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INDIAN JOURNAL OF ANESTHESIA AND ANALGESIA

January - February 2021
Volume 8 Number 1

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Greetings from the Desk of Editor-in-Chief

Pallavi Ahluwalia

On behalf of Indian Journal of Anesthesia and Analgesia (IJAA), the editorial board, and the whole Editorial team, I extend my greetings for this wonderful year 2021 ahead. It is a great honour and privilege for me to be appointed as Editor-in-Chief of the IJAA. I hope to follow the benchmark laid by my preceding editor, Dr. K. K. Mubarak and strive to improve it further.

The importance of critical peer review and ethics in manuscript handling for ensuring scientific values of publication work, as well as the importance of editorial team efficiency, cannot be undermined. The success of any scientific journal is primarily dependent on the submission of high-quality manuscripts, the dedication of its editorial board members, and the excellence of those reviewing the manuscripts. In an era when major journal publication can take several months after a paper is accepted, the open-access online format of IJAA provides a platform for timely publication without undue delay. The goal of a scientific publication is to advance the knowledge of the discipline as a whole, not just to add to an author's publication list or simply fulfilling the requirement of professional advancement.

We will take the utmost care in conducting rigorous peer reviews of all submitted manuscripts to accept only high-quality content with no conflict of interest for publication. I'd like to take this opportunity to remind all authors to follow the journal's guidelines while preparing their manuscripts to avoid unnecessary delays in the editorial process and the disappointment of rejection.

We have had many good research articles on issues related to current COVID pandemic. This year we will plan special issues related to relevant topics and a post graduate issue, which will be of immense help to our post graduate students. Currently the type of articles published includes Editorial, review, mini-review, systematic review, meta-analysis, and clinical research, Letter to Editor and case reports. We will try to expand it further to View points and Clinical guidelines.

We are constantly working to increase the number of reviewers who will be assigned to future journal submissions. I will explore new ways to improve journal manuscript handling efficiency using modern electronic applications and tools with my editorial staff. We will strive for a quick turnaround time from submission to decision, as well as the addition of review articles of current interest and more subsections for the benefit of authors and readers. I will work with my editorial team to improve quality, and we encourage the submission of more original articles as well as the citation of relevant Indian literature published in this journal in your future publications.

As I take on this new role, I welcome feedback from you, our readers and contributors, to improve the overall quality of the journal. I will work tirelessly with our editorial board's scholarly team to elevate the journal to the next level. IJAA welcomes your manuscript submissions and hopes that you have a pleasant experience working with our editorial staff.

With best wishes for a very happy and prosperous 2021.

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Potassium Chloride as an Adjuvant to Lignocaine and Bupivacaine in Brachial Block for Orthopedic Surgeries

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Abstract

Background: Brachial Plexus block is the easiest and simplest form of providing anesthesia for upper limb surgeries. It is known that potassium added to local anesthetics can increase the extracellular concentration, time of depolarization and prolongation of action of the local anesthetics. With this in background, this study was designed to observe the effect of potassium chloride as adjuvant to local anesthetics on onset of sensory and motor blockade and qualitative block for analgesia.

Materials and Methods: Forty patients of ASA I and II of either sex, aged 17 to 61 years posted for upper limb orthopaedic surgeries received either plain Inj. Xylocaine 1.5% (A1), Inj. Xylocaine 1.5% with Inj. Potassium Chloride 0.2 mmol (A2), plain Inj. Bupivacaine 0.375% (B1) or Inj. Bupivacaine 0.375% with Inj. Potassium Chloride 0.2 mmol (B2) in Brachial Plexus block through Supraclavicular approach. Patients were assessed for the onset of sensory and motor blockade, duration of anaesthesia and post-operative analgesia.

Result: Groups A2 and B2 (potassium added groups) had faster onset of sensory and motor blockade, and prolonged duration of action than A1 and B1 (plain Xylocaine and Bupivacaine) groups. The quality of blockade was better in groups with added potassium, more so with Bupivacaine than with Xylocaine.

Conclusion: Addition of Potassium chloride to Xylocaine and Bupivacaine had significant clinical advantage over Plain drugs specially Bupivacaine on onset time, duration and quality of sensory and motor blockade in Brachial Plexus block.

Keywords: Lignocaine; Bupivacaine; Potassium chloride; Brachial Plexus block.

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Introduction

Brachial plexus block is the easiest and effective form of providing anesthesia and analgesia to the major part of upper limb for upper limb surgeries. It is even the safest in emergency procedures where associated conditions may not advocate the rationale of General Anesthesia. Regional Anesthesia still stands highest potential in safety if done in expert hands. Advantages of regional anesthesia like less

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operation theatre pollution, safe alternative where facilities of general anesthesia are not available and prolonged post-operative analgesia still advocate for its use over general anesthesia unless absolutely contraindicated. Brachial plexus block with one-point injection helps to anesthetize larger area of upper limb. Various factors affect the action of local anesthetic agents used for Brachial plexus block – patient factors, systemic disease, technical factors in administering the drugs for the block, drug induced side effects when more volume is used to facilitate dense block and many more to list. Various local anesthetic agents have been used for the brachial block – if physiological environment be facilitated to reversibly inhibit the nerve conduction it can definitely have its action on the duration of drug used for block. It is known that potassium concentration and glucose level extracellularly can increase the time of depolarization and can increase the action of the local anesthetics. So we attempted to provide a more physiological environment rather than vasoconstrictor drugs to facilitate early onset and prolonged duration of the local anesthetics.

With this in background, this study was designed to study the effect of potassium chloride if added as adjuvant to local anesthetics, instead of vasoconstrictors, on the action of local anesthetics in respect to onset of sensory and motor blockade, duration of total block to facilitate post-operative analgesia and the qualitative effect of the block.

Material and Methods

The present randomized double blind study was carried out in a tertiary Care Hospital in Gujarat. Forty patients of age group 17-61 years of either sex of ASA gr I and II posted for upper limb orthopedic surgeries of various types were included for the study. After a detailed preoperative history of the patients, thorough local and systemic examination (Table 4), & all the requisite preoperative investigations including the bleeding profile, patients were selected for the study with following Inclusion criteria: patients without any serious systemic illness and comorbid conditions, not on anticoagulants, and willing to be a part of the study and Exclusion criteria: Patients with uncontrolled systemic diseases, on anti-coagulants, unwilling for regional anesthesia, failed block. After premedication with Inj. Glycopyrollate 0.2mg, Inj. Midazolam 1mg, Inj. Tramadol 50mg, Inj. Ondansetron 4mg, patients were randomly allocated to be subjected to Supraclavicular Brachial block (Winnie)6 under strict aseptic and antiseptic blind technique to receive either:

- Group A1 (N=10): to receive Inj. Xylocaine 1.5% 25 ml
- Group A2 (N=10): to receive Inj. Xylocaine 1.5% 25 ml + Inj. KCl 0.2 mmol
- Group B1 (N=10): to receive Inj. Bupivacaine 0.375% 25 ml
- Group B2 (N=10): to receive Bupivacaine 0.375% 25 ml + Inj. KCl 0.2 mmol

After administering the block, the patients were observed for immediate inadvertant complications if any, time noted for the onset of sensory and motor blockade (Table 1), and the duration of the block per operative and in the post-operative period and hence the time for requirement of first rescue analgesia and the results in all the groups were compared using Student t test for mean and standard deviation.

Observation and Results

Forty patients of either sex (Table 2) of ASA gr I and II comparable in terms of age, weight (Table 2) posted for planned orthopedic surgeries of upper limb (Table 3) were selected for this study and were randomly divided in four groups of N=10 to receive either of the drug for Brachial plexus block through Supra clavicular approach:

- Group A1 (N=10): to receive Inj. Xylocaine 1.5% 25 ml
- Group A2 (N=10): to receive Inj. Xylocaine 1.5% 25 ml + Inj. KCl 0.2 mmol
- Group B1 (N=10): to receive Inj. Bupivacaine 0.375% 25 ml
- Group B2 (N=10): to receive Bupivacaine 0.375% 25 ml + Inj. KCl 0.2 mmol

It was observed that onset of sensory block in groupA2 (8.1 ± 2.1min) was faster than groupA1 (8.6 ± 1.86min). Also, it was faster in B2 group (7 ± 1.65min) than B1 group (14 ± 2.6min) . (Figure 1). The onset of motor block also showed earlier onset in group A2 (9.8 ± 1.87min) as compared to group A1 (10.4 ± 1.74min) and group B2 (10.9 ± 1.65min) as compared to group B1 (17.6 ± 2.86min) (Figure 2). The earlier onset of sensory and motor block was more significant in the patients receiving Inj. Bupivacaine with Inj. Potassium Chloride compared to Plain Inj. Bupivacaine, which was not that significant in Xylocaine groups.

Figure 4 and Figure 5 show the sensory and motor

block score achieved after the block in all the groups which were comparable as far as the success of the block was considered. We have found that depth of sensory and motor blockade was significantly better in groups with added potassium as compared to plain local anesthetic groups.

Figure 3 shows the mean duration of analgesia in all the four groups. The analgesia in the post-operative period was much more in group B2 as compared to group B1 but the difference between groups A2 and A1 was not much significant.

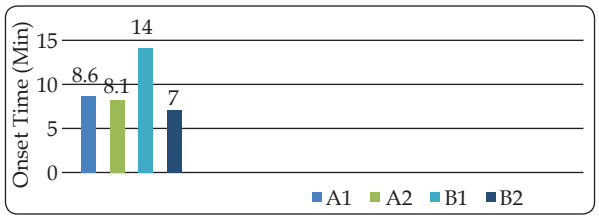

Fig. 1: Onset of Sensory Block in all Groups (Mean ± Sd).

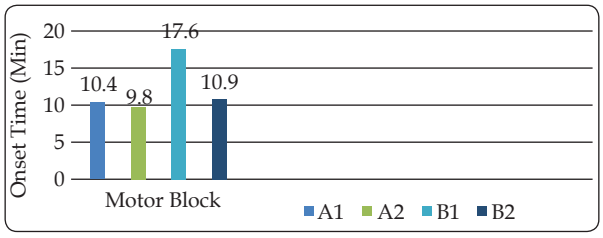

Fig. 2: Onset of Motor Block in all Groups (Mean ± Sd).

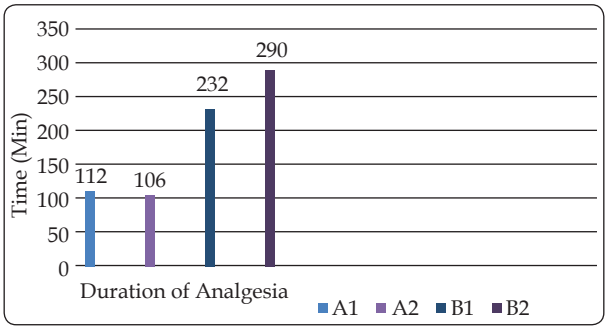

Fig. 3: Duration Of Analgesia (Mean ± Sd).

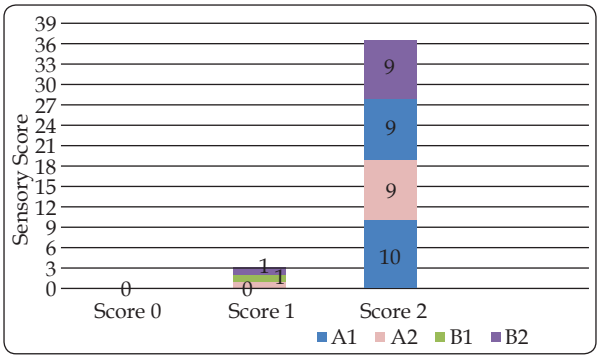

Fig. 4: Sensory Block Score.

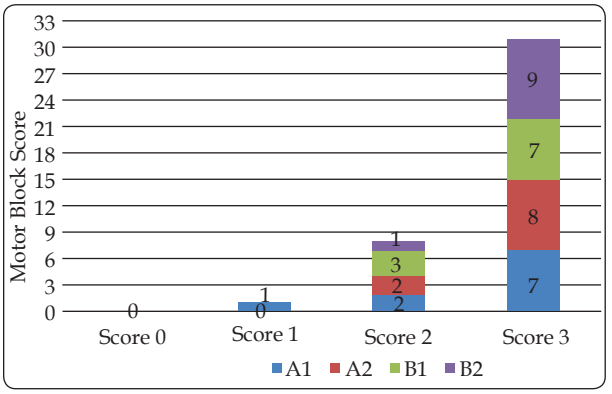

Fig. 5: Motor Block Score.

Table 1: Sensory And Motor Score.

Score	Sensory	Motor
0	Sharp Pain	Able to Move Arm Against Resistance
1	Pain on Touch	Inability to Move Wrist and Elbow Against Resistance
2	No Pain on Touch	Inability to Move Wrist and Elbow Against Gravity
3		Inability to Move Arm

Table 2: Demography Profile of Patients.

Age Group	Number of Patients	Percentage	Sex of the Patients	
Below 20	05	12.5	Male	Female
21-40	21	52.5	30	10
41-60	13	32.5		
Above 60	01	2.2		
Total	40	100	40	

Table 3: Planned Operative Procedure.

Sr. No.	Procedure	A1	A2	B1	B2	Total
1	Both Bone # Orif	02	03	06	05	16
2	Humerus Dcp Plating	01	03	03	02	09
3	K Wire Fixation of both Bone #	05			01	06
4	Tendon Repair	02	01	01	01	05
5	Sequestrectomy		01		01	02
6	Radial Head Excision		02			02
	Total	10	10	10	10	40

Table 4: Associated Medical Conditions.

Sr. No.	Procedure	A1	A2	B1	B2	Total
1	Pulmonary Koch's	02		03		05
2	Hypertensioin	02	03	04	01	10
3	Ischemic Heart Disease	03	03	02	04	12
4	Head Injury	01	01		01	03
5	Bronchial Asthma	02	03	03	02	10

Table 5: Complications.

Complications	Number of Patients	Percentage
Blood on Aspiration	02	5
Hematoma Formation	02	5
Total	04	10

Discussion

Brachial plexus block is widely used in practice for elective forearm and hand surgeries. It provides good intra- and post-operative analgesia. Many adjuvants have been added to local anaesthetic agents in an attempt to prolong their duration of action. Among them, addition of carbonated solution and potassium to local anaesthetic has stood the test of time. Addition of potassium chloride to local anaesthetic solutions increases the extracellular Potassium concentrations and depolarizes the membrane[3]. We conducted study on forty patients with demographic data in terms of age, weight and sex being similar in all groups posted for planned upper limb orthopaedic surgeries. After detailed assessment and explanation of the procedure,the patients were subjected to receive Brachial Plexus block with supraclavicular route (Winnie) bearing in mind complication of pneumothorax in the classical supra clavicular technique. The data collected was analysed for statistical significance by Student's t-test. The onset of the blockade in potassium group was significantly earlier when compared to plain bupivacaine group but not much significant as compared in the Lignocaine group. In our study, the mean onset of sensory and motor blockade in potassium group B2 was17.6 ± 2.86 and 10.9 ± 1.65 minutes, respectively. The results of our study support the findings of Parris and Chamber[7] (1966) who showed that addition of potassium chloride to bupivacaine significantly enhanced the onset of both sensory and motor blockade. In contrast to our study, the delayed onset of blockade proposed by Parris and Chamber[7] may be due to the lower concentration of bupivacaine (0.25%) when compared to our study (0.375%). Khosaand Gupta[5] also in a similar study found early onset of sensory and motor and prolonged duration of analgesia using KCl (5 mmol) as adjuvant with bupivacaine and no significant changes while using Lignocaine. We have found that depth of sensory and motor blockade was significantly better in potassium group when compared to other group. Local Anaesthetic agents are membrane stabilisers and efflux of potassium during the depolarisation prevents the propagation of the nerve impulse.[1,2] If the resting membrane potential is further lowered it will facilitate the halting of the impulse below the normal physiological 120mV. This is achieved by addition of potassium chloride in the extra cellular compartment which will cause some degree of depolarisation and enfeeblement of the membrane potential to prevent the passage of nerve impulse. Thus addition of potassium chloride as adjuvant will definitely shorten the onset time, prolong the duration of action and improve the quality of blockade in brachial plexus block by delaying the repolarisation.[3,4] Areas of further exploration like individual patient variations of anatomy, their response, different concentrations of potassium chloride, study of other agents and sites of blockade can be considered.[5-7]

Conclusion

The present study concludes that addition of potassium chloride to bupivacaine had a significant clinical advantage over plain bupivacaine on onset time, duration, and quality of sensory and motor blockade in brachial plexus block which was not seen with use of plain Inj. Xylocaine.

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To Compare the Effects of Atomized Intranasal Midazolam with Intranasal Dexmedetomidine as Premedication in Children

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Abstract

Background: Successful conduct of anaesthesia in children depends on adequate premedication which comforts the anxious child. Children are vulnerable to stress response because of limited energy reserves, larger brain masses and obligatory glucose requirements. This feeling of worry and nervousness is also seen in the parents of the children undergoing the surgery. Hence premedication becomes important in children in order to avoid anxiety in both children and parents.

Methods: A prospective observational study was conducted in 78 pediatric patients aged between 2 to 10 years of age in our institution. One group received atomized intranasal midazolam 0.3mg/kg (Group M) and the other group received intranasal dexmedetomidine 1mcg/kg (Group D) 30 minutes before the surgery.

Results: Mean sedation score was higher in Group M (1.58 ± 0.55) than in Group D (1.15 ± 0.36) with P value 0.002 at 5 minutes. Similarly the mean sedation score at 10 minutes for Group M was 2.34 ± 0.97 and Group D was 1.75 ± 0.71 with P value 0.008. Separation score and mask acceptance were better with Group M compared to Group D.

Conclusion: We conclude that in children, atomized intranasal midazolam produces better sedation levels, child parent separation and mask acceptance compared to intranasal dexmedetomidine.

Keywords: Children; Sedation; Premedication; Atomized; Intranasal; Midazolam; Dexmedetomidine.

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Introduction

Anxiety in children is characterized by subjective feelings of tension, apprehension, nervousness and worry expressed in various forms.[1] Studies have indicated that upto 60% of all children undergoing surgery present with negative behavioral changes. Age, anxiety of child and parents in preoperative holding area and anxiety during induction of anaesthesia have been identified as predictors of

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negative behavioral changes.[2] Preoperative anxiety activates human stress respone, leading to increased serum cortisol, epinephrine and natural killer cell activity. The stress activates the hypothalamic pituitary – adrenal axis, increases circulating glucocorticoids and is associated with alterations of immune function and susceptibility to infection and neoplastic diseases.[3] Surgical stress response may be detrimental, provoke a negative nitrogen balance and catabolism, delay wound healing and cause postoperative immunosuppression.[4]

Anxiety before surgery needs to be avoided and can be managed by pharmacological and non-pharmacological methods. To avoid stress to the child, drug must be easy to administer and non-painful. Intranasal administration of drugs is rapidly absorbed through the nasal mucosa, resulting in a rapid and reliable onset of action, with no painful injection and avoids first pass metabolism in liver.

Midazolam is one of the established drugs for premedication with high hepatic metabolism. Intranasal Midazolam atomizer / MAD (mucosal atomization device) delivers drug in form of droplets measuring 30-100 microns which helps in larger dispersion of drug.[5] Dexmedetomidine is an alpha 2 agonist having sedative, anxiolytic and analgesic effects, approved by Food and Drug Administration (FDA) in 1999. Few studies have been done comparing both these drugs as premedication, with different routes, different doses but with varied conclusions. Hence we wanted to compare midazolam and dexmedetomidine as premedication for children through intranasal route.

Material and Methods

After institutional ethical committee approval on 10th October 2016 (VIEC/2016/APP/126), a prospective randomized double blind study was conducted. Sample size was calculated based on onset of anxiolysis with alpha error of 5% and 20% beta error, sample size was calculated as 39 children in single arm.

78 children of both sex, aged between 2-10 years, ASA 1 & 2, scheduled for various elective surgical procedures like hernia, adenoidectomy, adenotonsillectomy, endoscopy procedures, major abdominal surgeries, syndactyly release, release of tongue tie, skin grafting, orchidopexy and fracture reduction surgery were included in the study.

We excluded children with active or recent upper respiratory tract infection, with known allergy or hypersensitivity and parents refusing to give consent.

All children were evaluated a day prior to surgery and informed written consent was obtained from parents or guardians after explaining the anesthetic plan and study details. Children were advised nil per oral as per standard guidelines. Children were then randomly assigned to one of the two groups of premedication.

Group M (n=39 children) - Children received atomized intranasal midazolam (0.3mg/kg), dispensed through proprietary drug atomizer in supine position during inspiration.

Group D (n=39 children) - Children received intranasal dexmedetomidine (1mcg/kg). The drug was loaded in a graduated syringe and sprayed in nostril with patient in supine position during inspiration.

The observer was blinded for the study drug. After IV cannulation, the premedicant was administered 30 minutes before induction of anaesthesia in the preoperative holding room, in presence of their parents. Perioperative pulse rate, blood pressure, electrocardiography, Spo_2, respiratory rate and sedation levels were monitored.

Six point Ramsay sedation score [Table I] was used to monitor sedation levels. When a sedation score of 4 or more was reached, child was transferred to operating room. At end of 30 minutes, even no satisfactory sedation level was achieved, anaesthesia induction was conducted.[6]

After achieving adequate sedation levels, the child was separated from its parents and was taken to the operating room. The response to the child parent separation was assessed and recorded according to a Four point scale [Table II].[7] A separation score of less than equal to 2 was considered relevant.

The ease of induction was assessed by mask acceptance by the child and recorded accordingly to a Four point scale during induction [Table III].[6] Induction / Mask acceptance score of greater than equal to 3 was considered satisfactory.

At the end of surgery the child was placed in the recovery position and allowed to wake up naturally. Behavior at awakening was assessed and recorded with a Four point wake up score [Table IV].[7] Wake up score less than equal to 2 was indicative of smooth recovery.

All observations and particulars of each child was recorded in the proforma. Statistical analysis was done using the following tests Mann Whitney

U test, Independent t test, Chi-square test and by using IBM SPSS version 21.0. P<0.05 was considered statistically significant.

Results

There was no significant difference between the two groups in terms of age, sex, pulse rate, blood pressure, respiratory rate and saturation.

Table I: Ramsay Sedation score[6]

Condition of the patient	Score
Patient anxious and agitated / restless or both	1
Patient cooperative, oriented and tranquil	2
Patient responds to commands only	3
A brisk response	4
A sluggish response	5
No response	6

Score >=4 is significant

Table II: Separation score.[7]

Child condition during seperation	Grade	Score
Child unafraid, cooperative, asleep	Excellent	1
Slight fear or crying, quite with reassurance	Good	2
Moderate fear, crying, not quite with reassurance	Fair	3
Crying and need for restraint	Poor	4

Score <=2 considered relevant

In Group M, 84.61% (33/39) of children reached adequate sedation compared to 64.10% (25/39) of Group D. The time taken to reach adequate sedation score in Group M was 13.18 minutes compared to 16.6 minutes in Group D.

Group M had a higher sedation score at 5 and 10 minutes. Group M had a lesser separation score and a higher induction or mask acceptance score as shown in Table V. In our study 89.74% children in midazolam group had satisfactory mask acceptance and 66.66% children in dexmedetomidine group had satisfactory mask acceptance. Hence Group M achieved better mask acceptance compared to Group D, with p value 0.0101. The wake up score between the two groups was statistically not significant. No adverse effects observed in our study.

Table III: Induction score / Mask acceptance score.[6]

Condition of the child during induction / mask application	Grade	Score
Afraid, combative, crying	Poor	1
Moderate fear of mask, not easily calmed	Fair	2
Slight fear of mask, easily calmed	Good	3
Unafraid, cooperative, accepts mask easily	Excellent	4

Score >=3 considered satisfactory

Table IV: Wake up score.[7]

Condition of the child while waking up	Score
Calm and cooperative	1
Not calm but could be easily calmed	2
Not easily calmed, moderately agitated or restless	3
Combative, Excited, Disoriented	4

Score <=2 indicative of smooth recovery

Table V: Comparison of Group M and Group D.

		Group M	Group D	P value
		Mean +/- SD	Mean +/- SD	
In relation to sedation score	Time (in minutes)	-	-	-
	5 minutes	1.58 +/- 0.55	1.15 +/- 0.36	0.0020[a]
	10 minutes	2.34 +/- 0.97	1.75 +/- 0.71	0.0081[a]
In relation to separation score	Separation Score (<=2 is relevant)	1.28 +/- 0.6	1.72 ± 1.02	0.0249[b]
In relation to induction / mask acceptance score	Induction score (>=3 is comfortable)	3.51 +/- 0.76	2.82 +/- 1.32	0.0056[b]

*Group M: Atomized intranasal midazolam group, Group D: Intranasal dexmedetomidine, SD: Standard Deviation, P<0.05 – statistically significant, [a]Mann Whitney U test, [b]Independent t test

Discussion

An ideal premedication in children, should sedate well, make the child quite on reassurance when separating from parent and easily calm the child during induction and wake up. Various drugs through different routes are used as premedication in children. Due to high first pass metabolism, oral midazolam have low bioavailability. In our study intranasal route of midazolam was used which has been preferred over oral midazolam as it has a rapid and reliable onset of action due to rich blood supply of airway mucosa. One study by Koppal R et al had used 0.5 mg/kg intranasal midazolam and concluded that it provided adequate sedation and separation scores with faster onset.[5] Studies suggested that atomized midazolam at 0.3mg/kg is safe, faster in action and better

separation scores compared to 0.2mg/kg[8] and recommended its use due to efficacy, cost, safety as well as availability.[9] One of the disadvantage of midazolam is, it can cause respiratory depression. Dexmedetomidine is an alpha 2 adrenergic agonist which provide sedation. We wanted to study the level of sedation, ease of child parent separation, ease of induction and condition of the child while waking up from surgery by comparing atomized intranasal midazolam (0.3mg/kg) and intranasal dexmedetomidine (1mcg/kg).

We premedicated the children 30 minutes before induction in preoperative holding room as done in other studies using dexmedetomidine.[5,12] Most of the children in our study were sedated by end of 10 minutes with intranasal midazolam which was similar to study done by Gupta et al. The study also claimed that intranasal dexmedetomidine yields a higher sedation level that intranasal midazolam. It is not clear whether they used atomized intranasal midazolam or not and their dose of midazolam was 0.2mg/kg compared to our 0.3mg/kg.[8]

In our study the separation score was better with intranasal midazolam compared to dexmedetomidine which is similar to study conducted by Arora et al. They had compared with oral administration of midazolam (0.5mg/kg) and dexmedetomidine (4mcg/kg). The dose of oral midazolam was not even twice the dose of our intranasal midazolam, but the dose of intranasal dexmedetomidine was four times our intranasal dose.[10]

Mask acceptance was also better in our intranasal midazolam group when compared to intranasal dexmedetomidine group. Similar results were observed by Akin et al when they compared intranasal dexmedetomidine (1mcg/kg) with intranasal midazolam (0.2mg/kg).[11] Kim et al did a meta-analyis on sedative effects of intranasal dexmedetomidine and other sedation methods.[13] He suggested that intranasal dexmedetomidine is associated with better sedative effects than oral benzodiazipines, which can be explained due to higher first pass metabolism.

In our study atomized intranasal midazolam has appeared to perform better than intranasal dexmedetomidine, though in some studies intranasal dexmedetomidine is better, it could be because we used atomized intranasal midazolam which help in better dispersion of drug over mucosa as compared to intranasal spraying from cut end of needle syringe for dexmedetomidine as atomized dexmedetomidine was not available.[10]

The draw back of our study is larger population of children need to be studied to rule out any adverse events and to compare atomized intranasal midazolam with atomized intranasal dexmeditomidine to achieve accurate results.

Conclusion

We conclude that atomized intranasal midazolam as a safe and effective sedative premedication for faster sedation levels, better child parent separation and better mask acceptance in children compared to intranasal dexmedetomidine.

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Comparison of Median and Paramedian Approach in Spinal Anaesthesia Using Whitacre Spinal Needle in Cesarean Surgery

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Abstract

Background: Spinal anaesthesia is the most common anaesthesia techniques used for Caesarean surgeries, median and paramedian approaches are two common techniques used for spinal anaesthesia. The present study was conducted to compare both median and paramedian approach in spinal anaesthesia in pregnant patients undergoing caesarean surgery in terms of incidence of PDPH, ease of each approach and skin to subarachnoid distance in both the approaches.

Materials and Methods: A total of 100 obstetric patients, undergoing cesarean surgery were included in the study. Patients were randomly allocated into two groups. Group M (n=50)- median approach and Group PM (n=50)- Paramedian approach.

Results: Mean number of attempts for successful spinal anesthesia were higher in Group PM (paramedian 1.90+0.65) as compared to Group M (median 1.54+0.68). Mean skin to subarachnoid distance was higher in Group PM (5.97 ± 0.13cms) as compared to Group M (5.05 ±0.19cms). Nine patients presented with Post dural puncture headache out of total 100 patients. In Group M, six patients (12%) developed PDPH out of 50 patients while in group PM, three patients (6%) developed PDPH, however, the difference was not statistically significant.

Conclusion: Paramedian approach is better than median approach in terms of reduction in the frequency of PDPH, though the results were statistically insignificant. Skin to subarachnoid distance (SSD) is significantly higher in paramedian approach as compared to median group.

