- Elevated blood lactate or rapid increase in blood lactate[18]
- Decreased central venous oxygen saturation[19] Increase in arterial to central venous oxygen saturation difference
- Decreased urine output[19]
- Increased peripheral skin temperature to core body temperature difference
- Echocardiographic Doppler-derived low cardiac index
- High inotrope requirement[20]

The mainstays of treatment include catecholamine, calcium sensitizers (levosimendan), and phosphodiesterase inhibitors (milrinone).[19]

The aim of this study is to compare the effect of prophylactically administered levosimendan and milrinone on postoperative parameters and outcomes in neonates and infants after corrective open-heart surgery and comparing postoperative parameters like heart rate, mean arterial pressure, arterial and venous blood gasses at certain particular points of time.

Postoperative outcomes were compared in terms of duration of ventilation, VIS (vasoactive inotropic score), intensive care unit stay and tissue perfusion in terms of lactate levels, mixed venous oxygen levels ($SmvO_2$), difference between arterial and venous saturation ($Da\text{-}vO_2$).

Materials and Methods

Study design

We performed a prospective observational study at our institute. Total 100 pediatric patients undergoing complex congenital cardiac surgeries to evaluate the efficacy of milrinone and levosimendan on intraoperative and postoperative outcomes.

Between November 2015 and October 2016 total of 323 complex congenital cardiac surgeries were performed at our institute out of which 100 pediatric patients were included in our study.

The study was approved by our institutional ethical committee. Informed written consent was obtained from the parents or guardians of the patients.

Inclusion criteria

Pediatric patients undergoing surgeries for complex congenital cardiac anomalies.

Cardiac conditions included in our study were:

- d-TGA (D- Transposition of great arteries) with intact interventricular septum
- d-TGA with ventricular septal defect (VSD)
- Double outlet right ventricle with VSD (Taussig-Bing anomaly)
- Total anomalous pulmonary venous connection (TAPVC) (supra cardiac, intracardiac and infracardiac type)
- Atrioventricular canal defect (AVCD) (partial and complete)
- Truncus arteriosus
- AP window (Aorto pulmonary window)

- Anomalous origin of coronary artery from pulmonary artery (ALCAPA)
- Cortriatrium

Surgeries performed in the study population included:

- Arterial switch operation
- TAPVC (Total anomalous pulmonary venous connection) repair
- AVCD (atrioventricular canal defect) repair
- Cortriatrium repair
- ALCAPA (Anomalous origin of coronary artery from pulmonary artery) repair

Exclusion criteria

- Infants and children undergoing closed heart surgeries
- Preoperatively intubated patients
- Preoperative patients in renal and hepatic failure
- Patients with preoperative sepsis and septic shock
- Age more than 6 years
- History of preoperative LCOS
- History of preoperative cardiopulmonary resuscitation
- History of treatment with one of the study drugs within the 4 weeks prior to enrollment.
- Children with tetralogy of Fallot
- Patients with residual atrial or ventricular septal defect in the post-operative echocardiography with the need of reoperation during the first postoperative 48 hrs.

Assessment

Both the groups were compared for intraoperative parameters including CPB time and aortic cross-clamp time.

Postoperative parameters compared in both the groups included:

- Heart rate (at three different time intervals, T1 (1 hour postoperatively), T2 (24 hrs. postoperatively) and T3 (48 hrs. Postoperatively)
- Mean arterial pressure at three different time intervals, T1 (1 hour postoperatively), T2 (24 hrs. postoperatively) and T3 (48 hrs. postoperatively)
- Arterial and venous blood gasses at three different time intervals, T1 (1 hour postoperatively), T2 (24 hrs. postoperatively) and T3 (48 hrs. postoperatively). (pH, PcO_2, Po_2, SaO_2, $SmvO_2$ and lactate levels).
- Vasoactive inotropic score (VIS) measured at three different time intervals, T1 (1 hour postoperatively), T2 (24 hrs postoperatively) and T3 (48 hrs. postoperatively)
- Duration of mechanic ventilation
- Intensive care unit (ICU) stay
- Postoperative morbidity and mortality.

Morbidity in terms of renal outcomes, low cardiac output syndrome (LCOS) was defined as mean invasive arterial BP of less than the 5th percentile (according to the height and age-based nomogram) after achieving an adequate preloading condition, along with any two of the following: arterial lactates >3 mmol/L on two consecutive readings, $ScvO_2$<50% or a decreasing trend, urine output <1 ml/kg/h for two consecutive hours, HR >90th percentile according to the age-based normogram and neurological outcomes were compared in both the groups.

Inotropic score for levosimendan was not designed so the maintenance dose of levosimendan i.e., 0.1 μg/kg/min (as par to the maintenance of milrinone of 0.5 μg/kg/min) was assigned a score of 5.

Additional inotropic support was initiated at the discretion of the senior consultant in charge. To estimate and make the levels of additionally administered inotropes comparable, the inotrope score previously described by Gaies *et al.*[23] was calculated.

Randomization was done by computerized allocation of patients to both the groups. Patients were divided into Group M (n = 50) who received milrinone and Group L (n = 50) who received levosimendan during the intraoperative period and the postoperative period.

Patients were visited in the preoperative period on the previous day.

Postoperative management

Patients were shifted intubated to the ICU. The rate of weaning from mechanical ventilation and the point of time of extubation were determined by the patient's fluid balance and gas exchange, pattern of breathing, and daily radiographic findings. Sedation was not prolonged and extubation was not

delayed for study reasons. Both the study drugs and additional inotrope/vasoconstrictor agents were tapered once the patients were hemodynamically stable and showed no signs of tissue hypoperfusion as assessed by clinical signs and serial arterial and venous blood gasses. Postoperative echocardiography was performed at regular intervals and at any particular instance where the patient showed major hemodynamic changes.

Results

Between November 2015 and October 2016, total 103 patients were assessed for eligibility for the study. Two patients from the milrinone group and one patient from the levosimendan group had to be excluded from the study in view of reoperation for major residual defects. One patient in the milrinone group had moderate left valve regurgitation in the postoperative echocardiography for which he was reoperated and on milrinone group had a residual ventricular septal defect after arterial switch operation for which the infant was reoperated 48 hours later in view of hemodynamic instability. One patient in the levosimendan group had a residual ventricular septal defect detected 24 hr. After arterial switch operation for which the child was reoperated on cardiopulmonary bypass. Remaining 100 infants were randomized and 50 infants allocated to each group.

Categorical variables are presented as numbers and percentages and analyzed using the $\chi 2$ test. Continuous variables are assessed for normal distribution and presented as means and standard deviation. Continuous variables are compared using student's t test for normally distributed variables and the mann-whitney U test fornon-normally distributed variables. The level of significance was accepted at $p < 0.05$. Statistical analysis was performed using SPSS, version 20.0 (CHICAGO, IL, USA)

Demographic data

The minimum age included in the study was 3 days and maximum was 2 years. The mean age in group M was 5.07 ± 3.09 months and in Group L was 5.34 ± 4.20 months. Mean weight in Group M was 4.26 ± 1.79 kg and in Group L was 4.59 ± 2.12 kg. The mean height in Group M was 57.8 ± 10.26 cm and in group L was 58.78 ± 11.59 cm. Age ($p = 0.715$), weight ($p = 0.401$) and height ($p = 0.656$) were comparable in both the groups (Table 1).

Table 1: Demographic data

	Group M	Group L	p value
Age (months)	5.07 ± 3.09	5.34 ± 4.20	0.715
Weight (kg)	4.26 ± 1.79	4.59 ± 2.12	0.401
Height (cm)	57.80 ± 10.26	58.78 ± 11.59	0.656

Preoperatively 49 of 50 patients in the milrinone had moderate to severe pulmonary arterial hypertension (PAH) and 48 of 50 patients in Group L had moderate to severe pulmonary arterial hypertension as stated in the 2-D echocardiography by continuous wave Doppler method (Fig. 1).

Procedural characteristics

The duration of cardiopulmonary bypass time in Group M was 111.4 ± 46.43 minutes and in Group L was 125.9 ± 32.6 minutes. The aortic cross clamp time in Group M was 80.88 ± 37.30 minutes and in Group L was 92.12 ± 26.97 minutes. Both the cardiopulmonary bypass time and aortic cross-clamp time showed no significant difference in both the groups (Table 2).

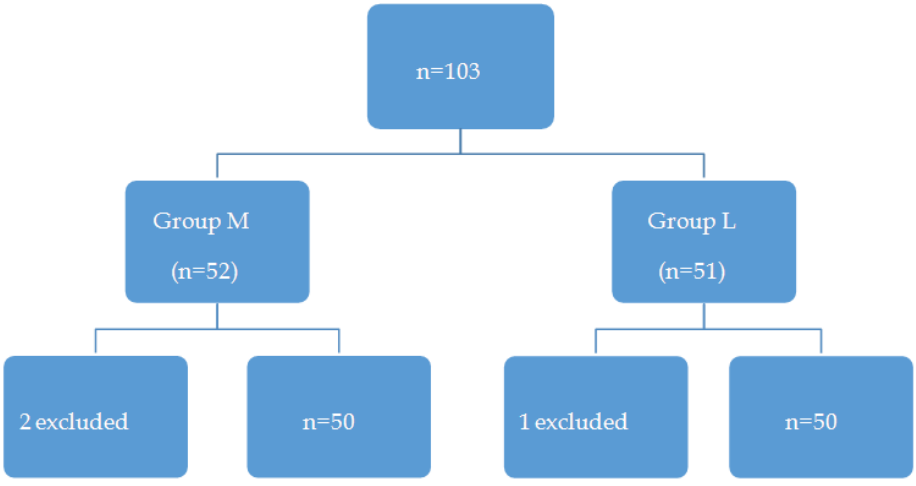

Fig. 1: Comparision of pulmonary hypertension in both the groups

Table 2: Intraoperative Parameters

	Group M	Group L	*p* value
CPB Time (minutes)	111.4 ± 46.43	125.9 ± 32.6	0.1549
AOX Time (minutes)	80.88 ± 37.30	92.12 ± 26.97	0.087

(CPB: Cardio Pulmonary Bypass), (AOX: Aortic Cross Clamp)

Hemodynamic parameters

Both the groups had similar baseline post-induction heart rate and mean arterial pressure. In the postoperative period, as shown in table 3, heart rate and mean arterial pressure at three different time periods (T1, T2 and T3) did not show any statistically significant difference in both the groups.

Table 3: Hemodynamic Parameters

	Group M	Group L	p value
Heart Rate (HR)			
Post Induction HR	137.68 ± 17.21	137.48 ± 16.69	0.953
1 hr PICU HR (T1)	145.76 ± 21.80	145.86 ± 22.65	0.982
24 hr PICU HR (T2)	145.06 ± 19.42	148.54 ± 20.87	0.390
48 hr PICU HR (T3)	142.3 ± 19.24	137.68 ± 21.64	0.262
Mean Arterial Pressure (MAP)			
Post Induction MAP	56.58 ± 9.23	60.46 ± 12.86	0.0862
1 hr PICU MAP (T1)	58.9 ± 12.07	63.82 ± 15.56	0.080
24 hr PICU MAP (T2)	61.5 ± 13.35	60.64 ± 11.86	0.734
48 hr PICU MAP (T3)	59.38 ± 11.67	58.64 ± 8.59	0.718

PICU: Pediatric ICU

Blood gasses

The arterial and venous blood gasses showed a significant difference in the pH in both the groups at T1, T2 and T3. There is no significant difference between arterial and mixed venous oxygen saturation in both the groups at all the time period. (T1, T2 and T3) There was no significant difference between arteriosus and venous serum lactate levels at all time points (Table 4).

Table 4: Comparison of Blood Gasses in Both the Groups

	Group M	Group L	*p* value
DAV			
1 hr PICU DAV (T1)	30.65 ± 11.35	28.74 ± 12.87	0.434
24 hr PICU DAV (T2)	26.27 ± 11.83	22.66 ± 9.01	1.674
48 hr PICU DAV (T3)	20.27 ± 11.14	21.08 ± 6.64	1.576
Arterial Blood Gas			
pH			
ABG 1 hr PICU pH (T1)	7.39 ± 0.06	7.45 ± 0.08	0.009
ABG 24 hr PICU pH (T2)	7.41 ± 0.07	7.40 ± 0.06	0.009
ABG 48 hr PICU pH (T3)	7.40 ± 0.06	7.38 ± 0.06	0.008
PCO_2			
ABG 1 hr PICU PCO_2 (T1)	38.99 ± 7.54	37.07 ± 6.78	1.066
ABG 24 hr PICU PCO_2 (T2)	38.95 ± 6.04	38.51 ± 5.88	0.854
ABG 48 hr PICU PCO_2 (T3)	37.26 ± 7.92	40.88 ± 7.37	1.120
PO_2			
ABG 1 hr PICU PO_2 (T1)	105.57 ± 62.23	131.06± 97.12	8.801
ABG 24 hr PICU PO_2 (T2)	178.62 ± 73.80	206.32± 75.49	10.43
ABG 48 hr PICU PO_2(T3)	167.39 ± 71.53	226.40± 96.03	10.116
SaO_2			
ABG 1 hr PICU SaO_2 (T1)	93.11 ± 11.86	97.03 ± 2.93	1.830
ABG 24 hr PICU SaO_2 (T2)	98.82 ± 1.46	99.14 ± 1.06	0.226
ABG 48 hr PICU SaO_2 (T3)	99.02 ± 1.24	99.17 ± 0.87	0.188
Lactate			
ABG 1 hr PICU Lactate (T1)	4.32 ± 2.87	3.70 ± 2.74	0.405
ABG 24 hr PICU Lactate (T2)	2.12 ± 0.94	2.07 ± 0.98	0.133
ABG 48 hr PICU Lactate (T3)	1.80 ± 1.01	1.83 ± 1.06	0.143
Venous Blood Gas			
pH			
VBG 1 hr PICU pH (T1)	7.34 ± 0.06	7.39 ± 0.07	0.008
VBG 24 hr PICU pH (T2)	7.36 ± 0.071	7.35 ± 0.05	0.010
VBG 48 hr PICU pH (T3)	7.35 ± 0.05	7.34 ± 0.05	0.008
PCO_2			
VBG 1 hr PICU PCO_2 (T1)	49.98 ± 9.09	45.09 ± 7.78	1.285
VBG 24 hr PICU PCO_2 (T2)	47.09 ± 7.35	45.16 ± 6.16	1.040
VBG 48hrs PICU PCO_2 (T3)	47.12 ± 7.22	48.47 ± 5.84	1.021
PO_2			
VBG 1hr PICU PO_2 (T1)	33.60 ± 7.58	35.54 ± 9.19	1.073
VBG 24hrs PICU PO_2 (T2)	42.63 ± 10.19	44.22 ± 8.64	1.441
VBG 48hrs PICU PO_2 (T3)	50.83 ± 24.94	45.26 ± 7.06	3.527
$SMVO_2$			
VBG 1 hr PICU $SMVO_2$ (T1)	62.19 ± 15.82	66.21 ± 12.51	2.441
VBG 24 hr PICU $SMVO_2$ (T2)	72.88 ± 12.50	76.48 ± 9.19	1.929
VBG 48 hr PICU $SMVO_2$ (T3)	79.52 ± 10.51	78.10 ± 6.54	1.585
Lactate			
VBG 1 hr PICU Lactate (T1)	4.37 ± 2.96	4.16 ± 2.48	0.419
VBG 24 hr PICU Lactate (T2)	2.23 ± 1.14	2.20 ± 1.07	0.162
VBG 48 hr PICU Lactate (T3)	1.77 ± 1.07	1.73 ± 0.62	0.152

Inotropic score

At least one catecholamine was administered on the decision of the senior consultant in 49 of the 50 patients in the milrinone group and 48 of the 50 patients in the levosimendan group for treatment of arterial hypotension refractory to fluid replacement or treatment of reduced myocardial contractility in the operation theater after weaning from cardiopulmonary bypass. The use of additional catecholamines, reflected in the vasoactive inotrope score did not differ between the groups in the initial 1 hour of PICU arrival and after 24 hours of PICU arrival (Table 5). An additional milrinone infusion was started after 48 hours in 8 patients in

Group L and in 15 patients in Group M, milrinone infusion was continued because of biologic and/or clinical signs of LCOS persisted. The VIS score after 48 hours showed a significant difference ($p = 0.0005$) between both the groups because of the prolonged action of levosimendan and its metabolite so the drug was weaned within 48 hours in Group L whereas milrinone was continued in Group M even after 48 hours in few patients due to the relatively shorter duration of action of milrinone compared to levosimendan.

Table 5: Comparison of Inotropic Score in Both the Groups

	Group M	Group L	*p* value
1 hr PICU Ionotropic Score (T1)	12.94 ± 4.27	12.24 ± 4.22	0.077
24 hr PICU Ionotropic Score (T2)	9.22 ± 5.16	9.08 ± 6.11	0.901
48 hr PICU Ionotropic Score (T3)	7.16 ± 6.24	4.68 ± 7.59	0.0005

Serum creatinine

Preoperative renal parameters (serum creatinine) showed a significant difference in both the groups. The serum creatinine estimated at T2 and T3 Showed a statistically significant difference. (p value at T2=<0.001, p value at T3=0.002) (Table 6).

Table 6: Comparison of Serum Creatinine in Both the Groups

	Group M	Group L	*p* value
Pre induction Sr. Creatinine	0.462 ± 0.109	0.387 ± 0.098	0.0009
24 hr PICU Sr. Creatinine	0.502 ± 0.097	0.435 ± 0.099	<0.001
48 hr PICU Sr. Creatinine	0.536 ± 0.250	0.408 ± 0.138	0.002

This finding extrapolates to the significant reduction of the incidence postoperative acute kidney injury (6 vs. 16) in Group L.

Postoperative outcomes

The duration of ventilation in Group M was 68.1 ± 56.02 hours and in Group L was 46.26 ± 41.23 hours. Duration of ventilation showed a significant difference ($p = 0.0297$) between both the groups with a reduction of ventilation duration in the levosimendan group. There was no statistically significant difference in the duration of ICU stay in both the groups (Table 7).

Table 7: Comparison of Postoperative Parameters in Both the Groups

	Group M	Group L	*p* value
MVT (hrs)	68.1 ± 56.02	46.26 ± 41.23	0.0297
ICU Stay (days)	8.06 ± 5.74	7.5 ± 3.33	0.5521

MVT: Mechanical ventilation time. ICU: Intensive care unit

ICU Morbidity and Mortality

There was no loss of atrioventricular synchrony or any sustained and serious atrial or ventricular tachyarrhythmia in the 100 patients who finished the study. Eight Patients in the Group L and six patients in the Group M had their chest left open at the end of the surgery. Both drugs were well tolerated in the immediate postoperative period and no serious adverse event occurred throughout the ICU stay. None of the patients needed mechanical circulatory support. Eight patients in Group M had postoperative surgical drainage and were re-explored in the first 12 hours where as two patients were re-explored in the levosimendan group.

Six patients in the milrinone group and ten patients in Group L had low cardiac output syndrome (LCOS) as measured by echocardiography. Sixteen patients in Group M and six patients in Group L had immediate postoperative acute kidney injury which was managed by peritoneal dialysis. Nine versus four patients in Group M and Group L respectively were re-intubated as they could not maintain adequate saturations on conventional oxygen therapy. Four patients in Group M expired in the intensive care unit. Out of the four, two patients developed severe sepsis and septic shock and were hemodynamically unstable even on high inotropic support and later expired. Two patients developed pneumonic patch after extubation and were re-intubated later succumbed to sepsis and expired. Four patients in the levosimendan group expire due to which two developed acute kidney injury and expired and two of them succumbed due to sepsis.

Discussion

Levosimendan improves myocardial contractility without increasing myocardial oxygen consumption, impairing diastolic relaxation, or causing an increase in intracellular calcium concentration.[22,23]

Levosimendan has been extensively evaluated in the adult population[24,25] but has received little attention in the pediatric field in the past and has been gaining greater attention in the last few years.

Due to its mechanism of action through calcium sensitization and its additional inotropic and vasodilator properties, levosimendan might be considered superior to milrinone in prevention and treatment of LCOS after open-heart surgery in children and infants.

We conducted a prospective observational study in 100 infants, who underwent surgeries for complex cardiac conditions on cardiopulmonary bypass and prophylactically received either a loading dose of milrinone (Group M) or levosimendan (Group L) followed by a maintenance dose, immediately after aortic cross clamp removal to evaluate the effect of these inotropic agents on hemodynamics (heart rate, mean arterial pressure), markers of tissue perfusion like lactate, mixed venous saturation, difference between arterial and venous saturations and the effects on postoperative outcomes, duration of ventilation, ICU stay, morbidity (renal, cardiovascular and neurological) and mortality.

In a piglet model, Stocker *et al*.[26] showed that prophylactically administered levosimendan as well as milrinone protected against reduction in CO and prevented from increase in left ventricular afterload early after cardiopulmonary bypass. In this animal model, levosimendan but not milrinone, improved myocardial contractility and led to an increase of CO above baseline. In our study we found no difference in the heart rate and mean arterial pressure in both the groups. The markers of tissue perfusion did not show any statistical difference between both the groups.

In a recently published randomized controlled trial in children after congenital heart surgery, Momeni *et al*.[27] compared the prophylactic use of milrinone against the prophylactic of levosimendan in a small and heterogeneous group of study subjects of various ages with all-age spectrum of diagnoses and different types of cardiac surgery. The primary endpoint, serum lactate concentrations[4] hrs after surgery, did not differ between the groups as was seen in our study. The only statistically significant difference found in the artrial was mean heart rate in the levosimendan group after 24 and 48 hrs. Our findings are consistent with their observations and the difference in the heart rate did not reach significance in our study.

Considering that the quantitative measurement of cardiac index in the pediatric population is limited, most pediatric intensivists use clinical and biochemical signs to support the diagnosis of LCOS. Among biochemical markers routinely used to support the diagnosis of LCOS, the serum lactate level is considered as one of the most important biochemical markers of early adverse outcome after complex congenital cardiac surgery.[28–30]

Duke *et al*.[28] showed that 4 hours after pediatric intensive care unit admission, lactate remained a clinically significant predictor of a major adverse event when greater than 4.5 mmol/L. Our study population did not show any significant difference in arterial and venous lactate levels at all time points in both the groups.

Milrinone and Levosimendan have different pharmacokinetics

Milrinone acts immediately when intravenously administered. The onset of action of levosimendan takes 3 to 4 hrs and exceeds the duration of administration because it acts through metabolites.

This prolonged duration of action of levosimendan led to a significant difference in the postoperative inotropic score at 48 hours (p value = 0.0005). Lecher *et al*.[31] in their study proposed no difference in the inotropic score in both the groups, but the study used the IS score proposed by Wernovsky *et al*.[32]

Two major drawbacks of the IS score proposed by Wernovsky *et al*.[33] were that it neither included milrinone or levosimendan and that it did not include vasopressin in the score which was used in few cases in our study.

In our study vasoactive inotropic score (VIS score) proposed by Gaies *et al*.[33] was used and the usual maintenance dose of levosimendan (0.1 μg/kg/min) was given a score of 5 so as to match the inotropic score of the maintenance dose of milrinone (0.5 μg /kg/min) which in the VIS score had a score of 5. The use of additional catecholamines did not differ between the groups.

To avoid a heterogeneous study population, we intentionally excluded patients with single ventricle lesions and with preoperative myocardial failure.

Our study patients were possibly not sick enough to form a valid study population. One could speculate that in a study population with pre-existing congestive heart failure or more complex cardiac lesions, levosimendan might have been more advantageous due to its inotropic properties and pharmacologic profile.

A further remarkable finding of this study is that levosimendan was very well tolerated and did not cause arterial hypotension, increased heart rate, and increased fluid requirement, or an excessive need of inotropes or vasoconstrictors when administered through a continuous infusion.

Both the groups showed a statistically significant difference in the duration of mechanical ventilation. Serum creatinine measured 24 hrs and 48 hrs Postoperatively showed a significant difference between both the groups likely due to the peripheral vasodilatory effect of levosimendan. The

postoperative renal outcomes showed a significant difference between both the groups with a significant reduction in the incidence of postoperative acute kidney injury in the levosimendan group.

Limitations

Overall, this study and its findings were limited by its small number of included study subjects.

One limitation of our study was the fact that there are currently no pulmonary artery catheters of appropriate size available for infants. Therefore, we could not perform invasive measurement of CO.

We could not include patients with preoperative ventricular dysfunction where the expected effect of levosimendan seems to have better outcome as stated in several adult studies and one pediatric retrospective study.

However, the study demonstrates that levosimendan can be used in children and that its use is associated with an overall trend toward hemodynamic benefit in a critically ill pediatric patient population.

To evaluate the effect on duration of ventilation which is a major contributing factor for the ICU stay larger study population are required.

Further studies are required on the Reno protective effect of levosimendan observed in this study to confirm its effect. This effect of levosimendan can advocate for its utilization in patients with acute kidney injury due to LCOS and or various etiologies in the immediate postoperative period.

Several subsets like premature infants, low-birth weight children, cyanotic heart disease, infants with preoperative ventricular dysfunction and infants with preoperative altered renal parameters have to be evaluated to confirm the superiority of this drug over various available inotropic and indicator agents.

Conclusion

In our prospective observational study of 100 infants undergoing surgery for complex congenital cardiac conditions, postoperative hemodynamic parameters and markers of tissue perfusion overtime were similar in infants with administration of either levosimendan or milrinone.

We observed decrease in the VIS score in the levosimendan group after 48 hrs. Due to the prolonged action of levosimendan and its metabolites compared to milrinone.

Duration of mechanical ventilation was significantly reduced in infants administered levosimendan in the immediate perioperative period.

The renal parameters showed a significant difference in both the groups with a significant reduction in the incidence of postoperative acute kidney injury.

This prospective observational study has primarily serve experience using the new drug levosimendan in neonates and infants and to initiate further multi center trials in pediatric patients.

Our results might be the basis of future controlled trials of levosimendan in children with a special focus on duration of mechanical ventilation and the incidence of renal complications.

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Original Research Article

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A Study on Bupivacaine and Bupivacaine Plus Midazolam for Caudal analgesia in Children's

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Abstract

Pain is the commonest and most troubling impact of sickness and medical procedure. It has been an extraordinary test and worry to analysts. Entirely torment is an unmeasurable substance and any plan for its evaluation in man must be available to both subjects and spectator mistake. Aim of our study was to study on Bupivacaine and Bupivacaine plus Midazolam for caudal analgesia in children's. *Materials and Methods:* The examination was embraced in 60 patients between the age gathering of 3 months and 12 years, and weighing between 4.5 kg and 25 kg, experiencing the elective medical procedures performed beneath the umbilical region. *Conclusion:* Caudal additional dural course has been favored in youngsters for its higher consistency, as respects to specialized parts of area of room and viability of relief from discomfort with medications regulated by this course.

Keywords: Bupivacaine; Bupivacaine plus Midazolam.

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Introduction

Pain is the commonest and most troubling impact of sickness and medical procedure. It has been an extraordinary test and worry to analysts. Entirely torment is an unmeasurable substance and any plan for its evaluation in man must be available to both subjects and spectator mistake.

All the joy humanity can pick up is not in quest for delight however in mitigating torment. Quick and successful alleviation of torment is satisfying.

Concentrates in the course of recent years found that deficient torment the executives is normal in youngsters.[1] Contrasting of pain relieving utilization among grown-ups and youngsters demonstrated reliably that kids get less, less successive, and littler portions of intense narcotics.[2] Purposes behind retention absense of pain are various and incorporate an abrogating concern in regards to respiratory gloom and a thought that kids don't react to agony to indistinguishable degree from do grown-ups.

The medications utilized as postoperative analgesics ought to be powerful and ought not deliver symptoms, for example, emesis, respiratory sadness or habit when utilized for significant lots.[3]

Neighborhood invasion of agent entry point destinations with nearby analgesics have been

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utilized for quite a while and are viable adjuvants to any sedative system.

Oral organization of opioids, Acetaminophen, NSAIDS can be empowered in postoperative youngsters who are taking oral liquids. This course as often as possible can not be utilized in the quick postoperative period on account of queasiness and retching or ileus.[4]

IM and IV courses have the inconveniences of territorial blood stream impacts, pinnacles and valleys of focuses and soak variances in blood levels, aside from trouble of torment by IM course. While PCAs are upheld in more established youngsters, persistent IV mixture has been attempted in littler babies.

Constant intrapleural absense of pain has been portrayed for kids experiencing chest, upper stomach and bother bladder medical procedure.[5]

In 1991 J.L. Pedraz *et al.* contemplated the pharmacokinetics and appropriation of Ketamine and its biotransformation items in canines after extradural organization of Ketamine at 1.4–1.5 and discovered Ketamine demonstrated a more prominent proclivity for mind stem, while Norketamine and Dehydronorketamine were conveyed for the most part in cerebellum and kidney separately.

In 1993 Sudha A Ved Mark Pinosky *et al.* announced, case reports of ventricular tachycardia and brief cardiovascular fall in two newborn children after caudal anesthesia utilizing a 'Bupivacaine–Epinephrine' arrangement and inferred that two coincidental intravascular infusions of Bupivacaine and epinephrine amid the execution of caudal anesthesia in babies.[6] These were related with wide complex tachycardia and hypotension that were fleeting, and likely spoken to epinephrine danger. The creators prescribed routine test portions and moderate fragmentary organization of the whole neighborhood analgesic portion when performing caudal epidural square in kids.[7-8]

Aim of our study was to study on Bupivacaine and Bupivacaine plus Midazolam for caudal analgesia in children's.

Material and Methods

A clinical report was embraced to assess the quality and term of absense of pain after caudal (epidural) Bupivacaine, and Bupivacaine with midazolam given in youngsters for elective infraumbilical medical procedures.

The examination was embraced in 60 patients between the age gathering of 3 months and 12 years, and weighing between 4.5 kg and 25 kg, experiencing the elective medical procedures performed beneath the umbilical region.

Nitty-gritty history and a total preoperative examination was attempted in order to prohibit patients with any fundamental illness particularly neurological infections and draining diathesis. A past filled with NSAID consumption if any was cautiously gotten and avoided such patients from the examination, chose patients had a place with American culture of anesthesiologist's order review 1 (ASA–1). All youngsters were submitted to routine examinations like total pee investigation and complete blood picture.[9]

Preceding booked activity a composed and educated assent was gotten by emergency clinic board of trustees and furthermore the idea of study was disclosed to patients and their folks. Youngsters taken up for the examination were not premedicated with pain relieving drugs and were fasted for least of 4 hours. A resting preanesthetic record of circulatory strain, beat rate, respiratory rate was recorded.[10]

All kids were anesthetized with standard enlistment system of Thiopentone 5 mg/kg gone before by 20 microgram/kg of infusion Atropine intravenously. Intubation was performed under suxamethonium 1.5 mg/kg unwinding. General anesthesia was kept up by inward breath technique, utilizing nitrous oxide (66.66%) oxygen (33.33%) and halothane 0.5% to 2%, utilizing a Rees alteration of Ayre's T piece and unconstrained ventilation. Contingent upon their body weight, new gas stream was determined and set in connection to body weight.

After acceptance of anesthetia, all kids were swung to left sidelong position. Inj. Bupivacaine 1 ml/kg additive free (0.25% arrangement) or inj. bupivacaine with inj.midazolam 50 microgram/kg additive free was infused into the caudal epidural space under strict aseptic conditions.

Results

To assess the adequacy of bupivacaine and bupivacaine with midazolam which were given caudally for intraoperative and postoperative absence of pain, The examination was embraced in 60 patients between the age gathering of 3 months and 12 years a place with ASA review 1, every one of those experiencing medical procedures performed

Group	Pulse rate (mean ± S.D)	Blood pressure Systolic (mean ± S.D)	Blood pressure Diastolic (mean ± S.D)	Respiratory rate (bpm) (mean ± S.D)
B	117.86 ± 11.36	86.8 ± 6.27	59.6 ± 6.87	26.87 ± 3.56
B+M	128.24 ± 12.23	94.0 ± 8.15	63.6 ± 7.735	24.58 ± 4.69

underneath the umbilicus and lower limit. Normal term of medical procedure was 30 minutes.

All preoperative vital parameters were comparable without any statistical significance ($p > 0.001$).

According to convention the examination was twofold visually impaired and randomized. Every one of the kids were premedicated with inj. Atropine i.v. 20 microgram/kg, incited with inj. Thiopentone sodium (5 mg/kg) intubated with suxamethonium 1.5 mg/kg and kept up on unconstrained ventilation by utilizing N_2O (66.66%), O_2 (33.33%) and halothane 0.5% to 2%, using Rees alteration of Ayre's T piece. Caudal epidural square was executed according to irregular pick, and kids were checked intraoperatively.

All kids were watched postoperatively and recorded agony scores at 0, 15 minutes, 30 minutes, 45 minutes, 60 minutes, 1½ hours, 2 hours, 3 hours, 6 hours, 12 hours and 24 hours.

Torment power was determined at each time in contrast with basal dimension. Agony force alone when contrasted among the gatherings was found with have no factual centrality. However when time is thought about the agony power in all gatherings indicated measurable hugeness ($p < 0.001$).

In Bupivacaine amass the agony force was altogether increasingly following 3 hours. The power of agony was huge following 6 hours in the gathering of Bupivacaine + Midazolanm ($p < 0.001$).

Postoperatively all kids were watched for unfriendly impacts like sickness, retching, maintenance of pee, engine soft spot for 24 hours.

Discussion

Post-agent uneasiness that emerges from agony is irritating for the tyke and guardians. Some genital and perineal surgeries, for example, anoplasty and hypospadiasis adjustment are trailed by moderate to serious postoperative agony. Feeling the torment after the surgeries, may make the kid control the agent site, which thusly may prompt post-agent dying, contamination, or other careful complexities, and furthermore result in long-haul mental issues.

Surveying torment in kids presents a bigger number of issues than does in grown-ups. The formative phase of youthful youngsters does not allow them to express their enduring verbally, in all age gatherings of kids relapse when they are hospitalized and went up against with serious postoperative torment. They decline to talk, they just cry until a sensible relief from discomfort has been given. By and by there are no legitimate and all around acknowledged devices for precisely estimating torment in little youngsters. Pediatric agony scores are multitudinous. Absence of verbal correspondence by the tyke, faulty and partial understanding of torment motions by the going to staff makes it exceptionally hard to develop far reaching torment scores.

A needle might be set with in the caudal space more effectively than in the epidural space in kids. The non accessibility of suitable estimated epidural needles for pediatric use makes caudal infusion or caudal catheters a favored course for organization of epidural medications, for example, neighborhood analgesics, Midazolam in youthful kids.

In this examination caudal Bupivacaine (additive free) (0.25%) with a portion of 1 ml/kg weight and midazolam (additive free) with portion of 50 microgram/kg body weight were utilized.

Aside from the account of the seriousness of agony, degree and term of help with discomfort with different operators utilized in the investigation. The indispensable parameters viz. beat rate, pulse, and respiratory rate and symptoms were noted in each gathering.

Despite the fact that the quantities of cases examined were just fifty, they were sensibly dispersed between the age gathering of 2 months and 11 years in order to give smart thought of the convenience of the methodology, strategy and its acknowledgment. Seevers (1936), Ruston (1954 and 1957), Spigel (1962) Frotina (1967), Touloukian (1971) *et al*., considered in excess of 750 cases and contributed their encounters with the system in the pediatric age gather 0–14 years.

Every one of the youngsters in this examination experienced system, for example, inguinal hernia fixes, orchidopexies, urological methods, which are difficult in the postoperative period henceforth kids will in general be less agreeable. It was discovered that intraoperatively there was no raise in heartbeat rate, respiratory rate, and circulatory strain to careful upgrade in both the gatherings demonstrating sufficiency of absense of pain.

Up to 69% of youngsters in the Bupivacaine bunch were sans torment, (snickering, glad, fought, merry, energetic, and sleeping.) until 3 hours after medical procedure. Eighty percent of kids were without torment in Bupivacaine + Midazolam assemble as long as 3 hours following medical procedure. The perception in our investigation demonstrates that caudal Bupivacaine + Midazolam delayed postoperative help with discomfort which is related well with the before investigations of Jose-adolfo isles *et al.* (1985) and Naguib M *et al.* (1995).

Conclusion

Caudal additional dural course has been favored in youngsters for its higher consistency, as respects to specialized parts of area of room and viability of relief from discomfort with medications regulated by this course. Epidural Bupivacaine and Midazolam blend unquestionably drawn out the span of post agent help with discomfort in youngsters. It radically chops down the utilization of parenteral analgesics in the post-agent period. There were a negligible frequency of reactions like vomiting and maintenance of pee which reacted to moderate treatment.

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Original Research Article

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Comparative Study of Pulmonary Artery Catheter vs Central Venous Catheter in Coronary Artery Bypass Grafting Surgery Patients

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Abstract

Background: Pulmonary artery catheter and central venous catheter are an important and integral part of hemodynamic monitoring during coronary artery bypass grafting. *Methods:* In our prospective randomized survey, 180 patients received either pulmonary artery or central venous catheter after induction of anesthesia. Patients between 35 and 75 years with ejection fraction between 35 and 60% undergoing elective off pump coronary artery bypass grafting surgery were included. Both groups were compared regarding heart rate, mean arterial pressures, serum lactate and central venous saturation, need for inotropes, fluid challenge, blood and blood products use, postoperative complications and ICU stay. *Results:* There is no statistical difference in heart rate and mean arterial pressure in intra- and postoperative period in both CVC and PA group except in PA group where heart rate was significantly lower after grafting and mean arterial pressure was higher at T6 and T12 hrs. After 48 hours blood lactate level was significant lower in PA catheter groups. Both groups were similar in terms of central venous saturation, intraoperative fluid bolus use, blood, blood products use and output both intraoperative and postoperatively. Use of inotropes particularly noradrenaline and levosemandan was more in PA group. There was no statistically significant difference in respiratory, CNS and Renal complications (*p* value >0.05), ICU stays >48 hr and mortality in both groups. *Conclusion:* We can conclude from our study that PAC definitely provides additional information regarding cardiac output and cardiac index in comparisons with CVC but clearly it does not result in significant difference in postoperative ICU stay and outcome of patient in form of morbidity and mortality in coronary artery bypass patients with preserved LV function.

Keywords: Central venous catheter; Pulmonary artery catheter; Coronary artery bypass graft; Peripheral vascular disease.

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Introduction

The introduction and initiation of substantial hemodynamic monitoring ushered the successful era of coronary artery bypass grafting surgery. With further knowledge in medical monitoring, ever-increasing stress has been placed on establishment of a central venous catheter (CVC) and pulmonary artery catheter (PAC) for hemodynamic monitoring. In the last decade, PAC monitoring has become less common with the newer advanced methods of cardiac output monitoring, but it is still considered as standard method for hemodynamic monitoring during coronary artery bypass graft (CABG).[1,2] On one hand, The CVC gives an idea

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about fluid status but does not provide extensive hemodynamic information as PA. Advocates of routine PA catheter use cite the advantages of early detection of hemodynamic deterioration[3–5], precise monitoring of the effect of therapeutic interventions and evidence that mortality is related to indices of myocardial function, namely the cardiac index, measured with a PA catheter.[6]

For patients who undergo coronary artery bypass graft (CABG) surgery, the PAC remains the most frequently used monitor among cardiovascular anesthesiologists.[7] The PAC has been considered to be a valuable device in perioperative fluid and vasoactive drug management, for early detection of perfusion abnormalities potentially for establishing tissue hypoxia. The CVC is still considered a cost-effective monitoring tool for management of CABG. Also there are very few studies which include the patients undergoing CABG with proper unbiased patient selection with randomization which can decide if PAC or CVC is the desirable monitoring tool for both intraoperative and postoperative management of patients including in terms of morbidity and mortality.

So our aim of the study is to conduct prospective survey to compare PA catheter with CVP catheter in patients undergoing coronary artery bypass grafting in terms of intraoperative and postoperative management.

Materials and Methods

In our single centered prospective randomized study, 180 patients undergoing elective off pump coronary artery bypass grafting (CABG) between February 2015 and February 2016 were randomly divided into two groups by computerized method. Institutional ethics committee approval was taken and written informed consent from patients was obtained. Group A and Group B received Pulmonary artery (PA) catheter and Central venous catheter (CVC) respectively.

Inclusion criteria

Patients between 35 and 75 years with ejection fraction between 35 and 60%, with or without controlled systemic disease were included.

Exclusion criteria

Patient with recent (less than 24-hour) or ongoing myocardial infarction or if combined surgical procedures (including valve or ascending aorta procedures) or redo-operations were excluded. Patients with planned off-pump CABG surgery were excluded.

Patients with age more than 75 years or less than 35 year, severe left ventricular dysfunction (EF <35%), on intra-aortic balloon pump, post- Myocardial infarction ventricular septal rupture, ischemic MR, significant renal and hepatic dysfunction, neurological abnormality, peripheral vascular disease (PVD) and preoperative coagulation abnormality were excluded from the study.

All patients were given Tab. Alprazolam and Inj. Pantoprazole night before surgery.

Beta-blockers and other drugs except angiotensin-receptor blocker drugs were continued until the morning of surgery in all patients, and oral anti-diabetic agent like sulfonylureas was stopped and replaced with insulin at the time of hospital admission.