Keywords: Median approach; Paramedian approach; Post dural puncture headache; Caesarean surgery.

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Introduction

The first spinal anaesthesia was performed in 1898, by a German surgeon named Karl August Bier, by injecting 10-15 mg cocaine into his assistant's (Hildebrandt Bier) and his subarachnoid space and in seven other patients as well five of the subjects had the symptoms of post dural puncture headache. He suggested that the headache seen in these patients is due to loss of CSF.

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Regional anaesthesia, especially spinal anaesthesia, is most commonly used for caesarean delivery. Spinal anesthesia can be achieved either through the median or paramedian approach. Headache or PDPH is the commonest complication seen following spinal anaesthesia due to continuous leak of CSF from the puncture site that results in meningeal stretch. Commonly observed in young Females, pregnant females[1], age group (20- 40 years) & patients with history of previous Headache. Factors that may lower the incidence of postdural puncture headache are design as well as gauge of needle, parallel positioning of bevel to longitudinal dural fibres and approach.

Pencil point needles include Whitacre, Gertie Marx, and Sprotte, they are different in terms of gauge and design.[2-5] Because of favourable evidence, these needles are increasingly used in clinical practice for both spinal anesthesia and diagnostic lumbar punctures. Nevertheless, some studies have failed to confirm benefits of these new needles.[6,7] In 2000, Vallejo et al.,[8] concluded that frequency of PDPH was high with Quincke needles compared to the pencil-point needles. In 2000, Reina MA et al.,[9] hypothesized that Whitacre needles had lower incidence of PDPH, In 2018, Singh B et al., concluded that the paramedian approach reduced the incidence of postdural puncture headache and low backache as compared to median approach.

Materials and Methods

After approval from institutional ethical committee, randomized prospective comparative study was conducted in attached teaching hospital between years 2017-2019.

Our study included 100 patients and were divided into two groups of 50 each. Group M included 50 patients who received spinal anaesthesia with 25G Whitacre needle in median approach and patients in Group PM received in paramedian approach.

The patients under American Society of Anaesthesiology (ASA) Grade I/II and the patients with elective caesaren surgery under spinal anaesthesia were included in the study. Patients unable to give informed consent, with known comorbidities like hypertension, diabetes, preeclampsia, history of PDPH, chronic headache, coagulation abnormalities, bleeding diathesis and taken up on emergency basis were excluded from the study.

Patients were randomly allocated into two groups using chit system.

- Group M (n = 50) – Median approach.
- Group PM (n = 50) – Paramedian approach.

Median approach: The patient is placed in the sitting position. A stool was provided as a footrest and a pillow placed on the lap. The patient is maintained in a vertical plane while the patient's neck was flexed and the patient's lower back pushed out. The needle was inserted below the lower edge of the spinous process of the selected upper vertebrae. Inj. Bupivacaine heavy 0.5% was used to achieve spinal anaesthesia.

Paramedian approach: A skin wheal is raised 1 cm lateral and 1 cm caudal to the L4 spinous process. The spinal needle inserted 10 to 15 degrees off the sagittal plane in a cephalomedial plane. Once the cerebrospinal fluid (CSF) was obtained after ligamentum flavum punctured, standard dose of Inj. Bupivacaine heavy 0.5% injected. The level of analgesia and time to achieve were noted. After the block was administered, supine position was given and a wedge was placed to tilt the patient towards left side. In both the approaches, maximum of three attempts at L3-L4 space done. If not successful, the L4-L5 space was selected.

Skin to subarachnoid distance was assessed in each approach by marking over the needle at skin tip after injecting the drug using sterile marker. Patients were followed upto 72 hours postoperatively to find out the Occurrence of post dural puncture headache and any other associated symptoms. The degree of post dural puncture headache was assessed with the help of the Visual Linear Analogue Scale.

Statistical Data Analysis

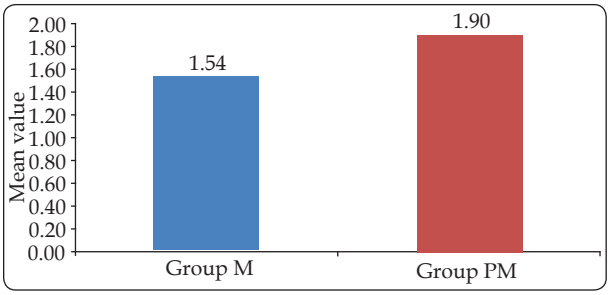
The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows. The data on categorical variables is shown as n (% of cases) and the data on continuous variables is presented as mean and standard deviation (SD) across two study groups. The inter-group statistical comparison of distribution of categorical variables is done using Chi-Square test or Fisher's exact probability test. The inter-group statistical comparison of means of continuous variables is done using independent sample t test. Intra-group comparison of means of continuous variables is done using paired t test. The underlying normality assumption was tested before subjecting the study variables to t test. All results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly.

In the entire study, the p-values less than 0.05 are considered to be statistically significant. All the hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference).

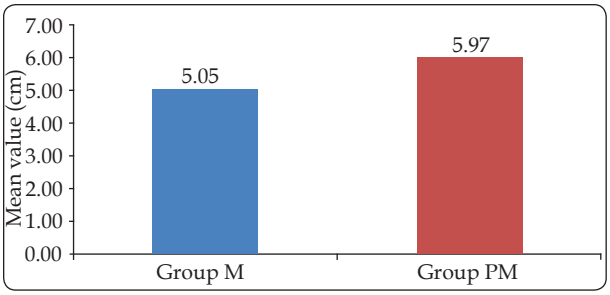
Result

Out of 100 patients, group M and PM were consists of 50 patients each. The mean ± SD of age of cases studied in GROUP M and GROUP PM was 26.88 ± 3.083 years and 25.98 + 2.53 years respectively. The minimum – maximum age range in GROUP PM and GROUP M was 20 – 33 years and 21 – 31 years respectively.

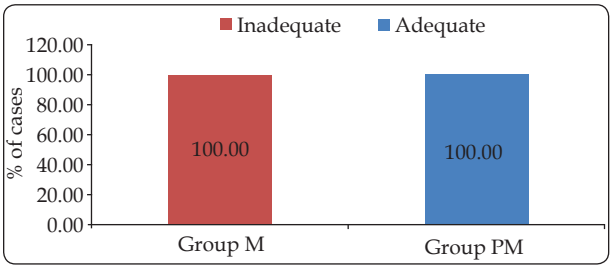
The mean ± SD of no. of attempts among the cases studied in GROUP M and GROUP PM was 1.54 ± 0.68 and 1.90 ± 0.65 respectively. Distribution of mean no. of attempts among the cases studied is significantly higher in GROUP PM compared to GROUP M (P-value<0.01). (Graph 1)



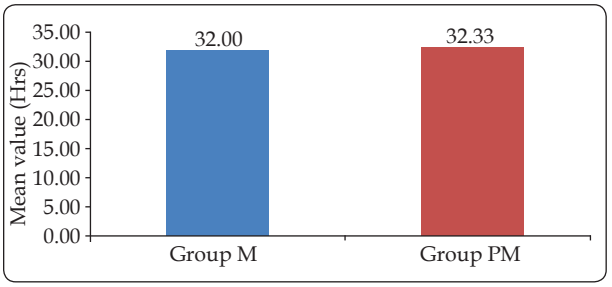
Graph 1: Inter-group comparison of mean number of attempts.



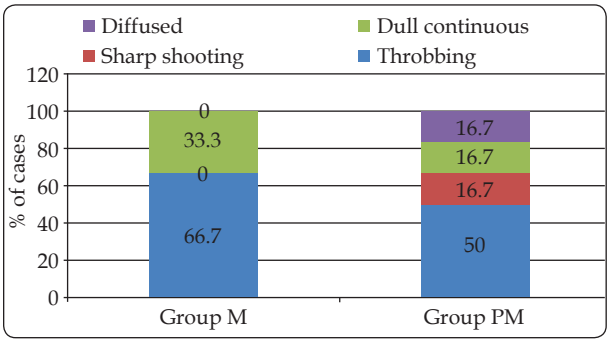
Graph 2: Inter-group comparison of mean skin to subarachnoid distance (SSD).



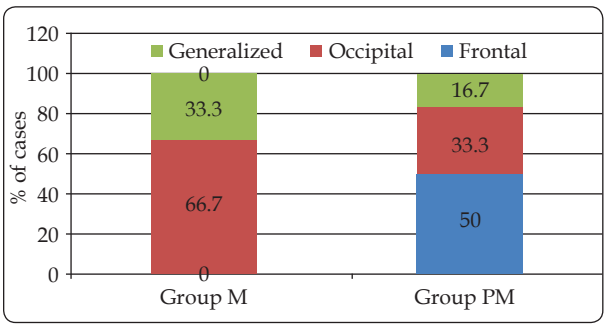
Graph 3: Inter-Group Distribution of adequacy of action intraoperatively.



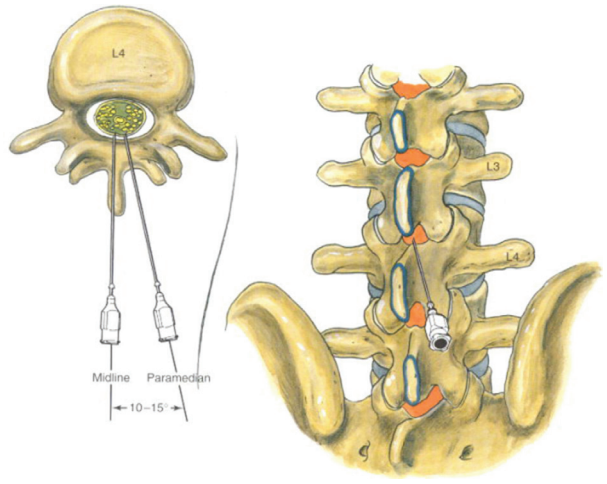
Graph 4: Inter-Group Distribution of Mean Time of Onset of PDPH.



Graph 5: Inter-Group Distribution of Nature of PDPH.



Graph 6: Inter-Group Distribution of Location of PDPH.



The mean ± SD of skin to subarachnoid distance among the cases studied in GROUP M and GROUP PM was 5.05 ± 0.19 cms and 5.97 ± 0.13 cms respectively. Distribution of mean skin to subarachnoid distance among the cases studied is

significantly higher in GROUP PM compared to GROUP M (P-value<0.001). (Graph 2)

Of 50 cases studied in GROUP M, none had inadequate action. Of 50 cases studied in GROUP PM, none had inadequate action (Graph 3). Of 50 cases studied in GROUP M, 44 (88.0%) had no pain, 6 (12.0%) had mild pain requiring no treatment. 50 cases studied in GROUP PM, 47 (94.0%) had no pain, 3 (6.0%) had mild pain requiring no treatment.

The mean ± SD of onset of PDPH among the cases studied in GROUP M and GROUP PM was 32.33 ± 2.94 Hrs and 32.00 ± 3.46 Hrs respectively. The minimum – maximum range of onset of PDPH in GROUP M and GROUP PM was 30 – 36 Hrs and 30 – 36 Hrs respectively (Graph 4).

Of 6 cases who had PDPH in GROUP M, 3 (50.0%) had throbbing, 1 (16.7%) had sharp shooting, 1 (16.7%) had dull continuous and 1 (16.7%) had diffused type of PDPH. Of 3 cases who had PDPH in GROUP PM, 2 (66.7%) had throbbing, 1 (33.3%) had dull continuous type of PDPH (Graph 5). Of 6 cases who had PDPH in GROUP M, 3 (50.0%) had it at frontal location, 2 (33.3%) had it at occipital and 1 (16.7%) had generalized PDPH. Of 3 cases who had PDPH in GROUP PM, none had it at frontal location, 2 (66.7%) had it at occipital and 1 (33.3%) had generalized PDPH. The mean ± SD of pain score (VAS) among the cases studied in GROUP M and GROUP PM was 3.83 ± 0.75 and 3.33 ± 0.58 respectively. The minimum – maximum range of pain score in GROUP M and GROUP PM was 3 – 5 and 3 – 4 respectively (Graph 6).

Distribution of adequacy of action, incidence, time of onset, nature, location, and mean pain score (VAS) of PDPH among the cases studied did not differ significantly between two study groups (P-value>0.05).

Discussion

The median approach may be technically difficult due to the exaggerated lumbar lordosis in pregnant patients. The paramedian approach is a useful technique in difficult or challenging situations like elderly and pregnant patients. The exact mechanisms leading to PDPH are still not completely understood. The signs and symptoms of PDPH result from loss of cerebrospinal fluid, traction on the cranial contents, and reflex cerebral vasodilation. Two most important factors influencing the frequency and severity of PDPH are the patient's age and the size of the dural perforation. The parturient is at particular risk of PDPH because of her sex and young age. Fine gauge spinal needles, 29G or smaller, are technically more difficult to use, and are associated with a high failure rate for spinal anaesthesia. 25G, 26G and 27G needles probably represent the optimum needle size for spinal anaesthesia.

Hence, we conducted a study by comparing median and paramedian approach using 25G Whitacre needle in patients who underwent elective caesarean surgery.

In our study 100 patients were included with 50 each in M and PM groups with mean age of group M patients was 26.88 ± 3.083 and group PM patients was 25.98 ± 2.53, similarly Manisha Kanagarajan et al.,[11] in 2017, and Afshan Nisar et al.,[12] in 2016, included similar ratio patients in median and paramedian approach, and with nearly similar mean age.

In our study the mean ± SD of no. of attempts among the cases studied in Group M and Group PM was 1.54 ± 0.68 and 1.90 ± 0.65 respectively. According to a study by Manisha Kanagarajan et al.,[11] in 2017, The mean ± SD of no. of attempts among the cases studied in Group M and Group PM was 2.6 ± 0.8 and 2 ± 0 respectively. In the study by Teena Bansal et al.,[13] in 2018, Single attempt was successful in 75 patients (75%) in group I and 80 patients (80%) in group II.

In our study mean ± SD of skin to subarachnoid distance among the cases studied in Group M and Group PM was 5.05 ± 0.19 cm and 5.97 ± 0.13 cm respectively. The minimum – maximum range of skin to subarachnoid distance in Group 1 and Group 2 was 4.7 – 5.4 cm and 5.7 – 6.2 cm respectively. Our results are comparable with the study by Behzad sohail et al14 in 2011 they compared the median and paramedian approaches in one hundred patients and demonstrated that the distance from skin to subarachnoid space was more in the paramedian group.

According to a study by Teena Bansal et al13., in 2018, Six patients presented with PDPH out of total 200 patients. In group I, five patients (5%) developed PDPH out of 100 patients while in group II, only one patient (1%) developed PDPH out of 100 patients; however, the difference was not significant statistically. This study was comparable with our study, as in our study also the difference of incidences of PDPH was not significant statistically.

Distribution of mean onset of PDPH among the cases studied did not differ significantly between two study groups (P-value>0.05). According to a study by Manisha Kanagarajan11 in 2017, The

mean duration of onset of PDPH was similar in both groups i.e. 2.8 ± 0.8 vs. 2.7 ± 1.2 days. Similar to the study by Teena Bansal et al.,[13] in 2018, nature of PDPH in our study also was not statistically significant.

In our study the mean ± SD of pain score (VAS) among the cases studied in GROUP M and GROUP PM was 3.83 ± 0.75 and 3.33 ± 0.58 respectively, while in the study by Teena Bansal et al.,[13] in 2018 Mean VAS of total patients was 2.34 ± 1.23 with minimum score of 2 and maximum score of.[14]

Conclusion

The mean number of attempts taken for successful spinal anaesthesia were more in paramedian approach compared to median approach. Skin to subarachnoid distance is significantly high in paramedian approach as compared to median approach. Incidence of post dural puncture headache is less in paramedian approach as compared to median approach.

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Comparison of Gabapentin and Pregabalin Premedication for Attenuation of Hemodynamic Changes in Elective Laparoscopic Appendicectomy

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Abstract

Introduction: General anaesthesia is the gold standard anaesthetic technique for laproscopic appendicitis. However, this procedure is not risk free. Carbon dioxide is used to create pneumoperitoneum in laproscopic surgeries causes various hemodynamic changes such as abrupt elevation of arterial pressure, systemic vascular resistance and decreased cardiac output. These changes are well tolerated in healthy patients. There is also an increase in circulatory catecholamines during laryngoscopy and intubation. Many pharmacological techniques were evaluated either in the premedication or during the induction to attenuate the hemodynamic response to pneumoperitoneum such as – deepening the anaesthesia, pretreatment with vasodilators, adrenoceptor blockers, calcium channel blockers and opiods. This study is designed to evaluate the hemodynamic changes associated by laryngoscopy, tracheal intubation and pneumoperitoneum in laparoscopic appendicectomy by premedicating the patients with Gabapentin (900mg) and Pregabalin (150mg).

Materials and Methods: The study was carried out as a hospital based double blinded randomized prospective comparative study after obtaining institutional ethics committee approval in the Department of Anaesthesiology, SMVMCH Puducherry. The sample size was calculated as 72 with 36 in each group. Patients scheduled for elective laparoscopic appendicectomy were selected for the study based on predetermined inclusion and exclusion criteria. The study drug, Gabapentin 900mg or Pregabalin 150mg, was sealed in a black covered envelope and was given to the patient with sips of water 1 hour before the induction of anaesthesia by an anaesthetist not involved in study. Anaesthetic and surgical techniques were standardized for all patients. HR, SBP, DBP, MAP, SpO2 were recorded at the following points of time:(i) Prior to induction, (ii) 2-3 minutes after intubation, (iii) Before creating pneumoperitoneum, (iv) After creating pneumoperitoneum, (v) 2 minutes after extubation, (vi) Intra op,every 5 mins till the end of surgery, (vii) Post op, every 10 mins for the 1st 30 minutes and then every 30 minutes till 3 hours, along with Ramsay sedation score.

cont...

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Results: Both the study groups were comparable in terms of age distribution, gender distribution, BMI distribution, duration of surgery. HR changes, SBP changes, DBP changes, MAP changes between the study groups were not significantly different at various different time intervals during intubation and pneumoperitoneum. Lower sedation scores were noted in Gabapentin group and was found to be statistically significant.

Discussion: Stress response with laryngoscopy and intubation, and pneumoperitoneum causes exaggerated hemodynamic response and increased intracranial pressure and manifest as tachycardia, hypertension and dysrhythmias. Haemodynamic changes between the study groups were not significantly different at various different time intervals neither during intubation and pneumoperitoneum nor during the surgery and post operatively. Lower sedation scores were noted in Gabapentin group as compared to that of the Pregabalin group at various different time intervals. Both the drugs showed a significant equal and comparable hemodynamic stability during intubation and subsequently during the course of the surgery.

Conclusion: Oral Gabapentin and Pregabalin produced similar attenuation of haemodynamic response to laryngoscopy tracheal intubation and pneumoperitoneum. However, lower sedation scores were noted in Gabapentin group as compared to that of the Pregabalin group.

Keywords: Pneumoperitoneum; Hemodynamic changes; Laparoscopic surgeries.

Introduction

Carbon dioxide is the most common gas used to create pneumoperitoneum in laparoscopic surgeries. Adverse cardiovascular effects of carbon dioxide pneumoperitoneum are abrupt elevation of arterial pressure, systemic vascular resistance, heart rate and decreased cardiac output.[1] These hemodynamic changes are mainly due to increased release of catecholamines, vasopressin, or both.[2,3] While this sympathetic response can normally be tolerated by healthy adults, it can be quite hazardous in patients having compromised cardiovascular function.Various anaesthetic techniques has been tried to blunt these deleterious hemodynamic responses like hypertension, tachycardia and arrhythmias in susceptible individuals.

During carbon dioxide pneumo-peritoneum, various physiological changes occurs on cardiovascular, respiratory and excretory systems. The intra-abdominal pressure and the position of patient placed on the operating table determines the severity of these changes. In cardiovascular system - carbon dioxide pneumo-peritoneum reduces the venous return from lower extremities; but the cardiac preload and vascular resistance are increased. In respiratory system - carbon dioxide insufflation causes hypercapnia, it can be easily monitored and corrected in a ventilated patient. There is 30% decrease in Splanchnic, especially mesenteric and renal blood flow.

Many pharmacological techniques were evaluated either in the premedication or during the induction to attenuate these adverse haemodynamic responses to pneumoperitoneum, such as deepening the anaesthesia, pre-treatment with vasodilators, adrenoceptor blockers, calcium channel blockers and opioids, with variable results.4,5 With adequate adjustments and pharmacological interventions, most of the alterations can be managed safely and prevented.[6]

More recently antiepileptic drugs like Gabapentin and Pregabalin have been used for the treatment of acute postoperative pain and to decrease postoperative opioid requirements. Gabapentin is a structural analogue of the neurotransmitter gamma-aminobutyric acid (GABA).[7] It is used to control neuropathic pain, to treat acute post-operative pain and to reduce post-operative opioid requirements. Gabapentin premedication provided perioperative hemodynamic stability during laparoscopic surgery. Gabapentin 900 mg, the recommended dose, when administered 1–2 h before surgery is generally well tolerated without any serious side effects. Therefore we selected 900 mg as the premedication dose of oral gabapentin for this study.[1]

Pregabalin is a structural analog of gamma amino butyric acid (GABA), and shares some characteristics with its predecessor, gabapentin.[8] Pregabalin is used in treatment of neuropathic, inflammatory pain, and acute post-operative pain.[9] Its mechanism of action is by decreasing the synthesis of neurotransmitter glutamate. The peak plasma concentrations of oral pregabalin is within 1 hour. Patients premedicated with pregabalin were haemodynamically stable perioperatively without prolongation of recovery time and side-effects.[10] The attenuation of haemodynamic response is

effective with a single oral dose of 150 mg pregabalin premedication. Therefore we selected 150 mg as the premedication dose of oral pregabalin for this study.

We therefore designed the study to evaluate the hemodynamic changes associated by laryngoscopy, tracheal intubation and pneumoperitoneum in laparoscopic appendicectomy by premedicating the patients with Gabapentin (900mg) and Pregabalin (150mg) 1 hour before the surgery.

Materials and Methods

The study was conducted in the department of Anaesthesiology at Sri Manakula Vinayagar Medical College and Hospital, Puducherry between October 2016 to May 2018 in patients scheduled for elective laparoscopic appendicectomy. Written informed consent was obtained from all patients and the study was approved by the Institutional Ethics Committee. It was a double blinded randomized prospective comparative study as per good clinical practice (GCP) guidelines by WHO, conducted on 72 patients in which 36 in Group A(received Gabapentin 900mg) and 36 in Group B(received Pregabalin 150mg) as premedication. Patients of ASA(American Society of Anaesthesiologists) physical status I and II of both gender, aged 18 to 60 years, Hypertensives with controlled hypertension were included in the study. Patients having BMI greater than 30, with renal or cardiac dysfunction, taking beta blockers, antipsycotics and anticonvulsants, pregnant or lactating women, patients who are refusing the procedure were excluded from the study. Eligible patients were randomly allotted into two different study groups randomly using sealed envelope technique.

Brief Procedure

All patients were thoroughly examined preoperatively and routine investigation were carried out. Patient were subsequently assessed for eligibility. Group A received Gabapentin 900mgand Group B received Pregabalin 150mg, as premedication 1 hour before surgery.

The group allocation and randomization were done based on computer generated serial number, using Epi-Info Software. The study drug was sealed in a black covered envelope and was given to the patient with sips of water 1hour before the induction of anaesthesia by an anaesthetist not involved in study. The anaesthesia was administered and observation was done by an experienced anaethetist who has no knowledge of whatever drug the patient has taken as premedication.

On arrival to the operation theatre, monitors were attached and baseline heart rate and systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and SpO2 were recorded. Mean arterial pressure (MAP) was calculated by formula MAP = (SBP+2 × DBP)/3.

The pre-operative level of sedation was assessed by the Ramsay sedation scale:

1. Anxious, agitated or restless;
2. Co-operative, oriented and tranquil;
3. Responds to command;
4. Asleep with brisk response to stimulus;
5. Asleep with sluggish response to stimulus;
6. Asleep with no response.

Anaesthetic and surgical techniques were standardized for all patients. An intravenous line will be started using 18 gauge venflon and the patient will be induced anaesthesia by:

(i) Inj.Glycopyrolate 0.2mg IV

(ii) Inj.Fentanyl 2mcg/kg IV

(iii) Inj.Propofol 2mg/kg IV

(iv) Patient was intubated using the appropriate size endotracheal tube and intubation was facilitated by Inj.Atracurium 0.5mg/kg.

(v) Anaesthesia was maintained by 33% O2 in N2O along with 2-2.5% Sevoflurane and intermediate doses of atracurium were administered as per requirement.

Carbon dioxide was insufflated into the peritoneal cavity to create pneumoperitoneum and intraabdominal pressure was maintained to 15 mm Hg. Ventilation was adjusted to maintain ETCO2 within range of 30-40 mm Hg.

In case of any acute/severe hemodynamic fluctuations the following interventions were done:

(i) If heart rate < 20% of the baseline, a bolus of 0.6mg Atropine was given IV.

(ii) If the mean arterial pressure falls < 20% of the baseline, a bolus of 6mg Ephedrine was given IV.

(iii) If the mean arterial pressure rises > 20% of the baseline, a bolus of 5mg Labetolol wasgiven IV.

At the end of surgery, Ondansetron 4mg was administered intravenously for prophylaxis against nausea and vomiting. Residual neuromuscular

block was reversed by using injection neostigmine (0.05mg/kg) and injection glycopyrolate (0.01mg/kg). Tracheal extubation was done when respiration is adequate.

The patients were transferred to the post-anaesthesia care unit and monitored for at least 3 hours, or until there were no signs of any drug-induced effects such as nausea, vomiting, any respiratory inadequacy or haemodynamic instability in form of hypotension/hypertension or tachycardia/bradycardia. If any side-effects were noted, they were treated accordingly.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO2 were recorded at the following points of time:

(i) Prior to induction
(ii) 2-3 minutes after intubation
(iii) Before creating pneumoperitoneum
(iv) After creating pneumoperitoneum
(v) 2 minutes after extubation
(vi) Intra-operative, every 5 mins till the end of surgery.
(vii) Post-operative, every 10 mins for the 1st 30 minutes and then every 30 minutes till 3 hours, along with Ramsay sedation score.

Statistical Analysis

Data was entered into Microsoft Excel data sheet and analyzed using SPSS 21.0 version software. Baseline characteristics were represented in the form of Frequencies and proportions. Chi Square test was applied to test statistical difference in proportions. Continuous variables were represented as mean and standard deviation. Comparison of means was done by independent sample 't' test and Mann Whitney U test was applied to test the statistical difference for the non-parametric data. A p-value of <0.05 was considered as statistically significant.

Results and Discussion

A total of 72 patients, 36 were received 900mg of Gabapentin (Group A) and 36 received 150mg of Pregabalin (Group B) as premedication. Both the study groups were comparable in terms of demographic and baseline characteristics viz, age distribution, gender, BMI, diagnosis and duration of surgery (Table 1). Haemodynamic changes between the Gabapentin and Pregabalin were not significantly different at various different time intervals during intubation and pneumoperitoneum (Table 2 & 3). Haemodynamic changes between the Gabapentin and Pregabalin were not significantly different at various different time intervals during the surgery and post operatively (Figure 1 & 2). Lower sedation scores were noted in Gabapentin group as compared to that of the Pregabalin group of study participants at various different time intervals (Table 4).

Both the drugs showed a significant equal and comparable hemodynamic stability during intubation and subsequently during the course of the surgery. After a detailed review of available literature it was noted that there is deficiency of established research findings comparing Pregabalin and Gabapentin in attenuation hemodynamic stress response to laryngoscopy, intubation and pneumoperitoneum. There were no studies available to the best of our knowledge, comparing the efficacy of Gabapentin and Pregabalin in attenuation of haemodynamic response to pneumoperitoneum/ laparascopy.

Mahoori A et al compared the effect of gabapentin (900mg) and pregabalin (150 mg) two hours prior to induction of anesthesia and stated that significant increase in heart rate and systolic blood pressure and diastolic arterial pressure was observed in placebo group after tracheal intubation, while statistically significant attenuation of hemodynamic changes was seen in gabapentin and pregabalin groups. No adverse outcome was reported in the study groups.[11] Similarly, Namratha S et al investigated the effects of oral gabapentin and pregabalin observed that when compared to gabapentin and pregabalin, there was a significant increase in HR and MAP in control group after laryngoscopy and tracheal intubation.[12] These findings of the above discussed studies were identical to the observations of the present study.

Namratha S et al demonstrated that Pregabalin being more sedative than gabapentin is better than gabapentin in suppressing the pressor response.12 This observation was similar to the present study result where it was noted that lower sedation scores were seen in Gabapentin group as compared to that of the Pregabalin group of study participants at various different time intervals.

In contrast to the identical effects of Pregabalin and gabapentin noted in the present study Waikar C et al evaluated the effect of clonidine 200 µg and gabapentin 900 mg and pregabalin 150 mg in attenuation of the hemodynamic response, reported that mean arterial pressure was well attenuated by pregabalin than others, and mean

Table 1: Demographic and Baseline characteristics of study patient in both groups.

S. No.	Variable		Group A Gabapentin (n=36)	Group B Pregabalin (n=36)	Total (n=72)	p-Value
1	Age in years					
		15-30	19	18	37	0.863
		31-45	9	11	20	
		46-60	8	7	15	
2	Gender					
		Male	21	20	41	0.812
		Female	15	16	31	
3	BMI					
		Underweight	1	4	5	0.534
		Normal	29	25	54	
		Overweight	5	6	11	
		Obese	1	1	2	
4	Diagnosis					
		Acute Appendicitis	25	27	52	0.568
		Sub acute appendicitis	10	9	19	
		Chronic appendicitis	1	0	1	
5	Duration of Surgery (in mins)		60.56±20.76	60.69±28.3		0.981

Table 2: Distribution of study groups based on heart rate changes at various time intervals

Time Interval	Group A Gabapentin (n=36)		Group B Pregabalin (n=36)		p value
	Mean	SD	Mean	SD	
Baseline	83.92	15.9	81.39	13.9	0.476
2-3 mins after intubation	90.39	16.3	88.14	14.9	0.544
Before pneumoperitoneum	89.9	16.3	82.3	14.2	0.038
After Pneumoperitoneum	91.92	19.2	85.5	16.7	0.135
2 mins after extubation	105.4	17.3	102.3	18.8	0.468

Table 3: Distribution of study groups based on MAP changes at various time intervals.

Time Interval	Group A Gabapentin (n=36)		Group B Pregabalin (n=36)		p value
	Mean	SD	Mean	SD	
Baseline	91.86	14.3	94.7	13.6	0.392
2-3 mins after intubation	89.1	18.5	84.3	14.4	0.226
Before pneumoperitoneum	83.5	11.9	77.4	11.6	0.032
After Pneumoperitoneum	91.1	13.4	88.3	15.3	0.406
2 mins after extubation	100.8	13.6	104.6	12.8	0.222

Table 4: Distribution of study groups based on sedation score at various time intervals.

Time interval (in mins)	Sedation Score	Study group		Total n (%)	p value*
		Group A Gabapentin n (%)	Group B Pregabalin n (%)		
Pre Surgery	2	36(100.0)	36(100.0)	72(100.0)	NA
10	3	36(100.0)	36(100.0)	72(100.0)	NA
20	3	36(100.0)	36(100.0)	72(100.0)	NA
30	2	3(8.3)	0(0.0)	3(4.2)	0.239
	3	33(91.7)	36(100.0)	69(95.8)	
60	2	13(36.1)	0(0.0)	13(18.1)	<0.001
	3	23(63.9)	36(100.0)	59(81.9)	
90	2	28(77.8)	1(2.8)	29(40.3)	<0.001
	3	8(22.2)	35(97.2)	43(59.7)	
120	2	35(97.2)	2(5.6)	37(51.4)	<0.001
	3	1(2.8)	34(94.4)	35(48.6)	
150	2	35(97.2)	7(19.4)	42(58.3)	<0.001
	3	1(2.8)	29(80.6)	30(41.7)	
180	2	35(97.2)	7(19.4)	42(58.3)	<0.001
	3	1(2.8)	29(80.6)	30(41.7)	
Total		36(100.0)	36(100.0)	72(100.0)	

heart rate following laryngoscopy and intubation was attenuated by clonidine group significantly.[13]

Bhagat NM et al compared the efficacy of oral premedication with pregabalin versus clonidine on stress response and hemodynamic stability during laryngoscopy in 60 adult patients aged 18-60 years. The study findings documented that Perioperative sedation levels were higher with pregabalin than with clonidine, without prolongation of recovery time. Statistically significant attenuation of mean arterial pressure and heart rate to laryngoscopy and laparoscopy was observed in the premedicated groups. The visual analogue scale scores of both the pregabalin and the clonidine group were significantly lower than that in the control group at 1, 4, and 8 h after surgery.[14] This haemodynamic attenuation by Pregabalin in the above study was similar to that of the present study findings among the Pregabalin group. Likewise, in a study by Gupta K et al it was observed in the study that Pregabalin and clonidine proved to have sedative and anxiolytic effects as oral premedicants and decreased the need of intraoperative analgesic drug requirement during laparascopic cholecystectomy.[15]

Saxena A et al evaluated the effectiveness of pregabalin as a premedication on the arterial pressorresponse to laryngoscopy and on hemodynamic variables and revealed that Pregabalin 75 mg at night and 150 or 300 mg 1 h before surgery adequately attenuates pressor response to laryngoscopy andintubation. Patients' hemodynamic variables were more stable in pregabalin groups as compared to control group (diazepam)during the intra-operative period.16 Chakraborty R et al evaluated the efficacy of preoperative 150 mg of oral pregabalin in attenuating haemodynamic response to laryngoscopy and endotracheal intubation and reported significantly less increase in systolic, diastolic and mean blood pressure in pregabalin groupof patients following intubation when compared to controls (p value = 0.02, 0.03, 0.02 respectively). Preoperative & post-operative sedation scores were relatively higher after pregabalin premedication.[17]

These findings by the above discussed research works were similar to the effects of Pregabalin observed in the present study. In addition, during laryngoscopyand intubation there was significant attenuation of SBP, DBP and MBP in Prebagalin administration as compared to placebo group as reported by Bhandari G et al in their study.[18] The mean arterial pressure was attenuated with oral pregabalin to statistically significant value (P<0.007). The requirement of analgesic drug was reduced with no postoperative respiratory depression, nausea, or vomiting and hemodynamic parameters remained stabilized perioperatively, in the study by Gupta K et al.[19]

Gabapentin also produced a haemodynamic attenuation effect to pneumoperitoneum/ laparasocopy in the present study, similar observations were noted in Prakash R et al study where the effect of oral clonidine and gabapentin premedication on intraoperative haemodynamic stability on 90 patients aged between 20-60 years was studied and noted that both clonidine and gabapentin group had significantly lower HR and BP changes than placebo group (P<0.05) during pneumoperitoneum.[20]

Bhandari G et al evaluated effects of gabapentin on arterial pressure and heart rate at induction of anaesthesia and attracheal intubation and reported that Pre medication with 900 mg gabapentin, 2 hours before induction of anaesthesia attenuatesthe tachycardia associated with laryngoscopy and intubation but not the pressor response completely.[18]

Also, Neogi M et al investigated the efficacy of gabapentin premedication and stated that mean arterial pressure in patients of group Gabapentin were significantly lower (P < 0.05) after tracheal intubation and pneumoperitoneum and remained lower, as compared to group placebo, throughout the pneumoperitoneum.[21] Similarly, heart rate in Gabapentin significantly lower (P < 0.05) after tracheal intubation and pneumoperitoneum and remained lower, in comparison to group palcebo, throughout the peumoperitoneum. These observations of the above research works were similar to that of the findings of the present study.

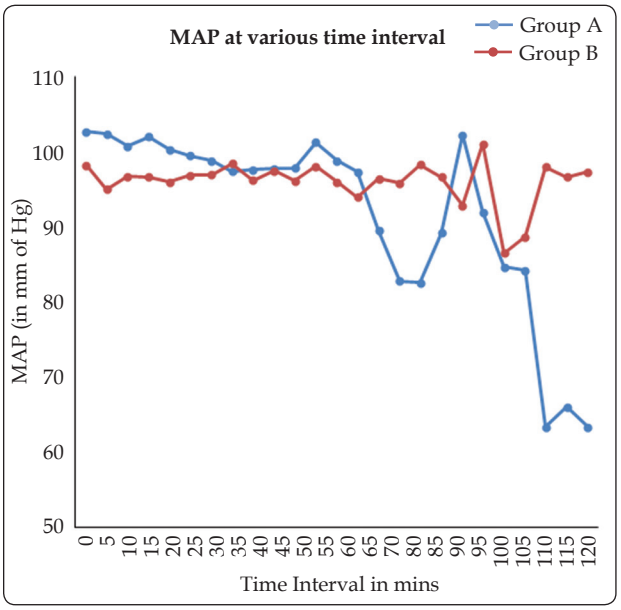

Fig. 1: Distribution of study groups based on HR at various time intervals during surgery.

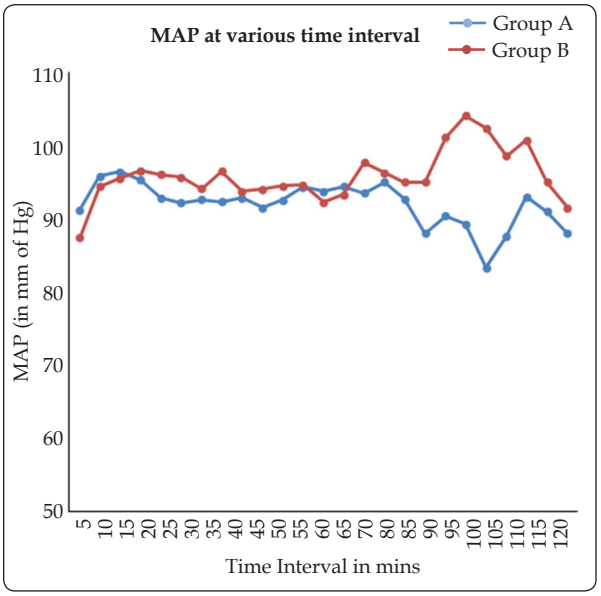

Fig. 2: Distribution of study groups based on MAP at various time intervals during surgery.

Conclusion:

Oral Pergabalin and Gabapentin produced similar attenuation of haemodynamic response to laryngoscopy and intubation. However, lower sedation scores were noted in Gabapentin group as compared to that of the Pregabalin group of study participants at various different time intervals.

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Comparative Evaluation of Dexmedetomidine and Fentanyl Infusion on Haemodynamic Response in Patients Undergoing Elective Surgery Under General Anaesthesia

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Abstract

Context: The procedures like laryngoscopy and intubation evoke stress response in patients undergoing elective surgeries under general anaesthesia.

Aims: To compare and evaluate dexmedetomidine and fentanyl on hemodynamic response like Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) in patients during intubation and extubation.

Settingsand Design: Doubleblinded Randomised Control prospective Study

Materials and Methods: AAfterobtainingethical clearance, 90 patients belonging to American Society of Anaesthesiologists class I/II, Scheduled for surgeries with duration of approx. 90mins were randomly divided into two groups. Group A received dexmedetomidine 1µg/kg as loading dose over 10mns prior to induction followed by infusion at 0.5µg/kg/hr until 10mins prior to extubation. Group B received IV Fentanyl 1µg/kg as loading dose over 10mins prior to induction followed by infusion at 0.5 µg/kg/hr until 10mins prior to extubation.

Exclusion criteria included cardiovascular disease, Obesity >30kg/m2, patients with anticipated difficult airway, on sedatives, hypnotics and who have allergy to the study drug. *Statistical analysis used:* Data analyzed- SPSS22.0 software. *Test of significance:* Chi-squaretest. Continuousdata: Mean standard deviation. Testof significance:Independentttest p value:<0.05-statistically significant.

Results: With respect to hemodynamic response during intubation and extubation, Group A has shown significantly lower HR, SBP, DBP and MAP in comparison to Group B. Post-operative Visual Analogue Score for first 24hrs was significantly less in Group A compared to Group B.

Conclusion: Dexmedetomidine is better and safe alternative to fentanyl in attenuating hemodynamic response during both intubation and extubation.

cont...

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Keywords: Dexmedetomidine; Extubation; Fentanyl; General anaesthesia; Hemodynamic response; Intubation; Post-operative pain.

Key Message: The haemodynamic changes that occur during intubation and extubation may sometimes lead to extreme cardiovascular disturbances. Intraoperative dexmedetomidine infusion has used successfully to maintain haemodynamic stability throughout the procedure.

Introduction

General anaesthesia is the plan of anaesthesia for major head & neck surgeries, neurosurgeries, laparoscopic and dental surgeries. Laryngoscopy and intubation are associated with sympathetic stimulation and major hemodynamic changes.[1] There was always a need to attenuate the sympathetic response to prevent perioperative stress induced ischemic changes.[2]

Maintenance of anaesthesia is done with inhalational agents. The requirement of volatile anaesthetics depends upon the intraoperative hemodynamic stability.[3] Patients requiring high MAC may take longer time for recovery from anaesthesia and thereby causing delay in extubation.[4]

One of the factors contributing for intraoperative hemodynamic instability include inadequate analgesia. Poor control of intraoperative pain may cause hypertension leading to increased bleeding at the surgical site.[5]

Extubation also is associated with stress response.6 Violent extubation may lead to development of pulmonary edema or bleeding from the pack sites especially in case of ENT surgeries.[7] Abrupt increase in blood pressure during extubation may lead to post-operative haematoma in neurosurgery cases.[8]

Post-operative analgesia is also of utmost concern for anaesthesiologist especially in first 24 hours. Inappropriate pain management may lead to immobility, deep vein thrombosis, poor rehabilitation and progression to chronic pain.[9]

The present study is being conducted to evaluate the efficacy of intraoperative dexmedetomidine and fentanyl infusion on hemodynamic changes during intubation, extubation and postoperative analgesia.

Objectives

Primary Objective

- To compare and evaluate dexmedetomidine and fentanyl on hemodynamic response like Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) in patients during intubation and extubation.

Secondary Objective

- To assess the inhalational agent requirement throughout the procedure
- To assess the pain in the recovery period by Visual Analogue scale (VAS)

Material and Methods

The ethical clearance was obtained before starting the study.

A thorough preanaesthetic check-up was carried out, history was taken and systemic examination done. Vitals were noted including weight of the patient.

Investigations asked prior to surgery include

- Complete haemogram
- Serum electrolytes
- Blood urea and serum creatinine
- Random blood sugar
- Bleeding time and clotting time
- ECG and Chest x-ray
- Urine analysis for sugar, albumin and microscopy
- No other specific investigations were asked

All patients were examined 1 day prior to the surgery, investigation reports were checked, anaesthetic procedure explained and informed consent was taken.

Fasting was ensured for 8hours and patients were premedicated with Tab.Alprazolam 0.5mg and Tab.Rantac 150mg, which were repeated again on the morning of surgery.

Preparation of drug for infusion

Dexmedetomidine 1ml ampule containing 100mcg

was diluted with normal saline till 20cc so that the solution contains drug of 5µg per ml

Fentanyl 2ml containing 100µg was diluted with normal saline till 20cc so that the solution contains 5µg per ml.

The drugs were administered using a syringe pump.

Patients were randomly divided into two groups by computer generated table-

GROUP A: IV Dexmedetomidine 1µg/kg as loading dose over 10mins prior to induction followed by infusion at 0.5µg/kg/hr until 10mins prior to extubation.

GROUP B: IV Fentanyl 1µg/kg as loading dose over 10mins prior to induction followed by infusion at 0.5µg/kg/hr until 10mins prior to extubation.

Venous access was secured with 18G IVC and fluids were started at the rate of 5ml/kg/hr.

Once the patient was shifted to OT their basal HR, NIBP, SPO2 were noted and monitoring started.

Before the induction of anaesthesia patients were premedicated with Inj.Glycopyrrolate 0.005mg/kg.

Loading dose of the study drug was started at the rate of 1µg/kg and given over 10mins. HR, SBP, DBP, MAP, RR and SPO2 were noted before the start of infusion.

Preoxygenation was done with 100% oxygen for 3mins and anaesthesia induced with Inj.Propofol at 2mg/kg till loss of verbal commands

After the loading dose was given, the required monitoring parameters were once again recorded and the study drug infusion rate was changed to maintenance dose of 0.5µg/kg/hr till 10mins prior to extubation.

Tracheal intubation with appropriate size oral endotracheal tube is facilitated by Inj.Succinyl choline 2mg/kg. Maintenance of anaesthesia is done by 60% nitrous oxide in oxygen, isoflurane and Inj.Vecuronium 0.1mg/kg as muscle relaxant. Isoflurane concentration was titrated to maintain stable hemodynamic.

Patient was mechanically ventilated to maintain ETCO2 between 30-35mm of Hg.

HR, SBP, DBP, MAP, RR, SPO2 were recorded 1min after intubation and then at 3min, 5min followed by at every 15 min interval till extubation.

Bradycardia will be treated by IV Atropine at 0.02mg/kg and hypotension will be treated by titrating isoflurane concentration or by rate of infusion of intravenous fluids.

Infusion of the study drug was stopped and isoflurane was discontinued 10mins prior to reversal.

The residual neuromuscular blockade was reversed with Inj.Neostigmine 0.05mg/kg and Inj. Glycopyrrolate 0.01mg/kg.

After observing the motor recovery and spontaneous breathing efforts, patient was extubated after thorough oral suctioning. Vitals were noted 1, 3 ,5, and 15min after extubation to check for extubation response.

Patient was transferred to post anaesthesia care unit for observation of any nausea or drug induced side effects.

For first 24 hrs patient was monitored for pain using VAS score and the number of analgesics used were noted.

Results

Present study compares the efficacy of both fentanyl and dexmedetomidine infusion on attenuating the pressor response during intubation and extubation. Study has been conducted on 90 subjects and all the patients were included in the study.The demographic data of age, sex, weight, ASA physical status were comparable between the groups. (Table no 1)

Table 1: PatientDemographicCharacteristics.

Parameters	Group A	Group B
Number (N)	45	45
Age (Years)	36.29±9.93	37.44±8.98
Weight(kg)	59.51±10.49	61.11±9.84
Gender (male/female)	20/25	24/21
ASA status (I/II)	33/12	31/14

ASA: American Society of Anaesthesioloigists

Baseline HR (bpm) was comparable in both the groups.

After start of dexmedetomidine infusion, HR decreased to 78.53±9.10 bpm in Group A. After intubation in 1st minute, there was slight increase in HR of about 80.73±8.57, which settled down to below the baseline 10mins after intubation. In the 1st minute after extubation, HR increased, which was 69.56±6.46 but still was lower than the baseline level.

In Group B, after start of fentanyl infusion, HR maintained at 82.73±7.32 which was same as baseline level (82.71±9.72). In the 1st minute after intubation, there was significant increase in HR

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which was 95±7.63. The increase in HR settled down to baseline level 15mins after intubation. In the 1st minute after extubation, there was again significant increase in HR of 87.38±8.47, which settled down to 77.36±13.86 after 5mins of extubation.(Fig. 1)

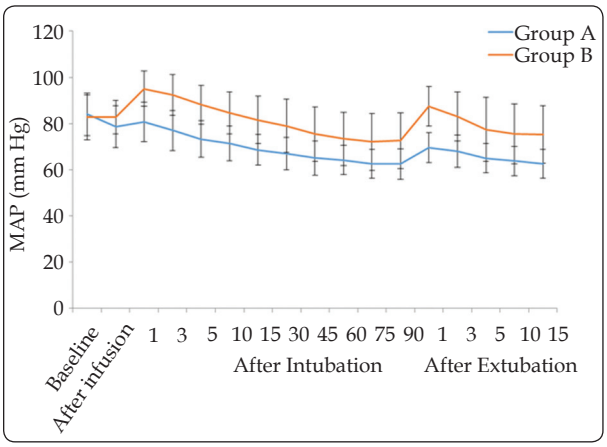

Fig. 1: Line Diagram Showing Heart Rate Comparison Between two Groups.

There was no significant difference in Mean arterial pressure (MAP) between two groups at baseline and also after the infusion of the study drugs. (Fig. 2)

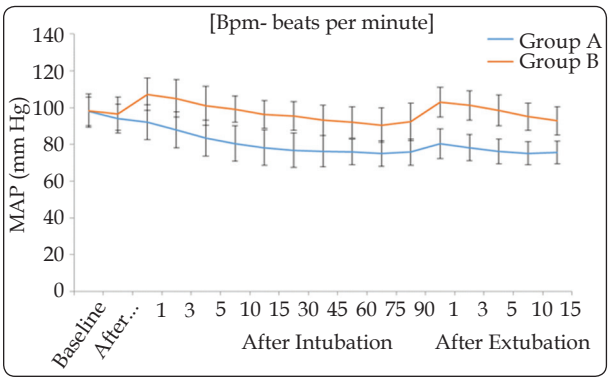

Fig. 2: Line Diagram Showing Mean Arterial Blood Pressure Comparison Between Two Groups.

Patients who received fentanyl had shown significant increase in MAP in the 1st minute after intubation from 96.71±8.99 to 107.31±8.69 and also in the 1st minute after extubation from 92.29±10.21 to 103.04±8.03.

Patients who received dexmedetomidine had shown no increase in MAP after intubation and also only mild increase in MAP in the 1st minute after extubation from 75.89±7.08 to 80.42±8.01.

VAS scores are significantly higher in fentanyl group when compared to dexmedetomidine at 0hr, 6hr, 12hr and 24hrs post-surgery.(Fig. 3)

There was significant difference in the requirement of rescue analgesics in the first 24hrs between the two groups. (Fig. 4)

62.2% of patients from Group A required only 2 rescue analgesics while 62.2% of patients from Group B required 3 rescue analgesics in the first 24hrs following surgery. [p value <0.001, significant]

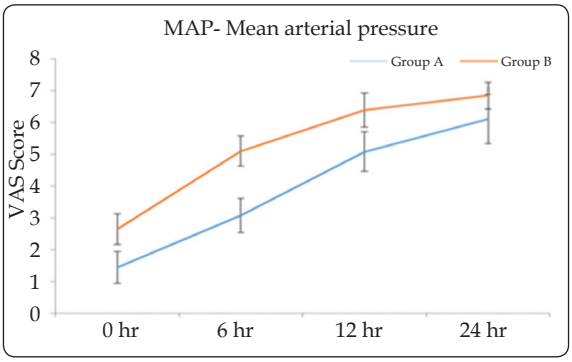

Fig. 3: Line Diagram Showing Vas Scores Comparison Between Two Groups.

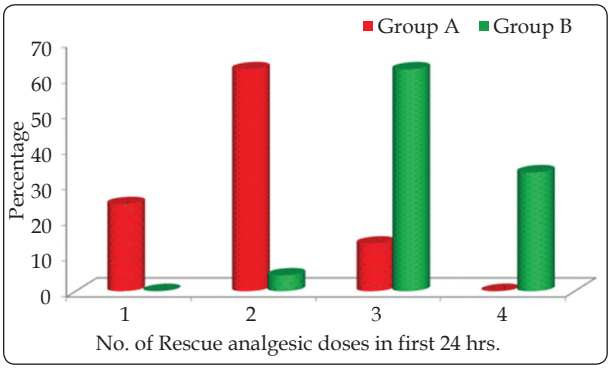

Fig. 4: Bar Diagram Showing Rescue Analgesics Comparison Between Two Groups.

Abbreviations

HR	Heart Rate
Bpm	Beats Per Minute
PR	Pulse Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
NIBP	Non-Invasive Blood Pressure
MAP	Mean Arterial Pressure
ECG	Electrocardiogram
SPO2	Peripheral capillary oxygen saturation
CVS	Cardiovascular system
PA	Per Abdominal
RS	Respiratory System
CNS	Central Nervous System
VAS	Visual Analogue Scale
Iv	Intravenous
ASA-PS	American Society of Anaesthesiologists – Physical Status
D5W	Dextrose 5% in water
NS	Normal Saline

CBC	Complete Blood Count
HB	Haemoglobin
WBC	White Blood Count
HS	Hora somni- at bedtime
RFT	Renal function tests
i.e.,	That is
µg/mcg	Microgram
Kg	Kilogram
Mm Hg	Millimetre of Mercury
cm	Centimetre
mg	Milligram
ml	Millilitre
mins	Minutes
Secs	Seconds
SD	Standard Deviation
Tab	Tablet
hr	Hour
ETCO2	Endtidal carbondioxide
No. of	Number of
Approx.	Approximately
Intraop	Intraoperative
Postop	Postoperative

Discussion

During general anaesthesia, the critical events include laryngoscopy, tracheal intubation and extubation. These events are associated with significant sympathetic stimulation. To mitigate the hemodynamic changes associated with sympathetic response, various techniques have been tried. These techniques range from application of local anaesthtetics, nerve blocks infiltration to various drugs. Short acting beta blockers like esmolol was tried initially to treat hypertensive episodes. But beta blockers are associated with side effects like bradycardia and conduction delays. Other drugs include calcium channel blockers, vasodilators, opioids and adrenergic blocking agents.

Dexmedetomidine is a highly selective α2 agonist.[11] It maintains hemodynamic stability through its central sympatholytic action. Dexmedetomidine has been extensively used as an adjuvant to general anaesthesia owing to its anaesthetic sparing and sedative properties. Fentanyl is synthetic potent µ receptor agonist. It controls both heart rate and blood pressure responses during intubation and extubation.[13]

This was a prospective double blinded randomized controlled study carried out at R L Jalappa Hospital and Research, Tamaka, Kolar, during the Academic year from January 2019-June 2020. Ninety patients of age group 20-50years with ASA grade I, II of either sex undergoing elective surgeries with duration of approx. 90mins like laminectomy, Oro-maxillary, ENT, Thyroid, laparotomies and laparoscopic surgeries under general anaesthesia were included. Patients were randomly divided into two groups each of 45 after obtaining the informed consent. Baseline vitals like HR, SBP, DBP and MAP were recorded. Loading dose of the study drug was started at the rate of 1µg/kg and given over 10mins. After the loading dose is given, the required monitoring parameters were once again recorded and the study drug infusion rate was changed to maintenance dose of 0.5µg/kg/hrPreoxygenation was done with 100% oxygen for 3minutes and premedicated with glycopyrrolate and induced with propofol. till 10mins prior to extubation. Group A received dexmedetomidine and Group B received fentanyl. The infusion of study drug was stopped 10mins prior to extubation. HR, SBP, DBP and MAP were again recorded until 15mins post extubation. VAS scores were recorded for first 24hrs post-operative period. The requirement of rescue analgesics was also compared between two groups.

Both the groups were comparable in terms of age, weight, gender and ASA grading in our study. In our study, we observed that there was significant difference in the heart rate after the intubation with less increase in dexmedetomidine group when compared to fentanyl group as in accordance with the study conducted by Tanuja et al.

From our study, we observed a significant increase in SBP, DBP and MAP after intubation with fentanyl group than dexmedetomidine group with p value less than 0.05. Our results were consistent with the study conducted by Patel CR et al, which has shown similar fluctuations in blood pressure after intubation implying the attenuating effect of dexmedetomidine on laryngoscopic response.[5]

From Our study, we found out that intraoperative hemodynamic were better maintained with dexmedetomidine infusion with MAP 20% less than baseline than fentanyl infusion. Bekker et alfrom his study concluded that dexmedetomidine infusion was able to blunt the perioperative blood pressure changes.[8]

By observing the significant increase in HR and MAP in our study after extubation in fentanyl group than dexmedetomidine group, we conclude that dexmedetomidine is better in attenuating the stress

response during extubation. Kotak N et alfrom his study concluded that 0.5µg/kg of dexmedetomidine over 10mins prior to extubation is effective in attenuating stress response to extubation.[6] Aksu et alfrom his study concluded that 0.5µg/kg of dexmedetomidine is effective in mitigating airway reflexes during extubation better than fentanyl 1µg/kg.[7] Study done by Garg A et aldemonstrated that intraop infusion of dexmedetomidine at 1 µg/kg over 10 min followed by 0.4 µg/kg/h reduces the emergence agitation after nasal surgery.

Post-operative analgesia is important for anaesthesiologist as it impairs the recovery of the patient. Our study demonstrated that patients who received intraop dexmedetomidine had less VAS scores when compared to fentanyl group with p value less than 0.05.

Our results were consistent with the study done by Vaswani JP et al, where they concluded that postoperative analgesia was higher in dexmedetomidine group.[10] Study done by Turgat N et al., demonstrated that fentanyl group required earlier rescue analgesic than dexmedetomidine group.

In our study there is insignificant difference in RR and SPO2 between two groups.

Dexmedetomidine has side effects such as bradycardia and hypotension. We did not encounter any such episodes in our study.

Conclusion

We hereby conclude from our study that, dexmedetomidine at 1µg/kg over 10mins followed by 0.5µg/kg/hr of infusion is better in attenuating the stress response to intubation, in maintaining the intraoperative hemodynamic and in attenuating extubation response. Dexmedetomidine also provides better post-operative analgesia when compared to fentanyl.

Conflict of Interest: Nil

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Prospective Randomised Comparative Study of Laryngeal Mask Airway in Relation to Laryngeal Inlet between Standard and Rotational Insertion Techniques using Fibreoptic Bronchoscope in Children

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Abstract

Background and Aims: Laryngeal mask airway is a novel device that bridges the gap in airway management between endotracheal intubation and face mask. In this study we wanted to determine the optimal insertion technique of LMA in children. The aim of this study is to compare the position of LMA in relation to laryngeal inlet between the two insertion techniques - the standard brain technique and rotational technique by using fibre optic bronchoscopy in children.

Methods: This is a randomised controlled study which included 60 patients divided in two groups of 30 each based on technique of insertion of LMA. After successful insertion, position of LMA is graded using fibre optic bronchoscope.

Results: In patients belonging to rotational technique group the incidence of FOB grade 1 is 96.67%and FOB grade 3 is 0%. Similarly, in standard technique group the incidence of FOB grade 1is 60% and FOB grade 3 is 3.33%.

Conclusion: Rotational technique of LMA insertion is associated with better positioning in relation to laryngeal inlet compared to standard technique as well as lesser attempts and decreased complications.

Keywords: Paediatric LMA insertion; Rotational technique LMA.

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Introduction

Many techniques are described to improve success rate of LMA placement in children. Fibreoptic assessment in paediatric population around the larynx demonstrates a high incidence of malposition of LMA. Suboptimal position of LMA can cause partial obstruction and incomplete seal around the larynx, thereby increasing the chance of regurgitation. In this study we have compared

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two LMA insertion techniques- the standard brain technique and rotational technique by using fibreoptic bronchoscope in children.