In all patient inj midazolam 0.05 mg/kg was given as premedication half an hour before surgery in preoperative room under close supervision of vitals.

Peripheral line and radial arterial line were inserted under local anesthesia prior to induction under aseptic precautions.

Anesthesia was induced in all patients by the administration of 0.1 mg/kg Midazolam, 5 µg/kg fentanyl and 0.2 mg/kg vecuronium bromide. After 3 min, patients underwent oral endotracheal intubation. In all patient CVC or PA catheter was put in right internal jugular vein after induction by Seldinger method. Intraoperatively, patients were administered 1 µg/kg Fentanyl, 0.04 mg/kg Vecuronium and Sevoflurane for maintenance of anesthesia.

All the patients were treated with 2 mg/kg heparin sodium for anticoagulation and protamine was used for heparin neutralization.

Heart rate (HR), Mean arterial pressure (MAP), Central venous oxygen saturation ($SvCO_2$) and Serum lactate in both groups was observed intraoperative after induction (AI), before grafting (BG) and after grafting (AG) and postoperative (T1) 1 hour (hr), (T6) 6 hr, (T12) 12 hr, (T18) 18 hr, (T24) 24 hr, (T36) 36 hr and (T48) 48 hr after surgery in postoperative ICU. In CVC group central venous pressure (CVP) was observed and in PA group CVP, Pulmonary capillary wedge pressure (PCWP), Cardiac output (CO) monitoring was done by thermodilution method and CO variable like Cardiac Index (CI) was observed

after induction, before grafting and after grafting during intraoperative and post operative at (T1) 1 hr, (T6) 6 hr, (T12) 12 hr, (T18) 18 hr, (T24) 24 hr, (T36) 36 hr and (T48) 48 hr after surgery in postoperative ICU. CVP and PCWP were maintained between 8 and 12 mm of Hg and 12 and 15 mm Hg respectively in both groups throughout perioperative period. Infusion of Inj. nitroglycerine was used for coronary vasodilation and to control perioperative hypertension. Hypotension was corrected first by giving fluid challenge with 250–300 ml crystalloids and if failed, either inotropes noradrenaline or dobutamine were started and/or blood transfusion done according to Hb to keep systolic blood pressure (SBP) and/or mean arterial pressure (MAP) above 90 mm Hg and 60 mm Hg respectively. In PA group hemodynamic management was done with CO monitoring. If the CI remained < 2.2 L/m^2/min with dobutamine (initial doses of 5 µg/kg/min), norepinephrine was added (starting dose of 0.02 µg/kg/min, with increments of 0.02 µg/kg/min until the desired MAP level was reached).

In postoperative period if CI < 2.2 L/min/m^2, pulmonary capillary pressure >16 mm Hg, and mixed venous saturation <60% in PA group and high CVP > 12, cold peripheries and central venous saturation <60% in CVP group suggesting patients experiencing (Low cardiac output syndrome (LCOS), dobutamine was started at a dose of 5 µg/kg/min, and if a hemodynamic response was not observed, the dose was increased to 7.5, 10, and finally to 12.5 µg/kg/min at 15 minute intervals. In patients in whom low cardiac output persisted, epinephrine was added as a second inotropic drug at a dose of 0.02 to 0.1 µg/kg/min. Inj. Levosimendan was started in hemodynamically unstable patient in which low cardiac index or cardiac output observed via cardiac output monitoring by PA catheter group and in CVP group it was started when hemodynamics was not maintained with other inotropes or large heart or poor contractility. Inj. milrinone 50 ug/kg bolus followed by infusion at 0.5 ug/kg/min is used if patients showed right ventricular failure in postoperative ECHO.

Criteria for extubation were partial pressure of oxygen PaO_2/FiO_2 more than 250, respiratory rate <25/min, arterial oxygen saturation between 98% and 100% at FiO_2 = 0.4 for 1 hour. Criteria for intensive care unit discharge were spontaneous breathing, hemodynamic stability without inotropic treatment, clear consciousness, and normal renal function.

Both these groups were compared with regards to need for inotropes, fluid challenge, blood and blood product use and postoperative complication. Intensive care unit stay in term of less than 24 hours, between 24 hours and 48 hours, more than 48 hours was observed in postoperative ICU. Any other complication like significant hypotension, arrhythmias, pulmonary complication, renal failure, CNS complication, death was observed.

Statistical analysis

Statistical analysis was performed using SPSS, Version 20.0 (Chicago, IL, USA). Sample size was calculated through http://www.raosoft.com/samplesize.html. Qualitative data were expressed as proportions whereas the quantitative data was expressed as mean ± SD. The chi-squared test and independent sample *t*-test were used to compare categorical and continuous variables respectively. The level of significance was accepted at $p < 0.05$.

Results

There was no significant difference between two groups regarding demographic data including age, weight, height and gender (Table 1).

All patients of both groups were similar in occurrence of left main, number of coronaries block in term of single vessel disease (SVD), double vessel disease (DVD) or triple vessel disease (TVD), ejection fraction, left atrium (LA) size and left ventricle (LV) diameter in both systole and diastole.There

Table 1: Demographic profile of both group

	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
Age	59.23 ± 9.57	57.81 ± 9.50	0.3186
Weight	61.44 ± 9.58	63.8 ± 12.22	0.1520
Height	158.27 ± 8.06	160.17 ± 7.74	0.1085
Gender distribution			
Male	56	63	0.3448
Female	34	27	

were no significant difference between two group in preoperative history of hypertension (HTN), diabetes mellitus (DM), cerebrovascular accident (CVA), recent myocardial infarction (MI) and chronic obstructive pulmonary disease (COPD) (Table 2).

The duration of surgery were 217.05 ± 45.02 min and 222 ± 48.85 in min in PA group and CVP group, respectively, (Table 3) while the numbers of vascular grafts was 3 ± 0.88 and 2.98 ± 0.76 in PA group and CVP group respectively. There were no significant differences between the groups in duration of surgery and number of graft in both groups ($p > 0.05$).

Both groups had similar baseline preoperative HR and MAP. In postoperative period there was increasing trend in HR than baseline HR in both groups. But in PA group HR after grafting were significantly lower than CVP group (p value <0.05) In postoperative period changes in HR in both group swere not significant (p value >0.05) exceptin T18 hr T24 hr and T36 hr (Table 4). There was no significant change in mean arterial pressure

Table 2: Preoperative Cardiac and Co morbid characteristics

	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
ECHO			
LA Size	28.63 ± 3.29	28.52 ± 3.30	0.8216
LV DD	46.04 ± 3.63	46.83 ± 3.38	0.1326
LV DS	29.92 ± 5.35	31.05 ± 5.44	0.1618
EF	47.05 ± 8.27	45.27 ± 6.76	0.1157
Coronary Angiography			
Left Main	37	25	0.0845
TVD	43	57	0.0512
DVD	10	08	0.8038
Comorbid Characteristics			
DM	46	41	0.5508
Recent MI	14	11	06664
COPD/BA	10	13	0.6552
CVA	06	02	0.2779
HTN	54	43	0.1349

LA: Left atrium, LV DD/DS: left ventricular dimensions in diastole (Dd) and systole (Ds), EF: Ejection fraction, TVD: Triple vessel disease, DVD: Double vessel disease, DM: Diabetes Mellitus, MI: Myocardial Infarction, COPD: Chronic Obstructive Pulmonary Disease, CVA: Cerebrovascular accident, HTN: Hypertension

Table 3: Duration of surgery and no. of graft

No. of GRAFT	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
2	16	12	0.5373
3	68	72	0.5907
4	06	04	0.7449
5	00	02	0.4770
Surgery duration	217.05 ± 45.02	222 ± 48.85	0.645

Table 4: Comparisons of Heart rate in both groups

(Heart Rate) HR	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
HR AI	76.51 ± 11.73	71.8 ± 9.79	0.00389
HR BG	76.82 ± 10.51	74.34 ± 9.34	0.0964
HR AG	78.2 ± 10.16	74.64 ± 9.14	0.0146
HR after 1 h	83.65 ± 15.62	82.96 ± 16.94	0.7770
HR after 6 hr	89.38 ± 15.31	85.93 ± 12.79	0.1021
HR after 12 hr	87.71 ± 14.13	85.7 ± 12.18	0.3080
HR after 18 hr	89.52 ± 12.56	85.88 ± 10.95	0.0400
HR after 24 hr	87.21 ± 13.11	82.43 ± 10.60	0.0078
HR after 36 hr	84.23 ± 11.15	80.27 ± 11.31	0.0192
HR after 48 hr	85.13 ± 9.11	82.98 ± 9.97	0.1339

(MAP) In both groups during intraoperative period however in postoperative period at T6 and T12 hours there was higher MAP in PA group than CVP group (p value <0.05) (Table 5).

There was no significant difference of blood lactate level during after induction and before grafting in both groups, but blood lactate level showed increasing trend after grafting in both groups and continued up to 18 hours in postoperative period. AT T12 hours and T18 hours blood lactate level are similar in both groups respectively. After 48 hours blood lactate level was significant lower in PA catheter groups in compare to CVP cathater groups (Table 6).

There was no significant difference of central venous saturation during intraoperative and postoperative periods in both groups (Table 7).

One patients in each group had incidence of IABP insertion because of hemodynamic instability during grafting. There was no need of convert to Cardiopulmonary bypass (CPB) in both groups.

Table 5: Comparison of change of MAP in both groups

Mean arterial Pressure (MAP)	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	p value
MAP AI	84.84 ± 11.81	84.41 ± 12.85	0.8141
MAP BG	88.51 ± 14.45	86.06 ± 12.63	0.2287
MAP AG	85.35 ± 16.03	84.37 ± 12.33	0.6471
MAP after 1 hr	81.65 ± 20.15	86.33 ± 16.91	0.0934
MAP after 6 hr	81.14 ± 13.03	86.94 ± 16.19	0.0088
MAP after 12 hr	79.4 ± 11.50	83.3 ± 13.39	0.0375
MAP after 18 hr	81.17 ± 10.64	83.17 ± 13.32	0.2674
MAP after 24 hr	82.33 ± 12.51	82.25 ± 13.25	0.9677
MAP after 36 hr	79.38 ± 8.34	81.7 ± 11.33	0.1210
MAP after 48 hr	81.6 ± 9.61	81.76 ± 10.93	0.9136

Table 6: Comparison of blood lactate level in both groups

	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	p value
LACTATE AI	2.04 ± 0.52	1.82 ± 0.47	0.0044
LACTATE BG	2.11 ± 0.65	1.91 ± 0.67	0.0465
LACTATE AG	2.03 ± 0.88	2.12 ± 0.94	0.5302
LACTATE after 1 hr	2.13 ± 0.96	2.39 ± 0.76	0.0477
LACTATE after 6 hr	2.91 ± 1.74	2.65 ± 1.29	0.2637
LACTATE after 12 hr	2.77 ± 1.72	2.76 ± 1.41	0.9698
LACTATE after 18 hr	2.90 ± 1.45	2.91 ± 1.20	0.9689
LACTATE after 24 hr	2.92 ± 1.25	2.70 ± 1.19	0.2295
LACTATE after 36 hr	3.03 ± 1.11	2.68 ± 1.02	0.2295
LACTATE after 48 hr	2.85 ± 1.09	2.45 ± 0.77	0.0048

Table 7: Comparison of central venous saturation in both groups

Central venous oxygen saturation	Group 1 Central Venous pressure	Group 2 Pulmonary artery	p value
$ScVO_2$ _AI	71.64 ± 4.27	70.26 ± 4.57	0.0383
$ScVO_2$ _BG	70.04 ± 4.41	69.52 ± 5.02	0.4598
$ScVO_2$ _AG	70.97 ± 4.38	69.27 ± 5.03	0.0167
$ScVO_2$ after 1 hr	71.85 ± 4.12	69.72 ± 4.87	0.0017
$ScVO_2$ after 6 hr	72.14 ± 4.17	70.83 ± 5.57	0.0759
$ScVO_2$ after 12 hr	71.7 ± 6.10	70.31 ± 5.96	0.1243
$ScVO_2$ after 18 hr	70.05 ± 5.44	68.72 ± 5.97	0.1191
$ScVO_2$ after 24 hr	68.71 ± 4.87	68.17 ± 4.70	0.4565
$ScVO_2$ after 36 hr	70.98 ± 4.17	69.66 ± 5.05	0.0574
$ScVO_2$ after 48 hr	71.75 ± 6.40	70.05 ± 7.07	0.0926

There was no significant difference in both groups in terms of intraoperative fluid bolus use, blood, blood products use in both intraoperative and postoperatively. Also there was no significant difference in IV fluid intake and output measured up to 48 hr in postoperative period in ICU (Table 8).

Complications

Incidence of hypotension was higher (31) in PA group in compare to (23) in CVC but failed to reach statistical significance (p value = 0.25). With regards to arrhythmias there were no statistically significant differences in either of the groups (p > 0.05). However, incidence of arrhythmias was 10 and 13 in CVC and PA catheter respectively which was lower side in CVC groups in our study (Table 9).

There was no statistically significant difference in Respiratory, CNS and Renal complication in both groups. (p value >0.05) Although incidence of Renal complication was more in PA (8) group as compared to (2) in CVP groups but it was not statistically significant (p value >0.05). In PA groups no patients had CNS complication in contrast to patients in CVC groups which might be due to more patients in CVC groups having history of CVA (6) as compared to (2) PA groups.

There was no significant difference in mortality in both groups. One patient in each group had mortality in postoperative period.

There was significant difference in noradrenaline use in both groups. In PA groups 56 patients noradrenaline was used in compare to 40 in patients managed with CVC. Use of levosimendan in PA and CVC groups was 13 and 4 respectively. However there was increased use of levosimendan in PA groups but it failed to reach significant level between two groups (p value >0.05) (Table 10).

There was no significant difference in other inotropes like adrenaline, dobutamine and ionodilator like milrinone in both groups.

There was no significant difference in prolonged ICU stays >48 hr in both groups. In CVP catheter group 22 had icu stays less than 24 hr vs 3 in PA

Table 8: Fluid and Blood Product Use

	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
Fluid bolus	32	43	0.1306
BLOOD	49	58	0.2246
POD1 input 24 hr	2046.4 ± 619.4	2148.7 ± 915.6	0.3809
POD2 input 24 hr	2527.7 ± 408.0	2452.8 ± 430.0	0.2319
POD1 output 24 hr	1728.7 ± 632.6	1770.7 ± 817.5	0.7007
POD2 output 24 hr	2141.0 ± 396.7	2098.6 ± 489.1	0.5239

POD-Postoperative Day

Table 9: Comparisons of complications in both groups

Complication	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
Hypotension	23	31	0.2549
Arrhythmia	10	13	0.6552
Respitatiory	04	02	0.6780
Renal	02	08	0.1037
Central Nervous System	04	00	0.1293

Table 10: Inotropes use in both groups

	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	*p* value
Noradrenaline	40	56	0.0250
Adrenaline	07	03	0.3290
Dobutamine	06	12	0.2141
Milrinone	01	00	1.0000
Levosimendan	04	13	0.067

Table 11: Duration of ICU stay

Intensive Care Unit stays	Group 1 Central venous catheter	Group 2 Pulmonary Artery Catheter	P value
ICU <24 hr	22	03	0.0001
ICU 24 to 48 hr	61	77	0.0082
ICU >48 hr	7	10	0.6102

catheter group (*p* value = 0.001). Discharged time from ICU was between 24 and 48 hr which was statically significant as 77 of patients managed with PA catheter was discharged from ICU in between 24 and 48 hr in contrast to 61 of patients in CVP groups *p* value (0.008) (Table 11).

Discussion

Routine versus selective use of pulmonary artery catheter (PAC) monitoring in coronary artery bypass grafting operations is a topic of significant debate[8]. Shoemaker, *et al*.[9] werethe first to report on the use of hemodynamic data from PAC to determine fluid therapy and the use of vasoactive drugs. Several studies[8,10] that have evaluated PAC in the setting of CABG surgery have suggested that the benefits of PAC outweigh their risks in patients undergoing major cardiac and vascular surgery. Off pump coronary artery bypass (OPCAB) surgery many times causes hemodynamic instability due to altered positioning of heart, interruption of coronary flow and placement of epicardial stabilizer. So vigilant hemodynamic monitoring is of utmost important during OPCAB surgery. So for this purpose, central venous catheter and pulmonary artery catheter are routinely used. Pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) and cardiac output monitoring via thermodilution method are obtained as additional information which helps to optimize patients and decide specific interventions during OPCAB. These parameters cannot be obtained in patients with central venous catheter and their management will only be based on CVP-guided approach in our study. We also measured central venous saturation and serum lactate in arterial blood sample in both groups to determine that whether it helped or not in hemodynamic management in OPCAB.

Many cardiac surgery centers continue to use PACs in a large majority of CABG cases on the basis that placement of a PAC will allow a more complete assessment of hemodynamics and early and more targeted pharmacologic or surgical intervention to restore homeostasis. However, a number of studies refute this and concurrently suggest that PAC use may represent additional unnecessary cost, particularly in low-risk patients with normal LV function. Also, however rare, PAC may have serious associated risks such as pulmonary artery thrombosis or rupture, infection, arrhythmia(s), myocardial or valvular injury, insertion problems, and misinterpretation of PAC data by care providers. Accordingly, whether and when to use PAC in CABG has become a topic of debate.

A study by the Canadian critical care clinical trial group[11] showed no benefit to therapy directed by PAC over standard care in elderly high-risk surgical patients.

This study[12] concluded that the PAC "does not play a major role in influencing outcome after cardiac surgery, that even high-risk cardiac surgical patients may be safely managed without routine PAC, and that delaying PAC until a clinical need develops does not significantly alter outcome, but may have an important impact on cost savings." This trial[12] suffered from lack of true randomization and crossover but remains the only large prospective evaluation of PAC use in patients undergoing coronary artery bypass grafting. Our study also agree with this trial that patient with mild-to-moderate left ventricular systolic dysfunction could be managed with CVP cathater alone but we also observed that routine use of PA cathater in patient with mild-to-moderate left ventricular dysfunction has no harm in terms of postoperative complication and mortality although there was increase duration of ICU hour stays in patients managed with pulmonary catheter (in first 24 hours) that was due to aggressive hemodynamic management with cardiac output monitoring.

A more recent retrospective review (Resano FG *et al*.) of outcomes in low-risk patients undergoing beating heart surgery showed that in the 69% of patients monitored with a PAC versus the 31% with a CVP, there was no change in any outcome variable (e.g., need to convert to bypass or insert balloon pump) including mortality rate. We also observed similar finding as one patient received IABP intra operative in both group in our study. However during surgery there was no need to convert on bypass in any patients in both groups.[10]

It was also suggested that measurement of cardiac output, prompted the frequent use of

inotropic agents to maintain a CI>2 L/min/m^2 in patients managed with PA catheter in contrast to CVP catheter. They also concluded that when confounding variables are controlled, use of a PAC was found to be a significant predictor of use of inotropic support at the end of the surgery. But we found that there was no significant difference in use of inotropes if hemodynamic management was done with PA cathater in off pump CABG. However in our study, we observed that more use of inotropeslike levosimendan in PA groups (13 vs 4) but it failed to reach significant level between two groups (p value >0.05). There was no significant difference in routine inotropes and vasopressors in both groups.

A 1989 study by Pearson and associates[7] prospectively randomly assigned 226 elective cardiac operation patients to either CVP, standard PAC, or oximetric PAC monitoring, but 46 of 74 patients randomly assigned to receive CVP had a PAC instead owing to anesthesiologist preference. They also observed no significant differences in mortality and ICU stays among the patient groups like our study. In our study we also observed that there was no significant difference in mortality and prolonged ICU stays >48 hours (p value 0.6102) in both groups. However we also found that more patients managed with CVP catheter was discharged earlier from icu stays because we observed significant difference in CVP catheter group 22 vs. 3 of PAC group had icu stays less than 24 hours (p value = 0.001). In our study most of patients managed with either PA or CVP catheter, discharge time from ICU was between 24 to 48 hours which was statistically significant as 77 patients managed with PA catheter was discharged from ICU in between 24 to 48 hour in contrast to 61 patients in CVP groups (p value 0.008). It was due to more patients discharged earlier in CVP group <24 hr.

We observed that there was no significant difference in postoperative complication like hypotension, renal, CNS, respiratory in both groups. However there was increase rate of CNS complication like stroke and cognitive defect in CVP group (4 vs. 0) compare to PA groups due to previous history of CVA found more in CVP group. Although in our study there was increase trend in hypotension (23 vs 31), arrhythmia (10 vs 14) and renal complication (2 vs 8) in both the groups respectively but it was not statistically significant (p value >0.05).

Our finding also supported by Stewart and coworkers[13] whom use six criteria to preoperatively identify 194 of 312 (62%) low-risk CABG patients who would be candidates for CVP as opposed to PAC monitoring. Of these, The CABG proceeded with CVP catheter in 133 patients, whereas there remaining 61 patients had a PAC inserted owing to surgeon or anesthesiologist preference. In these two subgroups, in hospital mortality was similar, although postoperative complications (morbidity) tended to be increased in PAC patients. The choice of monitoring catheter was not randomized in this study as compared to our study so there catheter selection bias might cause observed differences. Therefore, selection bias may have been introduced when the surgeon or the anesthesiologist selected a PA rather than a CVP catheter.

Interesting fact about our study that we also observed relation of serum lactate and central venous saturation because these parameters were very helpful in hemodynamic management particularly in postoperative period. We observed that in serum lactate showed increasing trend in postoperative periods. After 48 hours blood lactate level was significant lower in PA catheter groups in compare to CVC groups. However there was no significant change in central venous saturation during intraoperative and postoperative period in patients managed with either PA or CVP catheter in off pump CABG.

Limitations of our study

Patients with preserved left ventricular function with EF >40% (average) were included for study. These patients can better tolerate hemodynamic alterations during OPCAB than patients with depressed LV function and hence PA catheter might prove beneficial in this category. Further studies are needed to compare hemodynamic management based on either PA catheter or CVP catheter in off pump CABG in patients with compromised left ventricular function.

Conclusion

We can conclude from our study that PAC definitely provides additional information regarding cardiac output and cardiac index which can help for hemodynamic management of patient intraoperatively and postoperative ICU management in comparisons with CVC but clearly it does not result in significant difference in postoperative ICU stay and outcome of patient in form of morbidity and mortality.

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Comparison of Dexmedetomidine and Buprenorphine as an Adjuvant to Bupivacaine in Spinal Anesthesia for Femur Interlocking Surgeries

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Abstract

Background: Spinal anesthesia with bupivacaine is administered routinely for lower limb surgeries along with additives for better hemodynamics, prolonged sensory and motor blockade. Most commonly used additives being opiods. In the present study non-opiod like dexmedetomidine is compared with buprenorphine as an adjuvant for bupivacaine in patients undergoing femur interlocking nailing surgeries. *Materials and Methods:* In the present randomized controlled prospective double-blinded study a total of 90 patients from either gender, aged 20–60 years of ASA I and II undergoing femur interlocking nailing surgeries under spinal anesthesia were included. The patients were randomly divided into two groups (n = 45 each) by closed envelope technique. Patients in Group B received 15 mg of 0.5% hyperbaric bupivacaine with 45 µg of buprenorphine, and Group D received 15 mg of 0.5% hyperbaric bupivacaine with 5 µg dexmedetomidine for spinal anesthesia. The duration of motor and sensory blockade, time to first analgesic requirement and any adverse events were recorded. Data were analyzed using Fisher's exact test or Chi-square test for categorical data and analysis of variance for continuous data. The value of $p < 0.05$ was considered statistically significant. *Results:* In our study the subjects in Group D (dexmedetomidine) group had significantly longer period of motor blockade (190 ± 18.2 min) and sensory blockade (145 ± 20.2 min) compared to Group B (120 ± 17.2, 102 ± 13.5) respectively, which is statistically significant ($p < 0.05$ and $p < 0.05$* respectively). The time to first request of analgesic in the postoperative period was also longer (200 ± 21.9 min) in dexmedetomidine group when compared with Group B (130 ± 20), ($p < 0.05$*). There were no untoward complications (hypotension, sedation) in any groups. *Conclusion:* Intrathecal dexmedetomidine (5 µg) with bupivacaine for spinal anesthesia gives significantly longer duration of sensory and motor blockade than intrathecal buprenorphine (45 µg) with bupivacaine for spinal anesthesia.

Keywords: Dexmedetomidine; Buprenorphine; Femurinterlocking; Spinal anesthesia; Bupivacaine.

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Introduction

Subarachnoid block is the regional anesthesia technique of choice for lower limb surgeries,[1,2] as it has advantages like, preserving consciousness, maintains spontaneous breathing and provides adequate analgesia and muscle relaxation.

Local anesthetics in combination with adjuvants like fentanyl, buprenorphine are being used in sub arachnoid blocks since long as they shorten

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the onset of action, increase the quality of block, increase the duration of anesthesia and analgesia, and decrease the dose of local anesthetics.[2–4]

Dexmedetomidine, when used in subarachnoid block the analgesic effect is mediated via spinal α2 receptors by inhibiting the C-fiber neurotransmitter release and hyperpolarization of postsynaptical neuron.[5] Motor blockade duration is increased when dexmedetomidine binds with motor neurons in spinal cord.[6–9]

Prolonged analgesic property of buprenorphine is because of its action at both spinal and supraspinal levels.[4,10]

The main purpose of this study is to evaluate and compare the efficacy of dexmedetomidine 5 μg and buprenorphine 45 μg when used as an additive to 0.5% hyperbaric bupivacaine for spinal anesthesia.

Materials and Methods

The present study was conducted after taking informed written consent from participating patients. In the present prospective randomised controlled double blinded study, 90 patients of either gender in the 20–60 age group years, of American Society of Anesthesiologists (ASA) 1 and 2 undergoing femoral interlocking nailing surgeries were included. Patients with neurological, respiratory, cardiac, renal diseases, bleeding disorders, known hypersensitivity to local anesthetics, infection at lumbar spine were excluded from the study.

Patients were randomly assigned into two groups by a sealed envelope technique. Group B and group D of 45 each and the study drug is given as below.

Group B: 45 μg of buprenorphine with 15 mg of 0.5% hyperbaric bupivacaine.

Group D: 5 μg of dexmedetomidine with 15 mg of 0.5% hyperbaric bupivacaine.

Standard monitoring included ECG (Electrocardiogram), pulse oximetry, and NIBP (Non-invasive blood pressure). Ambient temperature was noted. Baseline vital parameters were recorded. IV access was obtained with 18G canula and IV fluids started.

Under aseptic precautions spinal injection of 15 mg of 0.5% hyperbaric bupivacaine with the study drugs (Buprenorphine and Dexmedetomidine) in the respective groups were given intrathecally in L_3-L_4 interspace using 25 G spinal (Quincke) needle in sitting position after confirming subarachnoid space with free flow of clear cerebrospinal fluid, and patients were made to lie in supine position immediately after the procedure.

Patients demographic data like age (years), sex, weight (kilograms), height (centimeters) and ASA physical status were noted. Vital parameters like heart rate, mean arterial pressure (non-invasive) were recorded every 5 minutes for first 30 minutes and every 15 minutes till the end of surgery. Bradycardia (HR <45) is treated with atropine 0.6 mg and hypotension (mean arterial pressure <65 mm hg) treated with injection mephentermine 6 mg IV bolus. Total number of patients requiring atropine or mephentermine were noted. After the surgery patients were shifted to postoperative ward.

Level of sensory block was tested using pinprick technique until thoracic (T10) level was achieved. Time taken for regression of sensory block to sacral (S1) were recorded.

Modified bromage (MB) scale has been used to assess the motor block.[11] Time taken to reach MB score 3 was noted.

Score 0: Full leg movement, full flexion of knees and ankle.

Score 1: Inability to raise extended legs, just able to flex knees, full ankle flexion.

Score 2: Inability to flex knees, some flexion of ankles possible.

Score 3: Unable to move legs or feet.

Time taken for motor block to regress to MB score 0 was assessed and noted.

Ramsay sedation scale was used to assess the sedation levels:[13]

Scale 1 — anxious, restless

Scale 2 — cooperative, oriented, tranquil

Scale 3 — responding to commands

Scale 4 — brisk response to stimulus

Scale 5 — sluggish response to stimulus

Scale 6 — no response to stimulus.

The level of pain was assessed at 1,6,12,18 and at 24 hours postoperatively, based on visual analogue score (VAS)[14], where 0 = no pain and 10 = severe pain. Time to first rescue analgesia was noted when VAS score was 4 and above. Number of patients requiring rescue analgesia (injtramadol 100 mg IV) for 24 hours were noted. Patients were monitored for any side effects postoperatively (sedation, hypotension, pruritus).

Statistical analysis

Descriptive statistical analysis was represented as Mean ± SD and results on categorical measurements are represented as percentages. Appropriate tests of significance like the independent *t*-test and chi-square test were used depending on nature and distribution of variables. Values of $p < 0.05$ were considered significant.

Results

There were no significant difference observed with respect to patients demographic data, ASA status and duration of surgery among the two groups (Table 1).

Table 1: Patient Characteristics

Variables	Group B	Group D
Age (years)	44.5 ± 10	41 ± 15
Height (centimeters)	160 ± 5	158 ± 4
Weight (kilograms)	65.4 ± 4	66 ± 6
Gender (male/female)	25/20	23/22
ASA grade (1/2)	38/7	36/9
Duration of surgery (minutes)	90 ± 10	94 ± 09

Data presented as mean ± standard deviation.

Among the spinal block characteristics (Table 2), time to regress to sensory level S1 was longer in Group D (145 ± 20.2) when compared to Group B (102 ± 13.5) which is statistically highly significant ($p < 0.05$). The time to motor block regression to modified bromage 0 was significantly ($p < 0.05$) longer in Group D (190 ± 18.2) when compared to Group B (120 ± 17.2). The time to first request for analgesia was longer in Group D (200 ± 21.9) than Group B (130 ± 20).

Table 2: Showing Spinal Block Characteristics in Patients

Variable	Group B	Group D	*p* value
Time to reach highest sensory block, T4 (min)	11 ± 5	15 ± 4	0.144
Sensory block-time to regression to S1 (min)	102 ± 13.5	145 ± 20.2	<0.05*
Motor block-time to reach modified bromage 3 (min)	8 ± 1.4	10 ± 1.2	0.7
Motor block regression to modified bromage 0 (min)	120 ± 17.2	190 ± 18.2	<0.05*
Time for 1st analgesia (min)	130 ± 20	200 ± 21.9	<0.05*

Data were expressed as mean ± standard deviation, median and range, min: minutes, TFA: Time to first request of postoperative analgesic, T: thoracic, S: sacral, *p value < 0.05 is statistically significant.

Hemodynamic parameters were stable in both groups and there were no complications in both the groups. No statistically significant differences were noted between the study groups with respect to number of patients who required atropine, mephentermine and tramadol in 24 hours (Table 3).

Table 3: Number of Patients Requiring Atropine or Mephentermine, and any Complications Present

Variable	Group D	Group B	*p* value
Patient requiring atropine (%)	2 (4.4)	3 (6.6)	0.266
Patient requiring mephentermine	3 (6.6)	3 (6.6)	1
Patient requiring tramadol 1 mg/kg	17 (37.7)	16 (35.5)	0.173
Hypotension (%)	7 (15.5)	8 (17.7)	0.266
Sedation	0	0	0
Pruritis	0	0	0

Data presented as mean ± standard deviation; mg: milligram; kg: kilogram; *p values <0.05 statistically significant.

The VAS score was higher in Group B when compared with Group D at any time interval, but statistically non-significant (Table 4).

Table 4: Showing Postoperative Visual Analogue Scale

Variables	Group D	Group B	*p* value
1 hr	0	0	0.0
6 hr	4	3	0.219
12 hr	5	5	1
18 hr	5	5	1
24 hr	4	5	0.202

Data presented as mode, hr: hour, *p value <0.05 is statistically significant.

Discussion

This study was done to compare the addition of buprenorphine 45 µg and dexmedetomidine 5 µg to 15 mg of 0.5% hyperbaric bupivacaine for patients undergoing femur interlocking nailing surgeries under spinal anesthesia.

Dexmedetomidine, a clonidine group of drug having properties of alpha-2 adrenoreceptor agonists, has been recently introduced. It is known for its sedative and anxiolytic effects by acting at the locus ceruleus in the brain stem. Dexmedetomidine, stimulates alpha-2 receptors in the spinal cord acting in the dorsal horn and reduces the sympathetic discharge, similarly it will regulate release of substance P and hence causes hyperpolarization of dorsal horn neurons.[11–15]

Buprenorphine, an opiod acts by partially

inhibiting delta opiod receptors at the same time stimulating kappa and mu receptors. It provides analgesia by acting at both supraspinal and spinal component.[10]

In this study patient characteristics like age, weight, height, ASA physical status are matched. There were no statistical difference noted with reference to hemodynamic parameters like heart rate and blood pressure and no significant side effects like sedation, pruritus, hypotension were seen among the groups.

Kanazi GE in his study showed that there was rapid onset of motor block with prolonged duration of motor and sensory block, when he used 3 μg dexmedetomidine as an adjuvant to intrathecal bupivacaine for spinal anesthesia.[11]

The study done by Vidhi Mahendru *et al.*[1], it was shown that there was prolonged duration of sensory and motor block with preserved hemodynamics and decreased postoperative analgesic requirement when he used dexmedetomidine 5 μg with 12 .5 mg bupivacaine for spinal anesthesia, and compared with clonidine 30 μg, fentanyl 25 μg, or 12.5 mg plain bupivacaine alone in patient undergoing spinal anesthesia.

In our study when dexmedetomidine 5 μg when added to intrathecal 15 mg of 0.5% bupivacaine significantly prolonged the time of regression for the sensory level to S1 level (<0.05*) when compared to Group B. It also showed that motor regression to modified bromage 3 and time to request for first analgesia was longer in dexmedetomidine group and was statistically significant when compared to Group B (<0.05).

Conclusion

Dexmedetomidine 5 μg when added to 15 mg of 0.5% heavy bupivacaine for spinal anesthesia in patients undergoing femur interlocking nailing provides longer duration of sensory and motor blockade when compared to that of buprenorphine 45 μg when added to 15 mg of 0.5% heavy bupivacaine for spinal anesthesia.

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Original Research Article

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Comparison of Oral Melatonin and Clonidine Premedication on Isoflurane Consumption and Postoperative Analgesia

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Abstract

Background: Premedication with oral melatonin and clonidine reduces anxiety and prolongs the postoperative analgesia. But there are few studies that have observed the isoflurane consumption when they are given as premedication, hence this study was conducted to compare the isoflurane consumption and duration of analgesia when oral melatonin and clonidine is given as premedication. *Methods:* Eighty-four patients whose aged between 18 and 60 years of American Society of Anesthesiologists one and two, undergoing surgery under general anesthesia were randomly allocated into three groups of 28 each. Group C received placebo (sugar pellet), Group M melatonin 3 mg orally and Group Cl clonidine 100 µg orally 60 min before surgery. *Results:* The end tidal isoflurane concentration at 30 min [Group C 0.78 (0.21), Group M 0.48 (0.15), Group Cl 0.64 (0.16) ($p < 0.001$)], at 60 min [Group C 0.75 (0.16), Group M 0.53 (0.2), Group Cl 0.64 (0.12) ($p < 0.001$)] was lower in Group M compared to Group Cl and C. Isoflurane consumption at 30 min [Group C 6.24 (1.3), Group M 3.84 (0.75), Group Cl 4.96 (0.98) ($p < 0.001$)] and at 60 min [Group C 10.8 (2.18), Group M 7.65 (1.11), Group Cl 9 (2.45) ($p < 0.001$)] was lower in Group M compared to Group Cl and C. Duration of analgesia was 267.60 ± 81.66 min in Group C, 507.00 ± 136.11 min in group M and 438.60 ± 111.01 min in Group Cl ($p < 0.001$). *Conclusion:* Premedication with oral melatonin resulted in lower end tidal isoflurane concentration and isoflurane consumption, however it did not prolong the duration of analgesia when compared with oral clonidine.

Keywords: Analgesia; Clonidine; Isoflurane; Melatonin.

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Introduction

Pain is the most feared discomfort in all perioperative patients. Although there are significant improvements in perioperative pain management, fear and anxiety are still the major hurdles that prevent several patients from undergoing surgical interventions. There are many drugs used orally to reduce anxiety preoperatively like midazolam, clonidine, melatonin, gabapentin, etc.

Melatonin is a hormone secreted by the pineal gland.[1] Melatonin has several functions that make it an attractive option for premedication including the regulation of circadian rhythm, sedative, analgesic, anti-inflammatory and antioxidant effects.[2] Clonidine is an α-2 adrenoreceptor agonist which produces analgesia by its central action.[3]

Some studies have shown that melatonin has similar efficacy compared to clonidine in reducing postoperative pain and narcotic consumption.[4]

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There are many studies which have inferred that clonidine reduces the requirement of isoflurane concentration,[5] but there are very few studies which have compared the anesthetic consumption when melatonin and clonidine are given as premedication.

Hence the present study was conducted to compare the effects of oral melatonin 3 mg and clonidine 100 μg as premedication on isoflurane consumption and postoperative analgesia in patients undergoing general anesthesia. The isoflurane consumption was considered as the primary outcome measure. The end tidal isoflurane concentration and postoperative analgesia were considered as the secondary outcome measures.

Materials and Methods

This prospective, randomized, double-blind control trial study was conducted from February 2018 to June 2018. Approval from the institutions ethical committee was obtained. The study was approved by Bangalore medical college and research institute ethical committee (BMCRI/PS/197/2017-18 dated 29/12/2017) and is registered in www.ctri.nic.in (CTRI/2018/02/012032). Eighty-four patients aged between 20 and 60 yrs of American Society of Anesthesiologists grade 1 and 2, who were undergoing surgery under general anesthesia, were randomly allocated into three groups of 28 each using a computer generated randomization sequence (www.random.org). Group C was considered as control and received placebo (sugar pellet), Group M received oral melatonin 3 mg and Group Cl received oral clonidine 100 μg. All the study drugs were given 60 min prior to surgery. Patients with systemic disorders (cardiovascular, respiratory, renal and central nervous system disorders), psychiatric illness, on chronic sedatives, opioid use or those with known drug allergies and duration of surgery more than 3 hours or less than 30 min were excluded from the study.

After obtaining informed written consent from patients, preanesthetic evaluation was performed. All patients were educated about the use of visual analog scale (VAS).[6] Preoperative investigations were performed as per the institutional protocol. Patients were fasted for 8 hr prior to surgery and were premedicated with 150 mg ranitidine and 0.25 mg alprazolam the night before surgery.

Patient's basal parameters like heart rate, non-invasive blood pressure (NIBP) and peripheral oxygen saturation were recorded. Based on the computer generated random list, patients were allocated randomly into Group C, Group M and Group Cl. The allocation based on the randomization sequence was concealed using sequentially numbered opaque sealed envelopes. The study drug was enclosed in opaque sealed envelopes and were opened by the principle investigator just before giving the study drug. The drug was given to the patient by an anesthesiologist not involved in the study. The group allocation was not revealed to any of the attending anesthesiologists until the end of the study. An 18G intravenous cannula was inserted and the study drug was orally administered with sips of water 60 min prior to surgery. Vital parameters were recorded every 20 min till the patient was taken up for surgery. Sedation was assessed at 60 min based on Ramsay sedation scale.[7] Questions relevant to the Hamilton anxiety scale[8] were asked to assess the degree of anxiety before giving the study drug and 60 min later. Patients were pre-loaded with 10 ml/kg body weight Ringer lactate. Any side effect like nausea, vomiting, headache, shivering, giddiness, etc. were noted. Once the patient was shifted to the operation theater, monitors like electrocardiogram, noninvasive blood pressure, pulse oximeter, entropy (Response Entropy/State Entropy) were connected and the basal parameters recorded. Patients were preoxygenated with 100% oxygen for 3 min and premedicated with glycopyrrolate 0.2 mg, ondansetron 4 mg, fentanyl 2 μg/kg and inj 2% preservative free lignocaine 3 ml (63.9 mg). Patient was induced with Inj propofol 10 mg every 5 sec till entropy was less than 60. The consumption of propofol and mean time of induction (from the time propofol was given till entropy of 60 was reached) was noted. Inj vecuronium 0.1 mg/kg was given and the patient was ventilated for 3 min. Under direct laryngoscopy trachea was intubated with appropriate size endotracheal tube. After confirming the proper position of the endotracheal tube, the agent gas monitoring line was connected and ventilation continued with Datex Ohmeda Avance S5™ GE healthcare, Finland (with an inbuilt software to calculate anesthetic consumption) anesthesia workstation ventilator. Anesthesia was maintained with 50% oxygen and air and isoflurane. Vital parameters were recorded before induction, after induction, after intubation and every 5 min thereafter till the end of surgery. Initial flows of 4l/min was kept till a minimum alveolar concentration of 1 or entropy RE/SE less than 60 was achieved and then flows were reduced to 1.5l/min. Isoflurane concentration was adjusted to maintain state entropy of 40–60. The depth of neuromuscular monitoring was monitored using

train of four (TOF), which was connected after the patient was induced but before the administration of muscle relaxant. TOF was maintained below a count of 2 with vecuronium increments. The end tidal isoflurane, end tidal oxygen and end tidal carbon dioxide were recorded every 5 min till the end of surgery. Isoflurane consumption was recorded every 30 min using a patented formula inbuilt in the software of the agent gas module of the anesthesia workstation. Any additional requirement of rescue propofol (10 mg) to maintain state entropy of less than 60, despite adequate administration of isoflurane (Minimum alveolar concentration of 1.5) was noted. Hypertension was defined as a rise in basal mean arterial pressure (MAP) more than 20% and tachycardia was defined as heart rate more than 100 bpm. Fentanyl 0.5 microg/kg was administered intravenously if tachycardia or hypertension persisted despite adequate depth of anesthesia (entropy <60). Intraoperatively, side effects like hypotension (defined as a fall in basal mean arterial pressure (MAP) more than 20%) and bradycardia (defined as heart rate less than 60 bpm) if any, were noted.