Methods

This study is a prospective randomised case control study conducted after getting approval from institutional ethics committee. Patients undergoing surgeries in day care surgery theatre at Institute of child health and hospital were assessed for inclusion and exclusion criteria after obtaining written informed consent from parents.

The study included 60 patients, divided into two groups. Group S, standard technique (standard brain technique) and group R, rotational technique. The primary objective was fibreoptic assessment of LMA position in relation to glottis. The secondary objectives are time taken for LMA insertion, number of attempts for LMA insertion, hemodynamic parameters and complications during LMA insertion intraoperatively and during postoperative period. The following are inclusion criteria: ASA 1 and 2, children aged 3 to 8 years, elective surgeries, valid informed consent obtained from parents or guardians. The following are excluded: ASA 3, 4, patients at risk of aspiration, anatomical abnormalities of airway or anticipated difficult airway, upper respiratory tract infection, patients with full stomach and history of asthma. Randomisation was done by computer generated table.

The children were premedicated with oral midazolam 0.5mg/kg 30 mins prior to shifting. In the operation theatre standard monitors attached. Baseline Heart rate, NIBP, Oxygen Saturation, and respiratory rate are recorded. After securing intra venous line, inj glycopyrrolate 10 mcg /kg i.v, fentanyl 2 mic/kg i.v are given. Child is induced with propofol 3.5mg/kg, inj xylocard 1.5mg /kg followed by insertion of LMA after adequate jaw relaxation. Vital parameters are monitored and FOB grading done. Following LMA insertion in both techniques, LMA was inflated with 10ml of air in size 2 and 15ml of air in size 2.5 LMA and seal was obtained. Cuff was inflated to maintain pressure around 45cms of water, measured using cuff pressure manometer. Successful placement was checked by chest expansion, reservoir bag movement and appearance of capnographic tracing in monitor. Maintenance of anaesthesia is with 50% O2 and N2O and 2% sevoflurane. Child is allowed to breathe spontaneously, airway patency checked clinically. The grading of FOB is as follows

Grade 1: larynx only seen

Grade 2: larynx and posterior epiglottis surface seen

Grade 3: larynx, epiglottis tip or anterior surface seen

Grade 4: Epiglottis downfolded and anterior surface seen

Grade 5: Epiglottis downfolded and larynx cannot be seen directly

Various grading scales are available. Brimacombe[1] proposed a similar grading scale and another fibreoptic grading scale was proposed by Julian Arevalo[2] using I gel.

Primary outcome measured is fibreoptic assessment of LMA position in relation to glottis. The secondary outcomes measured are time taken for insertion of LMA, number of attempts made, complications encountered, hemodynamic parameters, use of manoeuvres to relieve airway obstruction. Caudal block of 0.25% bupivacaine 1ml/kg was given for analgesia to both the groups. The intraoperative and post-operative complications were recorded

In case of gastric distension, decompression was done using nasogastric tube. Intraoperative laryngospasm was managed with 100% oxygen and additional dose of 1mg/kg propofol and repositioning of LMA done. At the end of procedure LMA was removed in deep plane of anaesthesia and face mask was used. After the child became conscious, child was shifted to recovery room.

Statistical analysis

Sample size was determined using this formula.

Formula $n=(Z\alpha/2+Z\beta)2*(p1(1-p1) +p2(1-p2))/(p1-p2)2$,

where $Z\alpha/2$ is the critical value of the normal distribution at $\alpha/2$(e.g. for a confidence level of 95 % αis 0.05 and the critical value is 1.96

$Z\beta$ is the critical value of normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p1 and p2 are the expected sample proportions of the two groups

Based on this the minimum sample size required for the study was calculated to be 27. Power of the study is 80%. In our study 60 subjects were chosen and divided into two groups of 30 each. (30 standard and 30 rotational) by computer allocated randomization number. Descriptive statistics was done for all data and were reported in terms of

mean values and percentages. Continuous variables were analysed with unpaired t tests and ANOVA single factor test. Categorical variables will be analysed with Chi square test and Fischer exact test. Statistical significance will be taken as $p<0.05$. The data will be analysed using SPSS version 16 and Microsoft excel 2007.

Both the groups were comparable in terms of age, gender, height, weight, LMA size, FOB grading, time for insertion, number of attempts, hemodynamic parameters , and complications.

By conventional criteria the FOB grading status between the rotational technique group and the standard technique group among study subjects is considered to be statistically significant since $p<0.05$ as shown in the table below.

By conventional criteria the time for insertion distribution between the rotational technique group and the standard technique group among study subjects is considered to be statistically significant since $p <0.05$ as shown in the table below.

Results

In patients belonging to the rotational technique group, the mean time for insertion is 8.43 minutes. Similarly, in standard technique group the mean time for insertion is 11 minutes. The decreased time for insertion in rotational technique group compared to standard technique group is statistically significant as the p value is <0.0001 as per unpaired t test indicating a true difference between the groups.

Table 1: Age Distribution.

Age Distribution	Rotational technique	%	Standard technique	%
≤4 years	6	20.00	3	10.00
5-6 years	14	46.67	14	46.67
7-8 years	10	33.33	13	43.33
>8 years	0	0.00	0	0.00
Total	30	100	30	100

P value unpaired test: 0.1015

Table 2: Gender Distribution.

Gender Status	Rotational technique	%	Standard technique	%
Male	28	93.33	23	76.67
Female	2	6.67	7	23.33
Total	30	100	30	100

P value Fischer's exact test: 0.0856

Table 3: Weight distribution.

Weight Distribution	Rotational technique	Standard technique
N	30	30
Mean	18.23	18.77
SD	3.46	3.43

P value unpaired t test: 0.5512

Table 4: FOB grading between two groups.

FOB Grading	Rotational Technique	%	Standard Technique	%
Grade 1	29	96.67	18	60.00
Grade 2	1	3.33	11	36.67
Grade 3	0	0.00	1	3.33
Total	30	100	30	100

P value Fischer's exact test: 0.0006.

Table 5: LMA size between two groups.

LMA Size	Rotational technique	%	Standard technique	%
Size 2	22	73.33%	18	60.00
Size 2.5	8	26.67%	12	40.00
Total	30	100	30	100

P value Fischer's exact test : 0.2910

Table 6: Time for insertion between groups.

Time for Insertion	Rotational technique	Standard technique
N	30	30
Mean	8.43	11
SD	0.86	1.31

P value unpaired t test: <0.0001

Discussion

Endotracheal intubation is the procedure for administration of general anaesthesia and a secured way of airway control. Laryngeal mask is a useful airway device both for GA and emergency airway maintenance. Advantages of LMA over endotracheal tube include speed of placement, improved hemodynamic stability during induction and emergence, lower incidence of coughing, sore throat and reduced anaesthetic requirement. Various studies including the one by SM Asida et al.,[3] and Wen Xian et al.,[4] have shown that LMA is a reliable paediatric supraglottic airway device demonstrating relatively low failure rates. Paediatric LMA plays a role in short day care procedures, maintenance of airway in inhalational anaesthesia or as a conduit for intubation using FOB and also plays a role in new-born resuscitation. Various insertional techniques have been studied to find an optimal method of LMA insertion. The

various methods of insertion include standard, rotational and lateral techniques with cuff inflated or partially inflated.[5,6] There are several methods to confirm the position of LMA and the gold standard being use of fibre optic bronchoscope.

In our study sample size was calculated based on study conducted by Babitha ghai et al.,[7] using FOB grading as the parameter. The induction can be either intravenous or inhalational induction. In our study we used inj fentanyl 2µg /kg with inj. Propofol 3.5mg/kg. This was similar to the study Seyedhejazi et al.,[8] which concluded that propofol 3.5mg/kg is equally effective for LMA insertion. in another study Ranju Singh et al.,[9] compared ketamine with propofol and fentanyl with propofol for LMA insertion in children and concluded that fentanyl with propofol provided the ideal insertion condition. There are several techniques described for LMA insertion, few common ones are standard, rotational and lateral. Standard technique is placement of LMA with the LMA aperture facing caudally which is advanced into hypopharynx till resistance is felt. McNicol et al.,[10] described an alternate technique of LMA insertion in which the LMA was introduced with aperture facing cranially with partially inflated cuff into pharynx and now turned to 180 degrees before it was advanced to final position. This was the reason why we took this study to know which method will be ideal in paediatric anaesthesia practice.

In our study success rate of LMA insertion by rotational technique was 100% in 1st attempt and in standard technique it was 83.3% in 1st attempt and 16.67% in second attempt. The attempt status was not statistically significant since p value was more than 0.4 which correlates with the study conducted by Babitha Ghai et al.,[12] comparing three techniques and found success rate at 1st attempt more with Rotational (96%), lateral (84%) and standard (80%). Further the airway seal provided by LMA is well maintained during surgery. This is also proved in a study by Richard et al where they showed that increase in cuff pressure during surgery in presence of no 2 is small and probably not a cause for clinical concern.

In our study the time for LMA insertion on an average mean was around 8.43 seconds in Rotational technique and 11 seconds in standard technique with mean difference of 2. 57 seconds. This was found to be statistically significant with p value of <0.0001 determined by unpaired t test indicating true difference among the study groups. This correlates with the study conducted by Babitha et al.,[12] in which the time taken for successful insertion is 12.24 seconds in rotational technique and 15.94 seconds in standard technique with significant p value of < 0.001.

In our study the incidence of FOB grade 1 was meaningfully more in rotational technique group compared to the standard technique group by 60% with percentage difference of 36.67 points. The incidence of FOB grade 3 was meaningfully less in rotational technique group compared to standard technique group by 3.33% with a percentage difference of 3.33 points. This difference is true and significant. Hence, we can infer that rotational technique significantly results in better seating of LMA than standard technique during positioning of laryngeal mask airway in relation to laryngeal inlet, studied using fibre optic bronchoscope in children. The above result was similar to the study conducted by Soh et al 13in which they found FOB grade 1 and 2 view with rotational technique was 92.3% and with standard technique was 61.5%. A similar study in adults by Kumar et al.,[14] also showed rotational technique to be easier with lesser complications compared to standard technique.

Common complications during LMA placement include coughing, gagging, apnoea, bleeding, laryngospasm and gastric distension. In our study the incidence of complications during insertion was more with standard technique when compared to rotational technique but not statistically significant. The incidence of intraoperative and post-operative complications were more with standard technique but were not statistically significant. Similar results were seen in study conducted by Nakayama et al[14] where there was lower incidence of complications like laryngospasm, apnoea and trauma in rotational technique compared to standard technique

In our study the heart rate, respiratory rate distribution oxygen saturation and blood pressure distribution between the two groups were compared and there was no statistical significance with p value >0.05.

Conclusion

In this study we conclude that rotational technique of LMA insertion is associated with better positioning of LMA in relation to laryngeal inlet when compared to Standard technique by using Fibre optic bronchoscope in children. Also, the LMA insertion time, number of attempts for LMA insertion and incidence of complications were less with rotational technique than standard technique.

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Comparative Study of Magnesium Sulphate and Lignocaine Viscous Gargle in Prevention of Postoperative Sore Throat – A Experimental Study

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Abstract

Background: Postoperative sore throat (POST) is a common occurrence following endotracheal intubation in general anaesthesia Pharmacological agents like local anaesthestics, corticosteroids, ketamine, magnesium sulphate($MgSO_4$) are tried for attenuating POST. In this study, we compared efficacy of magnesium sulphate with lignocaine gargle on attenuating incidence and severity of POST.

Methods: In this randomized double blind controlled study, total 60 adult patients were randomly allocated to two equal groups, Group M (n~30) and group L(n~30). In group M patients received Magnesium sulphate 20mg/kg, dissolved in 20 ml of 5% dextrose solution. In group L patients received 20ml of 2% lignocaine viscous solution. Patients were allowed to gargle slowly for 30 s, 15 min before induction of anesthesia with the solution as per allotment of the group. In post operative period patients were assessed for POST in a four-point scale (0-3) at 0, 1, 2, 4, 8, 12, and 24 hrs.). Heart rates (HR), SpO2, mean arterial pressure (MAP), were recorded.

Results: Incidence of POST in group M recorded lower than group L, and they are 26% vs. 56%, 16% vs. 46%, 10% vs. 40%, 6.6% vs. 33% 3% vs. 20% at 0,1,2,4,8 hrs respectively. Severity of POST was lower in Group M compared to Group L at 0,1,2,4 and 8 hrs. Hemodynamic variables were comparable and statistically insignificant.

Conclusion: We suggest the use of $MgSO_4$ gargle before induction of GA as an effective measure to decrease the incidence & severity of POST compared to lignocaine gargle.

Keywords: Lignocaine; Magnesium sulphate; Post-operative sore throat.

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Introduction

Postoperative sore throat (POST) is most common adverse effect following endotracheal intubation in general anaesthesia. Incidence of POST following endotracheal intubation ranges from 21-65%.[1,2] Various factors contribute to POST, foremost cause being trauma to airway mucosa, tracheal tube cuff pressure leading to mucosal erosion, mucosal inflammation and dehydration.[2,3]

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Multiple non pharmacological and pharmacological trials have been done for reducing incidence of POST. Using smaller size endotracheal tube, alternative airway devices such as LMA, gentle airway instrumentation, minimizing intracuff pressure, oral suctioning under direct visualization are the various non pharmacological measures attempted.[4,5,6] Pharmacological agents like local anaesthestics, corticosteroids, ketamine, magnesium sulphate ($MgSO_4$) are tried for attenuating POST.[7-14]

Magnesium sulphate a NMDA antagonist acts both on central and peripheral nervous system, it has both anti- nociceptive and anti- inflammatory properties which helps in reducing POST.[15] Various studies have been tried and results were controversial.[14,16,17]

To test this hypothesis, we compared efficacy of magnesium sulphate with lignocaine gargle on attenuating incidence and severity of POST.

Methodology

The study was conducted in Melmaruvathur adhiparasakthi institute of medical sciences and research in department of anaesthesiology after obtaining permission from institutional ethical committee. In this randomized double blind study, 60 patients undergoing elective surgery under general anaesthesia with endotracheal intubation were selected. After obtaining written informed consent, total 60 adult patients were randomly allocated to two equal groups every odd numbers allocated to Group M(n~30) and alternative patients to group L(n~30).

Patients undergoing elective surgery under general anaesthesia with endotracheal intubation of age group between 20-50 years of both sexes and American society of anaesthesiologist (ASA) grading I & II were included in this study. ASA III & IV, Patient refusal, Hypersensitivity to $MgSO_4$ and lignocaine, smoker, pregnant and lactating mothers, long term analgesic therapy and upper and lower respiratory tract infections are excluded from this study.

In preoperative assessment, general examination, systemic examinations and assessment of the airway were done. Patients received premedication of tab. Alprazolam 0.25mg and tab. ranitidine 150 mg orally the night before surgery and the morning of surgery with sip of water.Preoperative fasting of minimum 8hrs ensured before the surgery.

Patients were clinically examined, checked for written informed consent and procedure to be done were explained in detail as per patient information document. In group M patients received Magnesium sulphate 20mg/kg, dissolved in 20 ml of 5% dextrose solution. In group L patients received 20ml of 2% lignocaine viscous solution. According to group patients were asked to gargle for 30 s, 15 min before induction of anesthesia. The gargling solutions were given in nontransparent glasses and the person distributing the solution for gargling was also unaware of constituent of the solution and allotment of group.

On entering the operative room baseline monitors such as ECG, pulse oximeter(SPO2), noninvasive blood pressure (NIBP) were attached and parameters were recorded. Intravenous (IV) infusion of Ringers lactate started.

Patients were preoxygenated with 100% oxygen for 3mins, Inj. glycopyrolate (0.01 mg/kg), and Inj. Fentanyl (2 mcg/kg) were given intravenously. For induction, Inj. Propofol (2mg/kg) was given, followed by Inj. Succinylcholine 2 mg/kg IV was given. After 1 min of succinylcholine administration, laryngoscopy was done and intubated with a low pressure high volume cuffed polyvinyl chloride endotracheal tubeof internal diameter 8–8.5 mm for men, and 7–7.5 mm for women. Procedure was performed by a trained anesthesiologist. The endotracheal tube cuff was inflated until no air leakage could be heard with a peak airway pressure at 25cm H_2O and cuff pressure measured by handheld pressure gauge and pressure maintained between 15-20 cm H_2O. Capnograph was connected and ETCO2 was monitored throughout the procedure. Anaesthesia maintained with O2:N2O in the ratio of 1:2, and isoflurane maintained with 1-2% alveolar concentration. Muscle Relaxation provided using inj. Atracurium 0.5mg/kg of loading dose and maintenance dose was 0.1mg/kg. Fifteen minutes before the end of surgery inj. Ondansetron 4mg iv given. Inj. Myopyrrolate 5ml was used for reversal at end of surgery, oropharyngeal suction was performed under direct vision to avoid trauma to the tissues and to confirm that the clearance of secretions was complete. After extubation criteria was fulfilled, patient was extubated.

In post anaesthesia care unit (PACU) patients were assessed by an anesthesiologist at 0, 1, 2, 4, 8, 12, and 24 hrs. Four-point scale (0–3) was used for grading POST. Grade 0 = no sore throat; Grade 1 = mild sore throat (complains of sore throat only on asking); Grade 2 = moderate sore throat (complains of sore throat on his/her own); Grade 3 = severe sore throat (change of voice or hoarseness,

associated with throat pain). Heart rate (HR), SPO2, mean atrial pressure (MAP), were recorded in the post operative period. Cough, hoarseness of voice and any other adverse effects are noted.

Statistical analysis

Incidence of POST was 21-65% based on previous studies. Taking α error of 0.05, confidence interval of 95%, sample size calculation was made. On adding 10% for possible loss to follow-up, the sample size required was 30 patients per group. The collected data were analyzed using recent version of Statistical Package for Social Sciences (SPSS). Categorical variables were analyzed using the test. Normally, distributed continuous variables were analyzed using the independent sample t-test. Hemodynamic variables between the groups were compared with t-test. Differences in the incidence of POST among the groups were compared with Pearson's Chi-square test. p value <0.05 was considered as statistically significant.

Results

In this study total of 60 patients were included and they are randomly allocated in two groups of Group M and Group L and there was no attrition in this study. Demographic data such as age, sex, weight were analyzed and they are comparable in between groups. Duration of surgery were also comparable in both groups. Demographic variable and duration of surgery was not found statistically significant in between two groups. (Table 1)

Incidence of POST in group M recorded lower than group L, and they are 26% vs 56%, 16% vs 46%, 10% vs 40%, 6.6% vs 33%, 3% vs 20% at 0,1,2,4,8 hrs respectively. (Figure 1)

Severity of POST was lower in Group M compared to Group L at 0,1,2,4 and 8 hrs, they were significant with p value (<0.05) of 0.031,0.027, 0.023, 0.031 and 0.049 respectively. (Table 2). At 12hrs even though 3 patients of Group L had POST scoring of 1 compared to Group M but they are not significant. At 24hrs none of the patients had post operative sore throat.

Hemodynamic variables such as HR, SPO2 and MAP monitored over post operative period at 0,1,2,4,8,12, 24 hrs, they were comparable and statistically insignificant. (Table 3)

There were no significant adverse effects such as cough, hoarseness of voice in both groups.

Table 1: Patient demographics.

Variables	Group	Mean	Standard deviation	p-value
Age	M	35.73	11.93	0.575
	L	35.27	11.03	
Weight	M	59.53	6.30	0.648
	L	58.49	6.42	
Duration	M	115.00	30.34	0.678
	L	116.58	27.20	

Table 2: POST scoring.

Time	POST scoring	Group M	Group L	p-value
	0	22	13	
0 HR	1	8	14	0.031
	2	0	3	
	0	25	16	
1 HR	1	5	11	0.027
	2	0	3	
	0	27	18	
2HRS	1	3	10	0.023
	2	0	2	
	0	28	20	
4HRS	1	2	8	0.031
	2	0	2	
	0	29	24	
8HRS	1	1	6	0.049
	2	0	0	
	0	30	27	
12HRS	1	0	3	0.076
	2	0	0	
	0	30	30	
24HRS	1	0	0	0.095
	2	0	0	

*-none of the patients had a post score of 3 at any time of study.

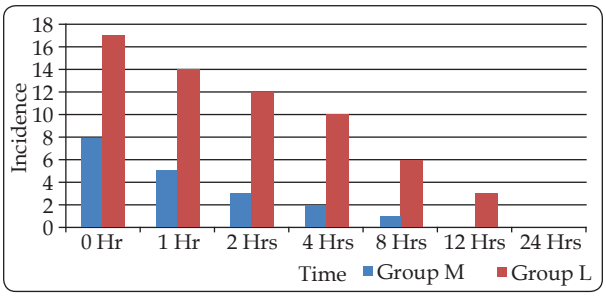

Fig. 1: Incidence of POST.

Table 3: Hemodynamic variables.

Variables	Group	0HR	1 HR	2HRS	4HRS	8HRS	12HRS	24HRS
HR (Min)	M	91.83±3.42	87.17±4.34	83.47±4.10	82.10±4.70	80.52±4.71	78.30±4.30	78.30±4.82
	L	91.07±3.62	85.87±5.17	83.86±5.4	82.87±4.3	80.25±4.74	79.57±4.25	78.00±3.41
	p-value	0.871	0.195	0.520	0.766	0.927	0.744	0.933
MAP (mm hg)	M	93.07±2.13	88.73±2.44	86.33±2.36	85.87±2.96	84.63±2.35	84.86±1.97	83.97±2.31
	L	92.73±2.49	89.37±2.71	88.00±2.24	87.33±2.79	85.63±3.48	85.17±3.30	85.00±2.92
	p-value	0.139	0.908	0.811	0.722	0.359	0.065	0.117
SPO2 (%)	M	99.23±0.81	99.40±0.56	99.40±0.56	99.43±0.72	99.43±0.62	99.40±0.62	99.47±0.62
	L	99.33±0.80	99.17±0.79	99.43±0.77	99.47±0.68	99.37±0.55	99.33±0.71	99.27±0.74
	p-value	0.96	0.81	0.31	0.63	0.31	0.40	0.40

Discussion

POST even though a minor complication, its incidence is very high after ETGA. Most common cause of POST being aseptic inflammation due to injury of pharyngeal mucosa, leading to oedema and congestion.[2,3] Even though it has delayed patient recovery, increased hospital stays and cost, there was only limited research were made in POST.[27] Various pharmacological andnon-pharmacological were tried with variable success rate for decreasing severity and incidence of POST.[4-14] So in this study we compared $MgSO_4$ and well known commonly used topical lignocaine 10% gargle for reducing severity and incidence of POST.

$MgSO_4$ has antinociceptive effects that are primarily based on inhibition of Calcium entry into cell and block NMDA-type glutamatereceptors.[15] Schempp CM et al also provedanti-inflammatory and antinociceptive properties of $MgSO_4$ after topical application.[19] Lignocaine the most common pharmacological agent used in preventing POST in several ways such as jelly, topical application, intravenous as well as spray with inconclusive effect.[7,8,10]

Demographic data such as Age and sex between group M and group L were found similar and they are statistically insignificant. Study conducted by Surajit Chattopadhyay et al showed similar results that age/sex has no implication over POST.[17] But controversy exists with age and gender in study conducted by Higgins et al. They found that female gender has more likely to have POST compared to male. Higgins et al also found elderly patients have higher incidence of POST.[18]

In our study duration of surgery in both groups were almost similar and comparable, they statistically insignificant. Surajit Chattopadhyay et al showed similar results that duration of surgery has no statistically significance for POST.[17] Aliya et al in controversy found that duration of surgery has a direct relationship with the occurrence of POST.[26]

Incidence of POST in $MgSO_4$ group recorded lower than lignocaine group at 0,1,2,4,8 hrs. Narinder P singh & suritit c in their respective studies found incidence of POST is less with use of $MgSO_4$ as compared to other drugs.[23] In other study conducted by SO Aigbedia lignocaine jelly group had higher incidence of POST when compared to ketamine gargle.[25]

Severity of POST is lower in group M compared to group L and they are statistically significant at 0,1,2,4,8 hours. Teymourian et al in their study comparing $MgSO_4$ and ketamine gargle observed lesser severity score in $MgSO_4$ group similar to our study.[20] Hung NK et al and Agarwal A,et al in both studies comparing benzydaminehydrochloride & lignocaine 10% spray in ET tube showed decreased severity score of POST in benzydamine hydrochloride than lignocaine group.[21,22]

Hemodynamic variables in both groups were comparable & statistically insignificant. This results similar to study conducted by Surajit Chattopadhyay et al.[27]

Conclusion

In this prospective randomized study $MgSO_4$ (Group M) gargle has lesser incidence & severity of POST when compared to lignocaine gargle (Group L). Hence we suggest the use of $MgSO_4$ gargle before induction of GA as an effective measure to

decrease the incidence & severity of POST.

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Conflicts of interest: Nil

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Original Article

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A comparison of Caudal Bupivacaine to Bupivacaine Infiltration with Rectal Diclofenac Suppository for Postoperative Analgesia in Pediatric Patients Undergoing Below Umbilical Surgeries

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Abstract

Aim: To compare the analgesic effects of caudal block using 1ml/kg of 0.25% bupivacine to a combination of local infiltration with 0.5ml/kg of 0.25% bupivacaine with rectal diclofenac suppository 2mg/kg in the management of postoperative pain following below umbilical surgeries in pediatric patients of age group 2-7 years.

Materials and Methods: 100 patients belonging to both sexes, aged between 2-7 years, with ASA Status I, II who were posted for below umbilical surgeries under general anaesthesia were included in the study The patients were randomly allocated into two groups. Group A : Patients received caudal block with 1ml/kg of 0.25% Bupivacaine Group B : Patients received local wound infiltration with 0.25% Bupivacaine 0.5ml/kg and rectal diclofenac suppository 2mg/kg .

Observation and Results: The pain scores, total duration of analgesia, number of rescue analgesics required, time for micturition and postoperative complications,if any were compared in both the groups.

Conclusion: We conclude that both caudal block and local infiltration with reactal diclofenac suppository are equ ally effective for postoperative analgesia in below umbilical surgeries.

Keywords: Bupivacaine; Diclofenac; Postoperative analgesia; Caudal block.

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Introduction

Pain in children is a complex phenomenon, as it is difficult to differentiate crying or restlessness due to pain from that of hunger or fear. Pain triggers complex biochemical and physiological stress responses and induces impairement in pulmonary, cardiovascular, neuroendocrinal, gastrointestinal, immunological, and metabolic functions.[1-2] It is now accepted that acute post-operative pain

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management is an integral part of the practice of paediatric anaesthesia.[3]

Pain relief can be achieved by various methods like systemic opioids, NSAIDS, central neuraxial block either intrathecal or epidural opioids, local anesthetic or by peripheral nerve block and infiltration of wound by local anesthetics, while the various non-pharmacological modalities are hypnosis, TENS, acupuncture and psychotherapy.[4]

Regional anaesthesia is an essential part of modern anesthesia practice, conveying many significant advantages such as superior analgesia, reduced MAC, hemodynamic stability,obtundation of hormonal stress response, reduced intra operative blood loss and improved GI function.[5] Regional anesthesia undertaken when the child is under GA can give prolonged analgesia in the postoperative period. Caudal block provides excellent analgesia for any surgery below umbilicus such as herniotomy, orchidopexy. Long acting local anesthetic alone or in combination with adjuncts prolong analgesia with minimal side effects.[6]

Infiltration of wound edges with local anesthetics (field block) or by directly instilling local anesthetic into a wound effectively provides intraoperative and postoperative analgesia for many minor and some major surgeries. The most commonly used local anesthetics for infiltration are lignocaine, bupivacaine and ropivacaine. Traditionally strong analgesics such as opioids have been used intraoperatively where as NSAIDS and paracetamol are most commonly given at the end of surgery as part of multimodal approach to postoperative analgesia.

Rectal route of drug administration is safe, easy and convenient for absorption in the pediatric age group as it bypasses the liver avoiding hepatic first pass metabolism.

This study was conducted to compare the analgesic efficacy of caudal bupivacaine to bupivacaine infiltration with rectal diclofenac suppository in pediatric patients undergoing below umbilicl surgeries.The pain scores, duration of analgesia, requirement of rescue analgesics and postoperative complications,if any were compared in both the groups.

Aims and Objectives

It is a prospective, randomized, comparative, observer- blinded study to compare the analgesic effects of caudal block using 1ml/kg of 0.25% bupivacine to a combination of local infiltration with 0.5ml/kg of 0.25% bupivacaine with rectal diclofenac suppository 2mg/kg in the management of postoperative pain following below umbilical surgeries in pediatric patients of age group 2-7 years.

Our aims and objectives are to compare:

1. Post operative hemodynamics
2. Pain scores in both the groups
3. Total duration of analgesia in both the groups
4. Number of rescue analgesics required
5. Time for micturition in both the groups
6. Complications if any, post operatively

Materials and Methods

Study Design and Equipment

After obtaining institutional ethical committee approval and informed consent from the parents, this prospective, randomised, comparative study was conducted in Rangaraya medical college/ Govt. General Hospital, Kakinada.

Inclusion Criteria

1. Age 2-7 years
2. Elective surgeries
3. ASA status I, II physical status.

Exclusion Criteria

1. Patient or parent refusal
2. History of allergy to any drugs used in the study
3. History of bleeding diathesis
4. Infection to site of caudal injection

Methods

100 patients belonging to both sexes, aged between 2-7 years, with ASA Status I, II who were posted for below umbilical surgeries under general anaesthesia were included in the study. Clinical examination and routine investigations were done to all patients. All of them had a thorough pre-anesthetic evaluation. Solid foods restricted for 8hrs, but clear fluids allowed upto 2hrs prior to surgery. Children were brought to the operating room and venous access achieved with a 22-Gauge i.v canula. Monitors such as pulse oximeter, ECG, and NIBP were connected. Patients were pre-medicated with

0.02mg/kg Atropine, 0.03mg/kg Midazolam. All patients underwent general anaesthesia with 3-5mg/kg Thiopentone Sodium and Endotracheal intubation was facilitated by Atracurium 0.5mg/kg. Maintained with 50% oxygen, 50% nitrous oxide, and sevoflurane at a concentration ranging from 0.5% to 2%. The patients were randomly allocated into two groups by picking random lots from a sealed bag.

Group A: Patients received caudal block with 1ml/kg of 0.25% Bupivacaine

Group B: Patients received local wound infiltration with 0.25% Bupivacaine 0.5ml/kg and rectal diclofenac suppository 2mg/kg.

In Group A, at the end of surgery patient is tilted on the lateral side and caudal

Block was performed under complete aseptic conditions by using loss of resistance technique. In Group B local wound infiltration was done before closure of the skin incision and diclofenac suppository placed per-rectally at the end of the surgery.

Vitals such as Pulse rate, MAP, Respiratory rate and Oxygen saturation were monitored through out the surgery. After completion of surgery, anesthetic agents were discontinued, anaesthesia was reversed with 0.05mg/kg Neostigmine and 0.02mg/kg

Atropine. 100% oxygen was administered through face mask for 3-5 minutes. The total duration of surgery was noted. When fully awake and hemodynamically stable, children were transfered to the PACU.

Postoperative hemodynamics Pulse rate and MAP were monitored for 8 hrs in the postoperative period. Postoperative pain was assessed using

FLACC Scale.

Flacc Scale

The Face, Legs, Activity, Cry, Consolability scale combines five types of pain behaviours ,including facial expression,leg movement, activity,cry and consolability and has been shown to have good inter-rate variability and validity in children. It is widely used because it is quick, versatile and can be applied to infants and older children including those with developmental disabilities. Pain was assessed at 0,15,30,45, 60min and every two hours thereafter until 8 hours following surgery or until patient requires rescue analgesic, whichever happened earlier was considered as the end point of observation. At the score ≥4 rescue analgesic i.v paracetamol 15mg/kg was given. The number of rescue analgesics required was also noted. The time for first micturition, the incidence of vomiting, urinary retention,or any relavant side effects were recorded. Children werealso monitored for effects of inadvertent intraarterial injection and intrathecal spread of the local anesthetic.

The data was statistically analysed and expressed as Mean ± S.D.

P value < 0.05 was considered significant.

Observations and Results

All the 100 patients enrolled completed the study. Both groups were similar in their demographic profile and baseline hemodynamic parameters like heart rate, mean arterial pressure (Tab.1).

Table 1: Demographic Data.

	Group A	Group B	P Value
Age (mean±SD)	4.80±0.93	4.84±0.84	0.8216
Sex (M:F)	34:16	36:14	
Weight (in kgs)	14.84±2.15	15.04±2.22	0.5485
ASA status(I/II)	39:11	35:15	

Data was expressed as mean +/- SD, ratio, absolute numbers.

P value found to be insignificant.

Table 2: Type of Surgery.

Type of Surgery	Group A	Group B
Herniotomy	23	24
High Ligation	10	7
Circumcision	9	10
Orchidopexy	8	9

Duration of Surgery

The duration of surgery between the two groups was compared using independent T test. Group A had a mean duration of 45.68 minutes, Group B had a mean duration of 46.90 minutes. It was found to be insignificant with a p value of 0.475 (Tab.3).

Table 3: Duration of surgery.

	Group A	Group B	P Value
Duration of surgery (mins)	45.68±1.74	46.90±1.30	0.475

Baseline Haemodynamic Parameters

Table 4: Baseline haemodynamic parameters.

	Group A (mean± SD)	Group B (mean± SD)	P Value
Heart rate	98.60±7.39	98.12±7.01	0.7391
MAP	56.07±3.14	56.40±3.25	0.8101

Data expressed as mean ± SD in both groups. P> 0.05 statistically not significant. The baseline hemodynamic parameters are equal in both the groups (Tab.4).

Table 5: Comparison of Post-Operative Haemodynamics between the two Groups.

	Group	Heart Rate (bpm) (Mean±SD)	P Value	MAP (mm of Hg) (Mean±SD)	P Value
15 mins	Group A	99.9±11.4	0.5302	57.90±4.40	0.4505
	Group B	101.30±12.8		58.50±4.30	
30 mins	Group A	100.8±10.7	0.5898	58.80±4.51	0.4628
	Group B	101.50±12.6		59.40±4.40	
45 mins	Group A	101.01±12.60	0.6023	59.03±4.50	0.5392
	Group B	101.56±13.02		59.65±4.42	
60 mins	Group A	101.13±11.7	0.6355	59.07±4.56	0.5469
	Group B	102.10±13.2		59.91±4.42	
2HR	Group A	101.31±10.9	0.6864	59.43±4.50	0.5434
	Group B	102.10±12.6		59.93±4.44	
4 HR	Group A	102.10±11.4	0.7244	59.92±4.41	0.5628
	Group B	102.70±12.06		60.04±4.54	
6 HR	Group A	102.60±12.52	0.7940	60.20±4.46	0.7818
	Group B	102.86±11.01		60.40±4.51	
8 HR	Group A	102.86±11.72	0.8427	60.54±2.26	0.8147
	Group B	103.90±11.01		60.86±3.15	

Data expressed as mean ± SD in both groups. P value is not statistically significant.

Postoperative hemodynamics are comparable between both the groups. (Tab.5)

Table 6: Comparison of Pain Scores between two Groups.

	Group A	Group B	P Value
15 MINS	1.22 ±0.41	1.28±0.45	0.487
30 MINS	1.72±0.45	1.60±0.49	0.205
45 MINS	1.96±0.34	1.94±0.31	0.759
60 MINS	2.08±0.34	2.04±0.34	0.557
2 HRS	2.74±0.44	3.00±4.36	0.675
4 HRS	3.20±0.61	3.26±0.66	0.638
6 HRS	4.20±0.75	4.32±0.74	0.422
8 HRS	5.24±0.62	5.24±0.55	1.000

Pain scores are compared at 15mins, 30mins, 45mins, 60mins, 2hrs, 4hrs, 6hrs and 8hrs postoperatively. Data expressed as mean ± SD. P value insignificant at all time intervals.Pain scores are equal in both the groups with no significant difference (Tab.6).

Table 7: Total Duration of Analgesia in two Groups.

	Group A	Group B	P Value
Duration in mins	227.17±19.52	226.36±19.10	0.834

Data expressed as mean ± SD. P value is insignificant. The total duration of postoperative analgesia is equal in both the groups (Tab.7).

Table 8: Requirement of Rescue Analgesics in two Groups.

	Group A	Group B	P Value
Number of rescue analgesics	0.48±0.50	2.06±0.51	0.0001*

Data is expressed as mean ± SD. P value significant (0.0001). Requirement of rescue analgesic is more in Group B compared to Group A. Two or more rescue analgesics were required in local infiltration with diclofenac suppository group (Tab.8).

Table-9 Comparison of time for Micturition in two Groups.

	Group A	Group B	P Value
Time for micturition in mins	274.17±18.80	187.37±24.79	0.0001*

Data is expressed as mean ± S.D. P value significant (0.0001)

Time for micturition in Group A is 274.17±18.80 minutes while in Group B it is 187.37±24.79 minutes.

Time for micturition is prolonged in caudal group(Tab.9) .

Side Effects

All the 100 children enrolled in the study were observed for any side effects in the post operative period such as Hypotension, bradycardia, nausea, vomiting and bleeding. None of them reported any of the above side effects.

Discussion

Pain is a subjective symptom that can be difficult to evaluate with regard to intensity, duration, tolerance, and threshold in pediatrics. Pain in newborns, infants, and children has the same negative effects as in adults. Thus, it is now widely accepted that infants and children require appropriate pain relief in the post-operative period.[7] Postoperative pain management not only minimizes patient suffering but also can reduce morbidity and facilitate rapid recovery and early discharge from hospital, which can reduce hospital costs.

Treatment of postoperative pain in children includes the use of i.v. opioids, nonopioid analgesics and regional nerve block techniques. This can delay the return to normal activity and discharge from

the hospital. Regional techniques for postoperative pain control in children such as caudal block or peripheral nerve block are well-established in postoperative pain control in children.

Postoperative pain is considered as the fifth vital sign of the patient. There is sensitisation of nerve endings leading to spontaneous firing of nerve fibres which constantly drives a pain system in the spinal cord after surgery. Regional anesthesia provides optimal postoperative analgesia as part of a balanced multi-modal approach to pain management.Caudal epidural analgesia is one of the most popular and commonly performed regional blocks in paediatric anaesthesia. It is a reliable and safe technique that can be used with general anaesthesia for intra and postoperative analgesia in patients undergoing infraumblical surgeries.

The weaker or milder analgesics with antipyretic activity, of which acetaminophen (paracetamol), salicylate (aspirin), ibuprofen, naproxen, ketoprofen and diclofenac are common examples, comprise a heterogenous group of NSAIDs and non opioid analgesics.[8]

These analgesic agents are administered enterally via the oral route or, on occasion, the rectal route. Parenterally administered agents including ketorolac, acetaminophen, and recently diclofenac are available for use when the oral or rectal route is not appropriate. Multiple studies and systemic reviews have shown opioid sparing and decreased pain associated with use of acetaminophen and NSAIDs, as well as cost effectiveness and reduced risk of opioid related adverse effects.[9]

Caudal epidural not only reduces the dose of general anesthetics but also attenuates the stress responses to surgery.[10-11] Performing caudal block in an anesthetized child demands proper positioning, identifying proper space and the cumbersome manoeuvre of positioning and repositioning without compromising the airway.

In this study we compared the analgesic efficacy of 1 ml/kg of 0.25% caudal bupivacaine (Group A) to 0.5ml/kg of 0.25% bupivacaine infiltration with rectal diclofenac suppository 2mg/kg (Group B) in pediatric patients undergoing below umbilical surgeries.The pain scores, total duration of analgesia, number of rescue analgesics required, time for micturition and postoperative complications,if any were compared in both the groups.

Demographic data such as age, sex, weight and ASA physical status insignificant in both the groups (Tab.1). There is no significant difference in the duration of surgery for both the groups (Tab.2, Tab3). The baseline and postoperative hemodynamic parameters are comparable between both the groups (Tab. 4, Tab. 5). Pain scores were assessed by FLACC scale at 15mins, 30 mins, 45mins, 60 mins 2 hrs, 4 hrs, 6 hrs and 8 hrs postoperatively (Tab 6). The pain scores and total duration of analgesia are equal in both the groups with no significant difference (Tab.7). Whereas the rescue analgesic requirement is more in group B(2.06±0.51) compared to Group A(0.48±0.50) (Tab.8). The time for micturirtion is significantly prolonged in Group A(274.17±18.80 mins) compared to Group B(187.37±24.79 mins) (Tab.9)

Moores et al.[12] compared the effects of rectal diclofenac with 0.25% bupivacaine administered caudally for postoperative analgesia in pediatric inguinal herniotomy.

Forty-three children were assigned randomly to receive either 1 ml/kg caudal bupivacaine 0.25% or rectal diclofenac 0.25 mg/kg intraoperatively to provide postoperative analgesia. They found that caudal bupivacaine although provided more pain-free patients at first; later the incidence of pain was similar in both groups and concluded that rectal diclofenac is a useful alternative to caudal blockade in this group of patients. In our study, none of the patients presented with pain in the early postoperative period, i.e. up to 220 min postoperatively. This may be because of the additional local infiltration of bupivacaine received by those in the diclofenac group in our study.

Seyed et al.[13] compared the analgesic effects of an acetaminophen (NSAID) suppository, bupivacaine wound infiltration, and caudal block with bupivacaine on postoperative pain in pediatric inguinal herniorrhaphy and observed that in children, bupivacaine infiltration group and the group who received caudal bupivacaine produce better analgesia than the third group who received suppository acetaminophen. They concluded that bupivacaine infiltration is better than a caudal block because of its simplicity, lower incidence of complications, and reduced failure rates. In our study diclofenac was used instead of acetaminophen. As suppository alone did not produce effective analgesia local wound infiltration was administered to the suppository group in our study.

Gupta et al.[14] studied postoperative analgesia in children undergoing infraumbilical surgeries. They concluded that rectal diclofenac in combination with caudal block provides good postoperative

analgesia in early as well as later in the postoperative period, in comparison to caudal block alone which provides analgesia only in early postoperative period or rectal diclofenac alone which does not provide good analgesia in the early or immediate postoperative period. As diclofenac suppository alone did not produce effective analgesia in postoperative period local wound infiltration was given in the suppository group in our study.

William and Splinter, Juan Bass, Lydia Komocar, et al.[15] compared the analgesic efficacy, adverse effects and the cost associated with supplementation of local infiltration with either intravenous ketorolac or caudal analgesia in children having an inguinal hernia repair. They concluded that, supplementation of intraoperatively administered local anesthesia with ketorolac results in a small improvement in pain, a lower incidence in vomiting and a more notable decrease in the time to micturition than a caudal block. These findings are consistent with our present study. However, the nonsteroidal antiinflammatory drug used here was intravenous ketorolac instead of diclofenac suppository used in our study.

Machotta et al.[16] compared between instillation of bupivacaine versus caudal analgesia for postoperative analgesia following inguinal herniotomy in children. They concluded that instillation of Bupivacaine into a wound provides postoperative pain relief following hernia repair, which is as effective as that provided by a postoperative caudal block which is consistent with the result of our study. We added rectal diclofenac suppository to the local infiltration group in our study.

Borkar Dave et al.[17] compared the analgesic efficacy of caudal block against diclofenac suppository with local anesthetic infiltration in children undergoing laparoscopy. They found that the analgesic efficacy of diclofenac suppository combined with local anesthetic infiltration at port sites were comparable to caudal block. Given the necessarily invasive nature of caudal block, they suggested the combined use of diclofenac suppository with local anesthetic infiltration at port sites as a useful and more economical alternative for analgesia following pediatric laparoscopy. Although these observations were for laproscopy, their conclusions are consistent with that of ours.

Gavrilovska et al.[18] compared the analgesic effects of caudal block with local wound infiltration in pediatric patients after inguinal hernia repair. The two groups did not differ in terms of patient characteristic data, surgical profile and hemodynamic changes as in our study. The duration of analgesia and time for first rescue analgesic are comparable between both groups. There were significant differences in incidence of adverse effects in caudal and local group including vomiting and urinary retention.

The results of this study are consistent with those of our study.

Conclusion

We conclude that both caudal block and local infiltration with rectal diclofenac suppository are equally effective for postoperative analgesia in below umbilical surgeries. As administration of caudal block is more time consuming and requires expertise, a less invasive and comparatively easier method of analgesia provided by diclofenac suppository and local wound infiltration of bupivacaine can also be used as an alternative for effective postoperative analgesia in children.

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Comparison of Effect of Norepinephrine Versus Phenylephrine Prophylactic Boluses on Spinal Anesthesia-Induced Hypotension During Elective Cesarean Delivery: A Double-Blind, Randomized, Clinical Study

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Abstract

Background: Spinal anesthesia (SA) onset induces maternal hypotension, which can be managed by vasopressors like phenylephrine (PE). However, PE (α-adrenergic agonist) tends to reflexively decrease the heart rate (HR) and cardiac output (CO). Norepinephrine (NE), being an α-agonist with weak β-adrenergic activity, maintains the blood pressure (BP) with less tendency to decrease the HR and CO, and hence, may be a more useful alternative to PE.

Objectives: To compare the effects of prophylactic boluses of NE and PE on SA-induced hypotension during elective cesarean section, as well as assess the neonatal outcomes and adverse reactions.

Methods: Sixty parturient belonging to ASA class I and II, scheduled for elective cesarean section, were randomly allocated between 2 groups: (i) Group NE (n=30) which received 5 µg intravenous (IV) NE, and (ii) Group PE (n=30) which received 50 µg IV PE as prophylactic boluses immediately after patient repositioning. Rescue bolus interventions using 5 µg NE or 25 µg PE were given for hypotension, respectively. Maternal hemodynamic variables were measured non-invasively. Neonatal outcomes and adverse effects, if any, were also noted and compared.

Results: Pre-operative and post-operative hemodynamic parameters (HR, SBP, DBP, MAP, SpO2), adverse incidences (of hypotension, bradycardia, and nausea) as well as neonatal outcomes were comparable between the two groups (P>0.05). However, the number of patients who required additional rescue vasopressor boluses was significantly greater in Group PE than in Group NE (OR for 2 vs 0 bolus = 9.75; OR for 2 vs. 1 bolus = 11.1428).

Conclusion: NE was more efficacious in preventing SA-induced hypotension with better preservation of maternal HR than PE, and hence, can be considered as an alternative to PE.

Keywords: Spinal anesthesia; Phenylephrine; Norepinephrine; Parturition; Blood pressure; Obstetric surgical procedures.

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Introduction

Spinal anesthesia (SA) is preferred for most of the abdomino-pelvic surgeries, including cesarean sections, since it is a simple and safe technique with rapid onset, allows the patient to remain awake, avoids airway management problems besides providing postoperative analgesia.[1-4] Hyperbaric bupivacaine (0.5%) is extensively used for SA.[4,5] However, a common side effect of SA onset is maternal hypotension due to SA-induced venodilation leading to a reduction in venous return and hence, cardiac output (CO), eventually reducing uteroplacental perfusion, causing both maternal morbidities (nausea, vomiting, inadequate cerebral perfusion, decreased consciousness, respiratory depression, and cardiac arrest) as well as adverse fetal effects (impaired fetal oxygenation, asphyxial stress, and fetal acidosis as it depends on the maternal uterine artery pressure for adequate uterine blood flow).[6]

Due to the poor efficacy of non-pharmacological techniques (like left uterine displacement to decrease aortocaval compression, leg elevation, and prehydration/preloading) to efficiently manage hypotension, a vasopressor such as phenylephrine (PE) is usually required to maintain the blood pressure (BP) during SA.[7-8] However, PE is a potent α-agonist without β-adrenergic activity, causing a dose-related reflex decrease in the heart rate (HR) and CO, which may be harmful in the presence of a compromised fetus.[9]

Norepinephrine (NE) may be a useful alternative to PE since it is a potent α-agonist with weak β-agonist action, thus counteracting the baroreceptor response to the α-effects. It can, therefore, maintain the BP with a low tendency to decrease the HR and CO compared to PE. Although hypotension management during SA is listed by the manufacturer as an indication for the use of NE, there is limited information available for its use in obstetric patients.[9]

The objective of the present study was to compare the effects of prophylactic boluses of NE and PE on SA-induced hypotension during elective cesarean section, as well as to assess the neonatal outcomes and adverse reactions.

Materials and Methods

This double-blind, prospective, interventional, randomized, controlled, clinical study was conducted at the Department of Anesthesiology, Maharashtra, from December 2017 to May 2019, after obtaining ethical clearance from the Institutional Review Board.

Sixty female patients, aged 18-35 years, singleton parturient with gestational age >36 weeks, ASA I or II physical status, and planned for cesarean section under spinal anesthesia, were recruited into the study after obtaining a written informed consent. Pregnant females with multiple gestations, abnormal placentation, essential or pregnancy-induced hypertension, history of significant systemic disorders (cardiovascular, respiratory, renal, or central nervous system), coagulopathies, spinal sensory loss above T6 dermatomal level, allergy to drugs intended to be used in the study and any other contraindications for spinal anesthesia were excluded from the study. The included patients were randomly divided (using computer generated codes and sealed envelope technique) into 2 groups depending on which prophylactic intravenous (IV) vasopressor was to be given – phenylephrine (Group PE) or norepinephrine (Group NE). For the purpose of this study, hypotension was defined as >20% decrease in the baseline mean arterial pressure (MAP).

Pre-anesthetic examination - On the evening before surgery, all patients underwent clinical examination (history, general condition, airway assessment by Mallampati grading,[10] nutritional status, height, weight, cardiovascular, respiratory, central nervous system, and spine examinations) as well as lab investigations (complete blood count, random blood sugar. blood urea, serum creatinine, blood grouping, Rh typing, coagulation profile, and urine analysis for albumin, sugar, and microscopy).

Pre-surgical preparation - A peripheral IV line was secured in a forearm vein with an 18-gauge cannula and connected to a three-way stopcock. Patients were preloaded with 500 mL of Ringer's lactate prior to the scheduled surgery and premedicated with IV Ranitidine (50 mg) and IV Ondansetron (4 mg). Baseline parameters were recorded after 15 min. In the operation theater, a multiparameter monitor was connected to non-invasively record and monitor the HR, systolic BP (SBP), diastolic BP (DBP), MAP, electrocardiogram (ECG), and oxygen saturation (SpO2%). Oxygen supplementation was given via a clear face mask at a rate of 4 L/min.

Study drug preparation - 0.5 mL of commercially available preparation of PE (10 mg/mL) was added to 100 mL of 5% dextrose to obtain a solution containing 50 μg/mL PE; 2 mL of this PE solution (50 μg/mL) was taken in a 5 mL syringe and further

diluted with 2 mL of 5% dextrose yielding a 25 µg/mL solution of PE. A similar solution containing 5 µg/mL NE was prepared by adding 0.5 mL of commercially available preparation of NE (1 mg/mL) to 100 mL of 5% dextrose.

Spinal anesthesia - Under strict aseptic precautions and with the patient in left lateral decubitus position, a lumbar puncture was performed at the L3-L4 intervertebral space with a 25-gauge Quincke spinal needle, using a midline approach. After obtaining a free flow of clear cerebrospinal fluid, 2.2 mL of hyperbaric bupivacaine (0.5%) injection was administered. Immediately after the spinal injection, the needle was withdrawn, the patient turned supine with continuous maintenance of left uterine displacement using a wedge, and a prophylactic bolus of the test drug administered.

Test drug administration - Group PE received 50 µg of IV PE and Group NE received 5 µg of IV NE as a prophylactic bolus and an additional rescue bolus of 25 µg PE and 5µg NE, respectively, every time the fall in MAP was >20% from baseline.

Post-anesthetic assessment - Motor block was assessed using modified Bromage scale.11 Bilateral sensory loss up to the T6 dermatomal level was tested using pinprick. Failure to achieve a dermatomal block up to T6 or attaining a higher level of sensory loss led to exclusion of the case from the study. HR, SBP, DBP, and MAP were noted at 1-min intervals for the first 5 min after intrathecal administration of hyperbaric bupivacaine injection, then every alternate minute for 15 min and after that, every 5 min, till the end of surgery. Fall in BP >20% of the baseline MAP was treated with an additional rescue bolus of the same study drug. Fall in the HR to <60 beats per min (bpm) for >30 s was treated with incremental doses of 0.3 mg of IV atropine. Any incidence of nausea (reported by patients) or vomiting (observed by investigators) was recorded, and if not associated with hypotension, was treated with 10 mg of IV metoclopramide.

Neonatal outcome assessment - After delivery, 20 IU of oxytocin injection was added to 500 mL of normal saline and given slowly intravenously. Blood was collected from the umbilical artery and immediately sent for arterial blood gas (ABG) analysis to estimate the umbilical artery blood pH, pO2, pCO2, lactate, and base excess. The neonatal status was assessed by APGAR score12 at 1 and 5 min.

Post-operative assessment - Post-operative monitoring of HR, SBP, DBP, and MAP of the patient was continued in the post-anesthesia care unit every 15 min for 1 h.

Statistical analysis - A sample size of 30 in each group was calculated by assuming a power of 90%, alpha error of 0.05 with a standard deviation (SD) of 0.07. The data was collected, compiled, and analyzed using the statistical software R version 3.6.1. Categorical variables are represented as frequency table and continuous variables are represented as mean ± standard deviation form. Chi-square test was used to check the dependency between two categorical variables. For mean comparison, t-test/repeated measures analysis (mixed models) was used. P value of ≤0.05 indicated statistical significance.

Results

Comparison of the demographic parameters between the two groups is presented in Table 1. The age of the study participants ranged from 20-22 years, weight between 46-74 kg, and height between 150-170 cm. Using two-sample t-test, no significant differences in these parameters were found between the groups.

Table 2 shows the comparison of pre-operative and post-operative hemodynamic parameters between the two groups over various time points, derived using mixed-model analysis. Variance between the subjects was taken as a random effect, and group and time points as a fixed effect. There were significant differences in the means of pre-operative SBP (P<0.0001), DBP (P<0.0001), and MAP (P<0.0001) over different time points, but this difference was not significant between the groups. There was also a trend for the HR to be significantly greater in Group NE than Group PE at different time points (P value was 0.005795 for interaction effect). However, there was no significant difference in the mean values of post-operative HR, SBP, DBP, and MAP between the groups over time.

Comparison of incidences of adverse events between the two groups is presented in Table 3. None of the patients reported vomiting. The Chi-square test showed no significant difference between the two groups with respect to the incidences of hypotension (P=0.176), nausea, and bradycardia. It revealed a significant difference between the groups in the distribution of the number of rescue vasopressor boluses required. Significant odds ratios were reported. The odds of having 2 rescue vasopressor boluses than no (nil) vasopressor boluses were 9.75 (CI: 1.7167-55.3725) times for PE group compared to NE group. Also,

the odds of having 2 vasopressor boluses than 1 vasopressor bolus were 11.1428 (CI: 1.9238-64.5378) times for PE group compared to NE group.

Comparison of neonatal outcomes between the two groups is summarized in Table 4. No significant difference between the two groups was found using two-sample t-test with respect to birth weight, APGAR score at 1st and 5th minute, pH, pO2 and pCO2, lactate, and base excess (P>0.05). A significant difference was noted in the distribution of APGAR score at 1 min and 5 min but not in its distribution between the groups, upon applying the generalized estimating equations technique by taking Poisson family with AR1 correlation structure.

Table 1: Comparison of demographic parameters between the two groups.

Parameter	Group NE	Group PE	P P value
Age (years)	25.9±3.65	26.43±3.65	0.574
Weight (kg)	60.87±6.91	61.6±6.46	0.6727
Height (cm)	159.93±3.89	159.23±4.53	0.5232

NE: norepinephrine; PE: phenylephrine.

Table 2: Comparison of hemodynamic parameters between the two groups.

Parameters	Time points	Group NE	Group PE	P P value
Pre-operative heart rate	Baseline	87.17±5.59	89.29±7.01	0.263288[a] <0.0001[b] 0.005795[c]
	15 min	91.63±11.42	86.16±10.32	
	30 min	86.36±8.75	84.83±7.36	
	45 min	84.53±7.54	82.83±7.61	
	1 h	85.4±8.83	82.4±7.01	
Pre-operative systolic blood pressure	Baseline	121.80±9.75	120.86±9.47	0.2591[a] <0.0001[b] 0.6112[c]
	15 min	109.93±9.45	107.57±9.98	
	30 min	110.4±11.07	108.7±10.24	
	45 min	115.33±10.79	111.66±9.01	
	1 h	116.43±9.41	112.83±8.64	
Pre-operative diastolic blood pressure	Baseline	77.93±8.29	76.83±8.07	0.3221a <0.0001b 0.2307c
	15 min	68.56±8.21	64.83±8.47	
	30 min	68.8±9.23	65.7±10.48	
	45 min	70.43±8.67	69.66±7.81	
	1 h	71.9±6.21	72.2±5.58	
Pre-operative mean arterial pressure	Baseline	92.53±8.01	91.48±7.83	0.2719a <0.0001b 0.6397c
	15 min	82.35±8.07	79.08±8.29	
	30 min	82.67±9.29	80.03±9.65	
	45 min	85.4±8.94	86.75±7.45	
	1 h	86.75±6.75	85.74±5.93	
Post-operative heart rate	15 min	82.5±6.82	80.83±6.53	0.51193a 0.09869b 0.11673c
	1 h	81.2±6.37	80.8±5.38	
Post-operative systolic blood pressure	15 min	116.83±8.28	114.46±8.78	0.2569a 0.5158b 0.8966c
	1 h	117.03±7.47	114.76±7.61	
Post-operative diastolic blood pressure	15 min	72.26±5.72	73.13±5.52	0.5476a 1.000b 0.8595c
	1 h	72.33±5.56	73.07±4.53	
Post-operative mean arterial pressure	15 min	87.12±6.20	86.91±6.15	0.8689a 0.7999b 0.9184c
	15 min	82.5±6.82	80.83±6.53	

NE: norepinephrine; PE: phenylephrine a: P P value for comparison of groups; b: P P value for comparison over time; c: P P value for interaction effect of group and time.

Table 3: Comparison of incidences of adverse events between the two groups.