At the end of surgery, isoflurane was discontinued and muscle relaxation was reversed with Inj neostigmine 0.05 mg/kg and glycopyrollate 0.008 mg/kg and trachea extubated when the TOF > 0.8 with sustained head lift and hand grip. Extubation time defined as the time between discontinuation of isoflurane to extubation was recorded.

Postoperatively side effects like nausea, vomiting, shivering, headache, etc. if any were noted. Vital parameters were monitored every 15 min for half an hour, then every 30 min for 2 hr and hourly till 6 hr. Sedation was assessed using Ramsay sedation scale and pain was assessed using VAS postoperatively at the end of 1 hr and 4 hr. When the VAS > 3, rescue analgesia was given using Inj Paracetamol 1g IV infusion. The time from the start of surgery to the first requirement of analgesia, i.e. duration of analgesia was recorded.

Statistical method and analysis: Sample size was calculated using www.openepi.com. Sample size was based on the pilot study, where the mean isoflurane consumption at 1 hr was 8 ml, assuming a standard deviation of 1.5 and normal distribution of values to detect a minimum of 15% difference in isoflurane consumption between 2 drugs, a minimum of 25 patients were required in each group. For further validation of the study we have taken 28 patients in each group assuming a dropout rate of 10%.

The Statistical software namely SPSS 18.0, and R environment ver. 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables, etc.

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

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, chi-square/ Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for Qualitative data analysis. Intergroup analysis has been done using the student *t* test.

Results

A total of 84 patients were enrolled and randomly allocated into three groups (Group C n=28, Group M n=28 and Group Cl n=28) [Fig. 1]. However 9 patients (Group C n=4, Group M n=3, Group Cl n=2) were excluded from the study due to protocol violation, prolonged duration of surgery > 3 hr and duration of surgery < 30 min due to inoperable tumor. A total of 24 patients in Group C, 25 patients in Group M and 26 patients in Group Cl were included for the final analysis.

Demographic parameters such as age, sex, weight and duration of surgery were comparable in all the three groups as shown in Table 1.

The mean dose of propofol consumption was significantly lower in Group M and Cl when compared to Group C as shown in Table 2. Intergroup analysis showed no significant difference in mean dose of propofol consumption (*p* value 0.528) between group M and group Cl.

The mean induction time was significantly lower in Group M and Group Cl when compared to Group C as shown in Table 2. Intergroup analysis showed no significant difference in mean induction time (*p* value 0.088) between Group M and Group Cl.

Intraoperative heart rate was higher in control group when compared to the clonidine and melatonin group as shown in Figure 2. There was an increase in heart rate after intubation which subsided 3 min after intubation in all the three groups.

The MAP was comparable in all the three groups of patients as shown in Figure 3. The MAP increased after intubation and subsided 3 min after intubation in all the three groups. All patients in melatonin group and clonidine group had a sedation score of 2, whereas in control group, 3 patients had a sedation score of 2 and 22 patients had a sedation score of 1 which was statistically significant with *p* value < 0.001. Intergroup analysis showed that the sedation score was similar in Group M and Group Cl (*p* value 0.9978). The anxiety score at 60 min after oral administration of the drug was 19.96 in the control group, 6.72 in the melatonin group and 7.4 in the clonidine group with a *p* value <0.001. Intergroup analysis showed that the anxiety score was similar in Group M when compared to Group Cl (*p* value 0.1172).

The end tidal isoflurane concentration in % at 30 min and 60 min was significantly lower in Group M and Cl compared to Group C as shown in Table 2 and Figure 4. Intergroup analysis showed that end tidal isoflurane concentration was lower in Group M compared to Group Cl at 30 min (*p* value <0.001) and at 60 min (*p* value 0.022). Isoflurane consumption at 30 min and 60 min was significantly lower in Group M and Cl compared to Group C as shown in Table 2. Intergroup analysis showed that isoflurane consumption was lower in Group M when compared to Group Cl at 30 min (*p* value <0.001) and at 60 min (*p* value 0.015). The

Table 1: Demographic parameters

	Group C n=24	**Group M n=25**	**Group Cl n=26**	***p* value**
Age (mean ± SD *) in yrs	37.4 ± 11.9	43.8 ± 12.0	38 ± 12.5	
Sex (M/F)	5/19	14/11	14/12	
Weight (mean ± SD) in kg	58.6 ± 9.7	59.9 ± 7.3	63.2 ± 7.3	
Duration of Surgery (mean ± SD) in mins	77.60 ± 11.62	75.13 ± 13.41	76.56 ± 12.52	0.944
Type of surgery (number of cases)				
Breast surgery	9	11	12	0.855
Upper abdominal surgery	4	5	5	0.914
lower abdominal surgery	3	3	5	0.662
Scalp and face surgery	8	6	4	0.426

*SD: standard deviation

Table 2: Comparison of end tidal isoflurane concentration, isoflurane consumption, propofol consumption, induction time, duration of analgesia, peripheral oxygen saturation, end tidal carbon dioxide, response entropy, state entropy and extubation time between the three groups.

	Group C	**Group M**	**Group Cl**	***p* value**
Endtidal Isoflurane Concentration (%)				
30 min [mean (SD)] (95% CI† of means)	0.78 (0.21) (0.69–0.86)	0.48 (0.15) (0.42–0.53)	0.64 (0.16) (0.57–0.70)	<0.001
60 min [mean (SD)] (95% CI of means)	0.75 (0.16) (0.68–0.81)	0.53 (0.2) (0.45–0.60)	0.64 (0.12) (0.59–0.68)	<0.001
Isoflurane Consumption (ml)				
30 min [mean (SD)] (95% CI of means)	6.24 (1.3) (5.73–6.74)	3.84 (0.75) (3.54–4.13)	4.96 (0.98) (4.57–5.34)	<0.001
60 min [mean (SD)] (95% CI of means)	10.8 (2.18) (9.94–11.65)	7. 65 (1.11) (7.21–8.08)	9 (2.45) (8.04–9.96)	<0.001
Mean dose of propofol consumption (mg) [mean (SD)] (95% CI of means)	96.40 (14.97) (90.53–102.26)	74.00 (13.84) (68.57–79.43)	76.40 (12.87) (71.35–81.44)	<0.001
Mean induction time (seconds) (95% CI of means)	76 (2.2) (75.14–76.86)	52 (1.66) (51.35–52.65)	53 (1.5) (52.41–53.59)	<0.001
Duration of Analgesia (mins) [mean (SD)] (95% CI of means)	267.60 (81.66) (235.59–299.61)	507.00 (136.11) (453.65–560.35)	438.60 (111.01) (395.08–482.11)	<0.001
Peripheral 02 saturation (%) [mean (SD)]	99.33 (0.51)	99.33 (0.51)	99.5 (0.54)	0.401
End tidal carbon dioxide (mm Hg) [mean (SD)]	33.96 (1.19)	34.26 (0.66)	33.98 (0.87)	0.524
End tidal oxygen (mm Hg) [mean(SD)]	38.9 (1.59)	39.69 (2.36)	39.6 (2.27)	0.068
Response entropy [mean(SD)]	55.4 (1.17)	55.2 (1.13)	55.5 (2.63)	0.845
State entropy [mean (SD)]	52.4 (0.84)	52.5 (1.08)	52.8 (1.61)	0.688
Extubation time (secs)	389.6 (39.63)	382.6 (30.8)	379.2 (31.61)	0.552

† Cl : Confidence interval

duration of analgesia was significantly prolonged in Group M and Cl compared to Group C as shown in Table 2. Intergroup analysis showed that the duration of analgesia was not statistically significant in Group M when compared to Group Cl (*p* value 0.0576).

Peripheral oxygen saturation, end tidal carbon dioxide, response entropy and state entropy are comparable between the three groups as shown in Table 2. Response entropy was maintained between 40–60 throughout the surgery as shown in Table 2. One patient in Group M, 6 patients in Group C and no patients in Group Cl received 20 mg of rescue propofol. Two patients had shivering in Group M which was treated with Inj Tramadol 100 mg IV. The extubation time was comparable between the three groups.

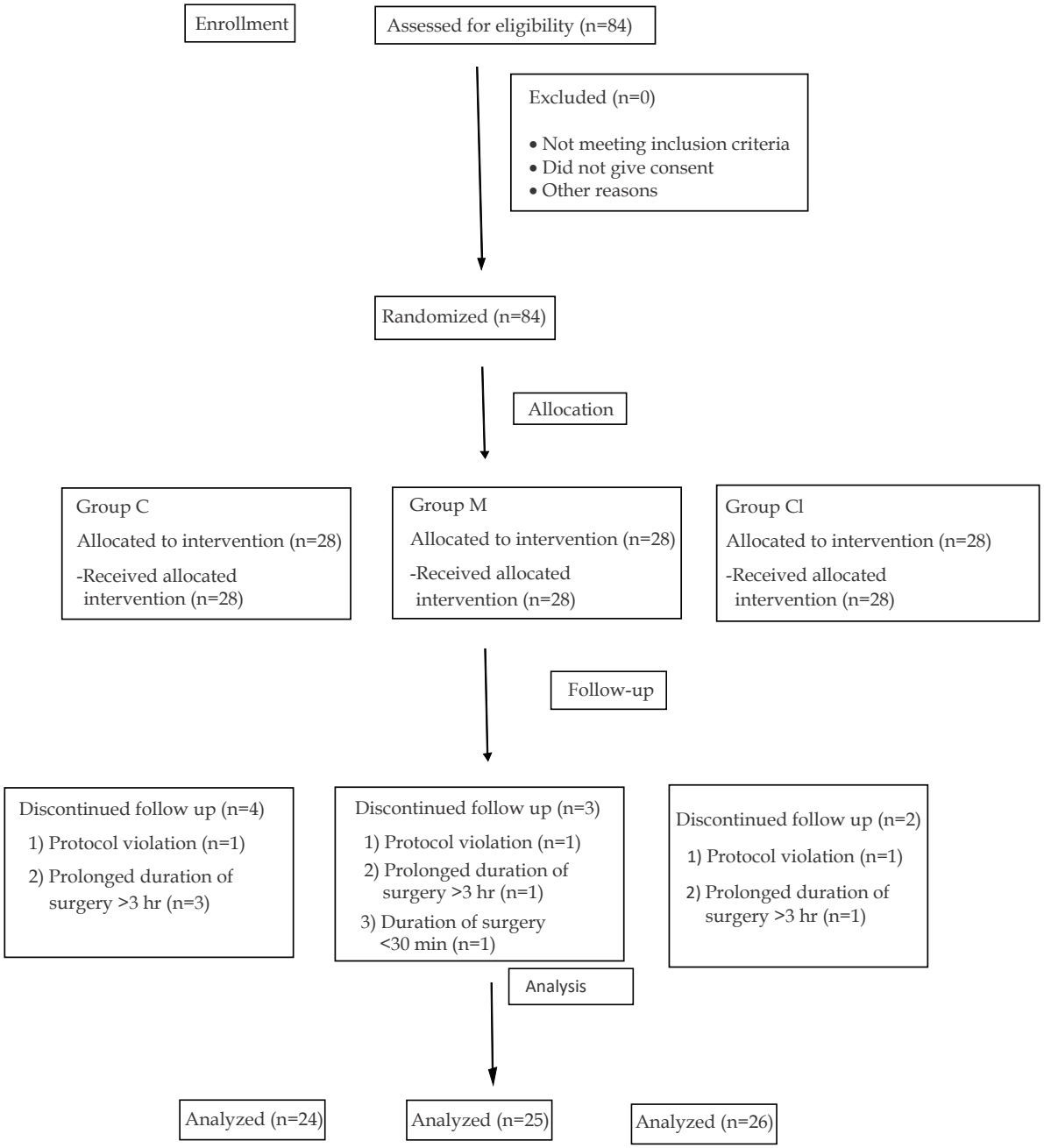

Fig. 1: Consort flow diagram

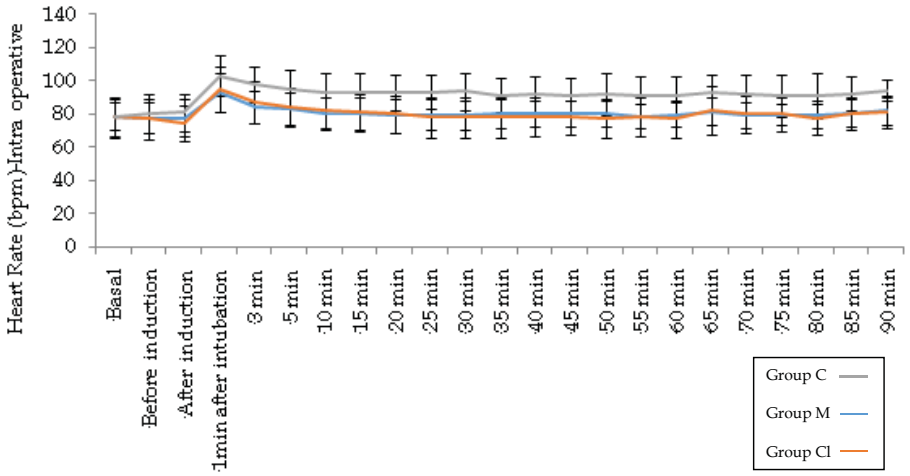

Fig. 2: Comparison of the trends of Preoperative and intraoperative heart rate between the three groups

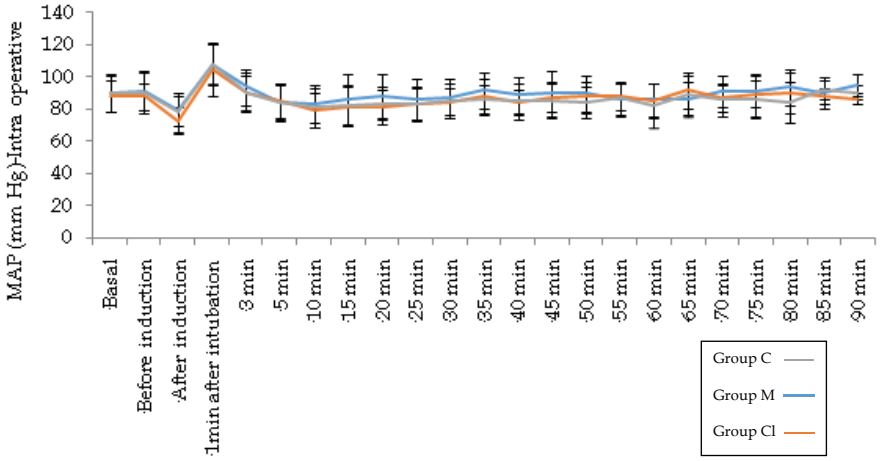

Fig. 3: Comparison of the trends of Mean arterial blood pressure between the three groups

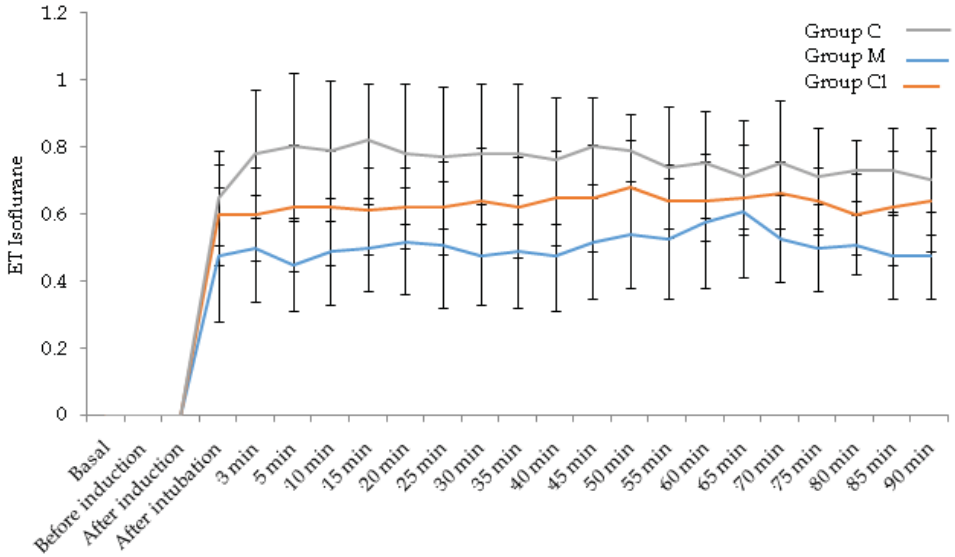

Fig. 4: Comparison of end tidal isoflurane concentration between the three groups.

Discussion

In this study it was observed that premedication with oral melatonin resulted in lower end tidal isoflurane concentration and lower isoflurane consumption, however it did not prolong the duration of analgesia when compared with oral clonidine.

There are many drugs used orally to reduce anxiety preoperatively like midazolam, clonidine, melatonin, gabapentin, etc. Midazolam is known to cause postoperative cognitive and psychomotor impairment.[9] Gabapentin causes nausea, vomiting and higher levels of sedation.[10] Hence a drug without these side effects is preferred.

Melatonin (*N*-acetyl-5-methoxytryptamine), discovered about half a century ago, is a hormone produced chiefly by the pineal gland[11] but also in much smaller amounts by the gastrointestinal tract, retina, platelets, respiratory epithelium, bone marrow, thymus, and skin. Melatonin has several functions that make it an attractive option for premedication including the regulation of circadian rhythm, sedative, analgesic, anti-inflammatory and antioxidant effects.[2] It interacts with multiple receptor sites including opioidergic, benzodiazepinergic, muscarinic, nicotinic, serotonergic, α_1, α_2 adrenergic and most importantly MT1/MT2 melatonergic receptors present in the dorsal horn of the spinal cord as well in the central nervous system.[12] The calculated serum half-life of melatonin is about 30–50 minutes.[13]

In a study the effect of melatonin 6 mg and pregabalin 150 mg as premedication on perioperative anxiety and postoperative pain was assessed and the authors concluded that both the drugs reduce preoperative anxiety and increase the postoperative duration of analgesia, but melatonin caused more sedation than pregabalin.[14] This sedation could be due to the higher dose of melatonin used.

Some studies have used two different doses of melatonin 6 mg and 3 mg to assess the efficacy of analgesia in patients undergoing cesarean section under spinal anesthesia. The incidence of headache in patients given 6mg was significantly higher than others ($p < 0.001$).[15] Hence in our study we have used 3 mg melatonin. None of the patients in our study had complains of headache or other side-effects like nausea or bradycardia.

Clonidine is an α_2 adrenoreceptor agonist which produces analgesia by its central action.[3,16] It is rapidly absorbed after oral administration and reaches a peak plasma concentration within 60–90 min. Clonidine stimulates alpha-2 adrenergic neurons in the medullary vasomotor center causing a decrease in the sympathetic nervous system outflow from the central nervous system to the peripheral tissues and central activation of non-adrenergic imidazoline preferring receptors. Decreased sympathetic activity is manifested as peripheral vasodilatation, hypotension, decrease in heart rate and cardiac output.

Some authors have studied the effect of oral clonidine 100 μg on postoperative pain and concluded that clonidine significantly reduces the severity of postoperative pain without any side effects.[17] Hence we have also used oral clonidine 100 μg as premedication in our study.

Studies have compared the effect of oral clonidine 3 μg/kg on propofol requirements during lower extremity vascular surgery and concluded that clonidine reduces the requirement for propofol.[18] Few authors have assessed the efficacy of oral melatonin 5 mg and clonidine 150 μg on pharmacodynamics and pharmacokinetics of propofol target controlled infusions and have inferred that there was no significant differences in the pharmacokinetics and pharmacodynamics of propofol infusion due to premedication with clonidine or melatonin.[19] Whereas in our study we observed that oral melatonin 3 mg and clonidine 100 μg premedication reduces the total requirement of propofol when compared to placebo.

Some authors performed a clinical trial and concluded that the induction time with sevoflurane was significantly longer in the placebo group compared to those who received clonidine 150 μg and 300 μg as oral premedication.[20] Our study demonstrates a similar result where patients who received melatonin and clonidine premedication had shorter induction time with propofol when compared to control group owing to their sedative effects.

In a study the role of oral melatonin 6 mg as premedication on attenuation of pressor response to laryngoscopy and intubation was studied and they concluded that melatonin 6 mg effectively attenuated the cardiovascular responses to laryngoscopy and intubation.[21] Whereas in our study we did not observe any attenuation of pressor response to intubation, which may be due to the lower dose of melatonin that we have used.

Some authors have studied the effect of oral clonidine 200 μg as premedication and concluded that it reduces the pressor response to intubation and laryngoscopy.[22] We did not observe any

attenuation of pressor response to intubation and laryngoscopy which could be due to the lower dose of clonidine used in our study.

In a study, the effect of oral clonidine 100 µg and melatonin 5 mg on postoperative pain and morphine consumption was compared and they concluded that their effect was greater than placebo and was equivalent between these two drugs.[23] There are studies which have assessed the efficacy of melatonin 6 mg, clonidine 200 µg and gabapentin 600 mg in reducing preoperative anxiety and postoperative pain in patients undergoing laparoscopic cholecystectomy and have found that the use of melatonin had an efficacy similar to that of clonidine and gabapentin in reducing preoperative anxiety, postoperative pain and narcotic consumption.[4] They have observed few cases of decreased blood pressure in those patients given clonidine, though it was not significant. We did not observe any such difference in MAP in all the three groups which could be because of the lower dose of clonidine used. In our study both melatonin and clonidine had lower anxiety scores and sedation scores compared to control. The basal heart rate was lower in the melatonin and clonidine group when compared to placebo, probably due to decreased anxiety. We also observed increased duration of analgesia in melatonin and clonidine group when compared to the control group.

Some authors have concluded that clonidine 2 µ/kg and 4 µ/kg, given as premedication reduces the MAC of sevoflurane in paediatric patients.[24] The effect of oral clonidine 150 µg premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy has been studied and inferred that clonidine 150 µg results in improved perioperative hemodynamic stability and a reduction in the intraoperative isoflurane concentration and postoperative analgesic requirements.[5] In our study melatonin 3 mg reduced the end tidal isoflurane concentration and isoflurane consumption significantly when compared to clonidine 100 µg.

In our study we observed two cases of shivering in patients who received melatonin. This may be due to the hypothermic properties of melatonin[25] or reduced operation theater temperature as the patient temperature was not monitored and the theater temperature was not kept constant in all the cases.

There are certain limitations in our study. We have not observed the effects of oral clonidine and melatonin on the recovery profile of the patients. The effect of melatonin on the sleep quality was also not assessed. The pain score was not analyzed as we have studied different varieties of cases with varied pain threshold. We did not find any literature, to the best of our knowledge and resources available, regarding the equipotent doses of melatonin and clonidine which could be because they belong to different groups of pharmacological classification.

To conclude premedication with oral melatonin 3 mg resulted in lower end tidal isoflurane concentration and lower isoflurane consumption, however it did not prolong the duration of analgesia when compared with oral clonidine 100 µg.

Conflict of interest: Nil declared.

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Original Research Article

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Efficacy of Dexmedetomidine in the Dose of 0.5 ug/kg as a Single Bolus Dose in Attenuating Hemodynamic Response to Laryngoscopy and Tracheal Intubation in Adult Patients

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Abstract

Aims and objectives: To evaluate efficacy of dexmedetomidine in the dose of 0.5 ug/kg as a single bolus dose in attenuating hemodynamic response to laryngoscopy and tracheal intubation in adult patients. *Materials and Methods:* We conducted a prospective, randomized, double-blind study, in which 60 patients scheduled for elective surgery under general anesthesia were enrolled for the study. Patients were randomly distributed in two groups (30 in each group). Group D received a bolus dose of 0.5 ug/kg dexmedetomidine group and Group C received 10 ml of normal saline (control group). *Results:* There was significant decrease in heart rate in Group D as compared to Group C from 1 minute after induction till 80 minutes ($p < 0.05$). There was significant decrease in SBP, DBP and MAP in Group D as compared to Group C from laryngoscopy till postextubation ($p < 0.05$). Complications like hypotension, hypertension, bradycardia, tachycardia, agitation and coughing was observed in 0%, 80%, 0%, 83.33%, 23.33% and 40% of Group C patients respectively while it was present in 10%, 0%, 10%, 0%, 0% and 13.33% of Group D patients respectively. *Conclusion:* Single bolus dose of dexmedetomidine 0.5 µg/kg prior to laryngoscopy and endotracheal intubation attenuates the airway reflexes and hemodynamic responses effectively during induction of anesthesia providing smooth intubation and provides adequate sedation and delays the need for analgesia in the postoperative period.

Keywords: Dexmedetomidine; Laryngoscopy; Tracheal intubation.

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Introduction

Laryngoscopy and endotracheal intubation are often employed to secure the airway during general anesthesia. However both laryngoscopy and intubation are noxious stimuli and are associated with stress and hemodynamic responses in the form of laryngosympathetic stimulation which is manifested as hypertension, tachycardia and arrhythmias. These hemodynamic responses are well tolerated in otherwise healthy individuals, but in patients with hypertension, coronary heart disease, cerebrovascular disease and intracranial aneurysm these transient changes can result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral hemorrhage.[1]

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Intravenous dexmedetomidine, a central alpha-2 agonist is being used in anesthesia practice as a premedicant. The advantages of dexmedetomidine as premedicant in anesthesia setting include sedation, analgesia, anxiolysis and improved hemodynamic stability. Because of these beneficial properties it has been found that the minimum alveolar concentration (MAC) of volatile anesthetics also decreases significantly up to 90% and hence decreases the requirement of anesthetics.[2] It has also been found that it can decrease the hemodynamic response to laryngoscopy and intubation.[3, 4]

The hemodynamic effects of dexmedetomidine result from peripheral and central mechanism. Alpha-2-adrenoreceptor agonists show a biphasic, dose-dependent, blood pressure effect at low doses the dominant action of α2-adrenoreceptor agonist activation is a reduction in sympathetic tone, mediated by a reduction of norepinephrine release at the neuroeffector junction, and an inhibition of neurotransmission in sympathetic nerves.[2] The net effect of dexmedetomidine action is a significant reduction in circulating catecholamines with a slight decrease in blood pressure and a modest reduction in heart rate.[5] This prospective, randomized, double blinded study was planned to evaluate the efficacy of dexmedetomidine in the dose of 0.5 ug/kg as a single bolus dose in attenuating hemodynamic response to laryngoscopy and tracheal intubation in adult patients.

Aims and Objectives

1. To evaluate the efficacy of dexmedetomidine in the dose of 0.5 ug/kg as a single bolus dose in attenuating hemodynamic response to laryngoscopy and tracheal intubation in adult patients.
2. To study changes in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure associated with laryngoscopy and intubation; and to monitor the hemodynamic and vital parameters at the time of endotracheal intubation and at 5 minutes and 10 minutes after.
3. To study any adverse effects associated, such as perioperative hypotension and bradycardia.

Materials and Methods

After approval by hospital research ethical committee, informed written consent for anesthesia was taken. A complete pre-anesthetic assessment of the patients was done. This included history of any systemic diseases like hypertension, bronchial asthma, cardiac and/or pulmonary disorder, psychiatric disorder, substance abuse and allergy to any drugs. Additionally a thorough general and systemic examination was carried out for each patient enrolled. The study was conducted as a double-blind trial from May 2016 to May 2017 at Mahatma Gandhi Mission Institute of Medical Sciences, Kamothe, Navi Mumbai. Sixty patients scheduled for elective surgery under general anesthesia were randomized into two groups.

Sample size: Sixty patients were enrolled for the study (randomly distributed in two Groups D and C [n=30 in each group]. Group D dexmedetomidine group and Group C control group).

Patient of both sexes with age between 18 and 60 yearshaving ASA physical status class I or II. Patients posted for surgeries under general anesthesiawith weight and height both within 20% of their respective ideal values were included.

Patients with comorbid diseases (cardiac, pulmonary, neurological disease), allergy to the drug to be used. Pregnancy, patients on alpha-2 adrenergic receptor agonist/calcium channel blocker/angiotensin converting enzyme inhibitor/ beta-blocker therapy, patient taking antipsychotic drugs and difficult intubation (patients requiring 3 or more attempts at intubation) were excluded.

Methodology

The patients were randomly divided into two groups as designated above and demographic data was noted. Baseline vital parameters were also noted. Patients were premedicated with Tab. Alprazolam 0.25 mg a night before and Tab. Ranitidine 2 hours prior on the morning of surgery with a sip of water. In the pre-op room, a good intravenous access was secured and vital parameters observed and recorded, which included heart rate (HR), mean arterial blood pressure (MAP), electrocardiogram respiratory rate and pulse oximetry (SpO_2). All patients were administered Ringer's lactate solution. Thereafter the patients were shifted to the operation theatre and all the monitors attached and baseline parameters were recorded. *Dexmedetomidine group (Group 'D'):* received a bolus dose of 0.5 ug/kg diluted in normal saline to 10 ml and injected intravenously slowly over 10 minutes, 10 minutes before induction. *Control group (Group C):* patients received 10 ml of normal saline, 10 min before induction.

The double-blind design of study was ensured by the fact that an anesthesiologist, not further involved in the study, prepared syringes immediately before induction of anesthesia. The syringes were thereafter marked dexmedetomidine/placebo together with the name of the patient. Thus the anesthesiologist responsible for the anesthetic technique was kept unaware of the content of the syringes.

Patients of both the groups were premedicated with 0.004 mg/kg of glycopyrolate, 0.02 mg/kg midozolam and 0.6 mg/kg of pentazocine given intravenously before induction. Alongside this, our study drug dexmedetomidine and placebo were randomly administered to the subjects selected for the study in a double-blinded trial as stated above.

Induction of anesthesia was carried out with Inj. Propofol in a dose sufficient to abolish eyelash reflex followed by 0.1 mg/kg of Inj.Vecuronium Bromide to provide neuromuscular blockade. The patient was preoxygenated with 100% O_2 for the next 3 mins. Thereafter, laryngoscopy was performed with an adequate size Macintosh blade and intubation was done with a cuffed endotracheal tube of appropriate size with a strict and vigil monitoring of hemodynamic and respiratory parameters at regular intervals of 1 minute for the first 5 minutes and thereafter at 5 minute intervals till the completion of surgery. Response to skin incision was also observed and recorded in a similar manner. During surgery, anesthesia was maintained with isoflurane and 70% nitrous oxide in oxygen. At the end of the surgical procedure, residual neuromuscular blockade was reversed with Inj.Neostigmine 0.05 mg/kg mg and Inj.Glycopyrolate 0.008 mg/kg intravenously (IV). Extubation was carried out routinely.

Results

Both the groups were comparable in terms of age, weight, height, gender ratio and ASA physical status.

At baseline the mean heart rate among the two groups was comparable (p = 0.402). There was significant decrease in heart rate in Group D as compared to Group C from 1 minute after induction till 80 minutes ($p < 0.05$). After that mean heart rate among the two groups was comparable ($p > 0.05$) (Table 1).

At baseline the mean SBP among the two groups was comparable (p = 0.593). There was significant decrease in SBP in Group D as compared to Group C from laryngoscopy till post-extubation ($p < 0.05$) (Table 2).

At baseline the mean DBP among the two groups was comparable (p = 0.402). There was significant decrease in DBP in Group D as compared to Group C from laryngoscopy till 90 minutes ($p < 0.05$) (Table 3).

Table 1: Comparison of Mean Heart Rate between Different Study Groups at Various Time Intervals

Heart rate	Group C		Group D		*p* value
	Mean	SD	Mean	SD	
Baseline	82.93	5.589	82.73	5.420	0.402
Before induction	83.13	5.244	80.07	4.741	0.412
1 min after induction	79.40	6.891	78.33	4.302	0.043
At laryngoscopy	103.53	6.642	72.40	3.802	0.004
At intubation	109.93	6.533	71.80	3.253	0.0001
5 min	102.53	5.649	71.73	3.991	0.0001
At skin incision	100.87	5.987	69.93	3.342	0.023
10 min	99.53	4.455	71.33	3.689	0.0001
20 min	96.33	6.707	72.93	3.393	0.016
30 min	96.60	6.790	71.33	3.536	0.0001
40 min	92.60	5.468	72.00	3.523	0.0001
50 min	88.13	5.557	73.67	3.763	0.006
60 min	86.73	4.770	72.07	3.084	0.0001
70 min	84.40	5.076	68.73	3.513	0.0001
80 min	83.47	5.029	69.93	3.393	0.002
90 min	82.07	4.017	69.13	3.137	0.256
120 min	81.80	4.156	76.07	3.473	0.085
Post-extubation	98.07	2.149	74.60	3.729	0.500

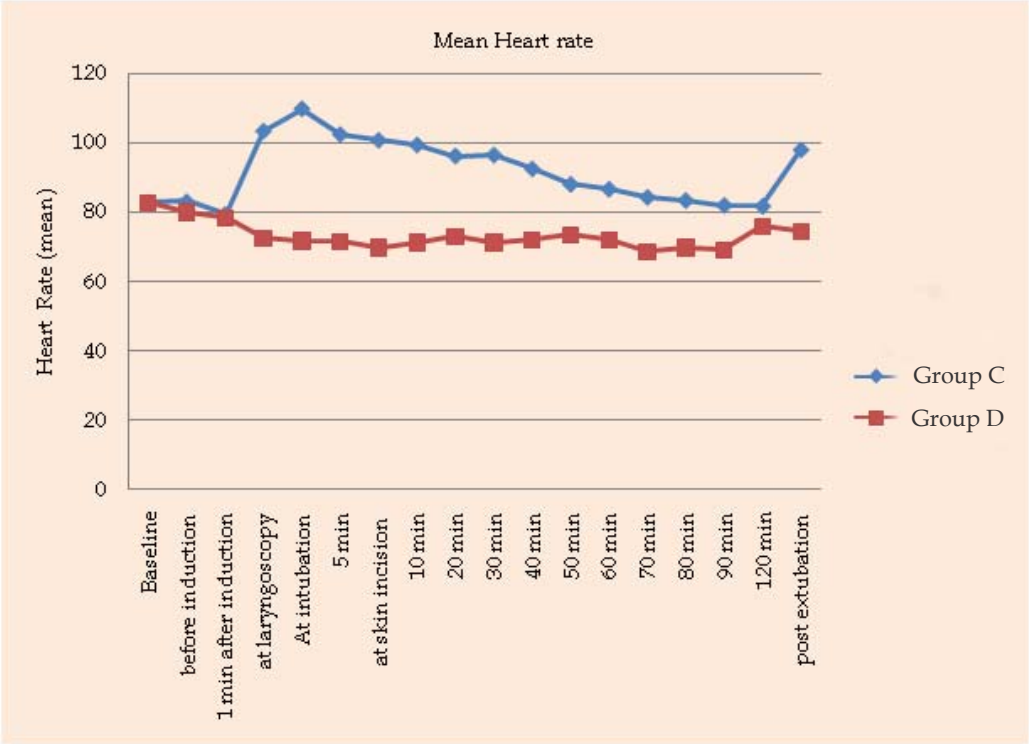

Fig. 1: Comparison of mean heart rate between different study group at various time intervals.

Table 2: Comparison of Mean SBP between Different Study Group at Various Time Interval.

SBP	Group C		Group D		*p* value
	Mean	SD	Mean	SD	
Baseline	129.93	11.356	128.40	10.705	0.593
Before induction	123.47	10.342	122.87	10.170	0.822
1 Min after induction	107.20	9.535	106.73	4.813	0.081
At laryngoscopy	156.60	10.036	99.93	6.741	0.0001
At intubation	145.53	9.864	100.47	5.600	0.0001
5 Min	134.07	7.565	103.47	3.919	0.0001
At skin incision	133.33	7.884	101.80	4.475	0.0001
10 min	132.20	9.445	102.20	3.253	0.0001
20 min	128.60	8.520	98.73	4.472	0.0001
30 min	126.20	8.735	96.13	5.198	0.0001
40 min	129.53	7.820	97.20	4.859	0.0001
50 min	132.53	7.873	100.07	5.139	0.0001
60 min	126.67	9.238	96.40	4.673	0.0001
70 min	128.87	8.431	98.67	2.832	0.0001
80 min	130.40	8.728	99.47	4.539	0.0001
90 min	132.33	8.023	105.27	4.690	0.0001
120 min	131.60	9.250	108.27	6.787	0.0001
Post-extubation	155.00	8.383	111.53	6.932	0.0001

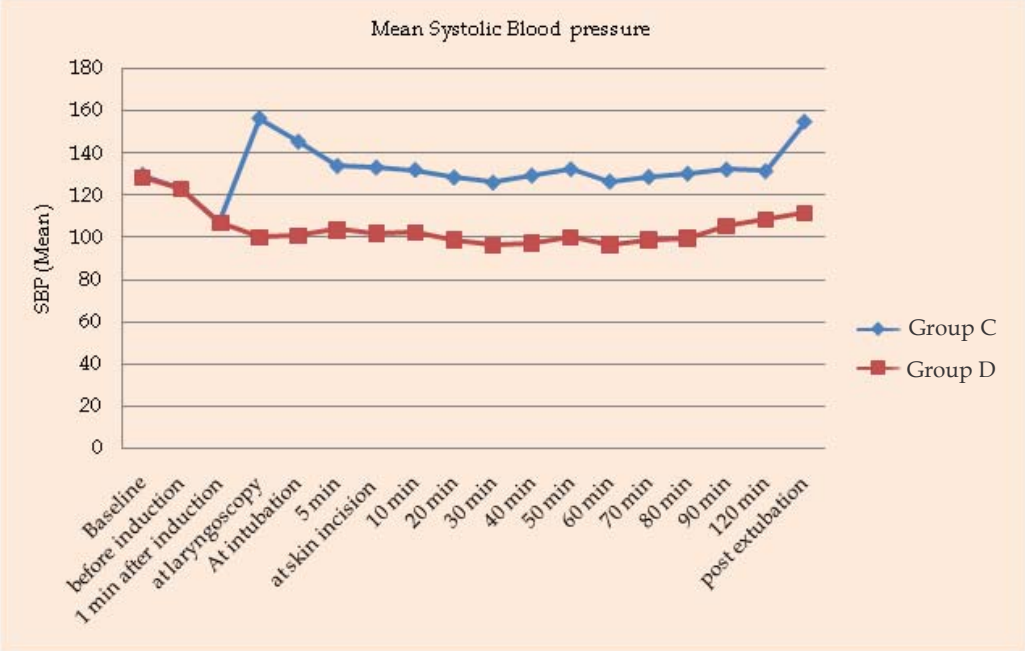

Fig. 2: Comparison of mean SBP between different study group at various time interval

Table 3: Comparison of Mean DBP between Different Study Groups at Various Time Interval.

DBP	Group C		Group D		*p* value
	Mean	SD	Mean	SD	
Baseline	85.50	5.283	84.90	5.307	0.662
Before induction	85.20	5.499	84.20	5.467	0.483
1 min after induction	85.13	5.425	83.13	6.425	0.536
At laryngoscopy	94.67	5.762	78.67	6.127	0.0001
At intubation	95.47	5.380	76.60	5.315	0.0001
5 min	94.40	5.103	74.07	4.806	0.0001
At skin incision	93.80	5.762	73.73	4.417	0.0001
10 min	94.87	5.987	70.93	4.660	0.0001
20 min	85.33	5.287	78.73	4.653	0.0001
30 min	84.33	5.827	76.33	4.521	0.0001
40 min	84.67	5.762	78.87	4.133	0.0001
50 min	86.67	5.511	79.93	4.315	0.0001
60 min	84.87	5.865	78.33	3.871	0.0001
70 min	85.33	5.287	84.67	5.020	0.001
80 min	86.00	5.452	85.60	5.315	0.018
90 min	84.07	5.953	83.93	4.891	0.030
120 min	83.00	5.960	82.47	6.361	0.739
Post-extubation	84.13	5.198	83.87	5.063	0.841

At baseline the mean MAP among the two groups was comparable (p = 0.294). There was significant decrease in MAP in Group D as compared to Group C from laryngoscopy till post-extubation ($p < 0.05$) (Table 4).

Complications like hypotension, hypertension, bradycardia, tachycardia, agitation and coughing was observed in 0%, 80%, 0%, 83.33%, 23.33% and 40% of Group C patients respectively while it was present in 10%, 0%, 10%, 0%, 0% and 13.33% of Group D patients respectively. There was statistically significant difference between various complications amongst different study groups (Table 5).

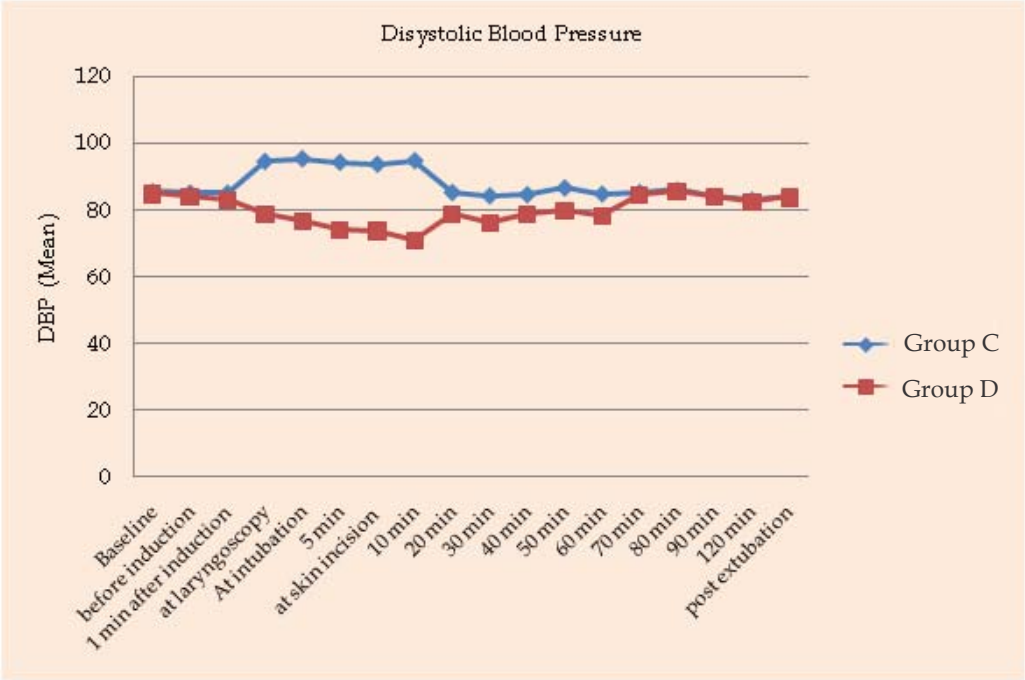

Fig. 3: Comparison of mean DBP between different study group at various time interval.

Table 4: Comparison of Mean MAP between Different Study Groups at Various Time Intervals.

MAP	Group C		Group D		p value
	Mean	SD	Mean	SD	
Baseline	79.20	3.773	78.20	3.537	0.294
Before induction	77.80	3.773	76.73	3.704	0.274
1 min after induction	74.33	5.492	73.47	5.164	0.531
At laryngoscopy	97.60	5.882	68.73	5.669	0.0001
At intubation	101.80	5.886	67.07	4.996	0.0001
5 min	102.60	4.875	66.27	4.563	0.0001
At skin incision	99.13	5.218	68.07	4.127	0.0001
10 min	97.73	4.510	66.73	4.118	0.0001
20 min	97.37	4.958	65.60	3.802	0.0001
30 min	96.80	5.209	64.93	3.778	0.0001
40 min	98.27	5.644	62.47	3.711	0.0001
50 min	99.40	5.781	66.40	3.793	0.0001
60 min	96.53	5.655	66.53	3.702	0.0001
70 min	98.00	4.136	68.27	4.118	0.0001
80 min	99.53	4.353	71.27	3.982	0.0001
90 min	100.67	5.738	74.73	4.051	0.0001
120 min	103.80	5.886	75.73	5.349	0.0001
Post-extubation	110.80	5.592	76.33	5.365	0.0001

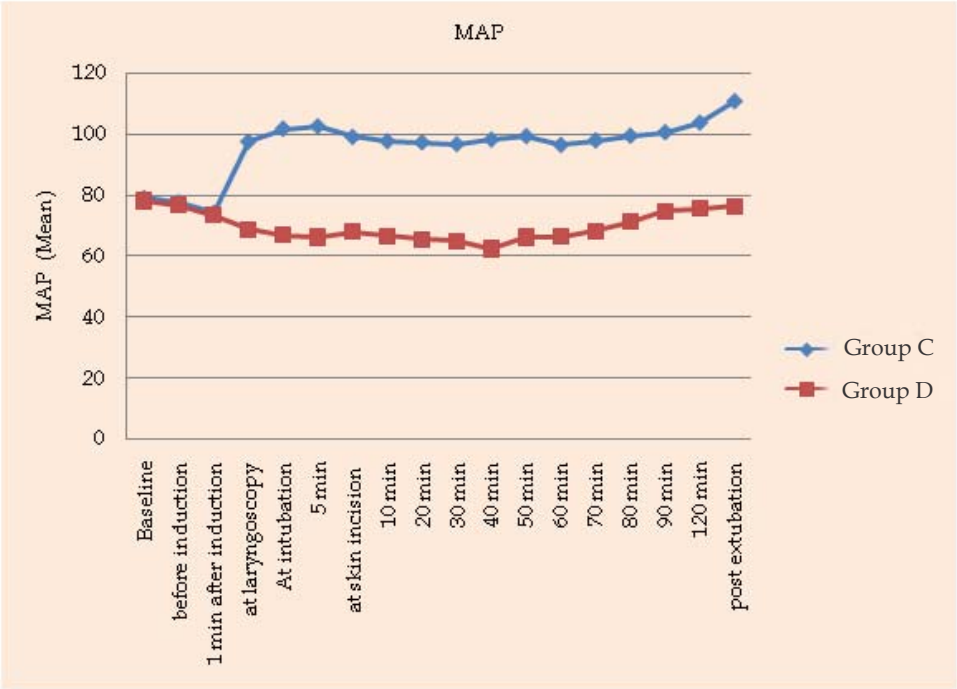

Fig. 4: Comparison of mean MAP between different study group at various time interval.

Table 5: Comparison of Various Complications amongst Different Study Groups.

Complications	Group C	Group D	*p* value
Hypotension	0 (0%)	3 (10%)	0.0001
Hypertension	24 (80%)	0 (0%)	0.0001
Bradycardia	0 (0%)	3 (10%)	0.0001
Tachycardia	25 (83.33%)	0 (0%)	0.0001
Agitation	7 (23.33%)	0 (0%)	0.0001
Coughing	12 (40%)	4 (13.33%)	0.0001

Discussion

Direct vision laryngoscopy for tracheal intubation stimulates the pharyngeal tissues and leads to a hypertensive pressor response due to reflex sympathetic discharge. Though these hemodynamic changes are short lived, yet they may be undesirable in patients with pre-existing myocardial or cerebral insufficiency.

The major stimuli to cardiovascular change during laryngoscopy and tracheal intubation are the forces exerted by the laryngoscope blade on the base of the tongue while lifting the epiglottis.[6] These include a pressor response and tachycardia along with an increase in catecholamine concentrations.[7]

The major part of this sympathoadrenal response is believed to arise from stimulation of supra-glottic region by the laryngoscope blade. Tracheal tube placement and cuff inflation cause minor additional stimulation.[8] It is also known that hemodynamic changes during laryngoscopy can cause unexpected adverse effects like cardiac dysrhythmias, acute surge of systolic blood pressure, left ventricular failure, or even pulmonary edema.

Out of various approaches for attenuation of hemodynamic pressor responses of laryngoscopy, intubation and laparoscopic surgery, pharmacological approach was considered best as it could reduce the heart rate as well as the blood pressure. Many pharmacological methods have been studied for premedication or during induction of anesthesia to attenuate the extent of these hemodynamic events including high doses of opioids, intravenous local anesthetics, beta adrenergic blockers, α_2 adrenergic agonists, magnesium sulphate, and vasodilators like nitroglycerine.

The precise mechanism that leads to the hemodynamic responses to laryngoscopy and intubation involves intense sympathetic discharges and release of catecholamine. Dexmedetomidine promotes sedative and hypnotic effects. The

presynaptic and postsynaptic effects of α_2 adrenoreceptors agonist diminish norepinephrine release and inhibit the central sympathetic outflow.

Heart Rate

In the present study, it was observed that there was a significant decrease in heart rate in all patients after induction and the difference in heart rate changes between the groups was statistically significant (p value <0.001). The primary action of dexmedetomidine on heart is negative chronotropic effect by blocking the cardio-accelerator nerves as well as by augmenting vagal nerve. The decrease in heart rate can be attributed to reflex response for transient hypertension following injection and subsequently due to decrease in central sympathetic outflow.

In the present study, the baseline heart rate at the start of study drug administration was comparable in both groups. At baseline the mean heart rate among the two groups was comparable (p = 0.402). There was significant decrease in heart rate in Group D as compared to Group C from 1 minute after induction till 80 minutes (p < 0.05). After that mean heart rate among the two groups was comparable (p > 0.05).

In the present study, there was a rising trend in heart rate in Group C from baseline value of 82.93 ± 5.5 as compared to Group D in which there was no rise in heart rate but instead the heart rate fell below the baseline 82.73 ± 5.4 following injection of dexmedetomidine and this difference was statistically significant (p value is <0.05). This shows that dexmedetomidine attenuates the sympathetic response to intubation effectively.

It was observed that incidence of tachycardia was 83.33% in Group C vs 0% in Group D. The increase in heart rate in control group was more persistent than dexmedetomidine group. This finding was in agreement with the study done by D. Jain *et al.*[9]

Similarly in the study conducted by D. Jain *et al.*[9], it was observed that, significant decrease in the pulse rate was observed in dexmedetomidine group from 7–10 minutes after the start of dexmedetomidine (p < 0.05), but no intervention was required as this fall in pulse rate was transient and did not affect the blood pressure. The pulse rate in dexmedetomidine group remained below the pre-dexmedetomidine values (baseline value), at all-time intervals following extubation. On the contrary pulse rate rose significantly (p < 0.05) in normal saline (control) group following extubation.[9]

In our study, bradycardia was observed in 3 patients (10%) in Group D which responded to injection atropine. This finding correlates well with the observation by Aksu *et al.*[10]

Similarly in the study conducted by M.L. Jakola *et al.* it was observed that after intubation maximum heart rate was 18% less in dexmedetomidine group compared with placebo. They also noted that there was a significant decrease in blood pressure in dexmedetomidine group.[4]

Systolic Blood Pressure

At baseline the mean SBP among the two groups was comparable (p = 0.593). There was a significant decrease in SBP in Group D as compared to Group C from laryngoscopy till post-intubation (p < 0.05). In the present study the mean systolic blood pressure (SBP) of patients in Group D (dexmedetomidine group) prior to dexmedetomidine injection was 129.93 ± 11.35 mm hg and in Group C (control group) it was 128.40 ± 10.70 mm hg. On inter-group comparison, there was no statistically significant difference in the systolic blood pressure between the two groups prior to injection of the study drug as p = 0.593. At base line the mean SBP among the two groups was comparable (p = 0.593). There was significant decrease in SBP in Group D as compared to Group D from laryngoscopy till post intubation (p < 0.05).

Similarly in the study conducted by Martina Aho *et al.* reported that increase in BP and HR was significantly less in dexmedetomidine group which received 0.6 μg/kg than in the saline group. At the same time they noted that in patients receiving dexmedetomidine 0.3 μg/kg, the increase in HR and BP did not differ from that of the saline group. The major findings of this study were that dexmedetomidine administered before induction at a dose of 0.6 μg/kg blunted the tachycardia response during endotracheal intubation.[11]

This is in agreement with the study conducted by Jain D *et al.* in which study group patients received 1 μg/kg of dexmedetomidine and they did not observe any significant change (p) in the blood pressure in dexmedetomidine group throughout the study period. On the contrary, the systolic blood pressure rose significantly (p < 0.05) in control group following extubation (172.13 ± 17.35) as observed in our study which we achieved with 0.5 μg/kg of dexmedetomidine.[9]

In our study none of the patients in Group D had hypertension as against 80% in control group. (p < 0.001).

Diastolic Blood Pressure

The diastolic blood pressure at the start of study drug injection was taken as baseline for inter-group comparison of patients in each group. In our study, prior to injection the mean diastolic blood pressure (DBP) of patients in Group D was 84.90 ± 5.3 mm Hg and in Group C it was 85.50 ± 5.2 mm Hg there was no statistically significant difference in the diastolic blood pressure between the two groups at the start of study drug injection (p value=0.5967). At base line the mean DBP among the two groups was comparable (p = 0.402). There was significant decrease in DBP in Group D as compared to Group C from laryngoscopy till 90 minutes (p<0.05). Similar findings were observed by Guler G *et al.*, in which diastolic arterial pressure increased significantly during extubation in both dexmedetomidine and control groups, but diastolic blood pressure was significantly lower in dexmedetomidine group than in control group at all times starting from 5 min after drug administration.[12] D. Jain *et al.*, in their study have not studied the changes in the diastolic blood pressure.[9]

MAP (Mean Arterial Pressure)

At baseline the mean map among the two groups was comparable (p = 0.294). There was significant decrease in MAP in Group D as compared to Group C from laryngoscopy till post extubation (p < 0.05). Thus, the MAP values were significantly lower in Group D compared to baseline values at all times from the time of dexmedetomidine infusion to post-extubation 15 minutes. This is in conjunction with the study conducted by Jain *et al.* in which study group patients received 1 µg/kg of dexmedetomidine and they did not observe any significant change (p) in the blood pressure in dexmedetomidine group throughout the study period.[9]

Comparison of adverse effects (complications)

In the present study, various complications like hypotension, hypertension, bradycardia, tachycardia, agitation and coughing was observed in 0%, 80%, 0%, 83.33%, 23.33% and 40% of Group C patients respectively while it was present in 10%, 0%, 10%, 0%, 0% and 13.33% of of Group D patients respectively. There was statistically significant difference between various complications amongst different study groups. Our findings are in agreement with G. Guler *et al.* in which bradycardia occurred in one patient and hypotension in three, within 3 min of dexmedetomidine administration. Atropine was administered for bradycardia, and hypotension was treated within 2 min by giving fluid infusion and reducing inhalation agents; no vasopressor was required. In Group D, no patients developed tachycardia as against in Group C, 26 patients (26.6%) developed tachycardia after extubation, but it reverted back to baseline within 3–5 min. Which was statistically very significant (p < 0.05).[12]

Agitation was observed in 6 patients (20%) in Group C following extubation whereas none of patients were agitated in Group D. this is statistically and clinically significant (p < 0.001). This observation is in conjunction with study done by Guler G *et al.* who conducted a study on the effect of single-dose dexmedetomidine in reducing the agitation and providing smooth extubation after pediatric adenotonsillectomy.[12]

Conclusion

Our study demonstrates that single bolus dose of dexmedetomidine 0.5 µg/kg body weight administered as premedication over 10 minutes, prior to laryngoscopy and endotracheal intubation attenuates the airway reflexes and hemodynamic responses effectively during induction of anesthesia providing smooth intubation and provides adequate sedation, maintaining patient's arousability and delays the need for analgesia in the postoperative period. Hence we recommend the use of dexmedetomidine in patients under GA and further studies are needed in larger population before it can be recommended in patients of CAD, hypertension, cerebral vascular diseases and Neurosurgeries.

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Original Research Article

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Comparison of Core Temperature by Noninvasive Method vs Invasive Method in Infants and Young Children

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Abstract

Context: Temperature is a vital parameter for monitoring under anesthesia. Induction of anesthesia leads to impairment of thermoregulatory center and results in redistribution of body heat from core to periphery. Hypothermia especially in children may results in increased morbidity and mortality. Sites of measurement of core body temperature are invasive and are not easily accesible. The purpose of this study is to evaluate the performance of skin temperature probe applied over the carotid artery in comparison to the nasopharyngeal, axillary, forehead temperature recordings. So that a better, safe and appropriate alternative to invasive temperature monitoring in pediatric age group can be used. *Aim:* To compare core temperature measured with invasive nasopharyngeal probe and noninvasive surface temperature measured with probe over axilla, forehead and skin over carotid artery. *Settings and Design:* The present study was a prospective, randomized and comparative study. We included 150 patients of age between 1 month and 60 months of ASA Grade 1 and 2, posted for elective abdominal and inguinoscrotal surgeries lasting more than 1 hour. *Methods and Materials:* Patients were randomly divided in 3 groups with 50 patients in each group. Group 1: Axillary vs nasopharyngeal temperature. Group 2: Forehead vs nasopharyngeal temperature. Group 3: Skin over carotid artery vs nasopharyngeal temperature. Standard General Anesthesia protocol was followed in all patients. We evaluated differences by monitoring and comparing invasive and noninvasive methods of temperature monitoring at above sites. *Statistical analysis used:* Software named statistical package for the social sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows. *Results:* Temperature noted throughout the surgery in Group 1 i.e. Axillary temperature v/s nasopharynx, temperature and we found that axillary temperature was lower by 1–1.5°C than nasopharynx temperature which was statistically significant (p-value being <0.05). Whereas in Group 2 i.e. Forehead temperature was lower by 2–3°C than nasopharynx temperature which was also statistically significant (p-value being < 0.05). However, in Group 3 we found that the temperature at skin over carotid artery (noninvasive) was almost equivalent to temperature at nasopharynx (invasive) with minimum difference of 0.2–0.3°C (p-value being >0.05), which was statistically not significant. This shows that temperature on skin over carotid artery almost equals to core, i.e. nasopharyngeal temperature in paediatric patients. *Conclusions:* We conclude that instead of using conventional invasive method of temperature monitoring, we can use equally reliable method of monitoring i.e. skin over carotid which is noninvasive, easily accessible with higher accuracy of estimating near core temperature.

Keywords: Hypothermia; Paediatric; Anesthesia; Core Temperature; Invasive; Noninvasive.

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Introduction

Temperature is a vital parameter for monitoring under anesthesia especially in infants and young children. They are more prone to develop hypothermia due to less insulating subcutaneous fat and higher surface area to volume ratio. They loose more heat through conduction and radiation than adults. Hypothermia especially in children may results in increased morbidity and mortality.[1]

Induction of anesthesia leads to impairment of thermoregulatory center and results in redistribution of body heat from core to periphery. Most commonly used sites for core temperature measurement are invasive like nasopharynx, distal esophagus, tympanic membrane, rectum and bladder. Non-invasive sites like axilla, forehead, skin over chest are easy to record but precision and accuracy of measurements may vary. Hence the measurement of core temperature is clinically more important.[2]

Nasopharyngeal temperature monitoring is used most oftenly in the operating room as it is easily accessible as compared to other invasive sites and gives more reliable core temperature. But this site also carries risk of injury to nasal mucosa, olfactory bulb, turbinates and readings may be affected by inspired anesthetic gases. Axillary temperature, among noninvasive techniques is used most extensively. However, axillary temperature monitoring is an unreliable method for measuring core temperature because the probes are often misplaced within the axilla.[3]

Skin temperature should correlate with changes in the core temperature. We hypothesize that skin over carotid artery temperature measurement may be an alternative method which provides rapid, easy and painless recording.

In this study, our aim is to evaluate the performance of skin temperature probe applied over the carotid artery in comparison to the nasopharyngeal, axillary, forehead temperature recordings. So that a better, safe and appropriate alternative to invasive temperature monitoring in pediatric age group can be used.

Materials and Methods

A study of a continuous response variable from three independent study groups with 1:1:1 patient ratio in Group 1, Group 2 and Group 3 are studied. In a previously published study the response within each patient group was approximately normally distributed. If the true intra-group difference in the mean response is approximately 1.5, we will need to study minimum 45 patients in each study group (i.e. total 135 patients) to be able to reject the null hypothesis that the population means of Group 1, Group 2 and Group 3 are equal with probability (power) 0.80. The Type I error probability associated with this test of null hypothesis is 0.05.

Therefore, the sample size we studied was 50 patients in each group (Total 150).

p value < 0.05 was considered as statistically significant.

After approval by institutional ethical committee, randomized prospective comparative study was conducted in attached teaching hospital. Study includes 150 patients, with 50 patients in each group randomly divided in three equal groups.

Group 1: Axillary vs nasopharyngeal temperature

Group 2: Forehead vs nasopharyngeal temperature and

Group 3: Skin over Carotid Artery VS Nasopharyngeal temperature.

We evaluated the differences by monitoring and comparing them in particular groups. Study includes children of age group 6 months to 5 years of both sexes and posted for elective urogenital surgeries lasting more than 1h with ASA Grade I and II. Neurological conditions affecting thermoregulatory function such as cerebral palsy were excluded. All patients were evaluated preoperatively.

Written informed consent was obtained from the parents. Standard *non per os* (NPO) guidelines for pediatric patients was followed.

Uniform Standard General Anesthesia protocol was followed in all patients. Temperature monitoring was started after 10 minutes of intubation and continued till extubation with every 10 minutes interval.

For temperature monitoring, surface probe used was attached to multiparameter cardiocap – DatexOhmeda monitor.

The nasopharyngeal probe (invasive method) is introduced into nasopharynx through one of the nasal apertures to a pre-calculated depth. The depth of insertion is determined before insertion by measuring the distance externally between the tragus and the nasal aperture. Simultaneously skin surface probe was placed over the axillary artery in the pit on the arm (noninvasive method) along the mid-axillary line in patients of Group 1.

In Group 2, probe is attached on the forehead (noninvasive) covering with adhesive dressing to avoid the effect of external objects affecting the temperature reading, while comparing it with the nasopharyngeal reading.

Finally, in Group 3 skin surface temperature probe is attached to the anterior part of the neck, centered to the site of maximum intensity of carotid artery pulsation at the level of thyroid prominence (noninvasive method), comparing it again with the nasopharyngeal reading (invasive method). The skin probe is secured in place and covered with adhesive dressing.

The operating room temperature was thermostatically maintained in the range of 20–22°C and relative humidity of 50%. All the patients received pre-warmed blanket applied over the lower extremity without disturbing the monitoring site.

The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS version 16.0, Inc. Chicago, USA) for MS Windows. The inter-group comparison of categorical variable is tested using chi-square test after Bonferroni's correction for multiple group comparisons. The intra-group comparison was performed using paired '*t*' test. The normality assumption was tested before subjecting the continuous variables to ANOVA and T test.

Results

The demographic data: age, weight in the groups were comparable did not differ significantly across three intervention groups (*p*-value >0.05 for all). Distribution of sex between group I vs II and I vs III was significant, which may be due to randomization.

Temperature noted throughout the surgery in Group 1 i.e. Axillary temperature v/s nasopharynx temperature and we found that axillary temperature was lower by 1–1.5°C than nasopharynx temperature which was statistically significant (*p*-value being <0.05). We found the fall in temperature in nasopharynx group from baseline, i.e. 36.7 ± 0.38 to 35.1 ± 0.42 at the end of procedure, whereas for axillary temperature it was from baseline 35.4 ± 0.48 to 33.1 ± 0.71 at the end of procedure.

Whereas in Group 2, i.e. Forehead temperature was lower by 2–3°C than nasopharynx temperature which was also statistically significant (*p* value < 0.05). The difference in nasopharynx group from baseline, i.e. 36.6 ± 0.35 to 34.4 ± 0.0 at the end of procedure, whereas for forehead temperature it was from baseline 34.7 ± 0.66 to 32.6 ± 0.0 at the end of procedure.

However, in Group 3 we found that the temperature at skin over carotid artery (non-invasive) was almost equivalent to temperature at nasopharynx (invasive) with minimum difference of 0.2–0.3°C (*p* value being >0.05), which was statistically not significant as shown in graph 3.

The mean nasopharynx temperature (from baseline 36.6 ± 0.42 to 35.7 ± 1.27 at the end of procedure) didn't differ significantly compared to temperature at skin over carotid artery (baseline 36.3 ± 0.55 to 35.5 ± 1.27). Thus temperature at skin over carotid closely resembles to that nasopharynx.

The intra-group comparison of temperature at each time interval throughout the surgery is almost equivalent in Group 3 compared to Group 1 and Group 2 as shown in Table 2.

This shows that temperature measured on skin over carotid artery almost equals to core temperature, i.e. nasopharyngeal temperatures in pediatric patients.

Discussion

Children loose more heat through conduction and radiation than adults, due to less insulating

Table 1: Distribution of Demographic Data of Cases Between Three Groups

Parameter	Group I	Group II	Group III	Gr I v II	Gr I v III	Gr II v III
Age – Yrs	1.58 ± 1.09	1.86 ± 1.25	1.83 ± 1.34	0.644 NS	0.502 NS	0.873 NS
Wt – Kg	10.06 ± 2.77	10.54 ± 3.25	9.80 ± 3.16	0.189 NS	0.098 NS	0.816 NS
Sex M:F	48 : 02	39 : 11	37 : 11	0.015*	0.004*	0.815 NS

NS: non-significant

Table 2: Comparison of Temperature at each Time Interval between group

Time (min)	Group 1 (N=50)			Group 2 (N=50)			Group 3 (N=50)		
	Nasopharynx	Axillary	*p*-value	Nasopharynx	Forehead	*p*-value	Nasopharynx	Skin over carotid artery	*p*-value
10	36.7 ± 0.38	35.4 ± 0.48	0.001*	36.6 ± 0.35	34.7 ± 0.66	0.001*	36.6 ± 0.42	36.3 ± 0.38	0.001 NS
20	36.5 ± 0.37	35.4 ± 0.49	0.001*	36.4 ± 0.42	34.5 ± 0.67	0.001*	36.3 ± 0.59	36.2 ± 0.37	0.061 NS
30	36.4 ± 0.42	35.3 ± 0.48	0.001*	36.2 ± 0.36	34.5 ± 0.76	0.001*	36.1 ± 0.72	36.1 ± 0.42	0.848 NS
40	36.1 ± 0.47	35.1 ± 0.52	0.001*	36.1 ± 0.31	34.4 ± 0.78	0.001*	35.9 ± 0.63	36.0 ± 0.47	0.744 NS
50	35.9 ± 0.56	34.9 ± 0.52	0.001*	36.0 ± 0.33	34.3 ± 0.82	0.001*	35.9 ± 0.56	35.9 ± 0.56	0.742 NS
60	35.9 ± 0.55	34.9 ± 0.54	0.001*	35.9 ± 0.31	34.3 ± 0.83	0.001*	35.8 ± 0.56	35.8 ± 0.55	0.959 NS
70	35.8 ± 0.65	34.8 ± 0.65	0.001*	35.9 ± 0.37	34.0 ± 0.95	0.001*	35.7 ± 0.63	35.7 ± 0.65	0.601 NS
80	35.7 ± 0.45	34.6 ± 0.68	0.001*	35.9 ± 0.35	34.1 ± 0.99	0.001*	35.6 ± 0.69	35.7 ± 0.45	0.195 NS
90	35.7 ± 0.45	34.5 ± 0.69	0.001*	35.7 ± 0.31	33.9 ± 0.98	0.001*	35.5 ± 0.73	35.5 ± 0.45	0.753 NS
100	35.7 ± 0.50	34.4 ± 0.77	0.001*	35.5 ± 0.34	33.6 ± 0.97	0.001*	35.3 ± 0.75	35.4 ± 0.50	0.191 NS
110	35.7 ± 0.55	34.3 ± 0.89	0.001*	35.3 ± 0.26	33.3 ± 0.96	0.001*	35.2 ± 0.74	35.3 ± 0.55	0.074 NS
120	35.6 ± 0.56	34.4 ± 0.97	0.001*	35.2 ± 0.44	33.6 ± 0.97	0.001*	35.1 ± 0.86	35.2 ± 0.56	0.401 NS
130	35.5 ± 0.61	34.2 ± 1.05	0.001*	34.9 ± 0.07	32.8 ± 1.28	0.001*	35.3 ± 0.72	35.3 ± 0.61	0.524 NS
140	35.5 ± 0.60	34.3 ± 1.22	0.007*	34.6	32.6	–	35.2 ± 0.85	35.2 ± 0.60	0.563 NS
150	35.5 ± 0.67	34.4 ± 1.36	0.0026*	34.4	32.6	–	34.9 ± 0.73	34.9 ± 0.67	0.111 NS
160	35.4 ± 0.51	34.4 ± 1.47	0.001*	–	–	–	35.1 ± 1.00	35.2 ± 0.51	0.580 NS
170	35.3 ± 0.38	34.5 ± 1.72	0.001*	–	–	–	35.2 ± 1.32	35.2 ± 0.38	0.999 NS
180	35.1 ± 0.42	33.9 ± 1.71	0.001*	–	–	–	35.7 ± 1.27	35.5 ± 0.42	0.999 NS

Values are Mean ± Standard Deviation. *p*-values for Intra-group comparisons by paired sample = '*t*' test. **p* value < 0.05 is considered to be statistically significant.

NS : statistically Non- Significant

subcutaneous fat and higher surface area to volume ratio. Hence, temperature monitoring is an integral part of management of anesthesia during surgeries, especially in infants and young children who are more prone to hypothermia.

A more severe loss of temperature, inability to generate heat inside the body and lack of thermoregulatory response, in children, make them more susceptible to hypothermia than adults. Therefore, correct and continuous measurement of the core body temperature, during surgery, is very important for controlling temperature conditions in patients, especially children.

Hypothermia can occur in up to 20% patients who undergo major surgeries. It is also accompanied by various symptoms that can increase the clinical consequences especially high-risk patients. These consequences include respiratory disorders, apnea, hypoxia, carbon dioxide retention, metabolic acidosis, hypoglycemia, left shift of oxygenation curve, heart disorders, platelet dysfunction, dysfunction of coagulation enzymes, increased bleeding, increased surgical site infection, change in drug metabolism and thermal discomfort.[4]

As core body temperature measurement sites (e.g. tympanic membrane, pulmonary artery, distal esophagus and nasopharynx) are not easily accessible, usually near core sites are used for monitoring. These sites include the mouth, axilla, bladder, skin surface, and rectum. The above mentioned core temperature measurement sites advocated as the most pertinent are relatively invasive and present as an elevated health risk to a varying degree. For example, probes in the nasopharynx can cause mild-to-severe epistaxis while rectal probes can occasionally cause trauma.

In some situations, none of the true core temperature sites are readily accessible such as during the immediate perioperative period with procedural sedation, or in patients with congenital malformations.

Replacing a malfunctioning invasive probe in a patient can also be challenging once a surgical procedure is underway. Furthermore, the risk of cross-infection among patients will be elevated in low resource settings due to the repeated use of a given invasive probe. A need therefore exists for a sufficiently accurate noninvasive form of thermometry.

Hence, we conducted a prospective randomized study by comparing invasive and noninvasive methods of temperature monitoring, to avoid such complications in children.

We compared mean nasopharyngeal and mean axillary temperatures (Group 1) and found that the difference between mean nasopharyngeal temperatures and axillary temperatures were around 1–1.5°C.

Axillary temperatures were found less than nasopharyngeal temperatures and the result was statistically significant. Androkites *et al.* conducted a similar study "On comparison of axillary and infrared tympanic membrane thermometers in a pediatric oncology outpatient setting. There results showed that the tympanic membrane site of temperature monitoring results in significantly higher temperature reading than the axillary method.[5]

In Group 2 we compared mean nasopharyngeal and mean forehead temperatures and found that the difference between the mean nasopharynx temperatures compared to mean forehead temperatures were around 2–3°C i.e. temperature on forehead is less than nasopharynx. This difference was statistically significant ($p < 0.05$).

In Group 3 we compared mean nasopharynx temperature and mean temperature of skin over carotid artery in study population and found that the difference between mean nasopharyngeal temperatures and mean temperatures at skin over carotid artery were around 0.2–0.3°C ($p > 0.05$), which was statistically not significant.

Similar studies was conducted by Imani *et al.* to measure skin temperature over the carotid artery and compare it with the rectum temperature, in order to propose a model for accurate estimation of near core body temperature.[6]

Selvaraj *et al.* also did a prospective double-blinded study to compare the correlation of skin temperature over carotid artery in the neck to that of simultaneously measured nasopharyngeal temperature in adult patients undergoing surgical procedures under general anesthesia.[7]

They also found that skin temperature over the carotid artery in the neck was strongly correlated to the nasopharyngeal temperature in adult patients.

We did similar study in pediatric patients comparing skin over carotid artery to nasopharynx as well as comparison with other sites and the results were almost equivalent to above study.

Skin over carotid is more reliable technique of temperature monitoring as compared to other peripheral sites, because of its close proximity to larger artery. This may be explained as there is thin layer of skin over the artery in children.

Nasopharyngeal temperature monitoring is considered as the primary indicator of intraoperative thermal status due its proximity to internal carotid artery. But nasopharyngeal temperature monitoring has its limitations because of the risks involved in it.

As oppose to this temperature measured on skin over carotid artery provides accurate, safe temperature measurement and without potential risks.

In conclusion, skin temperature measured over the carotid artery, provides an accurate noninvasive estimate of nasopharyngeal temperature in infants and young children undergoing elective surgery. This method completely eliminates risks (e.g., epistaxis, infection, etc.) associated with invasive core temperature measurements and also presents a reliable alternative.

The only limitation of our study is that we have included all types of surgeries more than 1 hour. In future, we can study this in specific type of surgeries where risk of hypothermia is more.

Conclusion

We conclude that instead of using conventional invasive method of temperature monitoring, we can use equally reliable non-invasive method of monitoring, i.e. Skin over carotid artery which is easily accessible and is devoid of complications.

Key Messages: Temperature monitoring over skin over carotid is reliable for core temperature.

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Original Research Article

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A Double-blind Randomized Clinical Study to Compare the Effects of Levobupivacaine Alone and with Dexmedetomidine in Brachial Plexus Block by Axillary Approach

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Abstract

Background: For regional nerve blocks, a combination of dexmedetomidine with local anesthetic like levobupivacaine has shown improved effectiveness by extending the duration of analgesia and reduction in postoperative analgesic requirement. This study was undertaken to evaluate the effectiveness and efficacy of levobupivacaine alone and levobupivacaine with dexmedetomidine in axillary brachial plexus block. *Materials and Methods:* We included 70 patients of ASA category I, II, and III, posted for elective hand and forearm surgeries and randomly assigned them into two groups to receive either 24 ml 0.5% Inj.levobupivacaine and 1 ml normal saline (Group L) or 24 ml of 0.5% Inj.levobupivacaine and 1 mcg/kg of Inj.dexmedetomidine diluted to 1 ml with normal saline (Group LD). *Results:* In Group LD the onset of sensory block (16.13 ± 4.001 min) and motor block (18 ± 3.889 min) was significantly shorter compared to that of Group L. Duration of sensory block in Group LD was 677.25 ± 99.54 min and in Group L was 494.38 ± 70.64 min and the difference was clinically significant ($p < 0.001$). Duration of motor block in Group LD was 710.88 ± 87.32 min and in Group L was 526.25 ± 70.229 min and was clinically significant. Duration of analgesia in Group L was 576.88 ± 76.306 min and that in Group LD was 764.38 ± 110.275 min. There was a significant change in hemodynamics in Group LD as compared to that in Group L. *Conclusion:* Levobupivacaine along with sdexmedetomidine provides faster onset of anesthesia with extended duration of analgesia. It offers efficacious and trouble-free method of anesthesia and better analgesia in postoperative period for hand and forearm surgeries.

Keywords: Axillary block; Dexmedetomidine; Peripheral nerve block; Levobupivacaine.

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Introduction

Regional anesthesia provides long-lasting and effective anesthesia at specific sites. Brachial plexus block is being used as a primary and sole anesthetic technique to facilitate painless surgery. It can be used for management of postoperative pain and chronic pain conditions.

Usually for upper limb surgeries, brachial plexus block is used regularly as regional anesthetic technique. Various approaches like interscalene, supraclavicular, infraclavicular and axillary are used. Among these, axillary approach to the brachial plexus block is popular because of its ease of access, safety of administration and reliable block. It is indicated in surgeries involving forearm and hand.

Levobupivacaine is a newer, long-acting local anesthetic agent having pharmacokinetic properties similar to bupivacaine. Various study

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trials have shown its wider safety and minimal myocardial toxicity in contrast to bupivocaine. The efficacy of local anesthetic is improved by addition of adjuvant thereby enhancing the onset of action, increasing the duration of action, and prolonging postoperative analgesia.

Dexmedetomidine which is used as an adjuvant to local anesthetics is a selective alpha-2 adrenoreceptor agonist. It is assumed to hasten the onset of action, prolong the duration of action, and postoperative analgesia.

The aim of the study was to compare the effects and efficacy of levobupivacaine alone and levobupivacaine with dexmedetomidine in axillary brachial plexus block for hand and forearm surgeries in terms of onset of sensory and motor block, duration of sensory and motor block and duration of analgesia.

Materials and Methods

Following Ethical Committee approval in our institution Subbaiah Institute of Medical Scinces and Hospital, Shimoga, 70 patients undergoing elective hand and forearm surgeries were randomized using closed envelope technique. Patients between the ages of 18 and 60 belonging to physical status of ASA I, II and III were included. Patients with weight <45 kg, pregnant patients, allergy to levobupivacaine or dexmedetomidine, coagulation abnormalities and infection at block site were excluded.

All patients underwent pre-anesthetic evaluation; written informed consent was obtained. All patients were kept nil by mouth 6 hours prior to surgery, tablet alprazolam 0.5 mg was given the night before the surgery, and premedicated with Inj. ranitidine 50 mg and Inj.perinorm 10 mg 2 hr before surgery. Baseline readings of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) were noted. Under all aseptic precautions, operative limb was positioned. Axillary block was performed by using 40 mm length 26G, short beveled, stimulating needle using nerve stimulator. Once the limb was positioned, the pulsation of axillary artery was felt in the upper one-third of the arm. 1 ml of inj. lignocaine 2% was injected subcutaneously just above and below the pulsation. By starting the stimulation with current intensity at 2.5 mA, location of each nerve was done. Then current intensity was decreased slowly to a minimum of 0.5 to 0.6 mA by changing direction of the needle to obtain the desired appropriate response. 6 ml of the drug solution was injected for each nerve (ulnar, radial, musculocutaneous and median nerve) after negative aspiration for blood.

Group L: Received Inj.levobupivacaine (0.5%) 24 ml and 1 ml of normal saline.

Group LD: Received Inj.levobupivacaine (0.5%) 24 ml and Inj. dexmedetomidine 1 mcg/kg diluted to make a volume of 1 ml with normal saline.

The anesthetist involved in preparation of drug combinations was blinded for study groups. Inj. dexmedetomidine 1 mcg/kg diluted to make volume of 1 ml with normal saline. Time of drug admistration was noted.

After giving the block hemodynamic parameters like HR, MAP, SBP, DBP, SpO_2 were noted every five min for the first 20 min, every 15 min for first 1 hour thereafter and every half an hour later on till sensory block regression. Sensory block was assessed by pinprick sensation using 22G needle in various dermatome of respective nerves using a three-point scale.

Motor block was assessed by ability to oppose, abduct and adduct the thumb for median, radial and ulnar nerve respectively and ability to flex the elbow for musculocutaneous nerve.[1]

The time of onset for sensory and motor block was noted separately. Level of blockade was assessed every five min for the initial 20 min intraoperatively and then every 15 min postoperatively till the resolution of sensory and motor functions. During postoperative period, time for requirement of primary analgesic was noted.

Surgery was started after 30 min of giving the block to ease the evaluation of sensory and motor block. If there was incomplete loss of pinprick sensation in the ulnar, radial, musculocutaneous and median nerve distribution with minimal motor block 25 min after the local anesthetic injection, intravenous (IV) midazolam 2 mg, and fentanyl 2 mcg/kg IV were given. If patients complained of pain despite supplemental analgesia with fentanyl, general anesthesia was administered and they were excluded from the study.

The time gap between the local anesthetic drug administration and full sensory block was taken as sensory onset time. Duration of sensory block was defined as time taken for complete resolution of the sensory block in all dermatome.

The time gap between drug administration and complete motor block was taken as motor block onset time. Time for recovery of complete motor activity in the hand and forearm was taken as duration of motor block.

Visual analog scale (VAS) was used for assessment of pain postoperatively. When VAS score >4, Inj.paracetamol 1 gm iv infusion was given and the time of requirement of first analgesic was noted.

Any untoward effects like desaturation (SpO_2 less than 94%) was treated with supplemental oxygen through face mask. Fall in BP more than 20% from baseline was treated by the IV fluids if required iv vasopressors were also used. Bradycardia with heart rate of less than 50 beats/min was treated with atropine 0.6 mg iv. Any other untoward side effects were recorded.

Statistical analysis

Statistical analysis of data was done using Statistical Package for the Social Sciences (SPSS) Version 20.0 software. Independent Student *t*-tests were used to compare qualitative demographic variable and surgical time between two groups. Chi-square test was used to compare gender distribution in two groups. Data is considered as statistically significant if *p* value is less than 0.05. For outcome data with continuous variables and to measure the variation in outcome independent Student *t*-tests were used for statistical analysis.

Results

Demographic Data

As shown in Table 1, there was no statistical difference between the two groups in regards to age, weight, gender distribution and duration of surgery with a *p* value of 0.65, 0.696, 0.639, 0.32, respectively.

Chi-square test was used for American Society of Anesthesiologist (ASA) category distribution. The difference was statistically insignificant ($p = 0.577$).

Onset of sensory and motor block

As shown in Table 2, the onset of sensory block in Group LD (16.13 min) was earlier compared to Group L (19.05 min) and mean onset time of motor block in Group LD was 18 min compared to 23.13 min in Group L which was statistically significant ($p \leq 0.001$).

Duration of sensory block, motor block and analgesia

As shown Table 2, the mean duration of sensory block, motor block and analgesia was significantly prolonged in Group LD as compared to that in Group L which was statistically significant ($p \leq 0.001$).