Parameter		Group NE (n=30) n (%)	Group PE (n=30) n (%)	P P value
Hypotension	Absent	13 (43.33)	8 (26.67)	0.176
	Present	17 (56.67)	22 (73.33)	
No. of rescue vasopressor boluses	Nil	13 (43.33)	8 (26.67)	0.01499MC
	1 bolus	13 (43.33)	7 (23.3)	
	2 bolus	2 (6.67)	12 (40)	
	3 bolus	2 (6.67)	3 (10)	
Bradycardia	Absent	29 (96.67)	25 (83.33)	0.01844MC
	Present	1 (3.33)	5 (16.67)	
Nausea	Absent	26 (86.67)	25 (83.33)	1MC
	Present	4 (13.33)	5 (16.67)	

NE: norepinephrine; PE: phenylephrine MC: P P value obtained by Monte-Carlo simulation.

Table 4: Comparison of neonatal outcomes between the two groups.

Parameter	Group NE	Group PE	P P value
pH	7.41±0.02	7.41±0.03	0.8419
pO2	94.91±2.71	93.74±3.14	0.1286
pCO2	39.93±1.74	39.63±1.99	0.5368
Lactate	1.5±0.26	1.56±0.25	0.3185
Base excess	-0.03 ± 1.217	-0.27 ± 1.311	0.478
Birth weight (kg)	2.68±0.23	2.69±0.34	0.895
APGAR at 1 min	7 (7,8)	7 (7,8)	<0.0001a
APGAR at 5 min	8.5 (8,9)	9 (8,9)	

NE: norepinephrine; PE: phenylephrine; pO2: Partial Pressure of Oxygen, pCO2: partial pressure of carbon dioxide; APGAR: Appearance, Pulse, Grimace, Activity, and Respiration a: P value for comparison between times.

Discussion

This prospective clinical study was conducted to compare the effects of prophylactic boluses of NE and PE on SA-induced hypotension during elective cesarean section, as well as to assess the neonatal outcomes and adverse reactions, if any. The usual approach to use vasopressors is reactive rather than proactive; however, since the SA-induced hypotension is hazardous to the mother and more so to the fetus, it is better prevented than treated. Hence, prophylactic vasopressors were used.

The demographic data were comparable in both the groups, thus avoiding confounding of the results. The hemodynamic parameters, adverse events incidences, and neonatal outcomes showed no significant differences between the groups, except odds of requiring rescue vasopressor boluses (PE>NE).

Various other researchers, who compared the roles of PE and NE in the management of SA-induced hypotension during cesarean surgeries, found similar results. Vallejo et al too noted that the maternal HR (P=0.17), SBP (P=0.25), DBP (P=0.15), CO (P=0.5), and stroke volume (P=0.5) were similar between the groups.[13] Dong et al observed no significant difference in the SBP over time (unlike the present study), but the HR at 2nd and 4th minute after SA was significantly higher in the NE group than PE group (P<0.05) indicating that NE is not only as effective as PE in preventing spinal hypotension but also has greater CO compared to PE.[6] Ngan Kee et al and Sharkey et al also reported that NE preserved maternal HR more effectively than PE (P=0.039) and had similar efficacy to PE in maintaining BP.[9,14]

Akin to the present study, no significant difference in the incidence of bradycardia was noted between the NE and PE groups by Vallejo et al (P=0.58).[13] However, it was found to be lower in the NE group by Dong et al (P<0.05), Ngan Kee et al (P<0.001), and Sharkey et al (P<0.001), which is quite contrary to the present study. Bradycardia seen with PE was not associated with hypotension but with a transient baroreceptor-mediated reflex mechanism. NE, on the other hand, may have annulled the bradycardia due to its weak positive chronotropic action by the stimulation of β-receptors.[6,9,14]

The present study also revealed that the incidence of hypotension was comparable between the two groups, but the number of patients who had more episodes of hypotension and thus required ≥2 rescue vasopressor boluses of the study drugs was significantly higher in the PE group than NE group. In line with these findings, Vallejo et al as well as Sharkey et al found no significant difference in the hypotensive incidences between patients on PE (65.8% and 39%, respectively) and those on NE (48.8% and 38%, respectively).[13,14] Sahu et al found an 85% prevalence rate for hypotension in similar settings, while McArthur et al found that 40-60% of women undergoing cesarean delivery needed treatment with vasopressor medications.[15,16] Sharkey et al also reported that the number of patients requiring additional vasopressor rescue boluses was significantly lower in NE group (7.2%) compared to PE group (21.4%) (P<0.03). This can be because, at term, the uterine vascular bed is maximally vasodilated and unable to autoregulate when the perfusion pressure is reduced. Consequently, a higher adrenoreceptor density renders uteroplacental blood flow potentially vulnerable to vasoconstriction induced

by α-adrenergic agonists like PE.[14] Contrary to the current study, the need for rescue boluses was comparable between both the groups (P=0.25) in Vallejo et al's study.[13]

The incidence of nausea, too did not show any significant difference between the two groups, in concordance with the results obtained by Dong et al (P=0.68), Ngan Kee et al (P=0.67), Vallejo et al (P=0.28), and Sharkey et al (P=0.57).[6,9,13,14]

The APGAR scores and measured umbilical artery metabolic markers were used to indicate the adequacy of placental perfusion, which showed no significant differences between the two groups, despite periods of maternal hypotension and transient HR reduction. This could be due to immediate correction of hypotension episodes and thus, the maintenance of uteroplacental perfusion in both the groups. APGAR scores at 1 and 5 min were >7 and pH never <7.2 in all patients. Similar findings have been reported by Dong et al, Ngan Kee et al, Vallejo et al, and Sharkey et al.[6,9,13,14] This has been explained by Robson et al who found that umbilical artery blood pH correlated well with maternal CO but not with BP itself.[17] Joupilla et al observed that IV preloading maintains the placental blood flow despite a moderate reduction in the maternal pressure, thus minimizing fetal acidosis.[18] In the present study, all patients were preloaded with 500 mL of Ringer's lactate solution, which probably would have maintained the placental flow during hypotensive episodes.

This study establishes that NE is more efficacious than PE in preventing SA-induced hypotension and maintaining the maternal HR, and hence, can be considered as an alternative to PE.

This study has its limitations in being a single-center study with a limited sample size. Multicentric, prospective studies with a larger sample size are encouraged to validate the results.

Conclusion

The hemodynamic profile offered by NE in preventing SA-induced hypotension during elective cesarean delivery is superior to PE with better preservation of maternal HR and decreased requirement of rescue vasopressor boluses. Neither of the drugs posed any adverse neonatal outcomes or unmanageable maternal side effects. Hence, NE can be considered as an effective alternative to PE.

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Study to Evaluate Usefulness of Magnesium Sulphate and Dexmedetomidine as Adjuvant to Bupivacaine for Lower Limb and Abdominal Surgeries Under Epidural Anaesthesia

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Abstract

Background and Objective: Central neuraxial blockade not only provides good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. To compare time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, adverse effects if any and number of rescue analgesia in first 24hours after surgery.

Materials and Methods: After ethical committee permission and patient consent, study was conducted on 90 patients aged 18 to 65 years belonging to ASA- I and II undergoing lower limb and lower abdominal surgeries, were randomly divided into 3 groups. GROUP A received epidural bupivacaine 0.5 % (17 ml) + 1ml 0.9% normal saline. GROUP B received epidural Bupivacaine 0.5 %(17 ml) + 1ml 0.5mcg per kg dexmedetomidine. GROUP C received epidural Bupivacaine 0.5 % (17 ml) + 1ml 50mg magnesium sulphate. Exclusion criteria include patient's with bradyarrythmias, cerebrovascular diseases, neurodegenerative diseases, renal and hepatic diseases, uncontrolled hypertension, bronchial asthma, ischemic heart disease, drug and alcohol abuse and uncontrolled diabetes mellitus.The Statistical software SPSS 22.0, 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. Test of significance were ANOVA and chi-square test. P value <0.05 statistically significant.

Results: Analgesia in postoperative period and less number of rescue analgesia was better in Group C, Duration of sensory and motor blockade was prolonged and better hemodynamic stability in Group B

Conclusion: Hence addition of magnesium sulphate to epidural bupivacaine provides better post-operative analgesia and dexmedetomidine to epidural bupivacaine increases duration of motor and sensory blockade with better hemodynamic stability.

Keywords: Bupivacaine; Epidural anaesthesia; Dexmedetomidine; Magnesium sulphate.

Key Message: Addition of magnesium sulphate and dexmedetomidine for epidural anesthesia along with bupivacaine has been observed with better hemodynamic stability, increased duration of motor and sensory blockade intraoperatively with good post-operative analgesia.

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Introduction

Many lower limb and lower abdominal surgical procedures are commonly done under neuraxial block, either spinal or epidural anaesthesia. Central neuraxial blockade not only provides us good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. Advantages include less airway related and pulmonary complications that include reduced chances of pulmonary aspiration and decreased stress response.

Epidural anaesthesia is a widely used and a standard technique that is practiced in many surgical procedures. There are various advantages of epidural anaesthesia over spinal anaesthesia that includes slow onset of hypotension, level of blockade and duration of blockade can be extended and the most important is the ability to provide post-operative analgesia through catheter. The most dreaded complication of postdural puncture headache can be avoided in epidural anaesthesia.

Bupivacaine is commonly used drug in epidural anaesthesia. Various drugs have been added as an adjuvant to bupivacaine to prolong duration of anaesthesia and analgesia and also it reduces dose dependent side effects. Dexmedetomidine a well-known alpha 2 agonist, 8 times more potent than clonidine when added as an adjuvant to bupivacaine administered via epidural route produces synergistic anti nociceptive effect and also prolongs the duration of blockade and analgesia.[1]

Magnesium which is a major cation and 4th most abundant mineral in the body produces anti nociceptive effects, due to antagonism of calcium and NMDA receptors. This blocks calcium influx and thus reducing acetylcholine release in neuromuscular junction. NMDA receptors after nociceptive stimuli are involved in pain processing by central sensitization, magnesium prevents this sensitization. Epidural magnesium prolongs duration of analgesia and is a rapid onset of surgical anaesthetic without increasing side effects.[2-4]

Aims and Objectives

To administer epidural bupivacaine with normal saline, epidural bupivacaine with dexmedetomidine, epidural bupivacaine with magnesium sulphate each in 30 patients undergoing lower limb and lower abdominal surgeries and document the time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability and adverse effects if any.

To compare the time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, adverse effects if any and number of rescue analgesia in the first 24hours after surgery.

Methods

After obtaining institutional ethical committee approval, 90 patients belonging to ASA I and II, aged between 18 to 65 of both genders posted for lower limb and lower abdominal surgeries. Patients were segregated into three groups of 30 patients each group based on computer generated randomisation after informed written consent. Exclusion criteria included patients with bradyarrythmias, cerebrovascular diseases, neurodegenerative diseases, renal and hepatic diseases, uncontrolled hypertension, bronchial asthma, ischemic heart disease, drug and alcohol abuse and uncontrolled diabetes mellitus.

Detailed clinical history of the patient was taken. Proper physical examination was done followed by systemic examination and investigations relevant to epidural anaesthesia were checked. Intravenous line was secured and IV fluid was connected.

GROUP A (control group) received epidural bupivacaine 0.5 % (17 ml) + 1ml 0.9% normal saline.

GROUP B received epidural Bupivacaine 0.5% (17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

GROUP C received epidural Bupivacaine 0.5% (17 ml) + 1ml 50mg magnesium sulphate.

As soon as the patient arrived the OT table, baseline vitals like pulse rate, non-invasive blood pressure, ECG and SPO2 were recorded and continuous monitoring was done. Patient group selection was done with computer generated randomised table. Patient was made to sit and under aseptic precautions parts painted and draped. Skin infiltrated with lignocaine 2% at the level of L3-L4. Then epidural performed with 18G tuhoys needle and space identified by loss of resistance technique and epidural catheter was secured and fixed at appropriate level. Test dose of Lignocaine 2% with adrenaline of 3cc was administered after confirming negative aspiration of blood and CSF. Now the patient was made to lie in supine position and the drug injected according to the group selected by computerised table.

The patients were monitored continuously during surgery and the first 24hours post operatively.

Documentation of onset and duration of sensory and motor blockade, duration of analgesia, hemodynamic stability (by monitoring vital parameters), adverse effects if any and requirement of rescue analgesics (number of doses) was done. Rescue analgesics, anti-emetics was administered whenever required.

Comparison was done between the three groups with the above mentioned variables to evaluate the usefulness of adjuvants (magnesium sulphate or dexmedetomidine) to epidural bupivacaine in order to prolong duration of sensory and motor blockade, duration of analgesia and minimize adverse effects in patients undergoing lower limb and lower abdominal surgeries under epidural anaesthesia.

Sample size of present study was based on time to acquire T10 by Vaibhav Shahi et al in a comparative study of magnesium sulfate vs dexmedetomidine as an adjuvant to epidural bupivacaine observed a variance estimate of four with 95% confidence interval with 80% power with equal allocation to detect a difference of 10% time in achieving T10 blockade, the required sample size per group was 30.

The one-way analysis of variance (ANOVA) was employed to determine whether there were any statistically significant differences between the means of three or more independent (unrelated) groups. Chi-square 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.

Results

Table 1: Comparison of Various Parameters.

Parameters	Group A	Group B	Group C
Number (n)	30	30	30
Age (years)	33.66.± 9.54	36.66 ± 8.54	35± 8.14
Weight (kgs)	62.8±10.21	69.07±9.19	63.17±9.06
Gender (male/female)	20/10	22/8	21/9
ASA status (I/II)	26/4	20/10	25/5
Surgical time (mins)	85.50±21.24	85.43±21.29	74.33±21.51

ASA: American society of Anaesthesiology.

Heart Rate

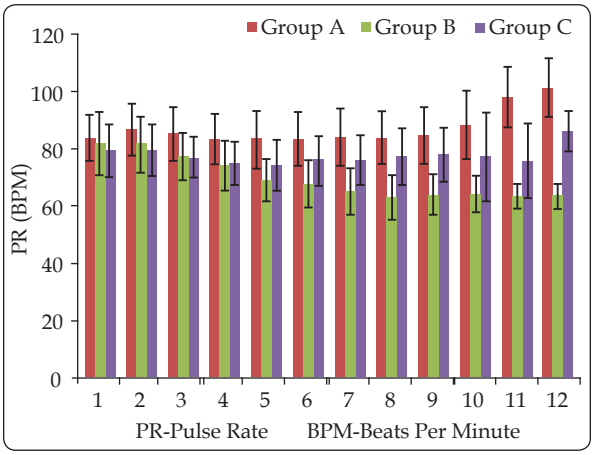

Fig. 1: Showing Comparison of Heart Rate in three Groups.

Baseline HR (bpm) were comparable in three groups, which were 86.43±8.98, 81.57±9.96 and 79.47±8.96 in group A, group B and group C respectively. (fig 1)

In group A there were no significant difference in PR, even after 30 minutes of epidural bupivacaine it remained at 83.97±9.96 and there was increased PR seen after 1hour of epidural bupivacaine with normal saline, it was 101.17±10.3 after 120min of epidural.

In group B after 10minutes of epidural bupivacaine with dexmedetomidine PR dropped to 64.87±8.25 and it remained on the lower side all though the procedure without tremendous increase in PR. It was 63.5±4.32 even after 120minutes of epidural.

In group C, PR remained the same all through the procedure, after 30minutes of epidural bupivacaine with magnesium sulphate it was 75±11.91 and it was 86±7.21 after 120minutes of epidural.

Systolic Blood Pressure

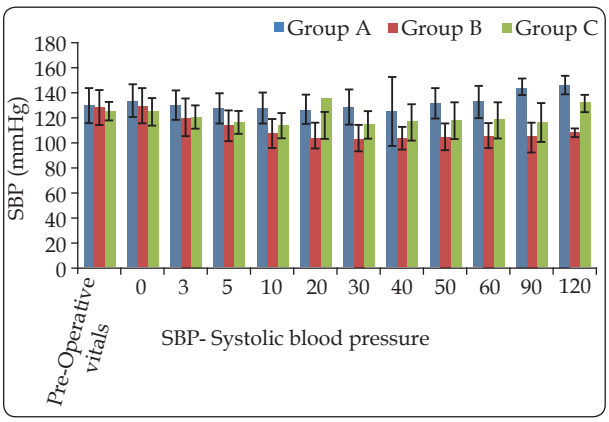

Fig. 2: Showing Comparison of Systolic Blood Pressure in three Groups.

Diastolic Blood Pressure

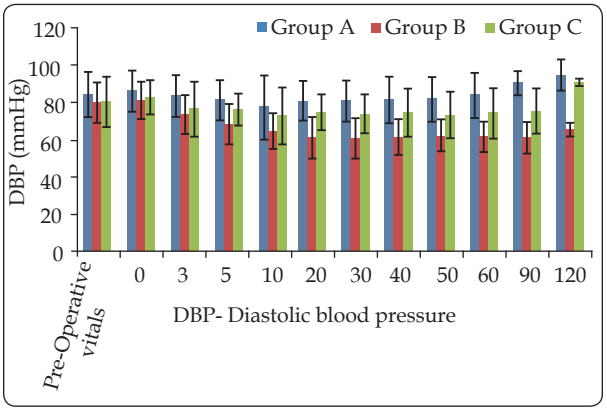

Fig. 3: Showing Comparison of Diastolic Blood Pressure in three Groups.

Mean Arterial Blood Pressure

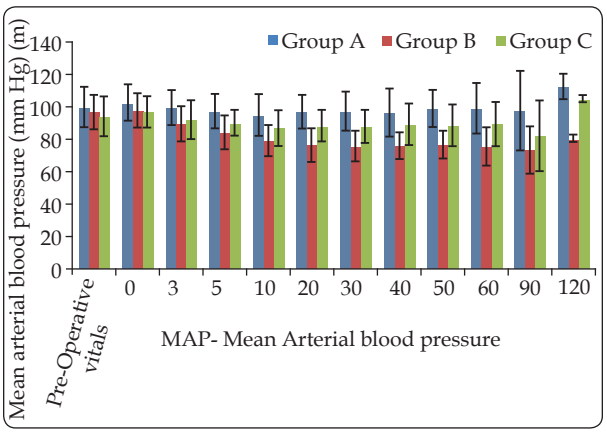

Fig. 4: Showing Comparison of Mean Arterial Blood Pressure in three Groups.

Baseline mean arterial blood pressure in all three groups was 101.90±11.35, 97.17±10.66 and 96.60±9.51 in group A, group B and group C respectively. (fig 4)

In group A MAP remains constant and there is no much fall in MAP, it was 95.70±14.79 after 40minutes of epidural, and it was 111.83±7.65 after 120minutes of epidural.

In group B significant reduction of MAP is seen after 30minutes of epidural and it was 74.93±9.51, it was stable all through the procedure and it was 79.67±2.16 after 120minutes of epidural.

In group C, MAP remains constant without increase or decrease from its basal value, it was 79.67±2.16 after 30minutes of epidural, and it was 104.33±2.08 after 120minutes of epidural.

Time taken for sensory block in group A was 14.12±6.18, in group B it was 4.63±1.22 and in group C it was 5.75±1.71, which signifies that time for onset of sensory block was seen early in group B.

Table 2 shows the time for complete motor blockade in group A was 17.17±2.01, in group B it was 7.02±1.70 and in group C it was 8.10±2.05, which signifies that early onset of motor blockade was seen in group B.

Time taken to achieve T6 level in group A was 13.22±1.43, in group B it was 4.73±1.32 and in group C it was 5.82±1.72, which imparts that time to achieve T6 level was seen early in group B

Time for two segment regression in group A was 86.77±3.60, it was 106.4±8.01 in group B and it was 102.7±8.05 in group C , which signifies that early two segment regression seen in group A, whereas longer time for two segment regression was seen in group B.

Time for recovery from motor blockade in group A was 102.7±8.05, in group B it was 121.6±8.42 and in group C it was 119.87±10.01 which signifies that time for regression of motor blockade in longer in group B when compared to other two groups.

Time taken for first analgesic request in group A was 1.90±0.28 hours, in group B it was 3.18±0.83hours

Table 2: Comparison of study variables in three groups of patients studied.

Variables	Group A	Group B	Group C	Total	P value
Weight (kg)	62.8±10.21	69.07±9.19	63.17±9.06	65.01±9.83	0.020*
Onset of Sensory Block	14.12±6.18	4.63±1.22	5.75±1.71	8.17±5.65	<0.001**
Onset of Motor Block	17.17±2.01	7.02±1.70	8.10±2.05	10.76±4.96	<0.001**
Time to achieve T6level	13.22±1.43	4.73±1.32	5.82±1.72	7.92±4.07	<0.001**
Duration of Surgery	85.50±21.24	85.43±21.29	74.33±21.51	81.76±21.76	0.071+
Time Two segment regression	86.77±3.60	102.7±8.05	106.4±8.01	98.62±10.94	<0.001**
Recovery from Motor block	97.77±5.03	119.87±10.01	121.6±8.42	113.08±13.53	<0.001**
Time to first Analgesic request	1.90±0.28	3.18±0.83	4.08±0.95	3.06±1.16	<0.001**

+Suggestive significance (P value: 0.05<P<0.10)
*Moderately significant (P value: 0.01<P ≤ 0.05)
**Strongly significant (P value: P≤0.01)

Table 3: Comparative assessment of VAS score in three groups of patients studied.

Variables	Group A	Group B	Group C	Total	P value
VAS First Analgesic	6.47±0.63	4.83±0.75	5.00±0.95	5.43±1.07	<0.001**
VAS 6hrs	6.30±0.65	4.70±1.21	4.47±1.04	5.16±1.28	<0.001**
VAS 12hrs	6.30±0.75	4.77±1.5	4.23±1.19	5.10±1.47	<0.001**
VAS 24hrs	6.13±0.57	4.93±1.31	4.03±1.19	5.03±1.37	<0.001**

+ Suggestive significance (P value: 0.05<P<0.10) * Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01) VAS: Visual Analogue Scale

and in group C it was 4.08±0.95hours, which signifies that analgesics during post-operative period was better with group C, that is magnesium sulphate.

Average time taken for surgeries in group A was 85.50±21.24, in group B was 85.43±21.29 and in group C it was 74.33±21.51.

Table 3 shows VAS score in all three groups postoperatively in 24hours shown, where it was less in group C after 6hours post operatively, which signifies that post-operative analgesic effect is better with group C.

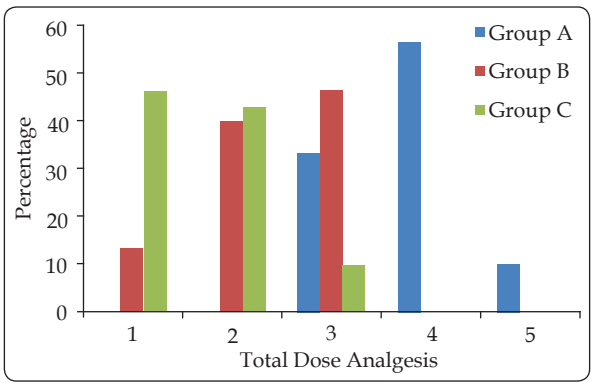

Fig. 5: Showing Total Analgesic Doses Required in 24 Hours in all three Groups.

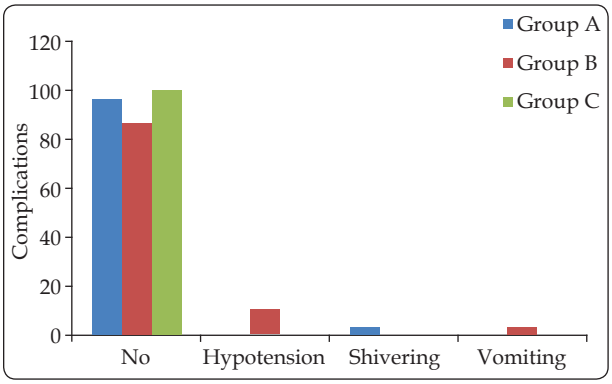

Fig. 6: Complications In Three Groups.

Fig 5 shows the no. of analgesic requests in all three groups which was maximum in group A and minimum in group C, which indicates that group C had better analgesic effect. In group A 10 required 3 doses of top up requirement in 24hours, 17 required 4 doses of top ups. In group C only 3 required 3 doses of top ups, 14 required only one dose and 13 required 2 doses.

Fig 6 shows the complication in three groups intra operatively and post-operative period of first 24hours, where 3 in group B had hypotension and one had vomit. 1 had shivering in group A and no complication was seen in group C.

Discussion

Central neuraxial blockade is most commonly and widely practised anaesthetic technique in many surgical procedures and bupivacaine is the most commonly used local anaesthetic in this technique. Many adjuvants have been added to bupivacaine to enhance the effect and analgesic quality of bupivacaine in neuraxial blockade. Many such adjuvants like midazolam, opioids and ketamine used in epidural. Opioids been associated with undesirable side effects which includes pruritus, nausea, vomiting, urinary retention, respiratory depression and somnolence.[6,7] there was search for an additive with low incidence of these side effects, where effectively it was replaced with alpha 2 agonists like clonidine and dexmedetomidine.[1]

In the last two decades there has been incredible increase in the use of alpha 2 agonist in epidural anaesthesia. When these drugs are administered in epidural it provides sedation, analgesia, anxiolysis and hypnosis.[10]

In 1999 dexmedetomidine came in clinical practice. Dexmedetomidine in regional anaesthesia was used in animals by many researchers, like Sabbe et al in 1994 and Eisench in 2001. Epidural dexmedetomidine prolongs the duration of analgesia, reduces the number of rescue analgesia. It establishes the faster onset of action of both motor and sensory blockade. Because of stable cardiorespiratory parameters it is even more

preferred adjuvant in regional anaesthesia[11]

The pharmacological properties of alpha 2 agonist have been largely studied and been employed clinically to achieve desired effects in regional anaesthesia. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis.[8,9] Introduction of dexmedetomidine, a newer prototype of alpha 2 agonist has widened the scope in regional anaesthesia. It was introduced in clinical practice in 1999. Epidural bupivacaine in a dose of 2mcg/kg given along with intrathecal bupivacaine causes significant prolongation in the duration of analgesia. The number of administered rescue analgesic doses is significantly less in patients receiving epidural dexmedetomidine. The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in the postoperative period, dose sparing action of local anaesthetics and stable cardiorespiratory parameters make alpha 2 agonist an effective adjuvant in regional anaesthesia.[14]

Parenteral magnesium, used for many years as an antiarrhythmic agent and for prophylaxis in seizures in pre-eclampsia. Noxious stimulation leads to release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. NMDA receptor signalling may be important in determining the duration of acute pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels. Magnesium can prevent the induction of central sensitization at the spinal action by blocking NMDA receptors in a voltage dependent manner. With same mechanism of action when small doses of magnesium was added to local anaesthetics for spinal anaesthesia the duration of action of spinal anaesthesia was prolonged and analgesic requirement postoperatively was reduced and side effects of high doses of local anaesthetics and opioids were reduced.[5]

Shahi V, Verma AK, Agarwal A, Singh CS in 2014 conducted a prospective randomized study of comparing dexmedetomidine and magnesium sulphate along with epidural bupivacaine in 120 patients to determine the motor and sensory onset of action and duration of analgesia post operatively, they have concluded that dexmedetomidine group showed rapid onset of action and prolonged duration of action with better post-operative analgesia when compared to magnesium sulphate group.[13]

Sonali Banwait, Sujata Sharma and Rajesh Sood in 2012 evaluated the efficacy of single bolus administration of magnesium epidurally as an adjuvant to epidural fentanyl for postoperative analgesia in 60 patients posted for total hip replacement under combined spinal epidural anaesthesia. The results of the investigations showed that a single bolus of epidural magnesium as an adjuvant to fentanyl for post-operative analgesic requirement results in prolonged duration of analgesia as compared to epidural fentanyl alone. Concomitant administration of magnesium reduces the requirement for breakthrough analgesics with no increased incidence of side effects.[12]

Conclusion:

From our study we conclude that when dexmedetomidine added as an adjuvant to epidural bupivacaine it provides fast onset of motor and sensory blockade with better hemodynamic stability. And magnesium when added as adjuvant to epidural bupivacaine it provides better post-operative analgesics not associated with any complications.

Conflict of Interest: Nil

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Study of Effect of Melatonin Premedication on Attenuation of Hemodynamic Response to Laryngoscopy and Intubation

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Abstract

Background and Aim: Laryngoscopy and endotracheal intubation cause increase in heart rate and blood pressure as well as abnormalities of cardiac rhythm due to reflex sympathetic discharge which is caused by epipharyngealand laryngo-pharyngeal stimulation. The aim is to study the changes in following parameters during laryngoscopyand endotracheal intubation up to 10 min with tab melatonin administration.

Material and Methods: The present study was carried out in the Department of Anaesthesiology, Government Medical College and S.S.G. Hospital, Vadodara, from November 2017 to October 2018. Randomisation was done according to computer generated list into two equal groups. Group C (Control group) - Patients received two tablets of vitamin D3 (placebo) 120 min before induction of anaesthesia.. Group M (Melatonin group) received oral melatonin tablets of 6mg (two tablets of 3mg each) 120 min before induction of anaesthesia. Vitamin D3 was used as placebo drug. Haemodynamic parameters such as heart rate: systolic, diastolic and mean blood pressures were recorded before the administration of drug (baseline), 120 min after administration of study drug, immediately after induction, at laryngoscopy and intubation, just after laryngoscopy and intubation and at 1, 3, 5 and 10 min thereafter.