Hemodynamic data

Heart rate

There was a statistically significant fall in heart rate between 25 min and 105 min in Group LD compared to Group L ($p < 0.05$). But there was no clinically significant bradycardia requiring treatment (Fig. 1).

Systolic blood pressure

There was a statistically significant fall in systolic blood pressure between 10 min and 480 min in Group LD compared to that in Group L ($p < 0.05$). But it was not significant clinically as none of the patients required vasopressors (Fig. 2).

Diastolic blood pressure

There was a statistically significant fall in diastolic blood pressure in Group LD compared to Group L between 10 min and 420 min ($p < 0.05$). But it was not significant clinically as none of the patients required vasopressors (Fig. 3).

Oxygen saturation

As shown in Figure 4, there was no fall in the oxygen saturation in either group.

Table 1: Demographic Data

Variables	Mean ± SD		*p* value
	Group L	Group LD	
Age	41.15 ± 15.22	39.5 ± 16.23	0.652
Weight	60.9 ± 5.945	60.33 ± 7.11	0.696
Gender			
Male	22	24	0.639
Female	13	11	
ASA			
I	15	16	0.557
II	19	16	
III	1	3	
Duration of Surgery (in min)	81.42 ± 17.23	85.98 ± 22.14	0.32

SD-Standard Deviation, ASA-American Society of Anesthesiologist

Table 2: Results Showing Onset of Sensory and Motor Block.

Variables	Mean ± SD (in min)		*p* value
	Group L	Group LD	
Onset of Sensory Block	19.5 ± 3.889	16.13 ± 4.001	<0.001
Onset of Motor Block	23.13 ± 3.37	18 ± 3.889	<0.001

Table 3: Results Showing Duration of Sensory Block, Motor Block and Duration of Analgesia

Variables	Mean ± SD (in min)		*p* value
	Group L	Group LD	
Duration of Sensory Block	494.38 ± 70.64	677.25 ± 9.54	<0.001
Duration of Motor Block	525.25 ± 70.23	710.88 ± 87.32	<0.001
Duration of Analgesia	576.88 ± 73.330	764 ± 110.23	<0.001

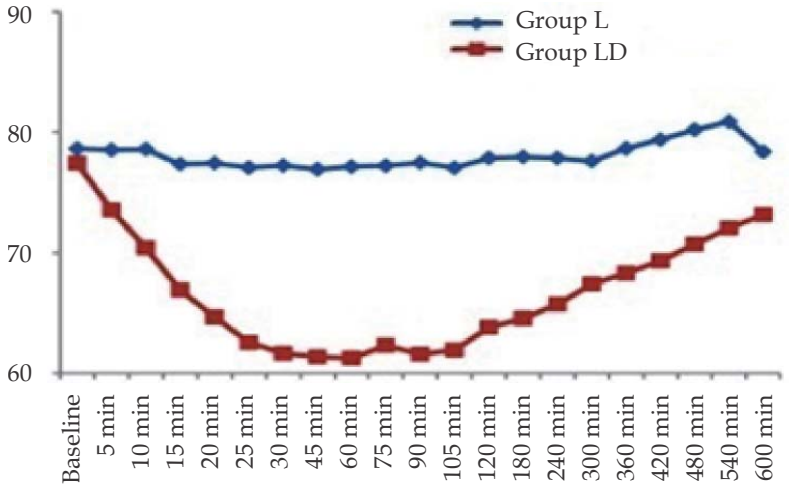

Fig. 1: Graph showing variation in the heart rate in both the groups

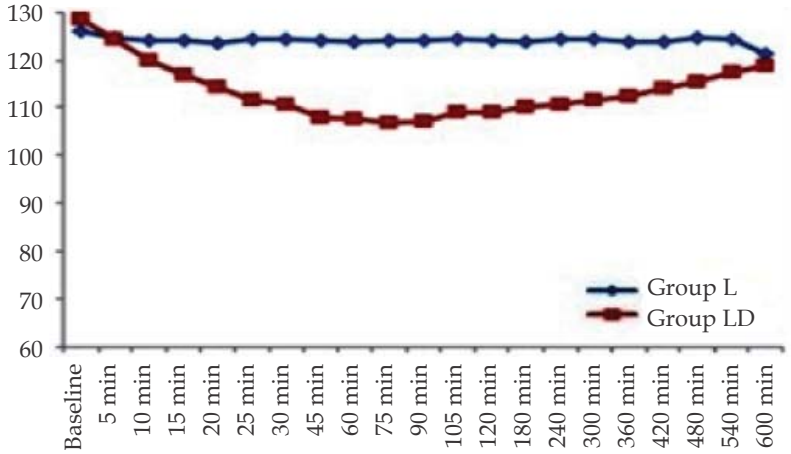

Fig. 2: Graphs showing variation in the systolic blood pressure in both the groups.

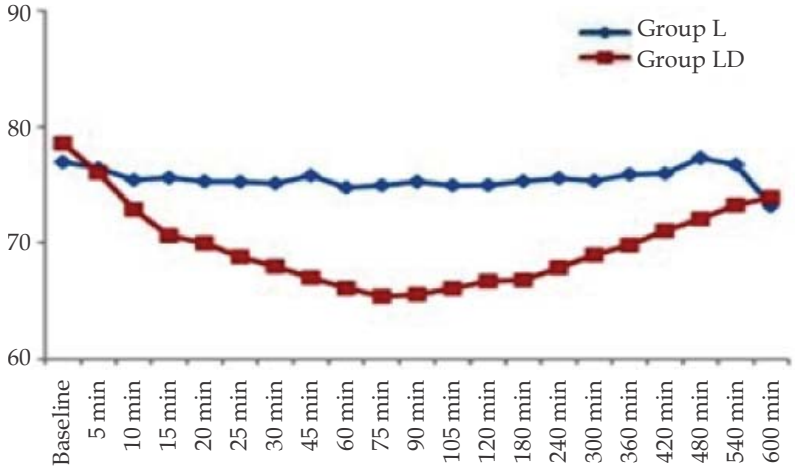

Fig. 3: Graphs showing variation in the diastolic blood pressure in both the groups

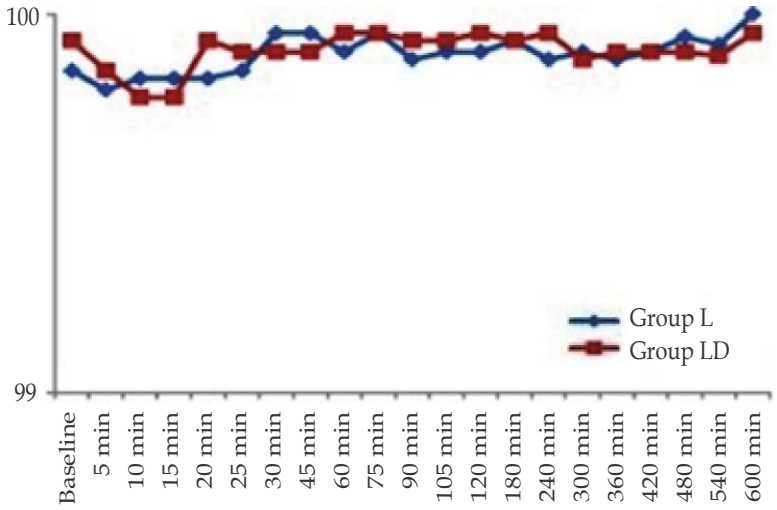

Fig. 4: Graphs showing variation in the oxygen saturation in both the groups

Discussion

The most commonly performed regional nerve block for surgeries on hand and forearm is the brachial plexus block. It offers many advantages over general anesthesia. Many complications like pneumothorax, vascular injuries which are common in interscalene, supraclavicular and infraclavicular brachial plexus block are less common in axillary brachial plexus block. Various anesthetic drugs have been used for axillary brachial plexus block. Different studies have compared bupivacaine, ropivacaine and levobupivacaine in brachial plexus block for upper limb surgery. Levobupivacaine is a good substitute for bupivacaine. Compared to ropivacaine, levobupivacaine provides a significantly longer duration of analgesia.[1] The long duration of sensory block associated with good analgesia and lesser cardiotoxicity than bupivacaine makes levobupivacaine a better choice for upper extremity blocks.

Local anesthetics along with adjuvant for axillary brachial plexus block intensify and extend the duration of block and analgesia.

Various parameters in demographic profile were comparable in both the groups. No patients in either group were excluded from the study.

In our study, we found that the mean onset time of sensory block was 16.13 ± 4.0 min in Group LD which was earlier and statistically significant (p < 0.001) than that in Group L which was 19.5 ± 3.8 min, and mean onset time of motor block was 18 ± 3.8 min in Group LD which was earlier andstatistically significant (p < 0.001) than that in Group L which was 23.13 ± 3.3 min (Table 2).

In this study, we demonstrated that addition of dexmedetomidine with levobupivacaine prolonged the duration of blockade and delayed the requisite for rescue analgesics (Table 3). Peripherally, alpha 2 agonists produce analgesia by reducing release of norepinephrine and causing alpha 2 receptor-independent inhibitory effects on nerve fiber action potentials. Centrally, alpha 2 agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of alpha 2 adrenoceptors in the locus coeruleus.[2-3]

Abosedira[4] in his study compared the effect of adding either clonidine or dexmedetomidine to lidocaine during Bier's block and reported that adding dexmedetomidine to lidocaine during Bier's block provides better quality of anesthesia, tourniquet tolerance, and reduced intraoperative and early postoperative analgesic requirement than the addition of clonidine.

Brummett *et al.*[5] in their study showed that perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat

Brummett *et al.*[6] in their study showed that perineural injection of dexmedetomidine added to ropivacaine causes dose dependent increase in duration of thermal antinociception in sciatic nerve block in rats and also found that on histopathological examination of myelin sheath was normal in both groups, in the same study also showed dexmedetomidine acts peripherally by causing hyperpolarization of nerve fiber and preventing the nerve from subsequent depolarization from resting membrane action potential. Kosugi *et al.*[7]

concluded dexmedetomidine reduced amplitude of compound action potential without stimulating alpha-2 adrenergic receptors.

The effectiveness of peripheral dexmedotomedine for analgesia has been recognized. This effect is dose dependent (not mediated by central action).

Very few studies on humans have been conducted to know the effects of α_2 agonists in peripheral nerve block. However various studies have showed that dexmedetomidine can be used safely in spinal anesthesia and IV regional anesthesia.[8-10] With this background, we determined the effects of addition of dexmedetomidine with levobupivacaine in axillary brachial plexus block. Although dexmedetomidine has an α_2/α_1 selectivity ratio that is eight times higher than that of clonidine, an equipotent comparative study of both the drugs in peripheral nerve block was conducted by Sudheer *et al*.[11] and it demonstrated that dexmedetomidine as adjuvants to levobupivacaine in supraclavicular brachial plexus block shortened the onset time of both sensory and motor blockade. It also prolonged the duration of sensory and motor blockade as well as duration of analgesia when compared to clonidine.

Erlacher *et al*.[12] concluded that the addition of clonidine has a different impact on mepivacaine, bupivacaine and ropivacaine in terms of onset and duration of block and found that ropivacaine has vasoconstrictor properties. Addition of alpha-2 adrenergic agonist did not change the quality of sensory or motor blockade. Masuki *et al*.[13] suggested that dexmedetomidine induces vasoconstriction via alpha-2 receptors in the human forearm (around the site of injection) which might delay the absorption of local anesthetics thus prolonging their effects. Agarwal Sandhya *et al*.[14] in their study showed that dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block.

Swami *et al*.[15] in their study showed that there was considerably enhanced duration of sensory and motor block of brachial plexus when dexmedetomidine was added to bupivacaine and the quality of block was comparable to that when clonidine was used as adjuvant. Prolongation of duration of blockade by dexmedetomidine reduced postoperative pain and requirement of post operative analgesics.

In our study none of the patients required sedation in group LD which can be explained by the fact that there is some amount of systemic absorption of dexmedetomidine.[16] Alpha-2 agonists act on dorsal horn neurons inhibiting the release of substance P in pain pathway and activate alpha-2 adrenergic receptors in locus coeruleus to produce sleep.

Limitation of study was the lack of facility for ultrasound guided blocks which could have helped us to reduce the volume and dosage of levobupivacaine, the block performance time and the number of needle passes. Though clonidine is preferred because of its low cost and is commonly used as an adjuvant compared to dexmedetomidine, we acknowledge that more study trials are essential to establish the cost-effectiveness and efficacy of dexmedetomidine compared to clonidine as an adjuvant in peripheral nerve blocks.

Conclusion

Dexmedetomidine used as an adjuvant to levobupivacaine provides more rapid onset of anesthesia and prolongs the duration of analgesia in axillary brachial plexus block and also provides expedient, simple, efficient anesthesia and painless postoperative period for foream and hand surgeries.

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Original Research Article

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Rocuronium and Succinylcholine: A Comparison of Intubating Conditions in a Rapid Sequence Induction with Thiopentone

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Abstract

Background and Aim: Succinylcholine is the gold standard for rapid sequence induction of anesthesia. An alternative neuromuscular blocker (NMB) with comparable quick onset and short duration is desirable in situations where its use is contraindicated. Rocuronium offers promise especially after the introduction of sugammadex. There is still some concern regarding the quality of intubating conditions provided at 60 seconds. *Methods and Materials:* Forty patients undergoing elective surgery under general anesthesia were randomly divided into two groups. For intubation Group R received i.v. rocuronium bromide 0.6 mg/kg and Group S received succinylcholine 1 mg/kg. Rapid sequence induction was performed with injection thiopentone 5 mg/kg followed immediately by the NMB according to the assigned group. Intubation was performed one minute after the NMB and intubating conditions assessed and graded on a four-point scale: Excellent = jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement; Good = jaw relaxed, vocal cords apart and immobile, some diaphragmatic movement; Poor = jaw relaxed, vocal cords moving, bucking; Inadequate = jaw not relaxed, vocal cords adducted, uncontrolled cough/bucking. Good and excellent conditions were together taken as clinically acceptable. *Results:* All the 20 intubations performed in group S and only 11 in Group R were rated as excellent one minute after the injection of muscle relaxant ($p < 0.001$). They were rated clinically acceptable in 18 patients in Group R compared to 20 patients in Group S ($p > 0.05$). *Conclusions:* Rocuronium provides clinically acceptable intubating conditions similiar to succinylcholine at 60 seconds and can be considered a safe alternative for rapid tracheal intubation in select situations where succinylcholine is contraindicated.

Keywords: Rocuronium; Succinylcholine; Thiopentone; Intubating conditions.

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Introduction

Modern anesthesia practice relies heavily on general anesthesia. Though a lot of development has been made in the field of supraglottic devices, tracheal intubation still remains the ideal choice to provide airway protection in patients at risk of gastric aspiration.[1] The technique most frequently employed is the rapid sequence induction, designed to minimize the interval between suppression of protective reflexes and accomplishment of intubation. The ideal neuromuscular blocker (NMB) should have a fast onset and brief duration of action.[2]

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Succinylcholine is the gold standard in muscle relaxants and consistently provides muscle relaxation within 60 seconds.[3] The duration of action is also short (4–9 minutes). Its use is, however, contraindicated in situations like myotonia, plasma cholinesterase deficiency, sepsis, head injury, perforated eye or susceptibility to malignant hyperthermia.[4]

Thus, a non-depolarising NMB with a short onset and duration; minus the disadvantages is desirable. The quest for 'non-depolarising succinylcholine' has led to the development of various NMBs including the short-acting mivacurium and rapacuronium. None of these has however stood the test of time. Rocuronium offers the fastest onset of action of all the clinically available drugs.[5] Intermediate duration of action however reduces the margin of safety and precludes its use in anticipated difficult intubations. The recent introduction of the specific reversal agent sugammadex, however, has made this choice lucrative.[3] Another concern is the quality of intubating conditions within one minute of injection. Incomplete relaxation can lead to unwanted movements and complications like coughing, bucking and laryngospasm. The choice of induction agent also makes a difference, and use of propofol is associated with better relaxation of the vocal cords.[6]

Thiopentone is another popular induction agent for emergency procedures because it offers advantage in hemodynamically unstable patients, but it provides considerably less relaxation than propofol. The main aim of this study was to assess the number of patients with excellent intubating conditions one minute after injection of low dose rocuronium (0.6 mg) given as a part of the rapid sequence induction, with thiopentone sodium as the induction agent and compare these to succinylcholine. The secondary aim was to assess clinically acceptable intubating conditions, onset and duration of rocuronium and succinylcholine, any difference in hemodynamic effects during induction and intubation, and complications of the study drugs.

Materials and Methods

After obtaining the ethics committee approval, 40 ASA physical status I or II patients of both sexes, aged 18–65 years and scheduled for elective surgery under general anesthesia were included in the study. Patients with anticipated difficult airway, pregnancy, obesity or malnourishment, presence of hepatorenal disease, any evidence of neuromuscular dysfunction or on medications known to interfere with neuromuscular function were excluded.

A careful preanesthetic assessment including routine laboratory investigations was performed a day before and informed written consent obtained. All patients were instructed to keep fasting for six hours before surgery.

The patients were randomly divided into two groups of 20 each by the chit in box method. An anesthesia assistant not involved in data collection would draw a chit and prepare drugs accordingly. Each chit was used only once. For intubation the Group S received succinylcholine 1 mg/kg i.v. and group R received i.v. rocuronium bromide 0.6 mg/kg.

On arrival in the operation theater, an intravenous (i.v.) cannula was inserted in a suitable vein on the forearm and 500 mL normal saline or Ringer lactate started. Routine monitoring including electrocardiogram (ECG), noninvasive blood pressure (BP) and arterial oxygen saturation (SpO_2) was established. All patients were premedicated with injection glycopyrollate (0.004 mg/kg), tramadol (1 mg/kg) and midazolam (0.02–0.05 mg/kg) given i.v. approximately 10 minutes before induction of anesthesia. Baseline Heart rate (HR) and mean arterial blood pressure (BP) were recorded just before induction; then before intubation, one minute after intubation and five minutes after intubation.

After preoxygenation for three minutes with 100% oxygen via face mask, rapid sequence induction was performed with injection thiopentone 5 mg/kg followed by 0.6 mg/kg rocuronium bromide or 1 mg/kg succinylcholine. Injection thiopentone was given over 20 seconds and infusion line flushed for 5–10 seconds to avoid incompatibility of the drugs. The muscle relaxant was given according to the assigned group. Ventilation with a mixture of oxygen and halothane was continued for one minute following which intubation was performed with appropriate sized cuffed endotracheal tube. The investigator performing tracheal intubation and assessing intubating conditions was summoned at the time of intubation and efforts were made to disguise the fasciculations produced by succinylcholine in order to remove observer bias. All intubations were performed by the same investigator and graded on a four point scale: Excellent = jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement; Good = jaw relaxed, vocal cords apart and immobile, some diaphragmatic movement; Poor = jaw relaxed,

vocal cords moving, bucking; Inadequate = jaw not relaxed, vocal cords adducted, uncontrolled cough/bucking. Good and excellent conditions were together taken as clinically acceptable. After intubation the cuff was inflated and tube placement confirmed. Controlled ventilation was started and halothane in a mixture of 50% N_2O and 50% O_2 was given for maintainence of anesthesia. Heart rate (HR), ECG, NIBP and SpO_2 were monitored continuously. At the end of surgery, all anesthetics were discontinued and patients breathed 100% oxygen. Respiratory efforts were allowed to return following which reversal of neuromuscular blockade was provided by neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Extubation was performed as per the clinician's judgement when adequate and regular spontaneous breathing was established and patients were able to open eyes to commands. Patients were oxygenated for five minutes and shifted to the recovery room for close observation.

For neuromuscular monitoring, the ulnar nerve was stimulated at the wrist with a peripheral nerve stimulator (Inmed Equipment, Vadodra) using a train-of-four (TOF) sequence and the resultant contraction of adductor pollicis muscle was observed visuallly. Baseline response was observed after the administration of thiopentone, but before the administration of muscle relaxant. Time from injection of muscle relaxant to complete ablation of first twitch of TOF (T_1) was taken as the onset of action of muscle relaxant. The time from injection to appearance of T_1 was taken as the clinical duration of action.

Statistical Analysis

After completion of the study, the data was compiled, tabulated and analyzed. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 17.0 software. Data is expressed as means and standard deviation (Mean ± SD) or numbers and frequency as appropriate. Chi-square test was used to compare categorical and student's '*t*' test for parametric data. *p* value of less than 0.05 was considered significant and less than 0.001 as highly significant. Sample size was calculated for the primary outcome based on previous studies. 18 subjects were needed to prove any difference with 95% confidence interval and power of 80%. The number was rounded off to include 20 patients.

Results

In the present study 40 patients were studied to assess the intubating conditions provided by low dose rocuronium (0.6 mg/kg) after induction with thiopentone and to establish its comparison with succinylcholine. The two groups were comparable with respect to the demographic data (age, sex and weight) (Table 1). The primary outcome was assessment of intubating conditions one minute after the injection of muscle relaxant. All the 20 intubations performed in Group S and only 11 in Group R were rated as excellent ($p < 0.001$) (Table 2). They were rated good in 7 patients, poor and inadequate in 1 patient each in Group R. Thus the clinically acceptable conditions were observed in 18 patients in Group R compared to 20 patients in Group S ($p > 0.05$). A significant increase in heart rate (HR) after induction was observed in the Group R ($p < 0.001$) (Figure 1). Both the groups had significant tachycardia one minute after intubation compared to baseline values ($p < 0.001$), however within five minutes, this returned to pre-induction heart rate ($p > 0.05$). The mean rise in HR after intubation was comparable between the groups ($p > 0.05$). A significant rise in mean arterial pressure (BP) was observed after intubation in both the groups ($p > 0.05$), however the rise in BP was comparable in the groups ($p > 0.05$) (Figure 2).

The onset of action of rocuronium was 97.20 ± 31.36 seconds compared to 58.20 ± 11.86 seconds with succinylcholine ($p < 0.001$) (Table 3). The clinical duration of action of rocuronium was 25.80 ± 5.05 minutes compared to 4.74 ± 1.55 minutes with succinylcholine ($p < 0.001$). No complications related to the use of the NMBs were observed.

Table 1: Demographic Data

Parameters	Group R (n=20) Mean ± SD	Group S (n=20) Mean ± SD	t / x^2	*p* value
Age (years)†	41.05 ± 15.63	36.00 ± 11.91	1.149	0.257
Weight (kg)†	61.40 ± 10.30	63.00 ± 8.49	0.657	0.519
Sex (Male/Female)*	6/14	8/12	0.440	0.507

† - *p* calculated by student's *t* test, *- *p* calculated by χ^2 test, $p > 0.05$ not significant, $p < 0.05$- significant, $p < 0.001$ highly significant.

Table 2: Intubating Conditions Observed in Study Group Patients

Intubating Conditions	Group R (n=20)		Group S (n=20)		x^2	*p* value
	No.	%	No.	%		
Excellent	11	55%	20	100%		
Good	7	35%	0	–	**11.61**	**< 0.001**
Poor	1	5%	0	–		
Inadequate	1	5%	0	–		

p > 0.05 non-significant, *p* < 0.05- significant, *p* <0.001 highly significant.

Table 3: Onset and Duration of Action of Intubating Dose of Muscle Relaxants in the Study Group Patients

Variables	Group R (n=20) Mean ± SD	Group S (n=20) Mean ± SD	t value	*p* value
Onset of Action (seconds)	97.20 ± 31.36	58.20 ± 11.86	5.202	<0.001
Duration of Action (minutes)	25.80 ± 5.05	4.74 ± 1.55	17.829	<0.001

p > 0.05 non-significant, *p* < 0.05- significant, *p* < 0.001 highly significant

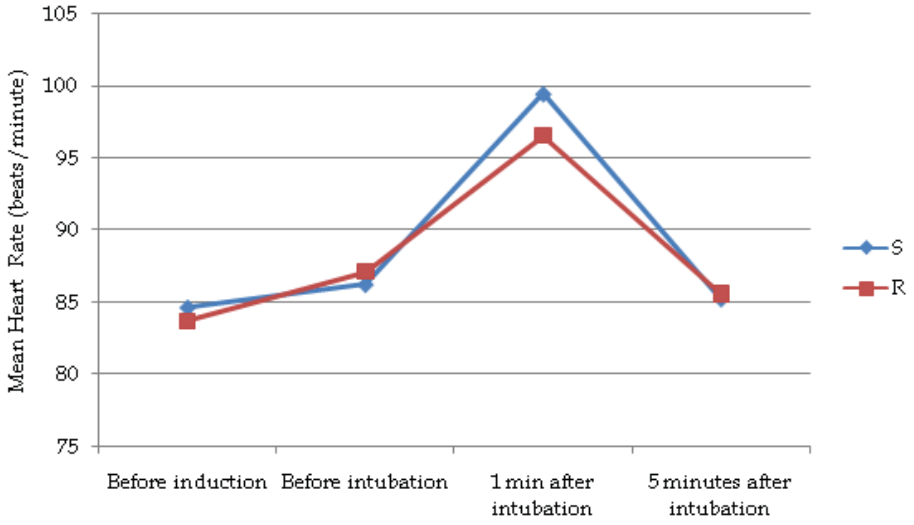

Fig. 1: Heart rate in relation to induction and intubation.

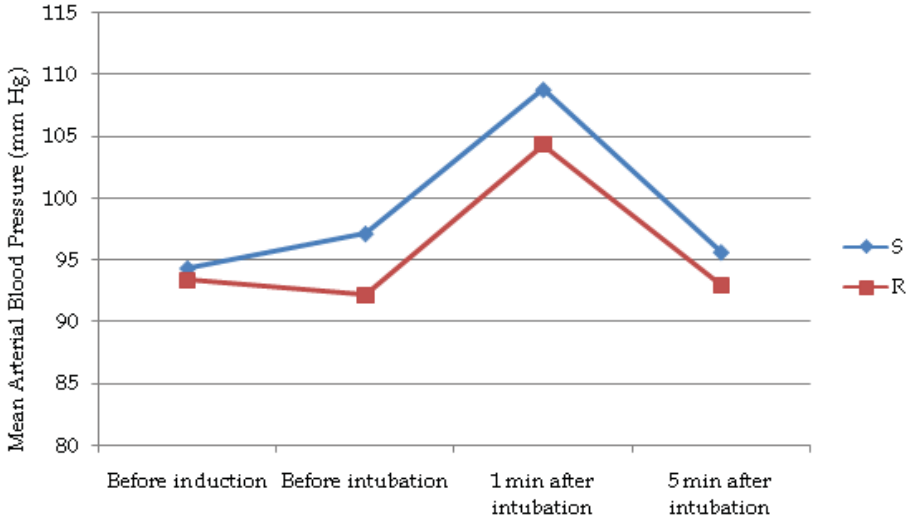

Fig. 2: Mean arterial pressure in relation to induction and intubation.

Discussion

Intubating conditions: The present study showed that low dose rocuronium (0.6 mg/kg) when used along with thiopentone sodium in the setting of rapid sequence induction, results in significantly less number of intubations graded as excellent (55%), compared to succinylcholine (100%). However, if diaphragmatic movement was ignored, the intubating conditions grouped together as clinically acceptable were comparable between the groups.

Cooper *et al.* observed excellent conditions in 95% patients receiving succinylcholine and 65% receiving rocuronium.[5] Those graded clinically acceptable were comparable in the two groups which is similar to our study. Misra *et al.* reported the incidence of excellent intubating conditions as 90% with succinylcholine and 70% with administration of rocuronium and thiopentone.[7] This was higher than our observation and can be explained by a difference in the definitions. They reported 56.7% patients with mild cough, citing delayed effect of rocuronium on diaphragm. In our study any cough or diaphragmatic movement was graded as good (clinically acceptable). Puhringer *et al.* and Huizinga *et al.* indicated that rocuronium and succinylcholine produce indistinguishable intubating conditions one minute after administration.[8,9] This could be attributed to the use of opioid premedication or propofol induction. Although these agents do not affect the neuromuscular blocking properties of rocuronium, they may promote the development of good intubating condtions on their own. Sparr *et al.* on the contrary reported excellent conditions in 80% and 40% patients intubated 60 seconds after succinylcholine and rocuronium respectively.[10]

Hemodynamic Parameters: Preoperative HR and BP in each group were taken as control. Significant increase in heart rate was observed post induction in the rocuronium group. Similiar observations were recorded by Misra *et al.* and Booth *et al*.[7,11] The rise in heart rate and blood pressure after intubation in all the patients is explained by the stress response to laryngoscopy and intubation. This response was comparable in the two groups and had completely abated five minutes after laryngoscopy, thus affirming that the two muscle relaxants do not cause any significant hemodynamic perturbations.

Onset of action: The observed onset of action was comparable to Naguib *et al.* who reported 97.9 ± 29 seconds and 55.1 ± 11.4 seconds respectively with rocuronium and succinylcholine.[12] Other authors also observed similar times.[5,13-15] However, considerably longer onset times were reported by some authors.[8,9,16]

Duration of action: Rocuronium has an intermediate duration of action, as was affirmed in our study. The mean duration of action with the 0.6 mg/kg rocuronium was 25.80 ± 5.05 minutes and 4.74 ± 1.55 minutes which was similiar to that observed by Huizinga *et al.* (24 ± 4, 5 ± 1) and Naguib *et al.* (23.7 ± 5.1, 4.2 ± 1.4).[9,12] Magorian *et al*., however reported considerably longer duration of 37 ± 15 and 9 ± 2 minutes with the same doses of rocuronium and succinylcholine respectively. The observed differences may be due to the difference in technique and the definition of the duration of action.[15]

Conclusion

From the present study, we conclude that 0.6 mg/kg rocuronium after induction with thiopentone provides an incidence of clinically acceptable intubating conditions that is comparable to succinylcholine at 60 seconds. Succinylcholine, however, ramains the gold standard as it offers unparalled relaxation. Rocuronium, therefore, should be considered as a safe alternative for rapid tracheal intubation in select situations where succinylcholine is contraindicated.

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Dexamethasone Adjunct in Ultrasound Guided Femorosciatic Block for Postoperative Analgesia in Below Knee Lower Limb Orthopedic Surgeries

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Abstract

Background and Aims: Since femoral sciatic block is not as famous as brachial plexus block for upper limb, and postoperative pain management in lower limb surgeries is limited to adjuvant in subarachnoid block or epidural analgesia. We intended to study the efficacy of ultrasound guided femorosciatic block in providing adequate postoperative analgesia, in patients undergoing below knee orthopedic surgeries. Also dexamethasone has been proved to be a useful adjuvant with local anesthetics in upper limb blocks, we considered to be studied in this block too. *Methods and Materials:* After approval of the institutional ethics committee, 65 patients planned for elective below knee orthopedic surgeries were enrolled in the study. Patients were randomly allocated to two groups: Group L and Group D. All the patients received subarachnoid block with 15 mg (3 ml) of 0.5% heavy bupivacaine for the surgery. In postoperative recovery room, when the level regressed to T10 level, ultrasound guided femorosciatic block was given. Group L received 20 ml of 0.25% levobupivacaine + 1 ml NS in femoral nerve block and 20 ml of 0.25% levobupivacaine + 1 ml NS in sciatic nerve block. The Group D received 20 ml of 0.25% levobupivacaine + 4 mg (1 ml) dexamethasone in femoral nerve block and 0.25% levobupivacaine + 4 mg (1 ml) dexamethasone in sciatic nerve block. In the postoperative period analgesia was given only on demand. The time of receiving first rescue analgesia was recorded along with the total number of rescue analgesics required in the 24 hours. The postoperative adductor muscle weakness and day of ambulation was also noted. *Results:* The demographic profiles of all the patients were similar. The postoperative analgesia was longer in Group D and also the number of rescue analgesics required in 24 hours was lesser in Group D. No patient had any block related or drug related side effects. *Conclusion:* Ultrasound guided femorosciatic block provides propitious postoperative analgesia in below knee orthopedic surgeries and can be used for providing postoperative analgesia in below knee orthopedic surgeries, without any side effects. Furthermore, adding dexamethasone to the block helps in prolonging the efficacy of the block by increasing the duration of analgesia provided and reducing the number of rescue analgesics required.

Keywords: Femorosciatic block; Levobupivacaine; Dexamethasone.

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Introduction

The introduction of ultrasonography in anesthesiology has been a captivating tool for the anesthesiologist. Peripheral nerve blocks have regained its importance owing to the much more safety provided by the ultrasound due to direct visualization of the nerve roots, needle and drug distribution.

Femorosciatic block is the most useful block for lower limb but has not been that popular owing to the technical difficulty of the blind blocks. Use of high

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resolution ultrasound has helped in identification of these nerves and facilitate the deposition of drug around the nerves.[1] It has been found, in a recent Cochrane review on USG for upper and lower limb block by Lewis SR and colleagues, that ultrasound guidance produces superior peripheral nerve block success rates along with reduction in complications such as nerve damage. They also suggest that it takes less time to perform the block when using ultrasound techniques alone rather than nerve stimulation.[2]

Effective post operative analgesia in orthopedic surgeries allows early embolization and physiotherapy which hastens the overall patient recovery. The postoperative complications such as thromboembolic complications and nosocomial infections, and hospital stay is also reduced provided adequate post operative analgesia in patients.[3] The search for ideal postoperative analgesia regimens following lower limb surgical procedures still continues till today, that would facilitates high quality analgesia with minimal complications in the postoperative period.[4]

The three most common alternatives for anesthesia or analgesia for lower limb orthopedic surgeries include spinal anesthesia, epidural anesthesia and the femorosciatic nerve blocks. It is generally accepted that both peripheral nerve blocks and spinal anesthesia provide sufficient anesthesia, better postoperative analgesia and satisfaction than general anesthesia, in addition to being minimally invasive and using less resources. But spinal block most of the times is associated with hemodynamic changes, making it unsuitable for high-risk patients.[5]

The second alternative is continuous epidural anesthesia or patient controlled epidural analgesia with promising results in managing post operative pain. A study by Osaka *et al.* comparing continuous sciatic nerve block and epidural analgesia for postoperative pain control in patients with fracture of the foot concluded that continuous sciatic nerve block developed good postoperative analgesia in these patients compared with continuous epidural.[6]

Therefore, femorosciatic blocks are being focused upon nowadays as the regional anesthetic technique following lower limb orthopedic surgeries, which are two of the most common blocks applied either in combination or alone.[7] Tran *et al.* compared femorosciatic nerve block with intraarticular infiltration in children undergoing Anterior Cruciate Ligament reconstruction. They found that femorosciatic nerve block provides better postoperative analgesia with fewer side effects.[8]

Many local anesthetics have been used in peripheral nerve blocks, of which bupivacaine, levobupivacaine and ropivacaine provide long duration of analgesia.

In a comparative study done by Fanelli and colleagues, ropivacaine, bupivacaine and mepivacaine were compared in femorosciatic block. They found no differences in the quality of sciatic nerve block as well as in the nerve block resolution times observed among the three groups.[9] Compared to ropivacaine, levobupivacaine provides significantly longer duration of analgesia.[10] Longer duration of sensory block along with less toxicity makes levobupivacaine a better choice for peripheral nerve blocks.[11]

Dexamethasone is a glucocorticoid with anti-inflammatory properties and has been used proficiently in various peripheral nerve blocks. It has been suggested in Cochrane Review by Pehora and colleagues that both perineural and intravenous dexamethasone may prolong duration of sensory block and are effective in reducing postoperative pain intensity and opioid consumption when used as an adjuvant to peripheral nerve block in upper limb surgery.[12] It has been studied with intrathecal levobupivacaine for labor analgesia and has been concluded to prolong the duration of levobupivacine.[13] This combination of levobupivacine and dexamethasone has also proven to be useful combination in axillary brachial plexus block[14], but has not been studied in lower limb blocks.

Therefore, we selected this useful combination in femorosciatic block for the overall patient satisfaction and better postoperative analgesia in below knee orthopedic surgeries.

Materials and Methods

After approval by institutional ethical committee, this study was carried out on 65 patients of both sex of ASA I-II physical status and in the 20–60 age group, who were scheduled for below knee orthopedic surgeries, between May 2018 and October 2018. The patients excluded were those with history of cardiac, renal or hepatic disease, CNS disorders, neuropathy, chronic treatment with calcium channel blockers. The patients having bleeding disorders, hypersensitivity to local anesthetics, local infection at the site where needle for block is to be inserted and allergic to study drugs or patient refusing the procedure were also excluded from the study. It was a prospective, double blinded controlled trial study. The study drug solution was prepared and given to the investigator by a nonparticipant staff. After explaining the procedure to the patients and

getting the informed consent, the patients were divided into two groups; Group L and Group D using random number chart.

Group L received 20 ml of 0.25% levobupivacaine + 1 ml NS in femoral nerve block and 20 ml of 0.25% levobupivacaine + 1 ml NS in sciatic nerve block. The Group D received 20 ml of 0.25% levobupivacaine + 4 mg (1 ml) dexamethasone in femoral nerve block and 0.25% levobupivacaine + 4 mg (1 ml) dexamethasone in sciatic nerve block.

All patients were kept nil orally for at least six hours before the procedure. They were given premedication in the form of tablet Alprazolam 0.5 mg and tablet Ranitidine 150 mg at 6:00 am on the day of surgery and were tested for Lignocaine sensitivity. On arrival to operation theatre, monitorings (i.e. five lead ECG, NIBP, SpO_2) were established along with starting of peripheral intravenous line in contra lateral hand with 18G IV canula. Baseline parameters were noted. All patients included in study were given subarachnoid block (SAB) in sitting position using 26G Quincke's spinal needle in L3–L4 interspinous space with 15 mg of 0.5% hyperbaric bupivacaine after free flow of CSF. After confirmation of adequate level (T6–T8), surgeon was allowed to proceed. After completion of surgery and covering of incision with the dressing, level of subarachnoid block was assessed in the patient in the recovery room. Once the level is regressed to T10, after proper positioning of patient, USG guided femoral and sciatic nerve block was given in allocated patients with respective drug solutions.

Under all aseptic precautions the inguinal area was draped, using linear probe (6–13 MHz frequency) of ultrasound, with sufficient application of sterile gel, a short axis view of femoral nerve and vessel was identified (Femoral nerve lies lateral to femoral artery in a groove formed by Iliacus and Psoas muscle). A 22G ecogenic needle was used by an ultrasound guided in-plane (lateral to medial) technique and positioned between the fascia iliaca and iliopsoas muscle near lateral corner of femoral nerve. After checking the exact location of the needle tip, drug solution was injected slowly to open the plane and drug distribution was seen as hypoechoic area.

Sciatic nerve block was given in supine position by same ultrasound probe. Leg of the patient was abducted and externally rotated so that the popliteal fossa was exposed for the access of probe. After draping popliteal fossa and applying sufficient gel, a short axis view of popliteal neurovascular bundle was obtained. A 22G ecogenic needle was used by ultrasound guided in-plane (lateral to medial) technique and under continuous ultrasound guidance, its tip was placed between the tibial and common peroneal component of sciatic nerve near the division and the drug was injected and drug distribution was confirmed.

The hemodynamics were measured continuously up to 2 hours in the recovery room and monitored for any side effects. The patients were then shifted to postoperative ward. Hemodynamics, pain and VRS was evaluated by the blinded investigator at 0, 2, 4, 8, 12 and 24 hours and the time of first rescue analgesia was noted. For the first 24 hours, the protocol for postoperative analgesia consisted of standard orders for i.v.diclofenac 75 mg on demand for VRS > 4. For breakthrough pain, patients were treated with IV tramadol 100 mg as and when required.

Patients were asked to rate average pain they experience over 24 hrs post operatively on a 10 cm VRS b/w 0-No pain and 10-Very severe pain.

After 24 hrs the patients were assessed for adductor muscle weakness by sideways leg raising test in which 0-Able to raise the leg sideways and maintain it for 10 seconds or more, 1-Able to raise leg sideways but for less than 10 seconds but more than 5 seconds and 2-Not able to raise the leg sideways or able to raise less but less than 5 seconds. The patients with score of 2 were taken as adductor muscle weakness present.

The patients were encouraged for embolization after 24 hours and were encouraged to perform 10 meter walk test, with the help of walking aid (as advised by Orthopedician). The day of completion of 10 meter walk test was taken as day of start of embolization.

The data was collected and entered in MS EXEL 2010. Statistical analysis was performed using SPSS software 17. The one sample Kolmogorov Smirnov test was employed to determine whether data sets differ from a normal distribution. Normally distributed data was analyzed using a repeat measures general linear model analysis of variance, whereas non normally distributed data was analysed using Mann-Whitney U test and categorical data was analyzed using chi-square test. Level of significance "p" was considered significant < 0.05.

Results

The total of 65 consenting patients were enrolled in the study. Out of the 65 patients, 2 were excluded due to inadequate sonographic anatomy, 1 patient was excluded due to lost follow up in postoperative

period and 2 were excluded due to inadverent rescue analgesics (dosage without need). Sixty patients were randomly divided into the 2 groups (Group L and Group D). The demographic profile was comparable in both the groups ($p > 0.05$) (Table 1).

The postoperative hemodynamics and respiration were stable in both the groups and were comparable, with no major side effects noticed in any of the two groups.

The duration of analgesia was significantly longer in Group D and thereby the number of rescue analgesics required were less in Group D with early ambulation recorded in the group ($p < 0.05$) (Table 2) (Fig. 2).

On comparing the adductor muscle weakness score, no patient in any of the two groups had adductor muscle weakness, i.e., score of more than 1.

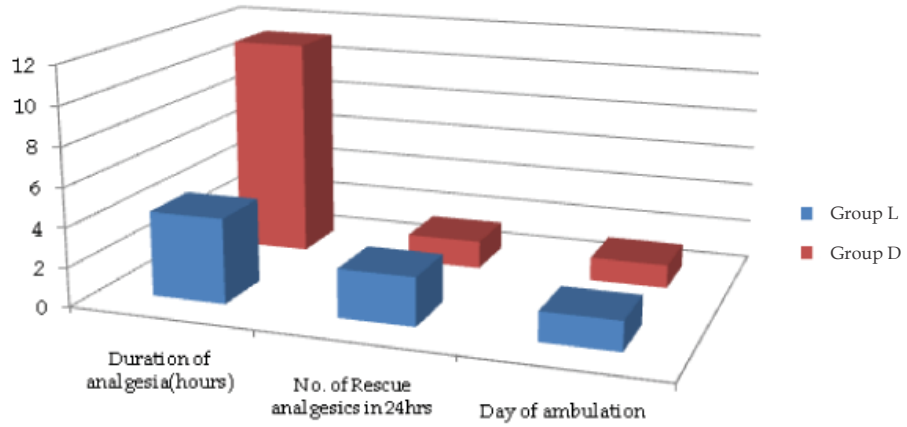

Fig. 1:

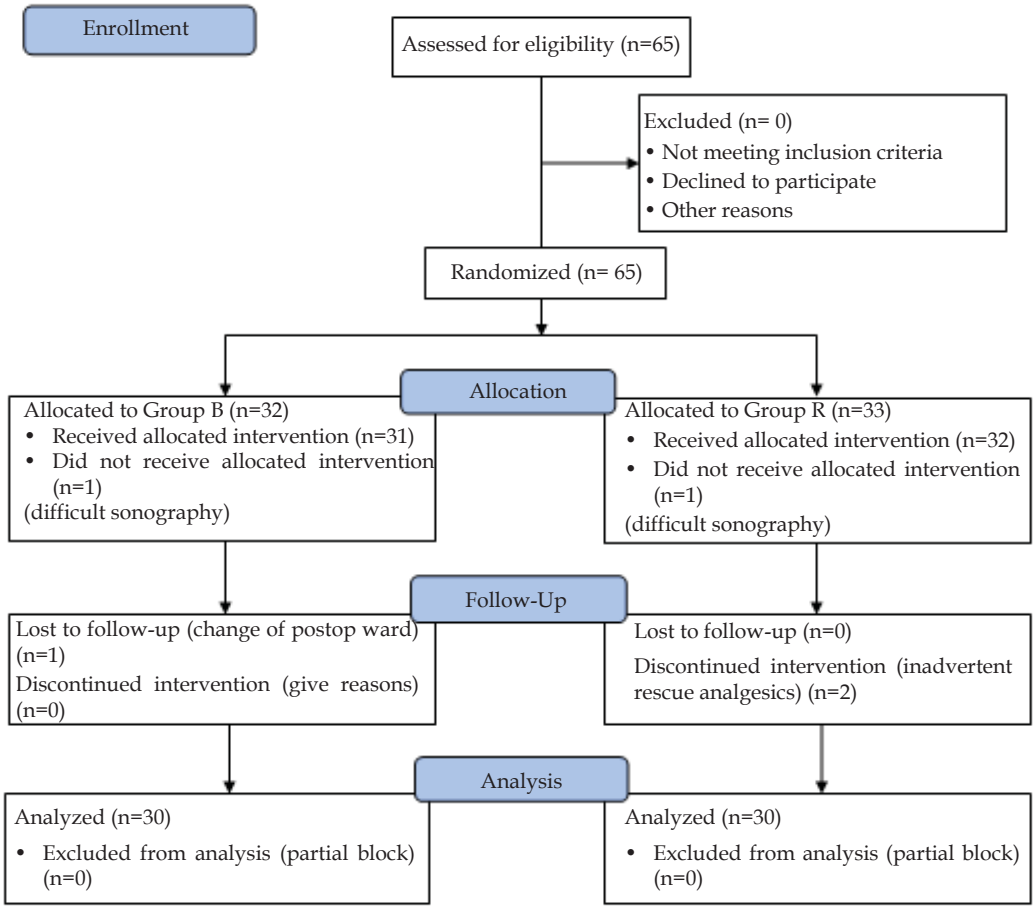

Fig. 2: Consort Flow Diagram

Table 1: Demographic Profile

	Group L	Group D	*p* value
Age (yrs)	40.87 ± 13.161	44.97 ± 15.897	.281
Weight (kg)	58 ± 6.181	57.53 ± 7.851	.799
Height (m)	1.60 ± 0.058	1.576 ± 0.092	.130
BMI (kg/m^2)	22.44 ± 2.306	22.13 ± 2.159	.240

Table 2: Comparison of duration of analgesia and postoperative ambulation

	Group L	Group D	*p* value
Duration of analgesia (minutes)	290.83 ± 24.986	673.50 ± 69.928	0.000
No. of rescue analgesics (24 hr)	2.47 ± .571	1.43 ± .568	0.000
Day of ambulation	1.50 ± 0.509	1.20 ± .407	0.015

Discussion

We have overlooked lower limb blocks for providing analgesia since decades. In our study, with the help of ultrasound guidance the femoral and sciatic nerves could be easily demarcated. Only 2 of the 65 patients had difficult sonographic anatomy and hence were excluded from the study. No block related side effects were noted, with no reports of adductor muscle weakness seen in any of the patients of the two groups.

On the other hand dexamethasone has been an integral part of anesthesiology, used for it anti-inflammatory and antiemetic action since ages. Even though its effect as adjuvant in peripheral nerve blocks is not fully understood, it has been proved to be a promising adjuvant.[12] Its anti-inflammatory and analgesic effects are through the inhibition of phospholipase A2 and activation of glucocorticoid receptors. The perineurally administered dexamethasone has been demonstrated to inhibit signal transmission of nociceptive C-fibers, decrease ectopic neuronal discharge, and decrease the release of local inflammatory mediators.[15,16]

In a meta-analysis done by Choi *et al.*, they concluded that adding dexamethasone to long acting local anesthetics prolongs the mean analgesic duration. They found no statistically significant difference in opioid consumption and no reported dexamethasone-induced neuronal damage.[17] In lower extremity nerve blocks studied by Fredrickson *et al.*, patients receiving 8 mg dexamethasone in sciatic nerve block reported lower pain score at 24 hours, but patients receiving dexamethasone in ankle nerve block had no added advantage.[18] However our study shows adding dexamethasone provided longer analgesia with lower requirement of parentral analgesics in post operative period. In another study done by Rahangdale *et al.*, compared intravenously versus perineuraly administered dexamethasone, it was concluded that perineural dexamethasone prolonged the duration of analgesia and motor blockade compared with the control group.[19]

The combination of levobupivacaine with dexamethasone has been studied in many upper limb blocks, which concluded that the combination provides longer duration of analgesia compared to levobupivacaine alone, and also reduces the rescue analgesics requirement.[20–23] The results are similar to our study, but the combination of femoral sciatic block has never been studied before. Another similar study done by Akkaya *et al.*, used 30 ml of 0.25% levobupivacaine with 8 mg dexamethasone for bilateral transversus abdominis plane block, concluded that there was significant reduction in postoperative opioid consumption, and this combination may be used as alternative to epidural opioid analgesia.[24]

Hence, the combination of levobupivacaine with dexamethasone is useful combination in femoro sciatic block too.

The limitation of our study was difficulty in achieving optimal limb positioning for the sciatic nerve block, for which an assistant was required to hold the patients leg in abduction and external rotation. Another limitation was the adductor muscle weakness was tested after 24 hours, at which the effect of block was weaned off.

Conclusion

The following conclusions were drawn from the study:

1. Ultrasound guided femorosciatic block provides propitious postoperative analgesia in below knee orthopedic surgeries. No patients in any of the studied groups had block related side effects.
2. The duration of analgesia was longer when dexamethasone was combined with levobupivacine for the block and the need of rescue analgesics was also lesser in the group. Also combining dexamethasone resulted in early ambulation and better patient satisfaction.

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Original Research Article

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Caudal Epidural Injection of Steroid and Local Anesthetic in the Management of Chronic Low-Back Pain

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Abstract

Objectives: The present study was carried out to assess the role of caudal epidural injections of steroid with local anesthtic in the management of chronic low-back pain. *Materials and Methods:* Fifty patients of chronic low-back pain were included in the study. Epidural injections of steroid with local anesthetic were administered to them via caudal approach. Follow up was scheduled after 1 month, 3 months, and 6 months. Assessment was done by using VAS score and ODI. *Results:* Fifty patients of chronic low-back pain were included in the study. 31 (62%) patients were male and 19 (38%) were female. Age of the patients ranges from 30 to 70 years with the mean age of 55.21 years. Mean VAS score of the patients before the intervention was 7.91 ± 1.60 which was reduced to 3.87 ± 1.21 at 1 month follow-up, 3.46 ± 1.32 at 3 months follow-up and 4.66 ± 1.56 at 6 months follow-up. Similarly, mean ODI of the patients before the treatment was 53.81 ± 6.12 which was reduced to 33.67 ± 4.89 at the end of 1 month, 32.65 ± 5.11 at the end of 3 month and 28.80 ± 4.71 at the end of 6 month. *Conclusion:* Caudal epidural injection of steroid with local anesthetic is an effective method for the management of chronic low-back pain in terms of pain relief and functional improvement in both short- and long-term results.

Keywords: Chronic low back pain; Steroid; Local anesthetic; Epidural; Radiculopathy; Spinal stenosis.

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Introduction

Chronic low-back pain is a common community health problem worldwide. Over 70% people in developed countries experience low-back pain at sometime in their lives.[1] In India, this figure is even more around 80%. Every year, around 3–4% of population in India is temporarily disabled, and 1% of working age population is disabled totally and permanently because of low-back pain.[2]

Low-back pain is defined as pain, muscle tension or stiffness localized below the costal margin and above the inferior gluteal folds with or without leg pain and it is defined as chronic when the duration of pain is 12 weeks or more.[3]

The origin of low-back pain can be various anatomic structures like muscles, fascial structures, nerve roots, bones, joints, intervertebral discs, and abdominal organs. Many times, the pain can arise from aberrant neurological pain processing which causes neuropathic low-back pain.[4,5]

Furthermore, low-back pain can also be influenced by psychological factors (like anxiety, depression and stress, etc.) and psychosocial factors.[6–8]

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Hence, the diagnosis of low-back pain is very challenging and must include thorough history taking about the symptoms as well as about psychological and psychosocial factors. A proper clinical examination and identification of origin of pain is the mainstay of diagnosis. Radiological investigations including MRI/CT scan should be advised wherever necessary.

Till now, various conservative, surgical and non surgical methods have been used for low-back pain with variable results.[9-13] Every patient with low-back pain is not a candidate for surgery and, in fact, surgery had been proven failure in approximately 25% of well selected cases.[14]

A cornerstone of non-surgical treatment for low-back pain is epidural steroid injection and still is the most commonly performed procedure for low-back pain.[10–13]

There are three different ways to perform epidural injection, viz. caudal block, translumbar approach and transforamial approach. In present study, we are using caudal epidural injection (CEI) approach to administer steroid and local anesthetic (LA) agent for the management of low-back pain.

Materials and Methods

The present study is a prospective study carried out in the department of anesthesia, Ananta institute of medical sciences, Rajsamand during the period of 1 year from January 2018 to January 2019. Fifty patients attended orthopedic OPD with the complaints of low-back pain were included in the study.

Sample size and sampling: Fifty patients of chronic low back pain.

Study type: Quantitative, Prospective

Duration of study: 1 year

Inclusion criteria

1. Pain on the low-back region, buttock and/or lower extremities while standing, walking and/or spinal extension.
2. Mild-severe lumbar central canal spinal stenosis identified by CT/MRI.
3. Lower extremity symptoms consistent with neurogenic claudication.
4. Must provide consent for study and should be able to complete the assessment instruments.
5. Age ≥ 30 years.

Exclusion criteria

1. Other comorbidities that could interfere with the results of the study concerning pain and function like painful peripheral neuropathy, fibromyalgia, Parkinson disease, dementia, stroke, amputees, other neurological disorders
2. Spinal instability requiring surgical fusion.
3. Severe osteoporosis
4. Known hip joint pathology
5. Bone metastasis
6. Allergy to local anesthetic and/or steroid.
7. Tuberculosis or other bone infection
8. Any other systemic disorder that limits ambulation of patient

Technique

The procedure was carried out in the operation theater. The patients were laid in prone position with a pillow in their inguinal region. Sacral hiatus was palpated and a 22G spinal needle was preceded into the hiatus at an angle of 45. Reaching the bone structures, the angle reduced to 10 and after preceding about 5 cm, hiatus was entered and epidural region was attained. Injection containing 2 ml (80 mg) methyl prednisolone with 4 ml of 2% xylocaine was injected into the epidural space without fluoroscopic guidance.

Data collection tool (score) used: Pain was assessed by using visual analogue scale (VAS) score (1–10). Functional status was assessed by using Oswestry disability index 2.0 (ODI).[15]

Follow-up: Follow up was scheduled at 1, 3 and 6 months.

Ethical clearance was taken from institutional ethical committee. Informed written consent was obtained from all the patients involved in the study.

Results

Fifty patients of chronic low back pain who met the inclusion criteria were included in the study. 31 (62%) patients were male and 19 (38%) were female. Age of the patients ranges from 30 to 70 years with the mean age of 55.21 years.

Mean VAS score of the patients before the

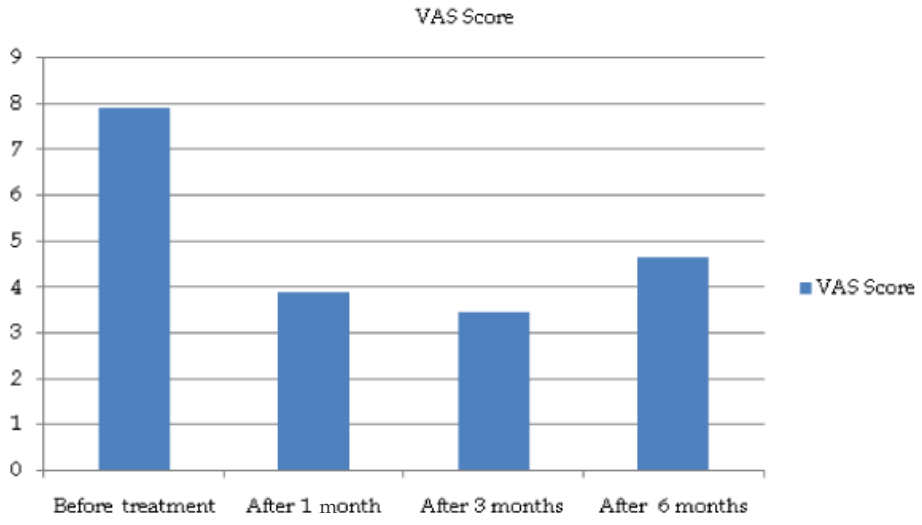

Fig. 1: MeanVAS score of the patients before treatment and at 1, 3, 6 month follow up.

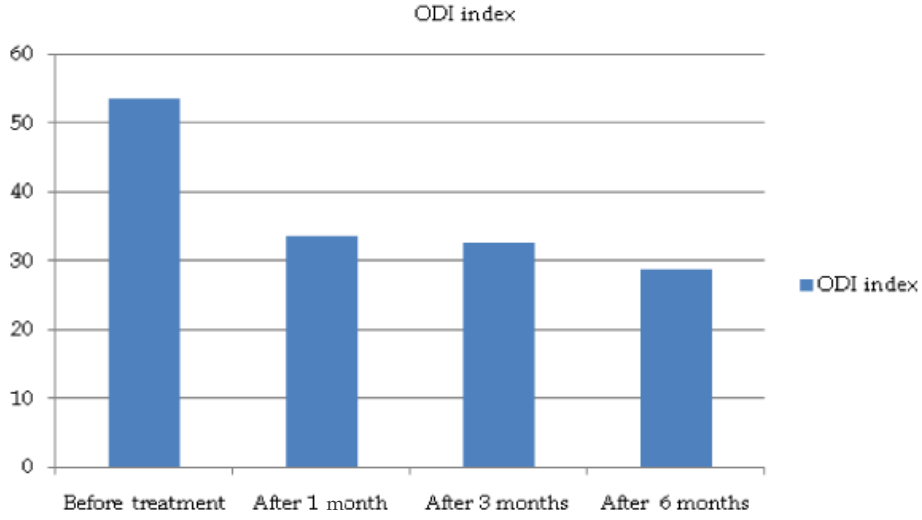

Fig. 2: Mean ODI before treatment and at 1, 3, 6 month follow up.

intervention was 7.91 ± 1.60 which was reduced to 3.87 ± 1.21 at 1 month follow-up, 3.46 ± 1.32 at 3 months follow-up and 4.66 ± 1.56 at 6 months follow-up. When compared to the VAS score before the treatment, the results were statistically significant (p-value < 0.05). Mean VAS score at six months follow up was higher than previous follow up values but the difference was not found to be statistically significant (p-value > 0.05) (Fig. 1).

In present study, mean ODI of the patients before the treatment was 53.81 ± 6.12 which was reduced to 33.67 ± 4.89 at the end of 1 month, 32.65 ± 5.11 at the end of 3 month and 28.80 ± 4.71 at the end of 6 month. When ODI values at each follow up was compared with ODI before treatment, the difference was statistically significant (p-value < 0.05) but when the ODI values at each follow up were compared with each other, the difference were not significant (p-value > 0.05) (Fig. 2).

Discussion

The present study was carried out to assess the role of caudal epidural injections of steroid with local anesthtic in the management of chronic low-back pain. The study showed positive outcome in both short- and long-term results in terms of reduction

in pain as well as good functional outcome.

The improvement in pain after epidural injections was assessed using VAS score. The mean VAS score of the patients before the intervention was 7.91 ± 1.60 which was reduced to 3.87 ± 1.21 at 1 month follow-up, 3.46 ± 1.32 at 3 months follow-up and 4.66 ± 1.56 at 6 months follow up. When compared with initial VAS score, the difference at follow up was statistically significant (*p*-value < 0.05), suggestive of positive outcome in both short- and long-term period. The VAS score at 6 months follow up was little higher than the previous follow up but the difference was not statistically significant (*p*-value > 0.05).

The improvement in mobility and function was assessed using ODI (Oswestry Disability Index).

ODI is calculated based on each score of the ODQ (Oswestry Disability Questionnaire), which consists of ten items. Each of the ten items is scored from 0 to 5, and the total is added and multiplies by 2. Therefore, the ODI ranges from 0 to 100.[15]

In present study, mean ODI of the patients before the treatment was 53.81 ± 6.12 which was reduced to 33.67 ± 4.89 at the end of 1 month, 32.65 ± 5.11 at the end of 3 month and 28.80 ± 4.71 at the end of 6 month. The difference was found to be statistically significant when ODI at each follow up was compared with ODI before treatment (*p*-value <0.05). The results are suggestive of good positive outcome in both short- and long-term follow up.

Manchikanti *et al.* performed a similar study in 2010 which included 70 patients of discogenic low-back pain. They compare the effect of caudal epidural injections (CEIs) of steroid and LA with CEIs of LA alone. Results were assessed using VAS, ODI, employment status and opioid intake. They got positive outcome for both short- and long-term results in both the groups. (86% in steroid + LA group and 74% in LA alone group). The results suggested that CEIs of steroid with LA are more effective than CEIs of LA alone in treatment of discogenic low-back pain.[16]

Ghahreman *et al.* also performed a comparative study in 2010 with 150 patients of low-back pain radiating to lower limb and concluded that CEIs of steroid with LA were effective than intramuscular injections in pain reduction secondary to radiculopathy.[17]

Wilson-Macdonald *et al.* performed a study in 92 patients of disc prolapse or spinal stenosis. They compared the effect of CEIs of steroid and LA with that of intramuscular injection of the same in the management of chronic low-back pain due to disc prolapsed or spinal stenosis. The assessment methods used were Oxford pain chart and ODI. They concluded that CEIs of steroid with LA was more effective in short-term results but was not found beneficial over intramuscular injections in long-term results.[18]

Iversen *et al.* also performed a study in 2011 to compare the effect of CEIs of steroid with that of placebo. 133 patients with unilateral lumbar radiculopathy were included in their study. The results were in contrary to our findings. They concluded that CEIs of steroid had no benefit over placebo in treating lumbar radiculopathy.[19]

Arden *et al.*, in 2005, studied the effect of CEIs of steroid with LA in 228 patients of sciatica and concluded that CEIs of steroid with LA had only short-term benefit over placebo in treating sciatica. Thus the results were partially in favor of present study.[20]

Bush K and Hillier S performed a placebo controlled study to assess the effect of CEIs of steroid with LA in the management of intractable sciatica and found that after 1 year follow up; subjective and objective measures were improved in both the groups. The improvement was greater in actively treated group but only the objective assessment, i.e. straight leg raise, was statistically significant.[21]

Another study done was by Breivik H *et al.* in the year 1976. Thirty-five patients of chronic lumbar radiculopathy were included in the study and a comparative assessment was done between the effect of CEIs of bupivacaine and methylprednisolone with bupivacaine followed by saline. They found improvement in both the groups but the improvement was greater in treatment group.[22]

In present study, caudal epidural injections of steroid with local anesthetic were found to be highly effective in both short- and long-term follow up. Both the VAS and ODI were improved till the 6 months follow up. ODI was slightly reduced at 6 months follow up than the previous value but the difference was not statistically significant.

An important limitation of present study was that we did not extend our treatment to control items for the comparison due to limitations of the time course. Replication of treatment results with the use of other control items would have provided a strong demonstration of experimental control,

strengthening the results of the study.

Conclusion

The results of the present study showed that caudal epidural injections of steroid with local anesthetic is an effective method for the management of chronic low-back pain in terms of pain relief and functional improvement. The results of present study are in favor of many studies done in the past but in contrary to some other studies. An important limitation of present study was that control items were not included in the treatment strategy. In future, controlled studies with large sample group and systematic reviews of various such studies are expected for further useful outcomes in the management of chronic low-back pain.

What this study adds to existing knowledge

The present study advocates the use of epidural steroid with local anesthetic injections for the management of chronic low-back pain. In comparison to previous study of using steroid alone or LA alone, the combination of steroid and LA have better results in both short- and long term follow up. Further, many patients in developing countries live with disability to avoid surgery but CEIs can be an effective alternative for them.

Conflict of interest: No conflict of interest exists. No financial relationship exists between authors and products or procedures related to the article.

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Original Research Article

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Comparison of Postoperative Analgesia Following Epidural Bupivacaine and Epidural Bupivacaine with Verapamil in Orthopaedic Lower Limb Surgeries

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Abstract

Introduction: Various attempts have been made to prolong neuraxial blockade. Calcium channel blockers have shown to inhibit pain pathway. In this study verapamil was added along with local anesthetic via epidural route. *Materials and Methods:* A double-blind randomized controlled study done with 40 ASA I and II patients undergoing elective lower limb orthopedic surgery by randomly allocating them into two groups each consisting of 20 patients. Under aseptic precautions epidural catheter was placed in L2–L3 interspace in all patients. Patients belonging to Group P received 12 ml of Inj. Bupivacaine 0.25% + 2 ml of normal saline and Patients belonging to Group V received 12 ml of Inj. Bupivacaine 0.25% + 5 mg of Inj.Verapamil diluted to 2 ml. And further supplementary doses were done with 6 ml of 0.25% Bupivacaine every 60 minutes. The intraoperative and postoperative vitals were monitored and intensity of pain was measured by using the verbal rating pain scale at 2, 6, 12, 24, 48 hour intervals. *Results:* The observations were analyzed using student *t* test. The postoperative pain score (verbal rating scale) was found to be low at all time intervals (2, 6, 12, 24, and 48 hrs) in Group V when compared to Group P. Significantly low-pain scores were observed at 2, 6, 12 and 48 hours intervals in patients belonging to Group V ($p < 0.01$ at 2, 6, and 48 hours intervals and $p < 0.05$ at 12 hours interval) than Group P. *Conclusion:* Pain relief was significantly better ($p < 0.05$) in patients who received epidural bupivacaine with verapamil mixture than the patients who received epidural bupivacaine with placebo.

Keywords: Epidural; Verapamil; Additive; Calcium channel blocker.

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Introduction

Neuraxial anesthesia is a technique by which the nerves around the spinal cord are blocked by instilling local anesthetics around the nerves. There are various approaches in achieving neuraxial blockade like subarachnoid blockade, epidural blockade and combined spinal-epidural techniques. Though neuraxial blockade is the widely used technique of choice for surgeries involving lower abdomen and lower limbs the biggest disadvantage is the limited duration of action.

Recently attempts have been made to prolong the action of local anesthetics in neuraxial anesthesia

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by adding various additives with them. Studies have shown that Calcium influx in the presynaptic membrane leads to release of neurotransmitters which are responsible for nociception and transmitting pain.[1] And by blocking calcium channels the pain pathway can be inhibited and by using calcium channel blocker concomitant to a local anesthetic can prolong the duration of local anesthetic.[2,3]

Verapamil is a dihydropiridine L-type voltage-gated calcium channel antagonist and evidence have shown that it potentiates the effect of local anesthetics by blocking calcium channels.[4,5] This study was done due to paucity of literature in the role of verapamil in neuraxial anesthesia. The aim of this study was to evaluate the analgesic efficacy of bupivacaine and verapamil mixture given through lumbar epidural route for postoperative analgesia in patients undergoing elective orthopedic lower limb surgeries.

Materials and Methods

After getting approval from institutional ethics committee the study was done on Government Stanely Hospital, Chennai, Tamil Nadu, India from a period of March 2006 to March 2008. The study design was of double-blind randomized control trial. A total of 40 patients of ASA I & II category who were admitted to undergo elective orthopedic lower limb surgeries were enrolled into the study. Patients with contraindications for epidural anesthesia and patients who did not satisfy the inclusion criteria were excluded from the study. A written informed consent was taken from all the study participants explaining the nature and possible ill effects of the study in their native language.

All the patients before enrolling to study were examined thoroughly and investigated with various routine biochemical tests, Electrocardiogram and chest X-ray to identify any preexisting life-threatening conditions. The patients were randomized into two groups namely Group P and Group V by means of computer generated numbers. All the patients were uniformly premedicated the previous night with tablet alprazolam 0.25 mg. The study drug were Injection Verapamil 5 mg diluted to 2 ml with sterile water for Group V and 2 ml of normal saline was taken as placebo drug for Group P. Before the patients were mobilized to operation theater the study drug will be loaded in a 2 ml syringe covered with black wrapper and will be handed over to the attending anesthesiologist.

On arrival in the operating room, baseline cardiorespiratory parameters, viz., Heart rate (HR), Systolic blood pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Respiratory rate (RR) were recorded. A good intravenous access was started at the non-operative side forearm of the patient using 18G IV cannula. Preloading with crystalloids (10 ml/kg) was done.

With the patient in sitting posture, after informing the procedure to the patient and under strict aseptic precautions, epidural space was identified at L2–L3 interspace using 17G Tuohy needle by Loss of Resistance technique. 19G epidural catheter was threaded in a cephalad direction and 4 cm catheter length was kept inside the epidural space. Test dose of 3 cc of 1.5% lignocaine with adrenaline (5 µg/ml) was given to check the position of catheter.

A standard anesthetic technique was followed in all patients.

Epidural 1st dose — 14 ml of 0.5% bupivacaine + 2 ml of placebo or injection verapamil.

Epidural 2nd dose — 6 ml of 0.5% bupivacaine.

Epidural 3rd dose — 6 ml of 0.25% bupivacaine.

Epidural 2nd dose was given exactly 60 minutes after the first dose and epidural 3rd dose was given exactly 60 minutes after the epidural 2nd dose. Patients with duration of surgery between 2–2:30 hours requiring standard 3 doses of epidural local anesthetics were only taken up for study. Unanticipated prolonged duration of surgery (requiring more than 3 doses) were excluded from the study.

Intraoperatively the patient was monitored with Electrocardiogram (ECG), Non-invasive blood pressure (NIBP), Pulse oximetry (SpO_2) and urine output. During the entire operative procedure, Heart rate (HR). Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), respiratory rate (RR) was continuously monitored and recorded every 5 minutes. All patients were given oxygen supplementation (4–5 L/min) through Hudson's face mask. All the patients were given anxiolytic — Injection Midazolam 0.05 mg/kg IV. No. intravenous opiod analgesics were supplemented during the study.

Intravenous fluid management was done based on mean arterial blood pressure and surgical blood loss. The intraoperative and postoperative observations were made by the attending anesthesiologist who was unaware about the nature of study drug.

Postoperative Monitoring

Postoperatively the patient was transferred to the recovery room and observed continuously for 60 minutes. Patient was then shifted to the postoperative ward where pulse rate, systolic blood pressure, diastolic blood pressure and respiratory rate were recorded at 2, 6, 12, 24, 48 hour intervals. The patients were assessed by the same observer in the postoperative period who was blinded for the group assignment. The intensity of pain was measured by using the verbal rating pain scale at 2, 6, 12, 24, 48 hour intervals.

Pain Score (Verbal Rating Scale)

Grade 0	No complaint of pain
Grade 1	Patient complaints of pain but tolerable. (Mild pain)
Grade 2	Patient complaining of severe pain and demands relief. (Moderate pain)
Grade 3	Patient restless and screaming with pain. (Severe pain)

When the patient complained of pain, i.e., the pain intensity was assessed based on Verbal Rating Scale, if the pain score reaches 1, patient was given injection diclofenac sodium 75 mg intramuscularly. The time of first rescue analgesia (TFA) was calculated from the time of injection of the study drug in the epidural space to the time when the verbal rating pain score reached 1.

Number of supplementary analgesics (Injection Diclofenac sodium 75 mg IM) required by each patient for period of 48 hours was noted in both the groups. Occurrence of significant side effects hypotension, bradycardia were noted.

Results

The observations were analyzed using Statistical Package of Social Studies Software Version 16 (SPSS 16). Qualitatve data were analyzed using chi-square test and quantitative data was analyzed using Student t test. Table 1 shows the distribution of demographic characteristics among the groups.

The intraoperative changes in hemodynamics were comparable between both the groups, there was no statistically significant differences between them, Figures 1 and 2 Show the Intraoperative heart rate and mean arterial pressure changes between the groups.

The postoperative pain score (verbal rating scale) was found to be low at all time intervals (2, 6, 12, 24, and 48 hrs) in Group V when compared to Group P. Significantly low pain scores were observed at 2, 6, 12 and 48 hours intervals in patients belonging to Group V ($p < 0.01$ at 2, 6, and 48 hours intervals and $p < 0.05$ at 12 hours interval) than Group P as shown in Table 2.

Table 1: Demographic Characteristics Among Groups

S. No.	Parameters	Group		*p* value
		Group P Mean ± SD	Group V Mean ± SD	
1.	Age (years)	35.10 ± 9.26	37.65 ± 11.60	0.447
2.	Height (cm)	166.50 ± 4.72	166.30 ± 4.66	0.893
3.	Weight (kg)	62.25 ± 6.41	62.80 ± 8.46	0.818
4.	Duration of surgery (hours)	2.15 ± 0.09	2.15 ± 0.08	0.913

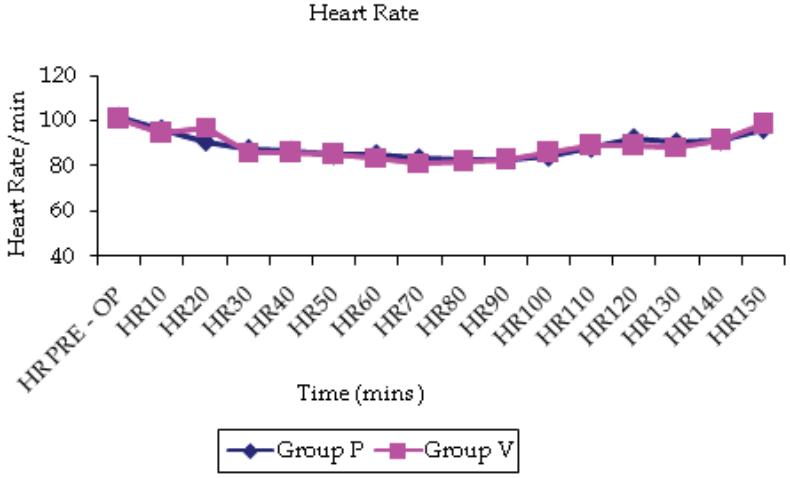

Fig. 1: Intraoperative Heart Rate Changes

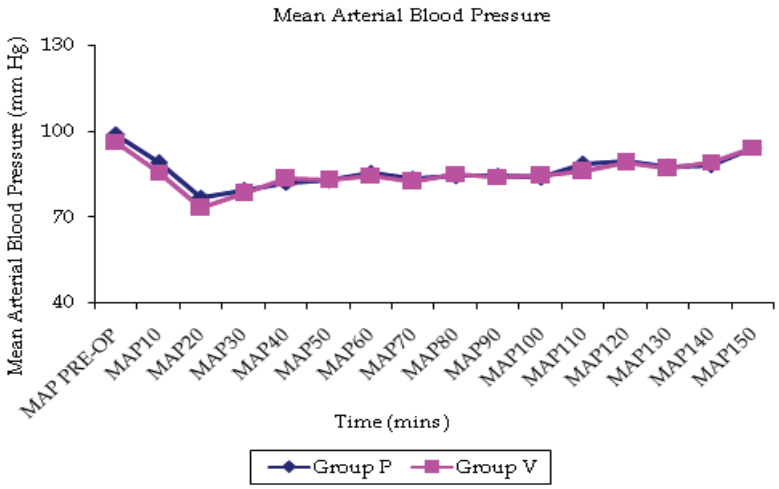

Fig. 2: Intraoperative Mean Arterial Pressure Changes

Table 2: Pain Score (Verbal Rating Scale)

S. No.	Parameters	Group		*p* value
		Group P	Group V	
		Mean ± SD	Mean ± SD	
1.	PS2 (hrs)	2.75 ± 0.44	0.00 ± 0.00	0.001**
2.	PS6 (hrs)	2.00 ± 0.46	0.45 ± 0.69	0.001**
3.	PS12 (hrs)	2.15 ± 0.49	1.70 ± 0.57	0.011*
4.	PS24 (hrs)	1.95 ± 0.69	1.60 ± 0.60	0.094
5.	PS48 (hrs)	1.85 ± 0.49	0.90 ± 0.31	0.001**

* $p < 0.05$ ** $p < 0.01$

Table 3: TFA and Total Postoperative Analgesic Requirements

S. No.	Parameters	Group		*p* value
		Group P	Group V	
		Mean ± SD	Mean ± SD	
1.	Time of First rescue analgesic (hr)	3.84 ± 0.46	6.42 ± 0.63	0.001**
2.	No. of supplementary analgesic doses (48 hr)	6.35± 0.49	4.25± 0.44	0.001**

* $p < 0.05$ ** $p < 0.01$

The study demonstrated that pain relief was significantly good ($p < 0.05$) in patients who received epidural bupivacaine with verapamil mixture than the patients who received epidural bupivacaine with placebo. Similar results were seen in time required for first analgesia and number of supplementary analgesic doses as summarized Table 3.

Discussion

Our knowledge of acute pain mechanisms has advanced sufficiently over the past decade so that rational rather than empirically derived therapy can be used by aiming specifically at interrupting the mechanisms responsible for the generation of clinical pain. Breakthrough pain after surgical procedures is now beginning to be recognized as constituting suboptimal management. This is an active research area. A number of clinical trials have been conducted to prove the efficacy of anti-nociceptive effect of Ca^{2+} channel blockers using different techniques and different types of drugs with conflicting results.[5,6,8,10]

The altered sensory processing caused by high-intensity noxious stimuli has several possible mechanisms, including an expansion of receptive fields and a decrease in thresholds of dorsal horn neurons; an enhancement of responses of dorsal horn neurons elicited by repetitive C fiber stimuli, which is known as wind-up phenomenon; and an increase in dynorphine gene expression6. Repetitive fast - transmitter activity of aspartate

and glutamate at α-amino-3-hydroxy- 5-methyl-4-isoxazolepropionic acid (AMPA)/ kinate receptors produces a membrane depolarization that counters a voltage-dependent blockade of the NMDA receptor by Mg^{2+}. Activation of neurokinin-1 receptors by substance P produces a slow, prolonged depolarization and enhances the influx of extracellular Ca^{2+} through voltage — operated Ca2+ channels. A further action of aspartate and glutamate on NMDA and metabotropic receptors produces an influx of Ca^{2+} through NMDA receptor-operated Ca^{2+} channels and activates phospholipase C.[7]

Phospholipase C catalyzes the formation of intracellular second messengers, which causes the release of Ca^{2+} from the endoplasmic reticulum. Increase in intracellular Ca^{2+} produced by these reactions results in increased gene expression and central sensitization, including wind-up and long-term potentiation.[3] Thus, calcium channel conductance is required for the nervous system to signal a painful situation. A disruption of calcium ion movement interferes with sensory processing and contributes to antinociception.[7]

This series of reactions may be prevented or attenuated either presynaptically by reducing the release of neurotransmitters, postsynaptically by blocking specific receptors, such as NMDA receptor, or by both mechanisms. Opioids and local anesthetics reduce the presynaptic release of the neurotransmitters.

Calcium channel blockers have antinociceptive effects in animals and show morphine potentiation in patients with chronic pain.[3,9] Substances with calcium channel-blocking effects and NMDA receptor antagonists may prevent pain and facilitate treatment of established pain states. In this study, we found that bupivacaine and verapamil administered epidurally, reduced the amount of analgesic that patients required postoperatively suggesting that verapamil may prevent central sensitization by surgical trauma.

In this double-blind study, we have evaluated the analgesic efficacy of bupivacaine with verapamil mixture given through lumbar epidural route in patient undergoing elective orthopedic lower limb surgeries.

Pain intensity was assessed using the verbal rating scale (VRS). Significant lower VRS scores after 2, 6, 12, 24 and 48 hours has demonstrated the clinical advantage of administering a single dose mixture of bupivacaine and verapamil through lumbar epidural route for effective postoperative analgesia.

Duration of analgesia was significantly more in Group V patients receiving bupivacaine and verapamil mixture (6.42 ± 0.63 hours) as compared to Group P (3.84 ± 0.46 hours). The demand for supplementary analgesic doses over 48 hours postoperatively was significantly low in Group V (4.25 ± 0.44 doses) than Group P (6.35 ± 0.49 doses).

Bradycardia with a heart rate < 60/ min was not encountered in any of the patient in both the groups.

Two patients of placebo group (10% of Group P) and one patient of verapamil group (5% of Group V) had episodes of hypotension with a MAP < 65 mm Hg during intraoperative period who were managed with a single dose of ephedrine 6 mg IV and crystalloids.

Postoperatively two patients of placebo group (10% of Group P) and one patient of verapamil group (5% of Group V) had episodes of hypotension with a MAP < 65 mm Hg. These patients were found to have an excessive blood loss seen in the operative wound drain, who are managed with compatible whole blood transfusion. No incidence of any bradycardia was noted in both the groups during postoperative period.

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Original Research Article

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Use of Dexmedetomidine as an Adjuvant in Pediatric MRI Procedures

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Abstract

Introduction: The success of sedation for MRI has typically been measured by two factors: comfortable immobility during the procedure enabling successful completion of the diagnostic examination and the safety of the sedation procedure. We have tried to assess the role of Dexmedetomidine as an adjuvant in pediatric MRI procedures. *Aims and Objectives:* To assess the effectiveness of intravenous dexmedetomidine as an adjuvant to the combination of Ketamine and Midazolam in pediatric patients undergoing MRI study and to compare incidence and severity of adverse effects found in the groups with and without Dexmedetomidine. *Materials and Methods:* After obtaining ethical committee approval and consent from the parents, 60 children posted for MRI study of duration less than 60 minutes, of age group 6 months to 5 years were selected for the study purpose and randomly divided into two groups. Children under group A received Inj. Ketamine 2 mg/kg + Inj. Midazolam 0.05 mg/kg. Children under Group B received Inj. Ketamine 0.5 mg/kg + Inj. Midazolam 0.03 mg/kg + Inj. Dexmedetomidine 2 mcg/kg. Monitoring of SpO_2, RR, HR were done with the help of MRI compatible monitors. 3-point score to assess grade of immobility during the procedure was used to assess the quality of sedation. Ramsay sedation score was used to assess duration of post-procedure sedation. Incidences of adverse events were noted. Inj. Propofol 0.5 mg/kg was used as rescue sedative and Inj. Atropine 0.02 mg/kg for treatment of bradycardia if any. All the patients received nasal Oxygen at 2 lt/min. *Observations and Results:* Movement during MRI procedure was noted in one patient from Group B. Postoperative Ramsay sedation scores were significantly higher >3 in 12 patients (40%) from Group A vs in 5 patients (16.7%) from Group B ($p < 0.05$). Intraprocedural quality of sedation was better with Group B ($p < 0.05$). 5.5% patients from group A desaturated within 10 min of administration of drugs which recovered spontaneously within 5 min of continuation of supplemental oxygen. *Conclusion:* Addition of Dexmedetomidine (2 mcg/kg) reduces doses of Midazolam and Ketamine hence reducing the incidence of dose related side effects without causing compromise in efficacy. It produces stable hemodynamics, better immobility during the procedure and enables early recovery from anesthesia.