Results: The mean pre operative pulse rate, the Systolic blood pressure(SBP), the Diastolic blood pressure(DBP), Mean arterial pressure(MAP) and the SpO2 were comparable in both groups but not significant statistically ($p>0.05$). At baseline and just before intubation, pulse rate was comparable in both groups. Nausea & vomiting was seen in one patient from study group & was treated with inj.Ondansetroniv. Hypotension was observed in 1 patient from the study group.

Conclusion: Administration of oral melatonin premedication 120 minutes before surgery results in Significant attenuation of the rise in systolic, diastolic and mean arterial blood pressure at the time of laryngoscopy & intubation and Transient increase in pulse rate which settled down within 1 minute after intubation and remained stable throughout the study period.

Keywords: Arterial blood pressure; Intubation; Laryngoscopy; Melatonin; Pulse rate

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Introduction

General anaesthesia is still one of the most common modes of anaesthesia for a variety of surgeries. It involves laryngoscopy and intubation as an integral and essential part. Laryngoscopy and endotracheal intubation cause increase in heart rate and blood pressure as well as abnormalities of cardiac rhythm due to reflex sympathetic discharge which is caused by epipharyngealand laryngo-pharyngeal stimulation. While the afferent limb of the reflex arc is via cranial nerves of the upper airway, the efferent limb is via sympathetic nerves.

Laryngoscopy and endotracheal intubation are considered potent noxious stimuli which provoke haemodynamic responses leading to a marked increase in heart rate and blood pressure.[1] This is probably of no consequence in healthy individuals. However, these events are especially detrimental in individuals who have limited myocardial reserve due to coronary artery disease, cardiac dysrhythmias, congestive heart failure, hypertension, cardiomyopathy and geriatric age group.[2] During intubation of trachea, the laryngeal and tracheal sensory receptors are stimulated which result in the release of endogenous catecholamines resulting in tachycardia and hypertension.[3] Stress response increases both SABP and DABP measurements increase by 36-40% in contrast to control levels. Heart rate levels increase more than 20% with tracheal intubation in contrast to laryngoscopy.[4,5] The pressor (stress) response reaches a peak 1-2min after laryngoscopy and tracheal intubation, and usually subsides within 5-6min, although tachycardia may persist for 10min.[6,7]

The hemodynamic response results in hypertension, tachycardia, and dysrhythmias, secondary to increase in circulating catecholamines. This sympathoadrenal response is usually transient, variable and unpredictable. It reaches a peak level within one minute and ends in 5-10 minutes after intubation. The pressor response is well tolerated by overall healthy patients, i.e. ASA I and II patients. However, it could be dangerous or even life threatening and therefore undesirable in susceptible patients(ASA III and IV); i.e. in those with systemic hypertension, coronary artery disease, intra cranial aneurysm, where circulation is already jeopardised.

The sympatho adrenal response increases the workload of myocardium which can lead to potentially deleterious effects like ventricular failure, myocardial infarction, pulmonary oedema, ventricular arrhythmias, cerebral haemorrhage, and rupture of cerebral aneurysm. Convulsion may be precipitated in a pre-eclamptic patient. Thus there is a need to suppress the hemodynamic response to laryngoscopy and intubation.

Since the invention of laryngoscopy and endotracheal intubation, various drug regimens and techniques have been used from time to time to attenuate these stress responses. Some of such agents being opioids (fentanyl, alfentanil), calcium channel blockers (verapamil, diltiazem), sympatholytics (clonidine, dexmedetomidine and methyldopa), beta blockers (esmolol, propranolol), benzodiazepines (midazolam, alprazolam), barbiturates, propofol, pregabalin and peripheral vasodilators (sodium nitroprusside, nitroglycerine).[8] However, each agent has some limitations such as respiratory depression, hypotension, tachycardia, bradycardia, rebound hypertension or allergic reactions. Hence, there has always been a need for a better agent. Melatonin (N acetyl 5 methoxytryptamine) is an endogenous sleep regulating hormone secreted by pineal gland. Exogenous administration of melatonin facilitates sleep onset and improves the quality of sleep. It is different from benzodiazepines and their derivatives in that it produces natural sleep pattern and does not lead to impairment of cognitive functions.[9] Various researchers have used this drug in different dose patterns as premedication in both adults as well as children. It has been mainly studied in view of pre operative anxiolysis, sedation in Intensive Care Unit, pre operative cognitive and psychomotor functions.[10] Moreover, administration of 1 mg of melatonin during the daytime to healthy young women decreased systolic, diastolic and mean arterial pressure along with the reduction of norepinephrine concentration the same depressant effect on BP and noradrenergic activation was observed in healthy men treated with melatonin.[11,12]

There are lots of studies regarding the sedative and anxiolytic effect of melation. But its use in attenuating pressor response to laryngoscopy and intubation has not been explored much. Hence study has been carried out to understand efficacy of oral melatonin in attenuation of hemodynamic response to laryngoscopy and intubation. The aim is to study the changes in following parameters during laryngoscopyand endotracheal intubation up to 10 min with tab melatonin administration.

Material and Methods

The present study was carried out in the Department

of Anaesthesiology, Government Medical College and S.S.G. Hospital, Vadodara, from November 2017 to October 2018. It was a prospective randomized controlled study of total 80 patients, approved by the Hospital Ethics Committee.

Inclusion criteria were: Patients belonging to American society of anesthesiologist (ASA) by physical status grade I and II, age 20-45 years of either gender, patients posted for planned surgery requiring general anaesthesia and endotracheal intubation

Exclusion criteria were diabetes, hypertension, psychiatric illness, intake of antipsychotics, sedatives, anxiolytics and antiepileptic drugs; sleep disorders, obesity and drug allergy. Likewise, patients with anticipated difficult intubation and those requiring more than one attempt or more than 20 s for laryngoscopy were excluded from the study.

Randomisation was done according to computer generated list into two equal groups. Group C (Control group) - Patients received two tablets of vitamin D3(placebo) 120 min before induction of anaesthesia.. Group M (Melatonin group) received oral melatonin tablets of 6mg (two tablets of 3mg each) 120 min before induction of anaesthesia. Each patient received either drug based on the generated list in a thick opaque, similar looking envelope by the pre-operative nurse. Both patient and investigator were unaware of the type of drug. Vitamin D3 was used as placebo drug.

In the pre-operative room, the study drugs were administered with a sip of water 120 min before surgery. Continuous monitoring of the pulse rate, respiratory rate, blood pressure and arterial oxygen saturation (SpO2) was done in the pre-operative period at an interval of 5 min by the nurse posted in the pre operative room.

On receiving the patient in the operation theatre, routine monitoring was commenced which included heart rate, electrocardiogram, arterial SpO2, non-invasive blood pressure (NIBP) and end-tidal carbon dioxide (EtCO2). All the patients were administered 100% oxygen for 3 min before induction. Glycopyrrolate 0.004 mg/kg and fentanyl 1 µg/kg were administered intravenously. Induction was attained with intravenous propofol 2 mg/ kg intravenously mixed with preservative-free lignocaine hydrochloride. Succinylcholine was given intravenously 2 mg/kg to facilitate endotracheal intubation with proper sized cuffed endotracheal tube by the same person each time. Maintenance of anaesthesia was attained with inhalation of sevoflurane 1 minimum alveolar concentration; nitrous oxide: oxygen 50:50. Muscle relaxation was attained with vecuronium bromide administered in the dose of 0.06–0.08 mg/kg

Intravenously as loading dose and one-fourth of the initial dose as maintenance doses. Mechanical ventilation was adjusted to maintain normocapnia (EtCO2 values of 35–38 mmHg). Intravenous infusion of injection diclofenac sodium 75 mg was administered slowly 15 min before completion of surgery for post-operative analgesia. After completion of the surgery, neostigmine 50 µg/ kg and injection glycopyrrolate 10 µg/kg were administered intravenously to reverse the residual neuromuscular blockade.

Haemodynamic parameters such as heart rate: systolic, diastolic and mean blood pressures were recorded before the administration of drug (baseline), 120 min after administration of study drug (just before induction), immediately after induction, at laryngoscopy and intubation, just after laryngoscopy and intubation and at[1,3,5] and 10 min thereafter. In the post-anaesthesia care unit, the patients received the standard post-operative care including oxygen administration via face mask at[4–6] L/min and monitoring of heart rate, NIBP, respiratory rate and SpO2. We observed for any episodes of nausea, vomiting, dizziness, headache, respiratory depression, arrhythmias, bradycardia, hypotension and restlessness till 24 h postoperatively. Complication like nausea/ vomiting, tachycardia, hypertension, hypotension, arrhythmia, drowsiness, restlessness, headache should be watched for preoperative intraoperative and postoperative period for 24 hours.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

The mean age, mean weight, ASA physical status and the ratio of Males to Females among patients in control group and in study group were comparable and not significant between both groups. ($p>0.05$) (Table 1)

The mean pre operative pulse rate, the

Table 1: Mean Age, Weight, ASA Grading and Duration of Surgery.

	Control Group(C)	Study Group(M)	p value
Age (years)	33.35 ± 2.98	32.20 ± 3.21	p = 0.1008
Mean ± SD			p >0.05
Weight (kg)	56.20± 4.57	55.32 ± 3.87	p = 0.19
Mean ± SD			p>0.05
ASA Grade	30/10	28/12	p = 0.082
I/II			p > 0.05
Gender	21:19	20:20	p = 0.139
Male:Female			p > 0.05

Table 2: Changes in mean pulse rate.

Time	Control group		Study Group		Inter Group
	Pulse rate	Intra group p value	Pulse rate	Intra group p value	p value
Baseline	77.10±6.42	N A	79.4±6.72	N A	p=0.305 p> 0.05
120 minutes after study drug	78.57±6.32	P=0.305 p > 0.05	78±6.82	p =0.357 p > 0.05	p =0.699 p> 0.05
Just after induction	76.22±6.43	P=0.542 p > 0.05	76.20±6.65	p =0.03 p< 0.05	p =0.989 p> 0.05
At laryngoscopy &intubation	82.52±6.45	P=0.0003 P<0.01	79.47±6.49	p =0.96 p> 0.05	p=0.037 p< 0.05
After 1 minute of intubation	83.97±6.4	p<0.0001	74.9±6.04	p =0.003 p< 0.05	p<0.0001
After 2 minutes of intubation	83.7±6.22	p<0.0001	72.85±6.07	p<0.0001	p<0.0001
After 3 minutes of intubation	80.72±6.21	p =0.124 p> 0.05	71.77±6.09	p<0.0001	p<0.0001
After 5 minutes of intubation	79.1±6.17	p=0.159 p> 0.05	70.65±12.6	p<0.0001	p<0.0001
After 10 minute of intubation	77.67±5.84	p=0.679 p>0.05	65.37±68	p<0.0001	p<0.0001

Table 3: Changes in Systolic Blood Pressure.

Time	Control group		Study Group		Inter Group
	SBP	Intra group p value	SBP	Intra group p value	p value
Base line	116.75±10.33	N A	117.78 ±7.78	N A	p = 0.615 p > 0.05
120 minutes after study drug	117.92±10.34	p=0.614 p> 0.05	113.93 ± 7.85	p=0.030 p < 0.05	p=0.66 p > 0.05
Just after induction	115.62±10.22	P=0.624 p> 0.05	110.93±7.98	p=0.0002 p<0.01	p=0.285 p > 0.05
Laryngoscopy & intubation	125.67±9.72	p=0.0002 p > 0.05	112.85±7.85	p=0.0061 p<0.01	p=0.0001 p < 0.01
After 1 minute of intubation	130.37±9.68	p<0.0001	105.43±7.29	p<0.0001	p<0.0001
After 2 minute of intubation	126.7±9.621	p<0.0001	101.63±7.23	p<0.0001	p<0.0001
After 3 minute of intubation	121.27±9.73	p=0.047 p < 0.05	99.2±7.08	p<0.0001	p<0.0001
After 5 minute of intubation	118.20±9.68	p=0.519 p> 0.05	97.82±6.79	p<0.0001	p<0.0001
After 10 minute of intubation	115.87±9.48	p=0.695 p> 0.05	97.17±6.47	p<0.0001	p<0.0001

Table 4: Changes in Diastolic Blood Pressure.

Time	Control group		Study Group		Inter Group
	DBP	Intra group p value	DBP	Intra group p value	p value
Baseline	76.66 ± 6.49	N A	74.83± 6.28	N A	p = 0.02 p < 0.05
120minutes after study drug	81.57±6.13	P=0.0040 p<0.01	72.42±6.75	p = 0.1023 p >0.05	P<0.0001
Just after induction	78.47±6.14	P=0.203 p >0.05	70.92±6.48	p = 0.0076 p >0.05	P<0.0001
At laryngoscopy & intubation	81.65±8.43	P=0.0040 p<0.01	74.37±6.22	p = 0.742 p >0.05	P<0.0001
After 1 minute of intubation	85.75±7.45	p<0.0001	68.67±5.64	P<0.0001	P<0.0001
After 2 minute of intubation	82.67±7.45	P=0.0002 p<0.01	65.ax30±6.0	p<0.01 p<0.0001	P<0.0001
After 3 minute of intubation	79.35±6.65	p = 0.07 p >0.05	64.27±5.96	p<0.0001	P<0.0001
After 5 minute of intubation	76.35±6.65	p = 0.833 p >0.05	63.42±5.89	p<0.0001	P<0.0001
After 10 minute of intubation	74.375±6.28	p = 0.123 p >0.05	62.82±6.28	p<0.0001	P<0.0001

Table 5: Changes in Mean Arterial Pressure.

Time	Control group		Study Group		Inter Group
	MAP	Intra group p value	MAP	Intra group p value	p value
Baseline	89.98±7.4	N A	89.26±6.13	N A	p = 0.09 p > 0.05
120 min after study drug	93.67±7.57	p = 0.03 p < 0.05	86.18±6.49	p = 0.032 p < 0.05	p = 0.9 p > 0.05
Just after induction	91.18±8.34	P=0.498 p> 0.05	84.28±6.44	P=0.0005 p<0.01	p = 0.03 p < 0.05
At laryngoscopy & intubation	96.28±8.2	P=0.0005 p<0.01	87.19±6.14	P=0.1354 p> 0.05	p < 0.0001
After 1 minute of intubation	99.72±9.13	p<0.0001	80.95±5.29	p<0.0001	p <0.0001
After 2 minute of intubation	97.37±7.7	p<0.0001	77.40±5.65	p<0.0001	p < 0.0001
After 3 minute of intubation	93.32±7.29	p =0.0391 p> 0.05	76.50±6.43	p<0.0001	p < 0.0001
After 5 minute of intubation	90.22±7.16	P=0.8351 p> 0.05	74.83±5.53	p<0.0001	p < 0.0001
After 10 minute of intubation	88.60±7.16	P=0.3992 p> 0.05	74.30±5.0	p<0.0001	p < 0.0001

Table 6: Intraoperative complications:

Parameter	Control Group		Study Group	
	No. of patients	%	No. of patients	%
Nausea & vomiting	0	0	1	2.5
Bradycardia	0	0	1	2.5
Hypotension	0	0	1	2.5
Arrhythmias	0	0	0	0
Headache	0	0	0	0
Respiratory depression	0	0	0	0

Systolic blood pressure(SBP), the Diastolic blood pressure(DBP), Mean arterial pressure(MAP) and the SpO2 were comparable in both groups but not significant statistically (p>0.05).

Table 2 shows the changes in pulse rate in both the study and control groups at various time intervals starting from baseline up to 10 minutes post induction. At baseline and just before intubation, pulse rate was comparable in both groups (p>0.05, statistically not significant).

On intragroup comparison, in the group M, there was only a minimal rise in pulse rate from baseline, at laryngoscopy & intubation (p>0.05-not significant). Whereas in the control group, there was a major rise in pulse rate at laryngoscopy & intubation(p<0.01, highly significant). On intergroup comparison; patients in the group M who received melatonin tablets before intubation, showed only minimal rise in the pulse rate when compared to the major rise in group C. But this difference in rise of PR between 2 groups became statistically significant only after 1 minute post intubation (p<0.01-highly significant).

Table 3 shows the changes in Systolic Blood Pressure starting from baseline up to 10 minutes of induction in both groups. On intragroup comparison, in the group M, there was no rise in SBP from baseline, at laryngoscopy &intubation (p>0.05-not significant). The SBP in group M was on decreasing side settled down and remained stable at lower side throughout the duration of 10 minutes post intubation (p<0.01-highly significant). Whereas in the group C, there was a majorrise in SBP at laryngoscopy & intubation (p<0.01, highly significant),which persisted at 1 min 2 min & 3 min readings(p<0.01, highly significant).After 3 min it started getting settle down & reached close to the base line at the end of 10 min(p >0.05- not significant)

Table 4 shows the changes in Diastolic Blood Pressure starting from baseline up to 10 minutes of induction in both groups. On intragroup comparison, in the group M, there was no rise in DBP from baseline, at laryngoscopy & intubation (p>0.05-not significant). The DBP in group M was on decreasing side settled down and remained stable at lower side throughout the duration of 10 minutes post intubation (p<0.01-highly significant). Whereas in the group C, there was a major rise in DBP at laryngoscopy & intubation (p<0.01, highly significant),which persisted at 1 min 2 min & 3 min readings (p<0.01, highly significant). After 3 min it started getting settle down & reached close to the base line at the end of 10 min (p >0.05- not significant)

Table 5 shows the changes in Mean Arterial Pressure starting from baseline up to 10minutes of induction in both groups. On intragroup comparison, in the groupM, there was no rise in MAP from baseline, at laryngoscopy & intubation (p>0.05-not significant). The MAP in group M was on decreasing side settled down and remained stable at lower side throughout the duration of 10 minutes post intubation (p<0.01-highly significant). Whereas in the group C, there was a majorrise in MAPat laryngoscopy & intubation (p<0.01, highly significant),which persisted at 1 min 2 min & 3 min readings (p<0.01, highly significant).After 3 min it started getting settle down & reached close to the base line at the end of 10 min (p >0.05- not significant)

Intra as well as inter group comparison showed no significant change in oxygen saturation throughout the intraoperative period.

Nausea & vomiting was seen in one patient from study group & was treated with inj.Ondansetroniv. Hypotension was observed in 1 patient from the study group. This was treated effectively with injection ephedrine 5 mg IV. Bradycardia was seen in one patient from study group & was treated with inj.atropine 0.6mg iv No other complication was observed in any of the two groups intraoperatively.

Discussion

The present study is aimed at assessing the role of melatonin in attenuating haemodynamic responses to laryngoscopy and intubation. Melatonin (N-acetyl-5-methoxytryptamine) is a pineal gland hormone which controls the circadian rhythm. It has been used for sleep disorders, jet lag, perioperative anxiolysis and sedation, cognitive and psychomotor functions.[9-12] It was assumed that its inhibitory actions on central nervous system responsible for sedation and anxiolysis may have a role in attenuating haemodynamic responses to laryngoscopy and intubation. Rosenberg et al. studied the role of perioperative melatonin in the modification of surgical stress response indicating that melatonin has sympatholytic activity.[13] This is in support of our assumption. The peak effect of exogenous melatonin ranges from 60 to 150 min.[14] Based on this, we made a hypothesis that melatonin can provide haemodynamic stability during laryngoscopy and intubation when given 120 min before the procedure.

The ratio of Male to Female in Group C is 21:19 and in Group M is 20:20. Other studies like

Priyamvada Gupta et al, 2016 and M Ahmed. A Mohammed et al, 2014 had almost similar gender ratio.[15,16]

The mean baseline pulse rate was 77.1±6.42 in Group C and 79.4±6.72 in Group M. It was comparable in both the groups, p>0.05 statistically not significant. However, in a similar study, no difference was observed in the changes of heart rate in the melatonin groups as compared to the placebo group.[16] The heart rate lowering effect of melatonin may be attributed to its anxiolytic actions. The underlying mechanism is probably the synergy between melatonergic and GABAergic systems. It also has analgesic effects as observed by various investigators and this may also contribute to the haemodynamic stability.[17]

The mean baseline systolic blood pressure (SBP) was 116.75±10.33 in Grp C and 117.78±7.78 in Grp M. It was comparable in both the groups i.e. p>0.05, not significant. In group C there was significant rise in SBP at laryngoscopy & intubation which only settled down 10 minutes post intubation. In group M there was no rise in SBP throughout the study period of 10 minutesas compared to baseline value . Similar trends were observed for diastolic and mean blood pressure.

It has been studied that melatonin reduces mean blood pressure in healthy volunteers.[18,19] A study on rats revealed that pinealectomy resulted in severe hypertension.[20] Mohammed et al. compared the role of oral melatonin 6 mg and 9 mg with placebo administered 1 h before surgery in attenuating pressor response to laryngoscopy and intubation. They observed that there was a reduction of blood pressure with regard to systolic, diastolic and mean blood pressure; and perfusion index in both melatonin groups as compared to the placebo group.

The mechanism of effect of melatonin on circulation is complex. The blood pressure lowering effect may be attributed to the specific binding of melatonin to melatonin receptors in the blood vessels, interfering with the vascular response to catecholamines.[21] It may interfere with the peripheral as well as central autonomic system, causing a reduction in adrenergic outflow and resulting catecholamine levels. Furthermore, it may induce relaxation of arterial wall smooth muscle by enhancing the availability of nitric oxide. In addition, it may also act via specific receptors melatonin type 1 or melatonin type 2 located peripherally in the blood vessels and centrally in blood pressure regulating area of the brain. It also has free radical scavenging effect leading to dilatation of blood vessels, and it may work via epigenetic mechanism at area postrema in the brain. The blood pressure lowering effect could also be due to the sedative action of orally administered melatonin. The sedative effect is mainly due to binding at GABA-A receptor and exerting its anaesthetic effect.[22]

The baseline SpO2 was 98.98±0.35 in Group C and 98.35±0.48 in Group M. In our study no significant difference in SpO2 was found in both the groups during the intra-operative period (p>0.05). Our finding are in consonance with those of others like Priyamvada Gupta et al, 2016 & Ahmed. A. Mohammed, 2014 in whom SPO2 was comparable in all the groups.[15,16] Nausea & vomiting was seen in one patient from study group & was treated with inj.Ondansetron iv. Hypotension i.e. systolic blood pressure < 90mmHg was observed in 1 patient from the study group. Bradycardia was seen in one patient from study group. No other complication was observed in any of the two groups intraoperatively. Various studies indicate that melatonin has an excellent safety profile. Very high doses up to 300 mg/day orally for 2 years have been administered safely.[23] Even in children doses up to 20 mg have been used without any significant side effects apart] from sedation.[24] Kain et al. safely used 0.4 mg/kg oral melatonin in children.[25] There is no liability to cause dependence and addiction. It may cause fatigue (4%) or nausea (3%). Dizziness, headache and irritability may be seen in some patients with use of very high doses in some previous studies of melatonin done for its anxiolytic action.[26] Thus, proving that melatonin is a useful drug for use as an adjunct in anaesthesia. The correct dosage in humans seems largely unknown and requires further studies.

The role of melatonin in anaesthesia and critical care has been elaborately discussed in the literature; it has been mentioned as a wonder drug with a wide spectrum of beneficial uses in anaesthesia and critical care including antioxidant and neuroprotective properties besides hypnosis, anxiolysis, analgesia and others.[27] The use of melatonin for attenuation of haemodynamic responses before laryngoscopy and intubation is superior to few other drugs studied for the same purpose. For instance, melatonin is superior to dexmedetomidine since the latter is associated with significant bradycardia and hypotension.[28]

Conclusion

Administration of oral melatonin premedication 120 minutes before surgery results in Significant

attenuation of the rise in systolic, diastolic and mean arterial blood pressure at the time of laryngoscopy & intubation and Transient increase in pulse rate which settled down within 1 minute after intubation and remained stable throughout the study period. After conducting the study we conclude that TabletMelatonin is a better alternative with minimal side effects in attenuating hemodynamic responses to laryngoscopy &intubation.

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A Comparative Study of Intrathecal Low dose Isobaric and Hyperbaric Levobupivacaine in Ambulatory Perianal Surgeries: A Prospective, Double Blind Study

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Abstract

Background: Perianal surgeries can be conveniently performed under saddle block . We intended to compare intrathecal low dose isobaric and hyperbaric levobupivacaine and study their efficacy in perianal surgeries under saddle block on ambulatory basis.

Methods: In this prospective, randomised controlled, double blind trial involving 20 patients in each group were randomised into two groups, Group I and Group H. Group I received 1ml of 0.5% levobupivacaine(5 mg) + 0.16 ml of Normal Saline (total volume-1.16 ml) and Group H : 1 ml of 0.5% levobupivacaine (5 mg) + 0.16 ml of 50% dextrose (total volume-1.16 ml). Duration for ambulation being the primary criteria, we also noted maximum cephalic spread, time to reach maximum height of sensory blockade, 2 segment regression, duration of motor and sensory blockade, time for voiding and time for rescue analgesia . Appropriate statistical tests were used for final analysis. P value less than 0.05 was considered statistically significant.

Results: There were no significant differences between the two groups in terms of the maximum height of sensory blockade and 2 segment regression that was achieved and request for first rescue analgesic. Duration of motor blockade, time to full recovery of sensory block and first voiding were all statistically significantly shorter in group H than group I.

Conclusions: We conclude that hyperbaric levobupivacaine is superior to isobaric form while being closer to ideal choice of anaesthetic agent on ambulatory basis required for perianal anaesthesia while both the concentrations are similar in their safety profile.

Keywords: Ambulatory; hyperbaric; Intrathecal; Isobaric; Levobupivacaine; Perianal.

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Introduction

Perianal surgeries are common procedures performed in the ambulatory setting. The primary goals are to reduce anaesthetic complications and to allow for early patient discharge. Saddle block is a preferred technique for perianal surgeries as it produces analgesia, anaesthesia, and motor

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block only in the perianal area.[1] However, this effect depends upon the volume, concentration, and doses of the drug used. Although hyperbaric local anaesthetic solutions like 0.5% hyperbaric bupivacaine have a remarkable record of safety, their use is not totally without risks. Hyperbaric solutions may cause hypotension or bradycardia after mobilization.[2]

Levobupivacaine, the S-enantiomer of racemic bupivacaine, is equipotent with bupivacaine when used in a similar concentration and dose. At the same time, levobupivacaine has lesser cardiac and central depressant action due to its faster protein binding rate.[3-6] Both hyperbaric levobupivacaine and isobaric levobupivacaine have been used in anorectal surgeries.[7] However, there are not enough data , whether one form is superior to the other.

We intended to compare intrathecal low dose isobaric and hyperbaric levobupivacaine and study their efficacy in perianal surgeries under saddle block on ambulatory basis.

Material and Methods

Patients undergoing anorectal surgeries for various ailments were included in the study after taking informed consent in this prospective randomised controlled , double blind trial. The study was performed under the Tenets of the Declaration of Helsinki after obtaining clearance from the hospital ethics committee and registration in Clinical trial registry bearing reference number CTRI/2020/09/027982.

Patients belonging to American Society of Anesthesiologists (ASA) physical status I and II, age between 18 to 50 years of either sex and done on elective anorectal surgeries (fistulectomy , fissurectom, haemorrhoidectomy, lateral internal sphincterotomy, perianal sinus, perianal abscess incision and drainage) were included in the study. Patients with diabetes and hypertensive status, previously on alpha agonists, steroids, antidepressants, any contra indication for neuraxial regional techniques, patient refusal and those with history of drug allergies were excluded from the study.

Patients were randomly allocated using computer generated randomisation (www.random.org) into 2 groups . Group I received 1ml of 0.5% levobupivacaine(5 mg) + 0.16 ml of Normal Saline in tuberculin syringe (total volume-1.16 ml) and Group H : 1 ml of 0.5% levobupivacaine(5 mg) + 0.16 ml of 50% Dextrose in tuberculin syringe(total volume-1.16 ml).

Pre anesthetic examination comprised of detailed history and systemic and airway examination. Preoperative investigations were done. All the patients were kept fasting for eight hours prior to surgery. Premedication with oral ranitidine hydrochloride 150 mg and alprazolam 0.25 mg given the night before the surgery.

Before surgery, patients were given instructions to use a 10-point Visual analogue scale (VAS) with 0 indicating no pain and 10 indicating the worst imaginable pain. In the operating room, electrocardiogram, pulse oximetry and non-invasive blood pressure (BP) were monitored, and baseline values recorded. All the patients were premedicated with Inj. Midazolam 1 mg IV. Following infusion of 500 ml lactated Ringer's solution, with the patient in the sitting position under aseptic precautions, lumbar puncture performed at L3-L4 interspace or L4-L5 interspace using 26 gauge spinal needle. The randomisation and loading of study drugs was done by a senior anaesthesiologist who was not involved further in the study. Just before spinal anaesthesia, syringe was handed over to the anaesthesiologist performing the subarachnoid block, who also monitored the patient subsequently. Thus, both the observer and the patient were blinded to the study drugs . The anaesthesiologist monitoring the patient intraoperatively and post operatively were not aware of the group allocation .

After intrathecal injection of drug , patients were made to sit for ten min, after which patients were placed in supine position . Intraoperatively heart rate, systolic BP, diastolic BP and mean arterial pressure, oxygen saturation and respiratory rate were recorded every 2 min for first 10 min then every 5 min till end of procedure . The sensory block level was assessed using cold swab for temperature discrimination along the midclavicular line and lateral part of dorsum of foot (S1) and perianal area . Motor level checked using Breen's Modification of Bromage scale . Sensory and motor block levels were noted after completion of 5 min when the patient was made supine and then every 2 min until the start of surgery . Maximum height of sensory block achieved was noted . If patient complained of pain during surgery, it was considered as failure of subarachnoid block and general anaesthesia instituted . Patients requiring general anaesthesia were not included for statistical analysis.