Keywords: Dexmedetomidine; Ketamine; Midazolam; MRI procedure; Pediatric.

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Introduction

MRI in children, due to high ambient noise warrants deep sedation for immobilization to complete the procedure successfully. Due to remoteness of MRI suite, lack of MRI compatible monitors and equipment, anesthesia for MRI becomes challenging. Total intravenous anesthesia (TIVA)

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continues to be the most widely preferred mode of sedation for children at remote locations like MRI suite.[1] An increasing number of procedures are done under TIVA since the range of drugs that can be safely used has expanded exponentially.

Propofol (2, 6-di-isopropyl phenol) is used for TIVA for short procedures in pediatric patients due to its rapidity of onset and offset.[2] However, the same property makes it unsuitable for MRI procedures since frequent additional doses are required for completion of MRI procedures which extend more than twenty minutes. Propofol is given in the form of a continuous infusion[3] for continued effect for prolonged period, but due to difficulty in obtaining MRI compatible supportive equipment required for an infusion; like IV stands and infusion pumps make its use unsuitable for MRI procedures. Also, Propofol does not possess intrinsic analgesic properties[4] and causes cardiorespiratory depression that discourages its use in MRI for paediatric patients.

Ketamine, an N- methyl-D-aspartate receptor antagonist anesthetic agent, is a well tried and tested drug that ensures safety and efficacy in remote areas especially for pediatric patients. Its intrinsic bronchodilator action combined with the anti-nociceptive effects at a spinal level preserves protective reflexes while providing profound analgesia. Conversely, its sole use in pediatrics pose the risk of sympathomimetic exacerbation and emergence phenomenon leading to cognitive impairment and delirium.[5]

Midazolam, a short-acting benzodiazepine, has excellent sedative effects but the respiratory depressant activity predominates and persist seven in titrated doses in pediatric patients.[6]

Dexmedetomidine, a centrally acting alpha-2 agonist drug, has been proven safe when used in titrated doses and does not differ in pharmacodynamics when used in pediatric population. It gives excellent sedation without respiratory depression[7] and has been proven effective even in high-risk cases.

Using a combination of drugs that have complementary action when used together produces excellent sedoanalgesia. Moreover, Ketamine and Dexmedetomidine by virtue of their counter balancing properties may produce stable hemodynamics while circumventing the complications of the said drugs.[6]

In present study, we have tried to evaluate and compare efficacy and safety of the combination of sedative doses of Ketamine (2 mg/kg) and Midazolam (0.5 mg/kg) versus the same drugs in reduced doses; Ketamine 0.5 mg/kg and Midazolam 0.03 mg/kg along with Dexmedetomidine at the dose of 2 mcg/kg[7] for MRI proceduresin pediatric patients.

Materials and Methods

After Institutional Ethics Committee approval and written parental consent, ASA physical status I-II children aged between 6 months to 5 years of both sexes undergoing MRI were included in this study. They were randomly divided into 2 groups by lottery method.

Group A received Inj. Ketamine at 2 mg/kg and Inj. Midazolam 0.05 mg/kg and 10 cc of distilled water in another prefilled syringe.

Group B received Inj. Ketamine 0.5 mg/kg plus Inj. Midazolam 0.03 mg/kg and 10 cc of Inj. Dexmedetomidine 2 mcg/kg diluted with distilled water in a prefilled syringe.

Patients with CNS/Extremity trauma with convulsions or with airway abnormalities, intubated and ventilator dependent patients, patients on sedatives or refusal of the parent for their child to be a subject were excluded from the study. Patients with known allergies to the study drugs or patients having received any study drug in the last 30 days were also excluded.

All subjects were kept nil per oral for solids and milk for 4 hours and clear fluids for 2 hours.

The prefilled study drugs were administered intravenously slowly over 10 minutes following which the MRI procedure was commenced. A blinded observer recorded baseline values and subsequent readings of Heart rate, SpO_2, RR, 3 point sedation scale every 5 minutes till the end of procedure. Post procedure for 30 minutes, the comfort of the patient, complications if any and wakefulness were assessed by Ramsay sedation score.

Statistical Analysis

Sample size was calculated based on in-patient admissions in the department of pediatrics in Bharati hospital spanning over six months. Taking the population (N) as 70 and margin of error as 5% with Z score 1.96 for a 95% confidence level, sample size was calculated using the following formula

$$\text{Sample size} = \frac{\frac{z^2 \times p(1-p)}{e^2}}{1+(\frac{z^2 \times p(1-p)}{e^2 N})}$$

and was found to be 56.

So sixty subjects were randomly chosen and divided into two groups by lottery method.

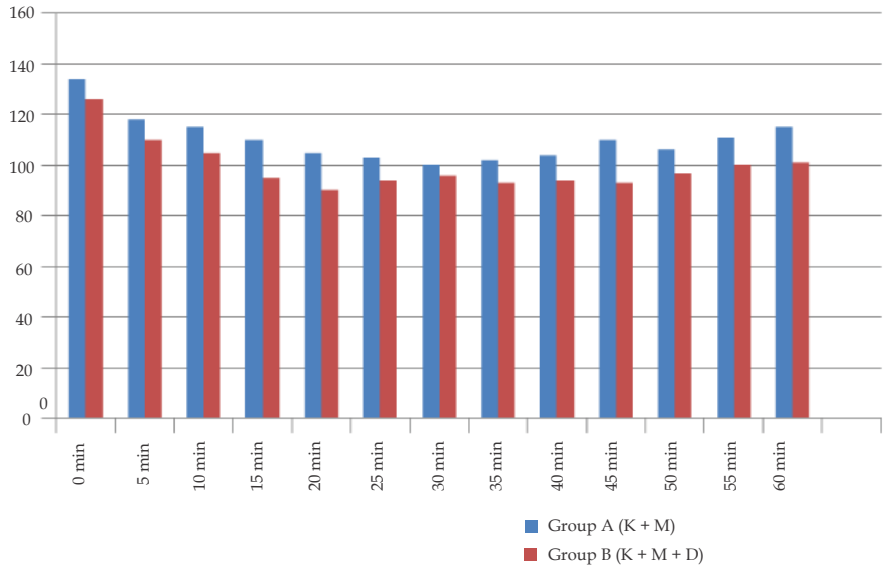
The data was entered in Microsoft Excel spreadsheet and analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used to analyze qualitative data represented as mean and standard deviation. Paired-*t* test was the test of significance used for paired data. '*p*' value of <0.05 was considered statistically significant.

Results

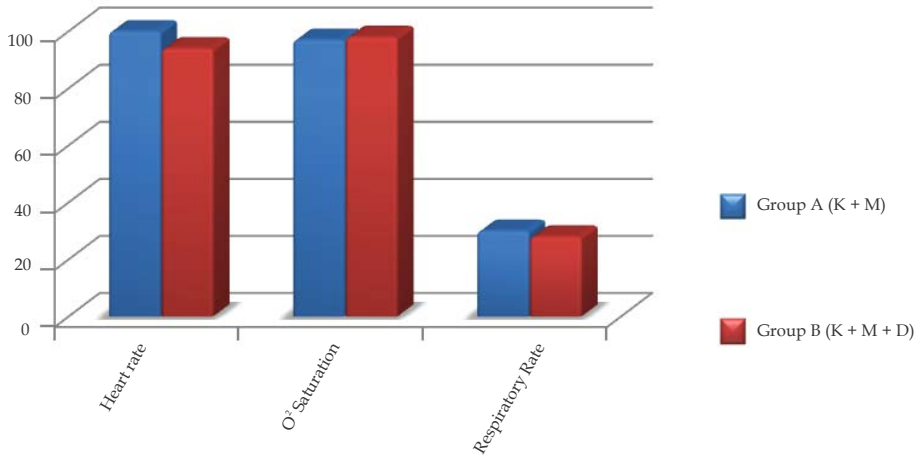
Demographic data was comparable with respect to Age, Weight, ASA physical status and gender status in both groups (Table 1). Throughout the procedure, the subjects maintained stable hemodynamics in both the groups (Table 2). Variation in heart rate was lesser in Group B when compared to Group A. however, the differences were statistically insignificant (Graph 2).

Table 1: Demographic Data

Demographic data	Group A (n=30)	Group B (n=30)	*p* value	Significance
Age (years)	2.1 ± 2.9	2.3 ± 2.7	> 0.05	Not significant
Sex (M)	20	19	> 0.05	Not significant
Sex (F)	10	11	> 0.05	Not significant
Weight (kg)	9.2 ± 4	8.9 ± 4.4	> 0.05	Not significant
ASA I	9	8	>0.05	Not significant
ASA II	21	22	>0.05	Not significant



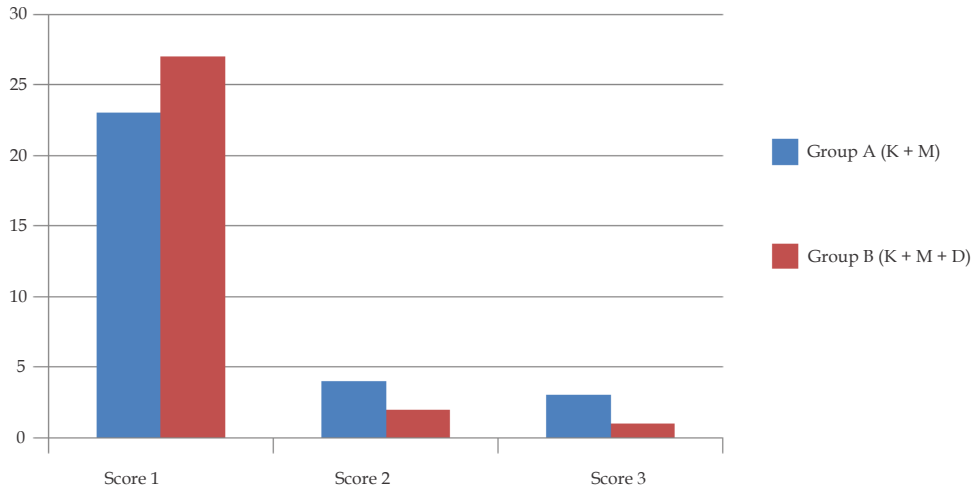
Graph 1: Comparison of variation in intraprocedural heart rates between the two groups



Graph 2: Comparison of Heart rates, Oxygen saturation and Respiratory rates between the groups

Table 2: Comparison of Hemodynamic Parameters

Parameter	Group A (n=30)	Group B (n=30)	p value	Significance
Heart rate	100 ± 30	94 ± 24	> 0.05	Not significant
SpO_2	97 ± 2	98 ± 2	> 0.05	Not significant
Respiratory rate	30 ± 4	29 ± 5	> 0.05	Not significant
Use of rescue analgesic	–	–	–	–



Graph 3: Comparison of intra-proceduralsedation scores between the groups

Table 3: Comparison of Adverse Effects during the Study Period

Adverse events	Group A (n = 30)	Group B (n = 30)
Tachycardia >20% baseline	1	–
Bradycardia <20% baseline	1	2
Movement during procedure	–	1
Respiratory depression (reduction in SpO_2 less than 90%)	3	–
Post-procedure Respiratory obstruction	5	–
Post-procedure agitation	1	–

Rescue analgesic was not required in any of the study subjects in both the groups.

Intraprocedural quality of sedation (Graph 3) was assessed by a 3-point sedation score where the scores were credited as follows:

Sedation Score

1 – No motion

2 – Minor movement

3 – Major movement requiring repeat scan

Optimal immobilization (Score 1) was observed in 90% of the subjects in Group B whereas in Group A, 76.67% of the subjects were adequately immobilized. Quality of sedation was found to be significantly better (p value < 0.05) in Group B as compared to Group A.

Bradycardia was observed in 2 subjects among the group receiving Dexmedetomidine which was treated with Inj. Atropine at 0.02 mg/kg but the procedure was continued; thereby, the sedation score was unaffected (Table 3).

Respiratory rates were observed to be decreased following bolus doses of the group a combination but stabilized following continuation of oxygen supplementation. Group B subjects showed adequate oxygenation which was assessed clinically by chest movements.

The subjects were observed in the recovery room for a period of thirty minutes post procedure. 16.67% of the subjects in Group A required continued oxygen supplementation in the post-procedure period. Once they regained complete consciousness they maintained on ambient atmosphere. Group B subjects were observed to have adequate oxygen

saturation in the post-procedure period and did not require supplementation.

Postoperative respiratory obstruction was relieved by extending neck in recovery position.

Overall respiratory adverse effects noted were more with group a patient.

Post procedure agitation was observed in 1 subject in group a, which subsided without any intervention within 10 minutes. No such incidence was observed in Group B (Table 4).

Table 4: Comparison of Post-procedural Sedation Scores between the Two Groups

Ramsay sedation scale	Group A (n = 30)	Group B (n = 30)
Postoperative RSS 3 or < 3	18	25
Postoperative RSS > 3	12	5

Ramsay sedation scale

1. Patient is anxious, agitated and restless
2. Patient is oriented, cooperative and tranquil
3. Patient responds to commands only
4. Patient exhibits brisk response to light tactile stimuli or loud auditory stimulus
5. Patient exhibits sluggish response to light tactile stimuli or loud auditory stimulus
6. Patient exhibits no response

Group B subjects showed spontaneous arousability at the end of the procedure with clear headed recovery which was contributory to the parents' (of the study subjects) satisfaction. 83% of the patients in Group B were arousable on light tactile stimulus by the parent whereas in Group A, 60% were spontaneously arousable. Also, the duration of sedation post procedure was significantly longer in group A. The difference was statistically significant ($p < 0.05$).

Both the groups did not show statistically significant deviation in hemodynamic parameters throughout the study period. In terms of hemodynamic stability, both the groups were comparable. Respiratory complications were observed in Group A while Group B had no such incidence. Intra-procedural sedation scores were better in Group B but the difference was statistically insignificant. Post procedure arousability, assessed with the aid of Ramsay sedation score (RSS), was significantly better in the subjects of Group B where 83% of the subjects had an RSS > 3 while compared to group A where only 60% had the same score. Intergroup difference was statistically significant. ($p < 0.05$)

Discussion

The success of sedation for MRI has typically been measured by two factors: the safety of the sedation procedure (lack of adverse events) and the effectiveness of the procedure (successful completion of the diagnostic examination).[3] Sedation of children for MRI is usually associated with inadequate or failed sedation because of difficulty in having patients motionless while maintaining hemodynamic and respiratory stability.

Various drugs have been tried from time to time in TIVA. Since no single drug can provide all the characteristics of an ideal intravenous agent, several drugs are used in different combinations to provide balanced anesthesia in TIVA, that is, amnesia, hypnosis and analgesia.[6]

Ahmet Koroglu *et al.*[7] compared the sedative, hemodynamic, and respiratory effects of Dexmedetomidine and Propofol in children undergoing magnetic resonance imaging examination. Their results suggested that, although Propofol provided faster induction and recovery, it caused hypotension and desaturation owing to its depressant action on upper airway reflexes. They also inferred that Dexmedetomidine was a better sedative than Propofol in pediatric patients.

In another study on same subset of patients for same purpose Haesesler *et al.*[8] inferred that co-administration of ketamine and midazolam by initial rectal and later supplemental intravenous route proved safer and useful alternative to general anesthesia.

Current guidelines for safe practice of TIVA in remote areas like MRI suite were put forth by Nimmo *et al.*[9] in 2018. According to their consensus document, continuous infusion of routinely used TIVA drugs like Propofol should be closely monitored to attain steady state plasma concentration with the help of target controlled infusions[9] (TCI) and continuous hemodynamic monitoring. As per their recommendations, in the circumstances where the above facilities are not available, only sedative doses of these drugs can be given. Ketamine with its intrinsic bronchodilatory activity complements the respiratory depressant activity of Midazolam. Dexmedetomidine, the wonder drug, further lowers the doses while enhancing the quality of sedation when used as an adjunct to the aforementioned drugs.[10,11]

In our study, we also tried to evaluate safety and efficacy of Dexmedetomidine as an adjuvant. We found that addition of it reduced the doses of

Ketamine and Midazolam without compromising depth of sedation. Our observations confirmed that it also offered the advantage of airway protection and early recovery.

Mason *et al*.[12] reviewed almost 200 studies and reports published regarding the use of dexmedetomidine in infants and children. They observed that the drug had minimal depressant effects on the respiratory system which maintained a patent airway. They also had a useful conclusion that besides providing and augmenting analgesia it diminished shivering as well as agitation postoperatively. In present study, we also did not observe any untoward emergence effects in Dexmedetomidine group.

Dexmedetomidine although not orally active, shows good bioavailability when administered via various other routes like intranasal, buccal, intramuscular and intravenous. Since its side effects are predictable and easily treatable, use of Dexmedetomidine in higher doses (>1.5 mcg/kg), has found place in fast-tracking anesthesia regimens like MRI in children.[13] So we selected 2 mcg/kg dose.

Ketamine, a general anesthetic agent, works primarily by antagonizing N-methyl-D-aspartate (NMDA) receptors. Electroencephalographic studies show that Ketamine anesthesia is associated with increased gamma and theta activity during administration and emergence.[5] This increased neuronal activity may prove detrimental in the presence on an underlying cerebral pathology which may trigger increased firing resulting in a seizure episode mid-procedure. Hence in our study, Midazolam with its anticonvulsant property[15] was used to counteract the above-mentioned effect of Ketamine.

Ketamine, with its cardio-stimulatory response on administration, causes a net effect of an increase in systolic blood pressure, heart rate and cardiac output.[5] In a study conducted by Gupta *et al*.,[10] Ketamine anesthesia administered with Dexmedetomidine at the dose of 1 μg/kg as a premedication in the study group and with Midazolam at the dose of 0.02 mg/kg in the control group. The group where Dexmedetomidine was administered, minimal deviations from baseline hemodynamic parameters were observed whereas in the control group, a significant rise of 27.5% from baseline systolic arterial pressure and a 17–25 beats per minute rise in heart rate were observed.

As per a meta-analysis by Shukry and Miller[14] Dexmedetomidine was used for sedation in monitored anesthesia care (MAC), airway procedures including fiber-optic bronchoscopy, dental procedures, ophthalmological procedures, head and neck procedures, neurosurgery, and vascular surgery. The literature suggested that Dexmedetomidine loading dose ranged from 0.5 to 5 μg kg^{-1}, and infusion dose ranged from 0.2 to 10 μg kg^{-1} h^{-1}. Dexmedetomidine was administered in conjunction with local anesthesia and/or other sedatives. Ketamine was administered with Dexmedetomidine and opposed its bradycardia effects.

Considering safety of Dexmedetomidine up to a bolus dose of 5 μg/kg[16], we ventured to use a dose of 2 μg/kg. We also tried to evaluate effect of addition of Dexmedetomidine (2 mcg/kg) in reducing the doses of Ketamine to 0.5 mg/kg and Midazolam to 0.03 mg/kg. Our secondary aim was whether it facilitates early and clear headed recovery immediately after the procedure without requiring additional incremental dose which can cause interruption in the ongoing procedure.

The particular combination of Ketamine and Dexmedetomidine for non-invasive diagnostic procedural sedation was studied by Tobias[13] in a meta-analysis consisting of four major cohort studies which established the utility of combination of Ketamine and Dexmedetomidine in the doses 1–2 mg/kg and 1 μ/kg respectively for non-invasive procedures.

Results of a valuable meta-analysis by Shukry and Miller[14] Ketamine and Dexmedetomidine suggested that they have counter balancing effects on hemodynamics rendering optimal conditions for pediatric sedation in remote areas.

Limitations

Intra-procedural monitoring of ECG, capnography and blood pressure was not done due to non-availability of MRI compatible monitors. The aforementioned limitations may have influenced the outcomes of the study.

Conclusion

Addition of Dexmedetomidine in dose (2 mcg/kg) not only reduced the dosage of Ketamine and Midazolam with resultant reduction in their side effects but also enhanced the quality of MRI while maintaining stable hemodynamics. Patients in Dexmedetomidine group had early, clear headed recovery when compared to those who did not receive it. Addition of Dexmedetomidine to

Ketamine and Midazolam proved more efficacious and safe in pediatric MRI patients.

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Original Research Article

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Comparison of Sedative and Cardiovascular Effects of Ropivacaine with Dexmedetomidine and Clonidine in Patients Undergoing Lower Limb Surgery: A Hospital Based Prospective Study

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Abstract

Background: Anesthetics are the agents used to induce sedation and analgesia in patients undergoing surgery. Combination of anesthetics plays major role in the major surgery and affect the various systems in the body. The present study aimed to evaluate the sedative and cardiovascular effects of ropivacaine with dexmedetomidine and clonidine in patients undergoing surgery. *Materials and Methods:* A total of 70 patients were included in the study. They were divided into two groups. G-A (Ropivacaine (0.75%/15 ml) + Dexmedetomidine (1 mcg/kg) and G-B Ropivacaine (0.75%/15 ml) + Clonidine (1 mcg/kg) were administered during surgery time. Study procedure was explained to all the patients and informed consent was taken. After administration of anesthetics to respective groups sedative and cardiovascular functions were recorded and analyzed. *Results:* 22 patients had a sedation score of 2 in Group A, whereas 35 patients had a sedation score of 2 in Group-B, 13 in Group A had score 3 at 10 min, No patient had sedation score 3 in Group B at 10 min. No one had sedation score 4 in both the groups, (Table 1). 32 patients, showed sedation score ≥ 2 in Group A compared to Group B where only 20 patients had sedation score ≥ 2 throughout the surgery. No one had a score of 3 in both the groups at the end of the surgery. Significant difference in heart rate was observed at 50 min and 70 min which got lowered in Group B when compared to Group A. No significant difference was noted in blood pressure monitoring and use of rescue drug for hypotension in both the groups. *Conclusion:* Epidural dexmedetomidine cause better sedation more cardiovascular stability compared to clonidine.

Keywords: Anesthesia; Clonidine; Ropivacaine; Dexmedetomidine; Epidural; Sedation; Hypotension.

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Introduction

Epidural anesthesia is a most common technique used in the lower limb surgery. This technique provides anesthesia along with analgesia in the post operative period. It provides better anesthetic effect and less postoperative complications. It also helps in fast mobilization with minimal side effects.[1-4] Bupivacaine is the most common anesthetic used in the epidural anesthesia. Recent clinical research results showed that use of ropivacaine is better than bupivacaine to induce the anesthesia. Ropivacaine has similar anesthetic effect but minimal cardiovascular adverse effects.[5] In clinical

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practice various adjuvant drugs used to increase the anesthetic and analgesic effect of local anesthetic agent. Use of combination can increase the effect and also reduce the toxic effects.[6,7] Studies showed that combination use of local anesthetic with alpha-2 agonist increase the quality and duration of analgesia and sedation with lesser cardiovascular effects. Dexmedetomidine and clonidine are alpha-2 agonist increase the effects of local ansthetics in epidural anesthesia.[8] Both drugs acts pre and post synaptic nerves terminals and also have central action which causes decrease the sympathetic flow leading to sedation and hemodynamic effects.[9,10] With this background the preset study aimed to compare the sedative and cardiovascular effects of ropivacaine with dexmedetomidine and clonidine in patients undergoing lower limb surgery.

Materials and Methods

Study setting and period

This prospective study was conducted for one year in the Department of anesthesiology, SreeMookambika Institute of Medical Sciences, Kulasekharam, Kanyakumri (Dist), Tamil Nadu.

Inclusion criteria

- Age between 18 and 65 years.
- Both genders.
- Patients fullfill the American Society of Anesthesiology Score 1 and 2.
- Patients undergoing lower limb surgery under epidural anesthesia.
- Patients undergoing lower abdominal elective surgeries under epidural anesthesia.

Exclusion criteria

- ASA score above 3.
- Patients undergoing spinal anesthesia.
- Alcoholics, drug addicts and on sedative drugs.
- Emergency surgeries.
- Not willing to sign on informed consent.
- Allergic to anesthetics.

Study groups

Group-A: Ropivacaine (0.75%/15 ml) + Dexmedetomidine (1 mcg/kg) (n=35)

Group-B: Ropivacaine (0.75%/15 ml) + Clonidine (1 mcg/kg)) (n=35)

Procedure

This study was started after approval of Institutional Research Committee and Institutional Human Ethics Committee. Study population was selected from patients coming to the anesthesia department. Based on the inclusion and exclusion criteria 70 patients were included in this study. All the selected patients were explained study protocol and procedure in detail. Informed consent was obtained from each patient. The selected patients were divided into 2 groups each of 35. The selected patients were asked to admit to the hospital one day prior to the surgery. They were kept fasting before 6 hr of surgery. On arrival to the operation theater, following insertion of an 18-G venous cannula, 500 mL of Ringer Lactate was infused to the patient before epidural anesthesia. Standard monitors like ECG, Non-invasive blood Pressure and SpO_2 probe was attached and baseline parameters recorded. Patients positioned and 15 ml 0.75% ropivacaine with adjuvant was administered epidural space in L3–L4 interspace through a standard midline approach using an 18-G Tuohy needle. Group-A was given Dexmedetomidine 1 mcg/kg with ropivacaine epidural space, whereas Group-B was given 1 mcg/kg of clonidine with ropivacaine epidural space. All patients were supplemented with oxygen-4L/min via a face mask throughout the procedure after positioning the patient. The level of sedation was assessed 10 minutes after grade 3 motor blockades and at the end of surgery based on the Ramsay sedation scale. Hemodynamic parameters were monitored every 5 minutes for the first 30 minutes, every 10 minutes thereafter till the end of surgery. Patient received inj. Atropine 0.6 mg when the heart rate fell below 20% of baseline (bradycardia) and Inj. Mephentermie in titrated bolus when there was hypotension (fall below 20% of baseline). Any side effects seen after administration of study drug was noted and treated appropriately.

Statistical analysis

Statistical Package for Social Sciences (16.0) version used for analysis. The data was expressed in number, percentage, mean and standard deviation. Unpaired *t* test applied to find the statistical significant between the groups. *p* value less than 0.05 ($p < 0.05$) consider statistically significant at 95% confidence interval.

Results

Total 70 patients were included in the study. They were divided into two groups each of 35 patients. 22 patients had a sedation score of 2 in Group A, whereas 35 patients had a sedation score of 2 in Group B. 13 in Group-A had score 3 at 10 min. No patient had sedation score 3 in Group B. No one had sedation score 4 in both the groups, (Table 1). 32 patients, that is 91% of patients showed sedation score ≥ 2 in Group-A compared to Group-B where only 20 patients, that is 57% had sedation score ≥ 2 throughout the surgery. No one had a score of 3 in both the groups at the end of the surgery. 0, 5, 10, 15, 20, 25, 30, 40, 45, 60, 80, 90, 100, 110 and 120 min not showed any significant difference compared heart rate between Group-A with B. Statistical significance in heart rate was observed between Group-A and B at 50 and 70 min ($p < 0.05$) (Table 3 and Graph 1). No significant difference was noted in blood pressure monitoring and subsequent use of injmephentermine for hypotension in both the groups.

Table 1: Comparison of Sedation Score at 10 min between the Group-A and Group-B

Sedation score	Group-A		Group-B	
	Number	Percentage (%)	Number	Percentage (%)
2	22	62.88*	35	100*
3	13	37.14*	0	0
4	0	0.0	0	0

(*p < 0.05 significant compared Group-A with Group-B)

Table 2: Comparison of Sedation Score at the end of Surgery between the Group-A and Group-B

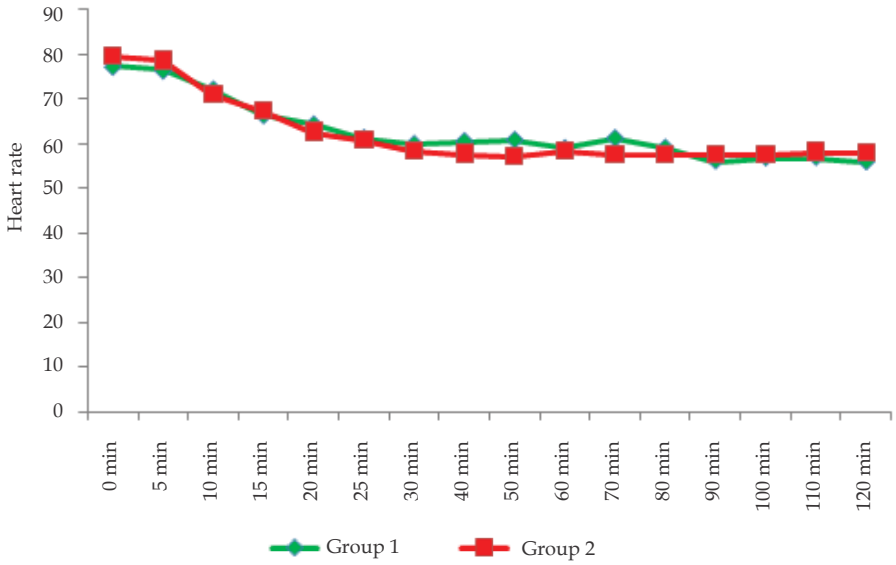
Sedation score	Group-A		Group-B	
	Number	Percentage (%)	Number	Percentage (%)
2	32	91.4*	20	57.14*
3	0	0	0	0
4	0	0	0	0

(*p < 0.05 significant compared Group-A with Group-B)

Table 3: Comparison of Heart Rate between the Group-A and Group-B

Heart rate	Group-A		Group-B		t	p
	Mean	SD	Mean	SD		
0 min	77.40	8.222	79.49	10.472	–.927	.357
5 min	76.57	9.319	78.49	10.752	–.796	.429
10 min	72.34	9.152	70.89	9.380	.658	.513
15 min	66.46	13.611	67.29	8.191	–.309	.759
20 min	64.43	6.984	62.57	7.072	1.105	.273
25 min	61.37	7.166	60.86	6.779	.308	.759
30 min	60.03	6.506	58.23	7.581	1.066	.290
40 min	60.60	6.779	57.66	6.633	1.836	.071
50 min	60.91	7.164	57.14	6.731	2.270	.026*
60 min	59.06	5.810	58.23	6.695	.553	.582
70 min	61.31	8.025	57.43	5.468	2.367	.021*
80 min	59.17	5.591	57.57	5.164	1.244	.218
90 min	56.20	7.136	57.60	4.894	–.957	.342
100 min	56.94	6.145	57.54	6.075	–.411	.683
110 min	57.03	7.115	58.09	5.564	–.692	.491
120 min	56.03	6.066	57.80	4.378	–1.401	.166

(*$p < 0.05$ significant compared Group-A with Group-B)



Graph 1: Comparison of heart rate between the Group-A and Group-B

Discussion

In this study, we found better sedation in the patients who received dexmedetomidine than those who received clonidine at both 10 minutes and at the end of surgery. This apparent change was also found to be statistically significant (p = 0.000). The similar study conducted by Oriol-Lopez *et al.*,[11] assessing the anxiolytic and sedative property of epidural dexmedetomidine in patients undergoing abdominal surgeries, dexmedetomidine was given at a dose of 1 mcg/kg. Following the injection, Ramsay sedation score was used for assessment of sedation. They found that 90% of the patients receiving dexmedetomidine were sedated to a score of 3 to 4 for 90 minutes after drug administration. The findings of Bajwa *et al.*,[12] also showed a significantly higher level of sedation in the patients who received dexmedetomidine in comparison to clonidine. These findings from the studies mentioned above concur with the findings from our study, showing that dexmedetomidine causes significantly higher sedation than clonidine when given epidurally. We found that heart rate significant fell in both the groups by 20 in 30 to 50 minutes after the epidural injection. Blood pressure decreased by 25% in 30 to 50 minutes following epidural injection. However, this change was not statistically significant (p > 0.05). Similar observations were observed by Bajwa *et al.* and Schnaider *et al.*[13] where a 15% fall of heart rate % blood pressure from the baseline which was not statistically significant.

We observed similar hemodynamic changes in both the study groups. We found no significant difference in the atropine and mephentermine requirement as rescue in both the groups. Findings were similar to studies done by Bagatini *et al.*, who also found no significant difference in terms of hypotension and bradycardia between the patients receiving dexmedetomidine or clonidine.[14] Nausea, vomiting and shivering was not observed in both the groups. We had two patients in Group R and one patient in Group RD who had dry mouth. The study conducted by Bajwa *et al.* showed a higher incidence of nausea, dry mouth during the postoperative period.

The limitations of our study was that as different surgeries were taken up in this study, therefore onset of pain at surgical incisional site may not give an accurate duration of analgesia. There is also need for larger studies, using different concentrations of both drugs to find equivalent doses of epidural dexmedetomidine and clonidine. There is a further requirement to assess the long-term safety and effects of epidural dexmedetomidine as most studies only determine the short-term effects.

Conclusion

The study results conclude that epidural dexmedetomidine induce better sedation compared to clonidine. Combination of dexmedetomidine with other local anesthetic produces the better sedation effect with less cardiovascular effects.

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Original Research Article

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Preemptive Gabapentin vs Pregabalin for Acute Postoperative Pain in Women Undergoing Cesarean Section Under Spinal Anesthesia: A Prospective Randomized Double-blind Study

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Abstract

Background: Appropriate management of pain is needed during the postpartum hospitalization period for preventing cesarean section (CS) related complications. Gabapentin and pregabalin have been used in treatment of neuropathic pain as well as postoperative pain with good results. However, there is paucity of studies in comparison with each other. The aim of current study was to compare the analgesic efficacy with respect to increase in duration of analgesia, reduction in total postoperative requirements of analgesics and study side effects and complications. *Methods:* A randomized, double-blind, placebo-controlled study was conducted in 90 women undergoing cesarean section who were anesthetized in a standardized fashion. Patients received 300 mg pregabalin, 600 mg gabapentin or placebo, 2 hours prior to surgery. Postoperative analgesia was given at visual analogue scale (VAS) ≥ 3. The primary outcome of present study was consumption of analgesic over 24 hours and patients were followed for time to rescue analgesia, pain scores, and side effects as secondary outcomes. *Results:* The consumption of diclofenac was statistically significant between both pregabalin and control groups, and gabapentin and control groups; however, pregabalin and gabapentin groups were comparable. Patients in pregabalin and gabapentin groups had lower pain scores in the initial hour of recovery. However, pain scores were subsequently similar in all the groups. Time to first request for analgesia was longer in pregabalin group followed by gabapentin and control groups. *Conclusion:* Prior to CS, a single dose of 300 mg pregabalin given 2 hours is equally effective to 600 mg gabapentin but superior to placebo. Both the drugs are better than placebo.

Keywords: Cesarean Section; Gabapentin; Postoperative pain; Pregabalin.

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Introduction

Adequate postoperative analgesia after cesarean section (CS) is necessary since these patients have a unique surgical recovery requirement which include breastfeeding and care of the newborn. Post-CS analgesic management should be efficient without impacting the ability of a mother to take care of the neonate and with minimum drug transfer through breast milk. Although multimodal

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approaches have been there for proper pain relief yet they are inadequate and unsatisfactory in many patients.[1] Inadequate pain management can result in increased morbidity due to thromboembolic events, inappropriate neonatal care and delay in discharge which makes postoperative pain control in this group of patients is more challenging than other surgeries.[2] Post-partum pain management in women undergoing CS differs among different regions based on facilities available at the center or region.

Pregabalin and its precursor, gabapentin, are structural analogs of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). These compounds have anticonvulsant, antihyperalgesic, and anxiolytic effects, and both bind to the alpha 2-delta (α2-δ) protein subunit of presynaptic, voltage-gated calcium channels extensively distributed in the both central and peripheral system. This inhibits calcium influx and reduces excitatory neurotransmitter (e.g., glutamate, substance P, calcitonin, noradrenaline, gene-related peptide) release in pain pathways.[3,4] Pregabalin is considered pharmacologically superior to gabapentin due to higher bioavailability (90% vs. 33%–66%), more rapid absorption (peak plasma level: 1-hour vs 3–4 hours), fewer drug interactions due to the absence of hepatic metabolism and linear increase in plasma concentrations when its dose is increased.[5,6] The lower doses of pregabalin required for its analgesic effect, compared to gabapentin, result in better tolerance and fewer side effects, making its use more advantageous.[7,8]

Pregabalin use as an analgesic in postoperative pain is still restricted to randomized control trials in patients of dental pain, hysterectomy, minor and day-case gynecological surgery and hip arthroplasty. To the best of our knowledge, there are no trials comparing pregabalin and gabapentin in postoperative pain in women undergoing cesarean section in the available literature. Thus, the study was undertaken to know whether the preoperative use of gabapentin and pregabalin will reduce the consumption of analgesics after cesarean section and to compare their efficacy and side effects with that of placebo.

Materials and Methods

After getting written informed consent from each participant, ninety women in the age group of 20–35, undergoing cesarean section, were enrolled. The inclusion criteria were ASA I and II with no contraindications to the use of gabapentinoids. Exclusion criteria were women of age more than 35; having history of central nervous system disorders, sedatives, chronic pain, using regular analgesics, anticonvulsants, impaired renal functions and 20% more than the ideal body weight.

The study was a randomized, double-blind and placebo controlled. A list of random numbers was generated by block randomization schedule using random number generator by a statistician and was handed over to the hospital pharmacist. Masking of study drugs was done by pharmacist by packing drugs in identical looking gelatine capsules. These capsules were further packed and sealed in an opaque envelope and labeled with study name, investigator name, and randomization number. Participants were assigned to their group according to their randomization number. The allocation sequence and enrollment of the patients was done by the same anesthetists who were involved in intraoperative and postoperative data collection. None was aware of allotted group till every woman was included and the assessments were done. Ninety women were allocated by sealed opaque envelopes bearing a code to each of the three groups to receive pregabalin 300 mg (Group P), gabapentin 600 mg (Group G) or a matching placebo (Group C) (n=30 each) prepared by pharmacy. The study drug was given orally 2 hours prior to surgery and no other sedative premedication was given. Patients were told how to use of a 10 cm linear visual analogue scale (VAS) for pain, where 0 denotes "no pain" and 10 denotes "worst imaginable pain", before surgery. In the operating room, electrocardiogram (ECG), noninvasive blood pressure (NIBP), peripheral oxygen saturation (SpO_2) and heart rate (HR) were monitored (Philips Intellivue MP70). Using an aseptic procedure, a 26-gauge Quincke needle was inserted intrathecally via a midline approach at the L3–4 interspace by the same anesthetist, who was unaware of allotted group. Following a successful dural puncture, the anesthetic solution (2.2 mL hyperbaric bupivacaine 0.5%) was injected. After completion of CS, all the patients were transferred to post-anesthesia care unit (PACU).

The primary outcomes of this study were to evaluate the time to the first requirement of analgesic and the total analgesic consumption in the first 24 postoperative hours. In this study, postoperative analgesia was defined as the time from the intrathecal injection of anesthetic solution to the first requirement of analgesic supplement. The pain intensity of patients was evaluated at the end of anesthesia in recovery room, then at 2, 4, 6, 8, 12, 18 and 24 hours after surgery. Rescue analgesia was given at VAS ≥ 3 with intramuscular diclofenac sodium 1 mg/kg.

The secondary outcome of this study included the assessment of sedation level and the incidence of vomiting. The sedation level of patients after surgery was measured according to modified Ramsay sedation score[9] using a 3-point scale with 1=anxious, 2=calm and oriented, 3=calm and drowsiness.

Any side effects like nausea, vomiting, skin rash, headache, dizziness, visual disturbances, peripheral edema and respiratory depression (sedation score > 2 and respiratory rate < 10 breaths/minute) were noted. Injection ondansetron 0.1 mg/kg was given when required.

Sample size was decided in consultation with a statistician. Sample size was calculated using a power of 90% and an α value of 0.05. Based on preliminary results from our department, the anticipated consumption of diclofenac sodium was 175 mg (standard deviation = 40 mg) in gabapentin group and a reduction in pregabalin group by 20% was considered significant. Based on these assumptions and sample size of previous trial also into consideration, a sample size of 30 per group was taken.[10] No adjustment to the Type 1 error rate was made to accommodate the multiple analyses associated with the secondary outcome measures. One-way analysis of variance (ANOVA) was used for comparison of total analgesic consumption over 24 hours and the time intervals to first analgesic.

Results

Ninety patients were enrolled in, completed the study protocol and were included in the data analysis. Failed spinal anesthesia and conversion to general anesthesia were encountered in one case from control group (C) which were replaced by another case to complete the sample size. Demographic characteristics in all three groups did not show any statistically significant difference (p value > 0.05) (Table 1). Time to first request for analgesia was 24.32 ± 9.2 minutes in pregabalin group, followed by 19.13 ± 14.2 minutes in gabapentin (p = 0.0983) and 9.00 ± 3.2 minutes in control group.

(Table 2). Sedation score analysis revealed significance in controlgroup in comparison to P and G groups (p < 0.001) at all measured times. Sedation scores are shown in Table 3. The common side effects in the study were nausea, vomiting and dizziness with no difference in the incidence of side effects between pregabalin and gabapentin groups.

Twenty-eight patients in the control group had nausea and vomiting in comparison to 13 in pregabalin group and 20 patients in gabapentin group (p < 0.001). Five patients reported dizziness in pregabalin group, nine in gabapentin group and one in control group. The incidence of sedation was 30% in pregabalin group, 40% in gabapentin group, 6.6% in control group. The incidence of headache, blurred vision, and skin rash was comparable in all the

Table 1: The demographic profile of patients in the three groups.

Demographic profile	Group P	Group G	Group C	p value
Age (yrs)	28.3 ± 5.2	27.8 ± 5.1	29.2 ± 4.2	0.529
Weight (Kg)	75.1 ± 12.4	76.5 ± 14.2	78.4 ± 12.1	0.613
Height (cm)	158.5 ± 4.6	157.4 ± 5.3	157.6 ± 3.4	0.662
Gestational age (week)	38.4 ± 1.2	38.2 ± 1.0	38.3 ± 1.1	0.782

Numerical data were expressed as mean ± SD. p value > 0.05 was considered insignificant.

Table 2: Time to first analgesic and requirement of rescue analgesic (mean ± SD)

Group	Time interval (minutes)	Diclofenac sodium (mg)
P	24.32 ± 9.2	162.32 ± 35.34
G	19.13 ± 14.2	171.21 ± 38.2
C	9.00 ± 3.2	200.00 ± 35.4

Table 3: Sedation score at different time intervals postoperatively (mean ± SD)

Group	1 hour	2 hour	6 hour	12 hour
P	1.98 ± 0.24	1.99 ± 0.12	1.92 ± 0.26	1.29 ± 0.42
G	1.87 ± 0.35	1.97 ± 0.18	1.90 ± 0.31	1.37 ± 0.43
C	1.45 ± 0.572	1.49 ± 0.46	0.88 ± 0.38	0.35 ± 0.27

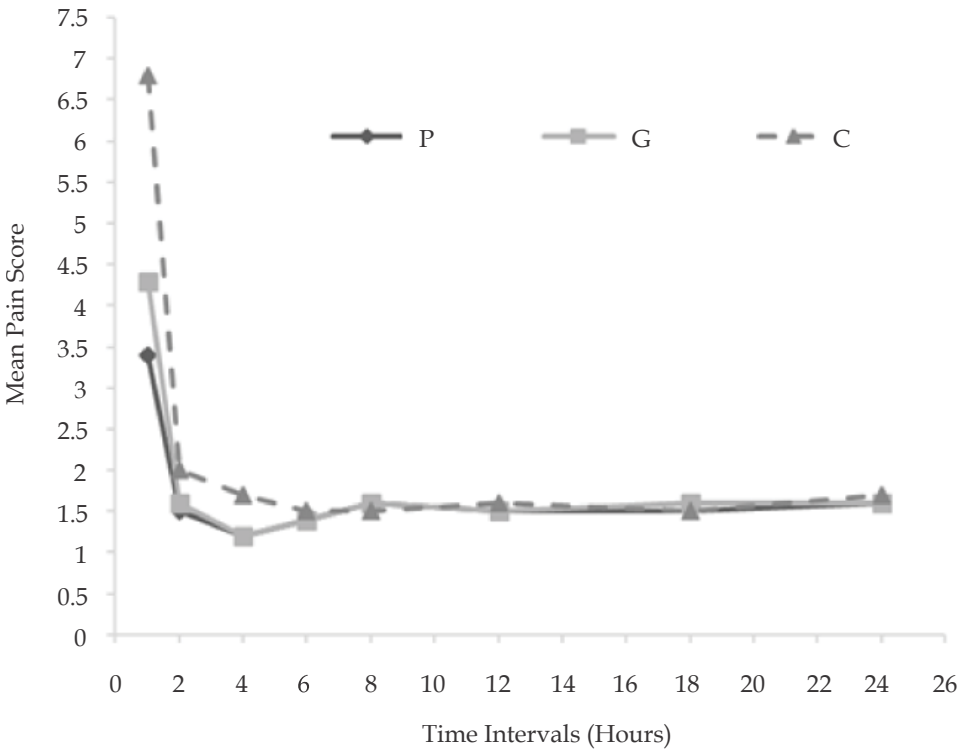

Fig. 1: Visual analogue scale (VAS) scores for pain at rest postoperatively in different time intervals. Time 0 is taken as admission to the recovery. Results are expressed as mean (SD). Patients in pregabalin and gabapentin groups had lower mean pain scores in the initial hour of recovery than placebo group. However, pain scores were subsequently similar in all the groups

groups. Figures 1 display postoperative pain scores over time. Patients in pregabalin and gabapentin groups had lower mean pain scores than placebo in the initial hour of recovery. However, pain scores were subsequently similar in every group.

Discussion

The study reveals that pregabalin 300 mg and gabapentin 600 mg, given orally 2 hours before LSCS significantly reduced postoperative analgesic requirement compared with placebo. This finding is in agreement with the pharmacokinetic profile of both the study drugs as they have short elimination life (6–8 hours) after a single dose. Their administration 2 hours prior to surgery appeared rational in order to attain maximal plasma concentration at the time of surgical stimuli though pregabalin is rapidly absorbed (peak: within 30 minutes to 2 hours) and gabapentin is slowly absorbed (peak: 2 hours). Two hours lapsed easily by the time patient received the drug and skin incision was given, which gave sufficient time to achieve peak effect of both the drugs.

In a study of patients undergoing infraumbilical surgery, it was found that gabapentin and pregabalin when given preoperatively in absence of an opioid or nonopioid analgesic, prolong the analgesic effects of spinal analgesia, which far exceeds the normal duration of spinal analgesia. The analgesic effect is longer lasting following pregabalin as compared to gabapentin (8.98 hr in Gabapentin vs 14.17 hr in Pregabalin group).[8] There are many studies showing that gabapentin in postoperative pain relief in various surgical procedures, but there is very little data regarding placebo-controlled studies of pregabalin in acute pain states. In comparison to the above studies, premedication with 150 and 300 mg pregabalin reduced analgesic consumption in laparoscopic hysterectomy.[10]

Mean pain scores was reduced with a preoperative dose of gabapentin and pregabalin in the initial hour of recovery in this study which is consistent with previous studies.[11,12] There was no difference after the initial hour. It may be due to the reason that gabapentin and pregabalin have a relatively short half-life and were given as a single preoperative dose. The incidence of side effects did not differ among all the groups except sedation and vomiting. Sedation with their use has been reported in previous studies also, but it had no effect on ambulation and discharge.[11,12]

Gabapentin and pregabalin also reduce movement-evoked pain which may cause enhanced functional postoperative recovery.[13] Postoperative opioid sparing is of questionable relevance since few trials have shown reduced opioid-related adverse effects. In one study by Jesper *et al.*[13] showed substantial reduction in movement-related pain 2 and 4 h after radical mastectomy after a single dose of 1,200 mg oral gabapentin administered preoperatively but reduction was not significant at rest. This could be explained by prevention or reduction of the development of central neuronal hyperexcitability induced by the surgical procedure as only evoked pain during movement was significantly decreased, in contrast to pain at rest.

Sedation and dizziness are the two most common side effects associated with gabapentin and pregabalin. The incidence reported in present study is similar to earlier studies.[11] This is usually not disabling and antianxiety effect has been found to be favorable in some studies.[14]

The limitation of the present study is that single dose of gabapentin and pregabalin has been used. The half-life of gabapentinoids is 5–7 hours and conclusions about the optimal dose and duration of the treatment cannot be made. Though no major difference was seen in pregabalin and gabapentin in the present study, further studies are needed to determine the long-term benefits, if any, of perioperative gabapentin and pregabalin comprehensively.

To conclude, postoperative analgesia was better with 600 mg gabapentin and 300 mg pregabalin than placebo during the early recovery after LSCS. Gabapentinoids like pregabalin and gabapentin are an effective drug in the treatment of postoperative pain.

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Original Research Article

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A Comparative Study to Evaluate the Efficacy of three Different Doses of Intraoperative Infusion of Intravenous Preservative Free Lidocaine in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Background: Surgical stress and pain elicit a consistent and well-defined metabolic response, involving release of neuroendocrine hormones and cytokines, which leads to a myriad of detrimental effects. Lidocaine is a local anesthetic and antiarrhythmic which has anti-inflammatory, analgesic and anti-hyperalgesic properties. There are studies comparing differentt doses of infusion for varying periods of time, our study was aimed to evaluate the efficacy of intraoperative infusion of three different doses of intravenous Lidocaine in patients undergoing Laparoscopic cholecystectomy. *Methods:* Forty-eight inpatients were divided into 3 groups of 16 each. All the groups received intravenous lidocaine infusion of 1.5 mg/kg bolus over 10 min, 30 min before the skin incision followed by 1 mg/kg/hr in Group A, 2 mg/kg/hr in Group B and 3 mg/kg/hr in Group C infusion throughout the surgery and continued for 1 hour after the skin closure. The outcome measures are the time at which first visual analogue scale (VAS) was more than 4 requiring rescue analgesia of Inj Tramadol, total number of doses and side effects of lignocaine in 24 hours of postoperative period. *Results:* Onset of breakthrough pain (VAS>4) was significantly prolonged in Group C than Group A and B. Time for first rescue analgesia was significantly prolonged in Group C than Group A and Group B. Overall Analgesic consumption was significantly lower in Group C than other groups. *Conclusion:* Intraoperative infusion of intravenous preservative free Lidocaine at 3 mg/kg/hour is more efficient than 2 mg/kg/hour and 1 mg/kg/hour in controlling postoperative pain and reduces the requirement of postoperative analgesics.

Keywords: Lignocaine infusion; Pain; Postoperative analgesia.

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Introduction

Acute postoperative pain is a complex physiologic reaction to tissue injury, visceral distension or disease which is manifested by autonomic, psychological and behavioral responses that result in patient specific unpleasant, unwanted sensory and subjective emotional experience. Moderate to severe acute pain, regardless of site, can affect nearly every organ function and may adversely influence postoperative morbidity and mortality. Opioids remain the primary pharmacologic therapy for moderate to severe postoperative pain with side effects such as nausea, vomiting[1], constipation, urinary retention and ventilatory depression. Non-opioid analgesics NSAIDS, COX-1 and COX-2 inhibitors is used to treat minor or moderate acute postoperative pain. These are hepatotoxic, affect platelet function with gastrointestinal bleeding risk.[2] Local anesthetic (LA) are increasingly being

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used in the treatment of chronic malignant and non malignant pain.[3] It provides effective postoperative analgesia, reduces opiate consumption, accelerates the recovery of bowel function and facilitates rehabilitation after surgery with a good safety margin.[4] There are studies conducted on the varying doses of preservative free lidocaine infusion from 1.5–5 mg/kg/hr[5–7] on the requirement of postoperative analgesics. Our study is aimed to evaluate the efficacy of intraoperative infusion of three different doses of intravenous (IV) lidocaine.

Materials and Methods

This randomized double blind clinical study was approved from Institutional Ethical Committee. Sample size was calculated assuming a difference in total analgesic requirement of at least 20% with different doses of IV lidocaine infusion. With the alpha error 0.05 and 80% power we found 14 patients were required in each group. We included 16 patients in each group to compensate for dropout. Forty-eight patients fulfilling inclusion criteria who were willing to give informed consent were included in the study. Then patients were divided into three groups of 16 patients each by using the computer generated randomization table (http://www.randomizer.org). Allocation concealment done by sealed envelope method into 3 study groups. Patients providing written informed consent voluntarily, posted for elective laparoscopic cholecystectomy, between 18 and 60 yrs of either sex, ASA Grade I and II with body mass index between 19 and 28 were included in the study. Patients with known hepatic or renal dysfunction, any cardiac dysrhythmias or atrioventricular block, allergic to the study drug were excluded from the study. During the preoperative assessment education regarding use of VAS was given to the patients. All patients were kept nil per orally for 8 hours. On arrival to the pre-operation room, intravenous access was secured. Non Invasive Blood Pressure (NIBP), Pulse Oximetry and Electrocardiogram (ECG) were connected. The baseline systolic, diastolic and mean arterial blood pressures (SBP, DBP and MAP), heart rate (HR) and oxygen saturation (SpO_2) were recorded. Drug infusion was prepared by the anesthesiologist who was not involved in the study. All the subjects in all the three groups received intravenous preservative free lidocaine bolus infusion at the dose of 1.5 mg/kg over 10 minutes, 30 minutes before the skin incision. Bolus dose was followed by continuous infusion as follows:

Group A received a continuous IV infusion at the dose of 1 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

Group B received a continuous IV infusion at the dose of 2 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

Group C received a continuous IV infusion at the dose of 3 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

On arrival to the operating room, NIBP, Pulse Oximetry and ECG were connected. SBP, DBP, MAP, HR and SpO_2 monitoring continued perioperatively. Intubation was done according to the Institute protocol. Persistent intraoperative tachycardia and hypertension was managed by deepening the plane of anesthesia with additional opioids who were excluded from further analysis. The patient was extubated once the consciousness regained and was transferred to the post-anesthesia care unit (PACU), where the infusion was continued for 1 hour following surgical skin closure. In PACU, hemodynamic variables and any signs of adverse effects like light headedness, perioral numbness, nausea and vomiting, Ramsay sedation score, arrhythmias, hypotension and Aldrete score were monitored and recorded at every 15 minute interval. Aldrete score more than or equal to 8 is taken as a discharge criteria from PACU to the surgical wards. In surgical wards hemodynamic variables and any signs of adverse effects were recorded every 2 hours for 24 hours after the discontinuation of intravenous lidocaine infusion. Intensity of pain was assessed and recorded immediately after extubation and then at the interval of 15 minutes for one hour in the immediate postoperative period and at the interval of 120 minutes for 24 hours after the discontinuation of lidocaine infusion. The intensity of pain was assessed with VAS by asking the patient to indicate on the 10 cm line at the point that corresponded to the level of pain intensity they felt. The distance in centimeter from no pain end of VAS (Appendix)[8] to the patient's mark was used as a numerical index of the severity of pain. Time for first rescue analgesia was recorded when patient's VAS score was more than 4 and was treated with Inj.Tramadol 50 mg IV. Further VAS score was assessed at the minimal interval of 2 hours in the first 24 hours and Inj.Tramadol was administered when the VAS score was more than 4. The total dose of analgesia consumed in 24 hours was recorded. Any adverse effects were monitored.

Statistical Analysis

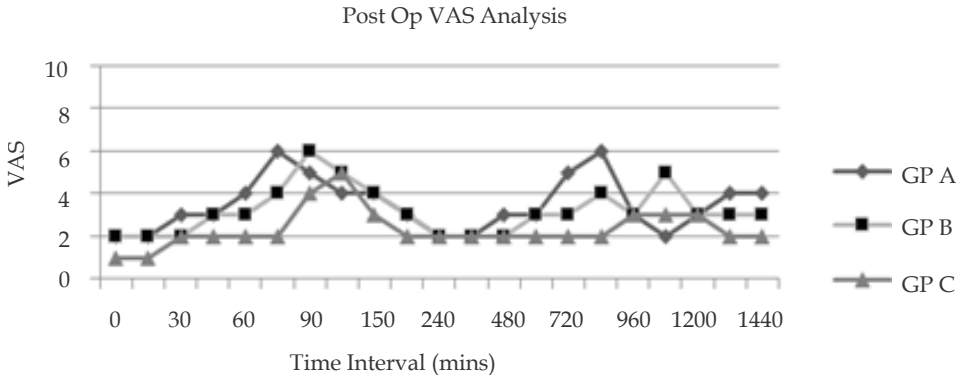
Data was entered into Microsoft excel sheet and was analyzed using SPSS 21 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for parametric data ANOVA test was used as test of significance for non-parametric data. *p* value of < 0.05 was considered to be statistically significant.

Results

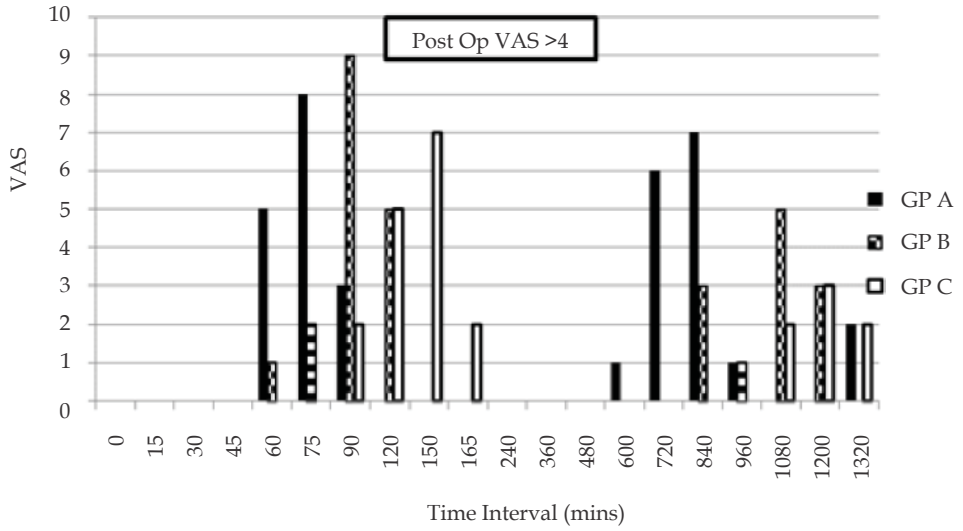
Demographic data (Table 1) did not differ significantly with respect to age, gender, ASA score, height, BMI and duration of surgery between the groups. Onset of breakthrough pain (VAS > 4) was significantly prolonged in Group C than Group A and B. Subsequent VAS were significantly

Table 1: Demographic Characteristics

	GP A	GP B	GP C
Age (yrs)	45.25 ± 5.56	43.94 ± 9.09	42.69 ± 7.49
Sex (M:F)	03:13	02:14	02:14
Weight (kg)	62.19 ± 6.96	61.44 ± 7.24	62.56 ± 5.96
Height (m)	1.64 ± 0.15	1.57 ± 0.20	1.59 ± 0.21
BMI (kg/m^2)	23.81 ± 2.67	23.92 ± 3.22	24.27 ± 2.33
ASA (1:2)	09:07	10:06	10:06
Duration of surgery (mins)	58.75 ± 9.57	58.13 ± 10.46	59.38 ± 9.258



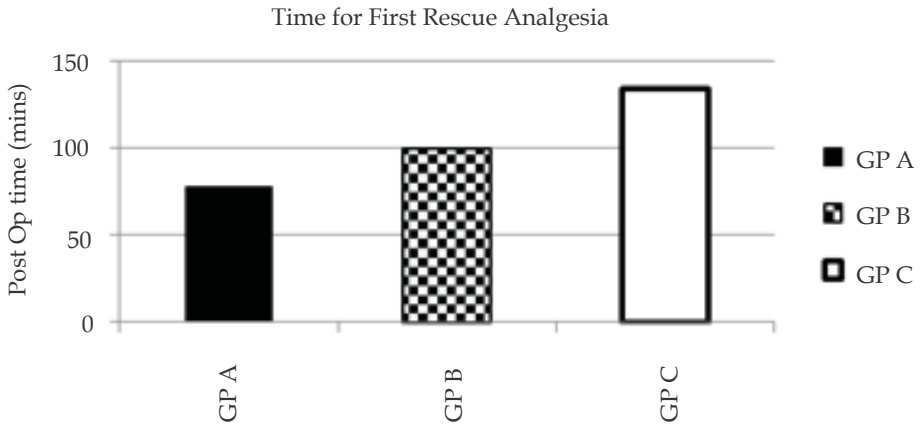
Graph 1: Postoperative VAS analysis



Graph 2: Postoperative VAS >4

Table 2: Time for First Rescue Analgesia

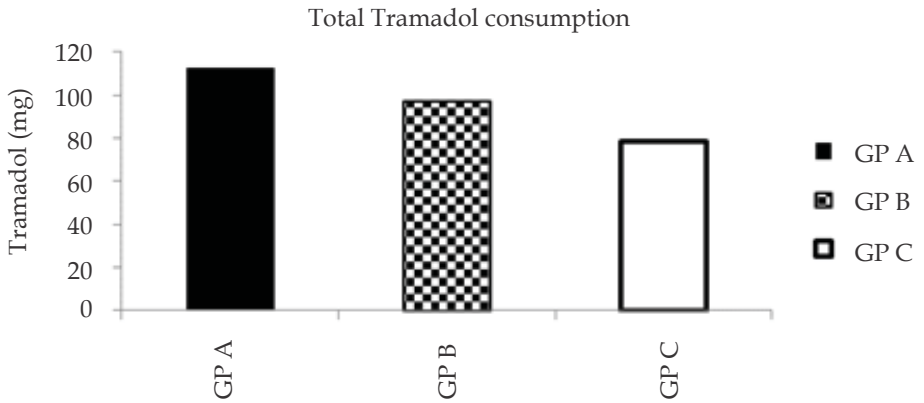
	GP A	GP B	GP C	*p* value
Time for First Rescue Analgesia (min)	77.81 ± 12.51	99.38 ± 17.21	134.06 ± 22.89	0.001*



Graph 3: Time for first rescue analgesia

Table 3: Total Tramadol Consumption in 24 Hours

	GP A	GP B	GP C	*p* value
Total tramadol consumption (mg)	112.50 ± 22.36	96.88 ± 22.12	78.13 ± 25.62	0.001*



Graph 4: Total analgesia consumed in first 24 hours

lower in Group C than Group A and B. Number of patients with VAS > 4 was significantly lower in Group C than other two Groups (Graph 1 and 2). Majority of the patients received their first rescue analgesia by around 75 min in Group A, 120 min in Group B and around 150 min in Group C (Table 2, Graph 3). Total tramadol consumption was 112 mg in Group A, 97 mg in Group B and 78 mg in Group C ($p < 0.001$) which was significantly lower than in Group A and B in first 24 hours (Table 3, Graph 4). There was delayed recovery in Group C when compared to other two groups.

Discussion

Lidocaine when administered intravenously reduces acute pain by decreasing ileus and postoperative nausea and vomiting.[9] IV lidocaine has analgesic[10], anti inflammatory[11] and anti hyperalgesic properties.[12] Molecular and genetic studies indicate that LA primarily inhibit glycine receptors.[13] LA block the generation, propagation and oscillations of electrical impulses in electrically excitable tissue both peripherally and centrally.[14,15]

Safety level of the IV lidocaine was considered with respect to the study[10,16,17] when administered as infusion where the plasma level of lidocaine was below the toxic level.

In our study, patients posted for elective laparoscopic cholecystectomy under general anesthesia with perioperative IV lidocaine being administered at 3 mg/kg infusion for 1 hour post skin closure had significantly prolonged onset of break through pain with VAS > 4 than in patients who received 1 mg/kg/hr and 2 mg/kg/hr infusion. Our study showed opioid sparing properties like nausea and vomiting which can delay the hospital discharge, increasing the expenditure[18,19] and patient dissatisfaction. Postoperative analgesic requirement was significantly lower in Group C than with Group A and B. But with lidocaine infusion of 3 mg/kg had delayed awakening from patients being less responsive to endotracheal tube. But study has showed PACU discharge was not delayed[20] in Group C. Perioperative lidocaine had the advantage of blunting sympathetic responses to tracheal intubation and extubation.[21] Complications related to lignocaine infusion was not noticed in our study.

Conclusion

With higher dosage of lignocaine infusion, rescue analgesia and total analgesic requirement was significantly lower. It improved postoperative pain scores in patients. It can be used as an alternative to epidural administration where it is difficult or contraindicated. Lidocaine provides the advantage of not requiring time and expertise in performing tranversus abdominal blocks.[22] Perioperative lidocaine improves postoperative quality of recovery in patients undergoing ambulatory surgery.[23] It is less expensive, easy to administer and relatively safe so can be used as an alternative intervention with wide potential applicability.

Limitations

We have not measured serum lidocaine levels. Also the effect of short-term lidocaine infusion on duration of hospital stay was not studied.

Source of support: Nil

Presentation at a meeting: Nil

Conflicts of interest: None

Appendix:

Visual Analogue Scale (VAS)

Ranging from zero (No pain) to ten (Maximal pain)

0 – No pain

1,2 – Mild, annoying pain

3,4 – Nagging, uncomfortable troublesome pain

5,6 – Distressing, miserabe pain

7,8 – Intense, dreadful horrible pain

9,10 – Worst possible unbearabe, excruciating pain

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Case Report

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Mucopolysaccharidosis and Anesthetic Challenges

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Abstract

Rare diseases and syndromes are of special interest to pediatric anesthesiologits, as each of them has very specific anesthesia concerns. Knowledge of the pathophysiology, symptomatology, treatment options of these diseases and tailored anesthesia management forms the basis of provision of safe anesthesia care to these groups of children. Mucopolysaccharidosis are a group of lysosomal storage disorders. They are caused by the total or partial deficiency of one of the eleven enzymes involved in the metabolism of glycosaminoglycans. This deficiency leads to gradual accumulation of glycosaminoglycans in the lysosomes leading to permanent, progressive cellular damage which affects appearance, physical abilities, organ and system functioning and mental development. From the anesthesiologist point of view, these patients have problems with airway management and positioning. Few anesthesiologists get to routinely care for these patients. But individual patients undergo multiple surgical procedures for improvement in quality of life. We present a case of an 11-year-old girl with MPS posted for herniotomy.

Keywords: Mucopolysaccharidosis; Difficult airway; Anesthesia

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Introduction

The mucopolysaccharidoses are a group of inherited, chronic progressive, metabolic diseases and include seven eponymously named syndromes caused by deficiency of 11 different lysosomal enzymes that are required for the catabolism of glycosaminoglycans (heparain sulfate, dermatan sulfate, chondroitin sulfate).[1] The incidence of MPS is 1:25,000. There is accumulation of glycosaminoglycans (GAG) in several body tissues leading to the involvement of multiple organ systems including airway, cardiac, respiratory and skeletal systems. systemic involvement and severity of the disease progress with time. MPS I (Hurler's syndrome) and MPS II (Hurler's syndrome) manifest tracheobronchial complications, cardiac disease (mitral valve involvement, aortic valve anomaly, left ventricular hypertrophy) and hepatosplenomegaly. Restrictive lung disease due to skeletal involvement is seen in MPS IV (Morquio's syndrome) and MPS VI (Maroteaux–lamy syndrome).

Airway obstruction occurs due to macroglossia adenotonsillectomy hypertrophy and deposition of GAG in the pharyngeal wall and larynx.[2] GAG infiltrate the connective tissues of the oropharynx and airways causing airway obstruction, obstructive sleep apnea, difficult mask ventilation and intubation. Submucosal GAG deposits in the upper airway (tongue, floor of mouth, epiglottis,

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ary-epiglottic folds) and tracheal wall impart a rigid anatomy. They also can have a short, immobile neck with limited mobility of the cervical spine and temporomandibular joint further contributing to difficult airway. Odonoid dysplasia and radiographic subluxations of C1 on C2 is common in MPS 1, IV, and VI and may cause anterior dislocation of the atlas and spinal cord compression. They can also have abnormal laryngeal and tracheal cartilage and copious secretions compounding the situation. Older age is associated with increased risk of difficult intubation, due to effect of alteration of MPS.

GAG accumulation in the cardiac tissues, causing valvular abnormalities and insufficiency (myocardial deposits). They also accumulate in the bones, joints, ligaments leading to atlantoaxial instability. Developmental delay and progressive neurological decline are also seen in these patients.

The incidence of anesthesia-related complications is high in MPS patients. Incidence of difficult intubation is 25–80% failed intubation is 2–10% and that of perioperative cardiorespiratory complications range between 5–25%.

In a retrospective review of anesthesia records of 19 children with MPS over a 9-year period, the incidence of respiratory and cardiovascular complications was 24% and 4% respectively.[3] The respiratory complications were airway obstruction at induction, difficult mask ventilation, difficult intubation and failed intubation. Airway obstruction during emergence occurred after 13 anesthetics. The cardiac complications were hypotension, bradycardia and perioperative circulatory arrest.

In a recently published retrospective analysis of 54 patients with MPS in an Italian tertiary referral center, 16 patients had at least 1 anesthetic complication during their clinical course.[4] Hypoxia, airway obstruction, hypoventilation and laryngospasm was observed in 11, 4, 4 and 2 procedures, respectively. 19 (29%) of intubation attempts were difficult and of these 3 were achieved with fiberoptic technique, 6 by video-assisted laryngoscopy and the remaining by repeated direct laryngoscopies. During 3 (1.8%) of these cases, face mask ventilation was inadequate to provide oxygenation, emergency intubation failed and patients were salvaged with the LMA. However, there is also a case report of failure of the LMA to secure the airway in a patient with MPS type II (Hunter's syndrome), where a subsequent rigid bronchoscopy revealed a pedunculated polyp just above the epiglottis, with diffuse infiltration of the pharyngeal and laryngeal mucosa and a smaller trachea.[5]

Postobstructive pulmonary edema during anesthesia in 5 patients with severe form of MPS has also been reported.[6] Chronic myelopathy can lead to central hypoventilation, which together with respiratory muscle weakness can lead to difficulty in extubation.

Case Report

An 11-year-old girl was posted for inguinal hernia repair. She was diagnosed as a case of MPS at one year of age and is under regular management with physiotherapy. At the time of diagnosis she was found to have a left inguinal hernia with bowel loops, left ovary and uterus as contents. She also had a small VSD. Because of these reasons, the hernia repair was deferred to a later age. At present, she was short for her age with delayed milestones. She was alert, very vocal and her intellect seemed to be normal. There was mild scoliosis and deformities of fingers. Facial features were coarse with flat nasal bridge, small mouth with crowded teeth and retrognathia. She had a history of snoring and slept comfortably only in lateral decubitus position. Her skin was dry with poorly visible veins. She had a skin dimple in the sacral region. Port-wine stains were present in the neck and chest. Lab investigations were within normal limits. Echocardiogram showed no evidence of residual VSD. Airway assessment showed a small mouth with crowding of teeth. Mallampatti was grade 2. MRI neck did not show any evidence of spinal cord compression.

An intravenous access was secured in the preoperative ward. Because of anticipated airway shifting on to the table, she was hooked on to monitors. Sevoflurane stepwise increase from 2% to 6% was used to induce the patient. Once induced, trial laryngoscopy was done. Vocal cords were not visualized with Cormack lehane grade 4. A size 2.5 LMA was inserted successfully and anesthesia maintained with O_2/N_2O 33%/66% and titrated Sevoflurane through a Jackson Rees circuit. Analgesia provided with 2 mics/Kg Fentanyl and hernia block with 10 mL 0.25% Bupivacaine. Intraoperative period was uneventful. Sevoflurane was cut at the last skin suture and LMA was removed after full recovery. Oxygen supplementation was given for 6 hours in the postanesthesia care unit and she was discharged after 36 hours.

Discussion

MPS are rare conditions, incidence varying from 1 in 24,000–5, 00,000 population.[7]

There are seven types of MPS. Hurler's syndrome being the prototype.

MPS cases are notorious for airway difficulties and are a challenge in anesthesia. They are rare and few anesthesiologists get to serve these patients. In contrast, these patients are in frequent need of medical attention. MPS causes accumulation of unmetabolized molecules in the connective tissue leading to swollen tongue and parapharyngeal tissues.[8] This can lead cause airway obstruction in a ball valve fashion in anesthetized and paralyzed patients. In addition, in some types of MPS there is a specific risk for compression of the cervical spinal cord (Metabolic myelopathy). Hurler's (1H), Morquio (IV), Maroteaux-Lamy (VI) and Sly (VII) syndromes are known for cervical canal narrowing.[8,10] This is due to thickening of duramater and hypoplasia of dens axis. These changes make direct laryngoscopic visualization of vocal cords both difficult and risky. Failure to control the airway is the largest single cause of perioperative mortality. Supraglottic airway devices like the laryngeal mask airway have been found to be useful in maintaining airway in this population. The advantage of LMA is the ease of positioning without excessive neck extension and without muscle relaxant.[2,9] The use of volatile induction and maintenance anesthesia (VIMA) helps in easy titration of depth thereby giving greater control over airway during induction. The deposits of mucopolysaccharides in lower airways results in diffusion defects — hypoxia and hypercarbia. This may lead to secondary pulmonary hypertension.[7,10] Supplemental analgesia with nerve blocks decreases requirement of opoids enabling earlier discharge from post Anesthesia Care Unit.

Conclusion

Children with congenital syndromes with multiple anomalies need a multidisciplinary approach to their care. It is advisable to actively look for specific anomalies associated with the particular syndrome. Systems that may be affected include cardiovascular, respiratory, airway, spine, coagulation, metabolic and endocrine systems. Specific websites and books are also available as references. An individualized tailored approach to anesthesia care is important to avoid anesthetic complications in these special groups of children.

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Case Report

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A Multidisciplinary Approach to Anesthetic Management of a Patient with Severe Aortic Stenosis for Bipolar Hemiarthroplasty: A Case Report

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Abstract

The increase in geriatric population with preexisting cardiac disease presenting for non-cardiac surgery is in escalating numbers. Aortic stenosis is a significant risk factor for the development of cardiac complications after non-cardiac surgery. According to the American college of cardiology recommendations, it is advisable to postpone any elective surgery in patients with aortic stenosis without proper optimization. We report about a 79-year-old female with severe aortic stenosis with left sided fracture neck of femur for bipolar hemiarthroplasty. Procedure was done under general anesthesia with fascia iliac block and intraoperative and postoperative course was uneventful.

Keywords: Aortic stenosis; Anesthesia; Non cardiac surgery.

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Introduction[1,2]

Patients with severe Aortic stenosis who require non-cardiac surgery poses a challenge to the anesthesiologist. The prevalence rates for severe AS range from 3.4% in subjects more than 75 years to 18% in older than 90 years.[3] The incidence of severe AS in patients who need surgery for hip fracture is between 5% and 10%.[6] Although after hip surgery 30-day mortality in severe AS is between 7% and 14%,[7–9] these data may be an underestimate since the diagnosis of AS is not uncommonly missed before surgery.[4] For these to undergo aortic valve replacement before the elective non-cardiac surgery the risk associated with the non cardiac surgery should be greater than the valve replacement procedure. AS most commonly occurs as an acquired condition but can occur as a congenital disease as well. Congenital bicuspid aortic valve are more prone for calcification with eventual stenosis.[5]

Case Report

A 79 year old female was admitted with left sided fracture neck of femur and was planned for bipolar hemiarthroplasty. Her weight was 60 kg. She was a known case of severe aortic stenosis. She was a diabetic for 7 years after having undergone Whipple's procedure for ca pancreas and on metformin. On examination she was conscious, her HR was 62/min, BP-140/100 mm Hg, SpO_2 - of 95% in Room air and Respiratory rate-15/min.

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She was edentulous with an interincisor gap of less than 2 fingers. There was an ejection systolic murmur not conducted to the carotids. There were no basal crepitations. Examination of other systems were normal.

Her routine blood investigations were within normal limits. Prothrombin time was 13.8, INR-1.1. ECG showed sinus rhythm with left axis deviation and ST segment depression in II, V1–V5. Echocardiography showed severe calcified aortic valve with pressure gradient 108.7 mm hg, and aortic valve area of 1 cm 2 mild AR and concentric left ventricular hypertrophy. Cardiologist opinion was sought and fitness was given under ASA III. T. Clopidogrel was stopped 5 days prior to the surgery.

In the OR the patient was noted to have an HR of 62/min with sinus rhythm, NIBP-156/62 mm hg, SpO^2 -97% in Room air. Inj phenylephrine, nor adrenaline infusions, defibrillator pads and airway crash cart were kept ready. Under aseptic precautions at injecting 2% lignocaine skin infiltration left radial artery was cannulated and secured for beat to beat BP monitoring. Preoxygenation was done for 3 minutes and premedicated with Inj ondansetron and Inj fentanyl 60 mcg, and induced with Inj etomidate 12 mg and Inj atracurium 30 mg, after giving 3 ml of 2% xylocard iv and lignocaine spray over the cords she was intubated and depth of anesthesia was achieved with oxygen, nitrous oxide and sevofluorane. Blood pressure dropped to 90/60 mm hg and hypotension was managed with Inj phenylephrine bolus dose of 30 mcg. Under ultrasound guidance fascia iliaca block was given with Inj 0.2% ropivacaine 15 ml + Inj lignocaine 2% 15 ml + distilled water 10 ml. intraoperatively HR was 57/min IBP-136/52 mm hg, SpO_2-100%, Urine output -40 ml/hr and $ETCO_2$ -37. There were no episodes of hypotension and no significant blood loss. The procedure lasted for around an hour. The patient was extubated fully awake after taking adequate precautions to prevent extubation response by giving 3 ml of 2% lignocaine iv and shifted to ICU for observation. She was shifted from ICU to ward the next day and discharged on postoperative day 4.

Discussion

Patients with severe AS have a low fixed Cardiac output and avoidance of hypotension is the critical step in the management of the case. Hypotension can initiate a cascade of events which can lead to cardiac arrest. If there is sudden decrease in contractility chest compressions will not maintain cardiac output.[6] Due to diastolic dysfunction and impaired relaxation of left ventricle the atrial contribution which accounts for nearly 40% of the cardiac output should be preserved. Ischemia leads to reducedcardiac output and decreased blood pressure further compromising coronary perfusion.[5] All possible attempts are to be taken to maintain sinus rhythm to maintain atrial kick. Any tachycardia and bradycardia should be avoided. Bradycardia is avoided because cardiac output becomes low in fixed aortic orifice state. Tachycardia can jeopardize diastolic filling time and increased left ventricular strain increasing oxygen demand.

General anesthesia is often preferred to epidural or spinal anesthesia because the sympathetic blockade produced by regional anesthesia causing hypotension leading to reduced coronary perfusion. Induction can be accomplished with an intravenous induction drug that does not decrease the systemic vascular resistance. An opioid induction agent may be useful if left ventricular function is compromised. Ketamine induces tachycardia and should be avoided.

Maintenance of anesthesia can be accomplished with a combination of nitrous oxide and volatile anesthetic agent and opioids or with opioids alone. Muscle relaxants with minimal hemodyanamic effects are best. Intravascular fluid volume should be maintained at normal levels since these patients are preload dependent.

Meticulous attention to hypotension is to be given and treated with alpha agonists such as phenylephrine that do not cause tachycardia and therefore maintain diastolic filling time. Persistent tachycardia is to be treated with beta blockers such as esmolol. Supraventricular tachycardia should be treated by cardioversion. Lignocaine, amiodarone and a defibrillator should be kept ready in the operating room since these patients have a propensity to develop ventricular dysrhythmias.

Patients of valvular heart disease may often be found on various medications like antibiotic prophylaxis for infective endocarditis, especially in patients with congenital heart disease, cardiac transplantation[8–10] anticoagulants, betablockers, statins, nesiritide etc. This patient was on T. clopidogrel. Patients with valvular heart disease often require anticoagulation for associated finding such as atrial fibrillation. Non-cardiac surgery in prosthetic valve patients poses risk of IE, bleeding and acute and subacute valve thrombosis with interrupted anticoagulation. The current guidelines recommend withdrawal of oral anticoagulation

72h before surgery to lower the INR to <1.5 and maintain anticoagulation with unfractionated heparin. The APTT is maintained twice the control value.[11] The use of beta-blocker in patients with stenotic valvular lesions has to be made on case-to-case basis and correlated with hemodynamic variables.[12] Statins exert their effect by plaque stabilization, anti-atherosclerotic, anti-thrombotic, vasodilative and anti-inflammatory properties.[13,14] Although there are no conclusive data to suggest the benefit of statin therapy in valvular heart disease, discontinuation of statin therapy is associated with worsened outcome.[14,15] Nesiritide is a recombinant brain-type natriuretic peptide (BNP), which decreases PA pressures and myocardial oxygen consumption while increasing coronary flow and urine output.[16]

Conclusion

Severe AS mandates a meticulous planning with thorough preoperative work up to make a rationale choice of management. General anesthesia is preferred in such cases to provide hemodynamic stability. Advantages of using fascia iliac block over neuraxial technique would be avoidance of hemodynamic stability, as a form of postoperative analgesia, better patient statisfaction and reduced number of complications. Identifying potential intraoperative problems and timely intervention is important in achieving desired goals.[7]

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Discussion

Include summary of key findings (primary outcome measures, secondary outcome measures, results as they relate to a prior hypothesis); Strengths and limitations of the study (study question, study design, data collection, analysis and interpretation); Interpretation and implications in the context of the totality of evidence (is there a systematic review to refer to, if not, could one be reasonably done here and now?, What this study adds to the available evidence, effects on patient care and health policy, possible mechanisms)? Controversies raised by this study; and Future research directions (for this particular research collaboration, underlying mechanisms, clinical research). Do not repeat in detail data or other material given in the Introduction or the Results section.

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List references in alphabetical order. Each listed reference should be cited in text (not in alphabetic order), and each text citation should be listed in the References section. Identify references in text, tables, and legends by Arabic numerals in square bracket (e.g. [10]). Please refer to ICMJE Guidelines (http://www.nlm.nih.gov/bsd/uniform_ requirements.html) for more examples.

Standard journal article

[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540-7.

[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, *et al*. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347-55.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3-9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792-801.

Unpublished article

[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

Personal author(s)

[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O,

Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. p. 7-27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

Reference from electronic media

[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/theme_health/HSQ20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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