Post-operatively, Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure(MAP), respiratory rate (RR), oxygen saturation (SPO2), Visual analogue

scale (VAS), sensory and motor levels were noted in immediate post-operative period and then 15 min in the first post-operative hour and then, every half hourly till next two hours, then every hourly till 6 hours or till patient was ambulated . Patient made ambulant when the following criteria were achieved (1) Able to perform partial knee bend (Bromage scale 6) (2) recovery of proprioception of great toe (3) return of perianal sensation (4) no postural hypotension on making the patient stand . Time for ambulation(primary criteria) was recorded from the time of SAB to the time when patient was made ambulant . Time for urination and side effects if any were also observed in the post-operative period. Side effects such as hypotension (defined as a decrease in mean arterial pressure >25% of the baseline value) treated with IV boluses of 6 mg ephedrine. Bradycardia defined as a pulse rate of <50 beat/min was treated with bolus of 0.6 mg atropine IV, Respiratory depression (RR <8 or SpO2 <95%) treated with oxygen supplementation and respiratory support if required, vomiting and others if any were noted.

Sample size

The sample size was calculated based on observations from previous studies.[8] Keeping the power of study as 80% and α error as 5% , to detect at least 15% difference in time to ambulation between two groups hypothesizing isobaric levobupivacaine causing better ambulation, a minimum of 17 patients is required in each group . For a better validation of results, we included 20 patients in each group . The patients were randomly allocated into two groups of 20 each using computer generated randomization .

Results

A total of 42 adult patients were assessed for eligibilty. One patient in Group H had technical failure of subarachnoid block and another patient had a complex fistula and hence duration of surgery was prolonged. Both were converted to general anaesthesia. They were excluded from statistical analysis. 20 patients in each group was randomly assigned using computer generated randomisation to one of two treatment groups [Fig 1].

The two groups were comparable with respect to age, gender, weight, height, ASA physical status type and duration of surgical procedure [Table 1] .

The maximum median cephalic sensory blockade levels achieved were S1 (L3– S2 interquartile range) and T12(L1– T10 interquartile range) in groups H and I, respectively. There were no significant differences between the two groups in terms of the maximum height of sensory blockade and 2 segment regression that was achieved. Duration of motor blockade, time to full recovery of sensory block, first voiding and time for ambulation were all statistically significantly shorter in group H than group I [Table 2]. There were no significant differences in the number of episodes of hypotension, bradycardia, nausea,vomiting, headache or respiratory depression requiring treatment between the two groups. In addition, time for request of first rescue analgesic was not statistically significant between the two groups.

Table 1: Demographic details, type and duration of surgery SD-Standard Deviation; min-minutes.

	Hyperbaric	Isobaric	P value
Age (in years), mean ± SD	38.3±4.2	40.2±3.0	0.10
Male:Female	8:12	10:10	
ASA physical status(I:II)	15:5	13:7	
Type of surgery			
Fistulectomy	6	4	
Fissurectomy	4	4	
Haemorrhoidectomy	4	6	
Lateral internal sphincterotomy	3	4	
Perianal sinus	1	2	
Perianal abscess incision and drainage	2	Nil	
Duration of surgery(min), mean±SD	46.5±7.7	50.40±6.2	0.08

Table 2: Comparison of various parameters between the hyperbaric and isobaric group along with the p-value. P-value ≤ 0.05 was considered to be statistically significant; min-minutes.

	Group H (mean ± SD)	Group I(mean ± SD)	p-value
Time to reach max height of sensory block (in min)	11.1± 2.6	12.0 ± 3.4	0.26
2 segment regression (in min)	61.2± 4.3	59.3± 3.2	0.19
Duration of motor blockade (in min)	127.6± 8.6	165.3± 9.1	0.0001
Full recovery sensory block (in min)	175.6± 13.2	198.6± 17.6	0.001
Time for ambulation (in min)	172±12.1	189±10.2	0.001
Time for first voiding (in min)	274± 28.4	309.6± 40.5	0.03
Time for rescue analgesia (in min)	228.6± 16.5	230.1± 14.4	0.76

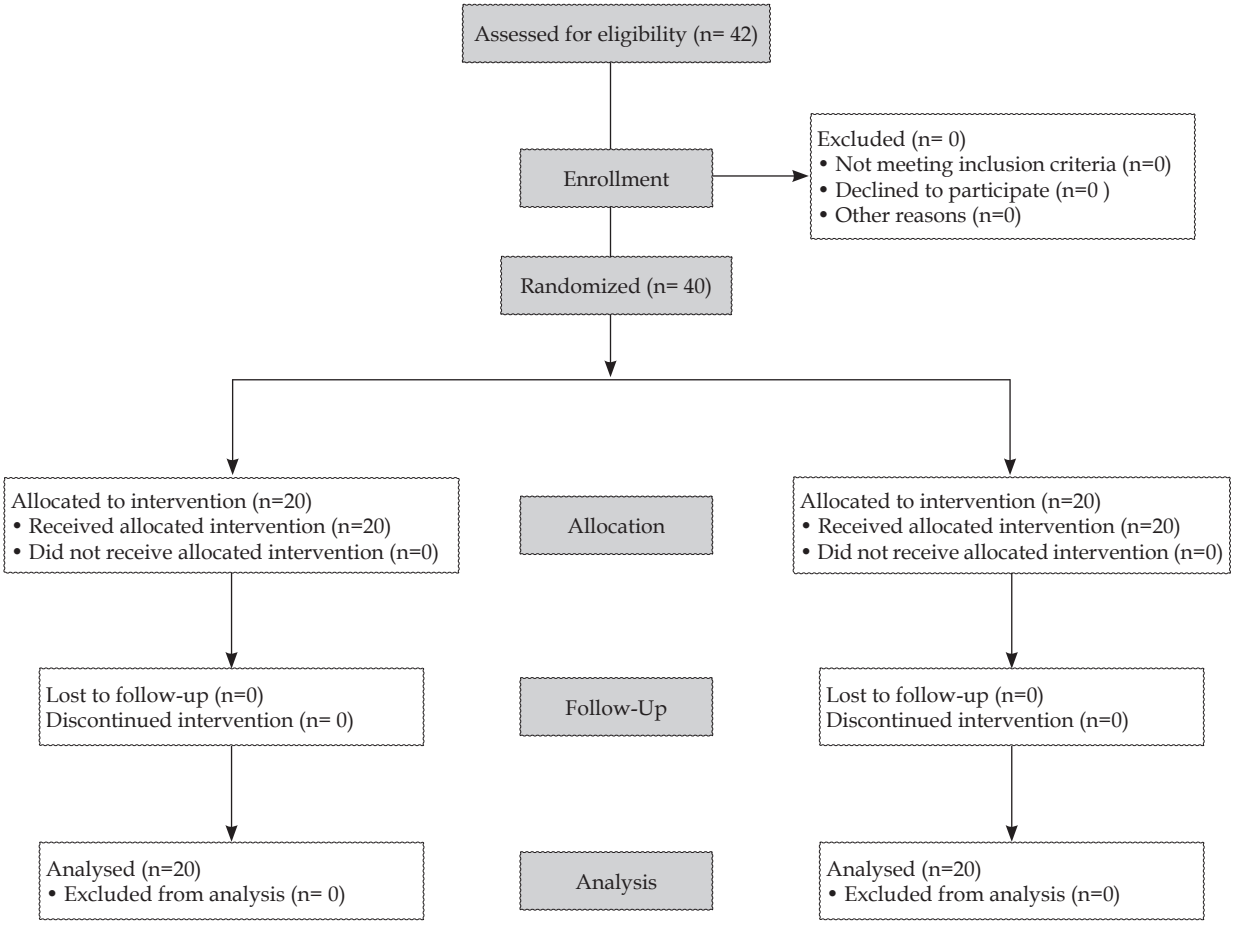

Fig. 1: Consort Flow Diagram.

Table 3: Frequency of adverse effects.

Adverse effects	Group H (n= 20)	Group I (n=20)	P value
Hypotension	1	2	0.5775
Bradycardia	-	-	-
Nausea	-	-	-
Vomiting	-	-	-
Headache	-	-	-
Urinary retention	-	-	-

Discussion

Our study compared block characteristics, clinical effects and complications of two different baricities of constant dose intrathecal levobupivacaine.

The effect of isobaric local anaesthetics has been not been consistent as shown in few studies. Levobupivacaine is available commercially in isobaric form. We prepared different baricity of levobupivacaine by adding 80 mg (0.16 ml) of 50% dextrose to isobaric levobupivacaine.

According to previous studies, limiting spinal block only to the dermatomal extent of the operative site provides better cardiovascular stability, faster motor and sensory recovery. Small doses of long-acting local anaesthetics have been used to obtain short-lasting spinal block.[9]

The ideal agent for day-case anaesthesia produces a rapid onset of a reliable block providing adequate surgical anaesthesia of appropriate duration and followed by a rapid regression of the motor and sensory blocks with minimal side-effects allowing rapid recovery and subsequent quicker hospital discharges.[10]

Smaller doses like 5-10 mg can be used in ambulatory surgeries . At such low concentrations, it produces a differential neuraxial block with preservation of motor function. The minimum local anaesthetic dose (MLAD) of intrathecal levobupivacaine is 5.68 mg for lower limb surgery.[3,4,11,12]

Naithani et al compared hyperbaric bupivacaine with isobaric levobupivacaine in lower limb orthopaedic surgeries, and found that although onset of sensory and motor block was significantly rapid, duration of sensory block was significantly longer in bupivacaine group as compared to levobupivacaine group. They proved that isobaric levobupivacaine offered effective clinical characteristics with stable hemodynamics and significantly decreased cardiovascular and central nervous system toxicity, so they concluded levobupivacaine to be a suitable alternative to hyperbaric bupivacaine in spinal anaesthesia.[2]

Sen et al also performed a similar study and proved that hyperbaric levobupivacaine had a faster onset of sensory and motor block with shorter duration of sensorimotor block than the isobaric form.[8] Similarly, in our study the onset was hastened and duration of block was longer in hyperbaric group than isobaric group but there was no difference in duration of analgesia between the two groups. Gulen G et al compared isobaric levobupivacaine with hyperbaric bupivacaine in caesarean section. In their study, time to reach maximum motor block in isobaric levobupivacaine was 11.36±2.35 min and in hyperbaric levobupivacaine was 6.13±1.56 min 13. We have obtained similar results. Few reviews have commented that use of hyperbaric levobupivacaine results in more predictable cephalad spread, also prolongs the duration of block, and also leading to a more rapid sensory and motor recovery.[4,12]

In the study by Alka Verma et al, in Group in which 50 mg dextrose was added to 7.5 mg levobupivacaine, 2 segment regression time was 49.2±3.09 min, which was significantly shorter than the times of other groups with 75 mg and 100 mg dextrose (56.76±3.68, 59.08±4.17).[14] Two segment regression in our study in hyperbaric group was 61.2±4.3 min whereas in isobaric group 59.3±3.2 min but the difference was not statistically significant.

In our study, the highest level of sensory blockade was seen in isobaric group reaching upto T12 whereas it remained confined to the site surgery in hyperbaric group reaching maximum L1 level. In the study by Sananlip et al, in which they studied characteristics of isobaric and hyperbaric levobupivacaine in gynaecological surgeries, isobaric levobupivacaine caused a wider range of peak levels (L1 to C8) compared with hyperbaric form (T7 to T2). They suggested that hyperbaric levobupivacaine had more predictable sensory block 3 . Similar maximum sensory block heights were also found in study comparing hyperbaric and hypobaric levobupivacaine in unilateral spinal anesthesia for elective ambulatory arthroscopic surgery of the knee by Kaya et al.[9] Few other studies did not notice any difference between the two groups in maximum height achieved when they compared isobaric levobupivacaine with hyperbaric solutions.[8,15] This difference may be due to the varying properties of drugs, their reaction to gravity and the movement of CSF due to postural changes. Gravity tends to keep the hyperbaric solution near the lowest point of the thoracic curve (T4/T5) in the supine position and preventing the flow further in a cranial direction .

This tendency to spread could be further increased with the viscosity of the hyperbaric solution, and prevent it mixing with the CSF. The plain solution, mixes freely with CSF, has neither gravitational nor viscous effect to restrict its movement within the displaced CSF and can spread unexpectedly high even after a reasonable time for fixation causing late complications like hypotension and bradycardia.[3,15,16]

Hyperbaric and hypobaric levobupivacaine both provided unilateral spinal anaesthesia more frequent in the hyperbaric group with good haemodynamic stability for arthroscopic surgery, in the study by Kaya et al.[9] Strictly unilateral sensory block was present in 30 min after injection (P -0.40), and unilateral motor block was observed in 94%, 93%, and 83% in groups Ropi-7.5, Levo-7.5, and Levo-5, respectively (P-0.31) in yet another study by Capellari et al.[17]

We found that time to achieve maximum sensorial blockade was prolonged in isobaric group compared to hyperbaric group though it was not statistically significant (12.0±3.4 vs 11.1±2.6 min, p=0.26). In the study by Ozgur et al, time for sensorial block to achieve T12 level was slower (12.5±2.2 min) in group containing less dextrose.[18] In contrast, Sasanlip et al found that hyperbaric levobupivacaine, compared with isobaric levobupivacaine, spread faster to T10 level (2.8 ± 1.1 versus 6.6 ± 4.7 minutes, P = 0.039) 3. Ajay Singh et al observed no difference in the block onset time or maximum block height.[15]

We found no difference in duration of analgesia between the two groups (228.6±16.5 vs 230.1±14.4 min, p=0.76) . Ajay Singh et al compared isobaric levobupivacaine with hyperbaric racemic bupivacaine in patients undergoing inguinal hernia surgery. The duration of anaesthesia was significantly shorter in group L compared with that in group B (206.2 ± 18.9 min vs. 224.1 ± 15.6 min, P < 0.001).[15]

With regards to full recovery of sensory block and duration of motor blockade, both were statistically significant (175.6±13.2 vs 198.6±17.6 min, p<0.01; 127.6±8.6 vs 165.3±9.1 min, p<0.001) being prolonged in isobaric group. Ozgur et al., in the group containing 80 mg dextrose, time to full recovery of sensory block was 154 min and duration of motor block was 105 min, both increasing with increase in density of levobupivacaine.[18] Kaya et al found that duration of sensory block although similar, motor block regression was faster in the hyperbaric group compared to hypobaric group.[9] This is due faster clearance of unbound levobupivacaine compared with plain bupivacaine represented by faster waning of the sensory block with levobupivacaine, duration of motor block being 185.9 ± 20.3 min as explained by Ajay Singh et al.[15] . Also, time for ambulation was significantly faster in group H compared to group I in our study.

We have found statistically significant difference in time for first voiding being 274±28.4 in hyperbaric group vs 309.6±40.5 min in the isobaric group (p=0.03). In the study by Ozgur et al, in Group I containing 60 mg dextrose was statistically significantly shorter than in the other groups containing 80 mg and 100 mg dextrose (p < 0.001).[18] Rapid return to bladder function is due to unilateral blocking of the sacral parasympathetic efferent ligaments innervating the detrusor muscle.

The incidence of hypotension was less in group Levobupivacaine (12%) compared to group Bupivacaine (32%) (P = 0.028) in the study by Ajay Singh et al.[15]. The difference in results can be attributed to the difference in the dose or baricity of the drugs used according to the nature of the surgery. Even in our study, all patients were hemodynamically stable and no significant difference was found in either of the groups. Herrera et al in their observational pilot study assessed the hemodynamic impact, hemoglobin and oxygen saturation of isobaric levobupivacaine versus hyperbaric bupivacaine for subarachnoid anesthesia in geriatric patients undergoing hip surgery. They observed lower incidence of intraoperative hypotension even in elderly.[19]

The main limitation of our study is that we did not compare time to mobilisation and actual discharge they may be affected by patient or surgery-related factors that are independent of the anaesthesia . The main issue with levobupivacaine is that hyperbaric formulations are not available commercially, so the we have to alter their baricity. This can potentially diminish spinal injection sterility and safety. Also, final anaesthetic solution density is less predictable than that of commercially available hyperbaric formulations.

To summarise, our results show that levobupivacaine with dextrose making it hyperbaric has significantly lesser duration of motor blockade, recovers from sensory blockade quite early and time for first urination being lesser compared with isobaric bupivacaine. None of the two groups being superior with regard to time for first rescue analgesic .

Conclusions

We conclude that hyperbaric levobupivacaine is superior to isobaric form while being closer to ideal choice of anaesthetic agent on ambulatory basis required for perianal anaesthesia while both the concentrations are similar in their safety profile.

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Comparison between Ultrasound Guided Peritubular Infiltration and Paravertebral Block for Postoperative Pain Relief in Percutaneous Nephrolithotomy

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Abstract

Background: Percutaneous Nephrolithotomy is most advanced and preferred technique for Renal calculi but associated with pain and discomfort in postoperative period. Aim of our study is to compare analgesic efficacy of peritubular infiltration with paravertebral block under Ultrasound guidance for postoperative pain relief.

Methods: In this prospective randomised study total 60 adult patients were allocated in two equal groups (A, B). After undergoing surgery under general anaesthesia group A patients received peritubular infiltration of 15ml of 0.25% inj.bupivacaine with inj. Dexmeditomidine 1ug/kg and group B patients received 15ml of 0.25% inj.bupivacaine with inj. Dexmeditomidine 1ug/kg in Paravertebral space T11, T12, L1 under ultrasound guidance. Postoperatively hemodynamic variables, VAS, Dynamic VAS, mean time for 1st demand of analgesia and total consumption of inj.tramadol were noted in both groups.

Results: At 4, 8, 12 hrs VAS, Dynamic VAS scores were lower in group B compared to group A($p<0.005$). Hemodynamic variables were comparable between groupsand demand for first rescue analgesia time were higher in paravertebral block group compared to peritubular infiltration group and total consumption of tramadol were low in paravertebral block.

Conclusion: Paravertebral block under ultrasound guidance is an effective analgesia for PCNL in postoperative period compared to peritubular infiltration.

Keywords: Paravertebral block; Peritubular infiltration; Percutaneous nephrolithotomy.

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Introduction

Renal calculi aremost common disease encountered in day to day practice. Various treatment modalities available such as percutaneous nephrolithotomy (PCNL), percutaneous nephrostomy (PCN), extracorporeal shock wave lithotripsy (ESWL) and open surgeries.[1,2] PCNL is the most common technique for removal of renal stones > 2 cm, staghorn calculi and multiple calculi. It is preferred

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because of less invasive, less time consuming than open surgery and increased clearance rate than ESWL.[1,2]

Percutaneous nephrostomy tube usually placed at the end of procedure to facilitate drainage of pelvicalyceal system to minimise bleeding relook and removal of residual calculi.[2] This Percutaneous nephrostomy tube placement is associated with severe discomfort and pain for patients which may require additional analgesics in postoperative period.[3] If failure to provide adequate analgesia may result in impaired ventilation, inadequate mobilization and prolonged hospitalization.[4]

Various modalities of treatments tried such as Nonsteroidal anti-inflammatory drugs, opioids, local infiltration, peritubular infiltration, paravertebral block, intercostal block and epidural anaesthesia.[5-9, 11-14] In our study we compared analgesic effect of paravertebral block and peritubular infiltration under ultrasound guidance with dexmeditomidine which was not studied previously.

Methodology

The study was conducted in Melmaruvathur Adhiparasakthi institute of medical sciences and research in department of anaesthesiology after obtaining permission from institutional ethical committee. In this study 60 patients of ASA I and II, age group between 18- 60 years undergoing elective PCNL surgeries are included in this study. Patient refusalASA III & IV, Hypersensitivity to Bupivacaine and dexmedetomidine, Patients requiring more than one puncture, supracostal puncture, Coagulopathy, Excessive bleeding and procedure more than 3 hours are excluded from the study. After obtaining written informed consent, total 60 adult patients were randomly allocated to two equal groups every odd numbers allocated to Group A(n~30) and alternative patients to Group B(n~30).

In preoperative assessment general examination, systemic examinations and assessment of the airway were done. Preoperative fasting of minimum 8 hrswas ensured before surgery. All patients received premedication of tab. Alprazolam 0.25mg orally the night before surgery as per anaesthesiologist order to allay anxiety, apprehension, and for sound sleep. The patients also received tab. Ranitidine 150 mg in the previous night and the morning of operation with sip of water.

Preoperatively patients were clinically examined and procedure was explained. On entering operative room (OR) standard intraoperative monitors such as ECG, pulse oximeter (SPO2), noninvasive blood pressure (NIBP) were attached, and baseline parameter recorded. Intravenous (IV) infusion of Ringers lactate started. After intubation end-tidal carbon dioxide (EtCO2) monitor was attached.

The patients were preoxygenated with 100% oxygen for 5min. Injection fentanyl (2 µg/kg) andinj. Glycopyrrolate (0.01 mg/kg) were given intravenously 3min before induction of anesthesia. Injection propofol 2mg/kg and Injection Succinylcholine 2 mg/kg IV was used for induction and intubation. After 1 min of succinylcholine administration, laryngoscopy and intubation were performed. The trachea was intubated with a soft seal cuffed sterile polyvinyl chloride ETT with a standard cuff and an internal diameter of 7–7.5 mm for women and 8–8.5 mm for men. Tracheal intubation was performed by an experienced anesthesiologist. Anesthesia was maintained with nitrous oxide 66% and oxygen 33% and isoflurane up to 1–2 minimal alveolar concentration and inj. Atracuririum for muscle relaxation.

At end of the PCNL procedure and before the extubation in Group A patients 23 G spinalneedle inserted up to renal capsule under ultra-sonographic guidance along the nephrostomy tube at 6 O'clock and 12 O'clock positions, 15 ml of 0.25% bupivacaine withInj dexmedetomidine 1µg/kg was infiltrated (7.5 ml in each tract) while gradually withdrawing the needle from renal capsule to the skin. Patients wereextubated. In post-anaesthesia care unit patients were observed for 24 hrs.

At end of surgery, Paravertebral block(PVB) was performed under ultrasound guidance at the T11, T12 and L1 levels using 0.25% bupivacaine with Injdexmedetomidine 1µg/kg at a total dose of 15 ml in group B. In ultrasound the paravertebral space was identified by between the costotransverse ligament, pleura, and transverse process. A 23-gauge spinal needle was advanced in the vertical-to-caudal direction using the in-plane technique. After the needle entered the paravertebral space, 5 mL of 0.25% bupivacainewith Inj dexmedetomidine 1µg/kg was injected in each dermatome level. The spread of the local anaesthestics was confirmed by anterior movement of the pleura in the paravertebral space. All blocks were performed by the experienced anaesthesiologist. At end of surgery, patients were reversed with injection glycopyrrolate 0.01 mg/kg and injection neostigmine 0.05 mg/kg and extubated when adequate spontaneous ventilation

was established.

During follow-up, patients were assessed for pain and side-effects by an observer blinded to the infiltration, immediately after extubation, and at 1st, 2nd, 4th, 8th, 12th, 24th hours respectively. The pain score was assessed using 0-10-point visual analogue scale (VAS) (0-no pain and 10-maximum, unbearable pain) and dynamic VAS (pain on deep breathing and coughing). When VAS score >4, the patient was administered intravenous tramadol 1.0 mg/kg slowly as a rescue analgesia, patient was reassessed and time of requirement noted. Total requirement of inj.Tramadol was also recorded.ECG (lead-II) and heart rate, SpO2, systolic BP (SBP), diastolic BP, mean BP, were recorded throughout the postoperative procedure. Side effects like nausea, vomiting, pneumothorax, hemothorax, wound site hematoma are noted.

Statistical analysis

All analyses were performed using SPSS Statistics software. Data were expressed as means with 95% confidence intervals for continuous variables. Continuous data were described as mean± SD, and categorical variables were given as numbers. (%). The chi-square test was used to compare categorical variables between the groups. Student's t-test or the Mann-Whitney U-test was used to compare continuous variables between two groups, depending on whether the statistical hypotheses were fulfilled. To evaluate changes in the measurements obtained in the time interval, a repeated measurements analysis was applied. The values are considered statistically significant when P value is < 0.05

Results

Demographic variables such as age, weight are comparable between groups and are not statistically significant. Duration of surgery are similar between groups and statistically insignificant. (Table 1)

Visual analogue score in immediate postoperative period at 0,1,2 hours between groups were almost similar and statistically insignificant with p-value 0.606, 0.506, 0.432 respectively (Table 2). At 4,8,12 hours VAS scores were lower in group B compared to group A with p-values 0.002, 0.003, 0.005 respectively and statistically significant. (Table.2) After 12 hours at 18, 24 hours VAS scores were comparable and not significant. Dynamic VAS scoring showed similar result as VAS and they were significant at 4, 8, 12 hours with p-value 0.02, 0.001,0.004 respectively (Table.2). Hemodynamic variables such as HR, MAP, SPO2 were comparable between groups (Table 3).

Mean time for first demand of analgesia were lower in group A compared to group B (480.50±33.53 vs 715.50±29.77 mins) and statistically significant (Table.4). Total consumption of tramadol in 24 hrs is also significant between group A and group B (113.67±29.82 vs 66.67±5.30 milligrams) (Table 4)

Table 1: Patient demographics.

Variables	Group	Mean	Standard deviation	p-value
Age	A	41.67	6.599	0.239
	B	43.50	5.619	
weight	A	66.50	6.781	0.132
	B	67.50	5.251	
Duration	A	128.65	25.34	0.778
	B	126.85	23.20	

Table 2: VAS and Dynamic VAS score.

Variables	Group	0HR	1 HR	2HRS	4HRS	8HRS	12HRS	18HRS	24HRS
VAS	A	1.63±	1.77±	2.20±	2.80±	5.43±	5.80±	4.27±	3.20±
		0.49	0.43	0.40	0.40	0.67	3.53	0.69	0.40
	B	1.40±	1.53±	2.00±	2.40±	3.00±	3.53±	3.80±	3.00±
		0.49	0.50	0.64	0.49	0.00	0.73	0.55	0.63
	p-value	0.606	0.506	0.433	0.002	0.003	0.005	0.077	0.433
Dynamic VAS	A	2.60±	2.43±	2.97±	3.70±	6.20±	6.00±	4.17±	3.47±
		0.49	0.50	0.61	0.70	0.76	0.00	0.64	0.62
	B	2.20±	2.13±	2.70±	3.53±	4.00±	4.40±	3.83±	3.17±
		0.55	0.50	0.615	0.50	0.00	0.72	0.64	0.37
	p-value	0.412	0.037	0.100	0.02	0.001	0.004	1.000	0.336

Table 3. Hemodynamic variables.

Variables	Group	0HR	1 HR	2HRS	4HRS	8HRS	12HRS	24HRS
HR (min)	A	91.20±	90.63±	88.93±	87.93±	90.20±	90.00±	83.13±
		2.82	2.26	3.22	2.49	4.14	3.43	4.45
	B	89.53±	89.20±	86.97±	86.57±	86.97±	84.67±	85.03±
		2.96	2.325	3.67	3.720	3.21	4.72	3.31
	p-value	0.921	0.076	0.383	0.036	0.186	0.086	0.09
MAP (mm hg)	A	92.13±	91.13±	90.97±	89.20±	88.10±	87.87±	87.03±
		2.12	1.88	1.92	2.51	3.54	3.14	3.24
	B	90.90±	89.90±	87.60±	87.80±	88.20±	87.10±	86.07±
		2.28	2.13	2.44	2.73	1.91	2.80	2.49
	p-value	0.613	0.202	0.083	0.903	0.085	0.746	1.910
SPO2 (%)	A	99.53±	99.40±	99.43±	99.37±	99.33±	99.47±	99.23±
		0.57	0.56	0.56	0.61	0.54	0.50	0.56
	B	99.37±	99.40±	99.40±	99.50±	99.37±	99.47±	99.40±
		0.61	0.49	0.49	0.57	0.55	0.50	0.49
	p-value	0.116	1.012	0.205	0.788	0.753	1.000	0.105

Table 4: Comparison of analgesic efficacy between groups.

Parameters	Group A	Group B	p value
Mean time for first demand of analgesia (mins)	480.50±33.53	715.50±29.77	0.003
Total consumption of tramadol in 24 hrs (mgs)	113.67±29.82	66.67±5.30	0.004

Discussion

Various surgeries like Percutaneous nephrolithotomy, Percutaneous nephrostomy and open surgeries involving removal of renal calculi are associated with pain invariably.[1,2] This pain can hamper post-operative respiration and devastating effects in postoperative period.[4] Various modalities of treatment were tried with variable success. In our study we compared analgesic effect of paravertebral block and peritubular infiltration under ultrasound guidance with dexmeditomidine for percutaneous nephrolithtomy.

The results of our present study showed that paravertebral block was more effective than peritubular infiltration in reducing postoperative pain. VAS score and DVAS score were lower in both group in initial postoperative period but duration of analgesia was prolonged in paravertebral block group compared to peritubular infiltration group. Geetha P Parikh et al as studied analgesic efficacy of peritubular infiltration of 0.25% bupivacaine in percutaneous nephrolithotomy also observed better low VAS score in immediate postoperative period compared to control group similar to our study.[15] Yayik AM et al as studied ultrasound –guided low thoracic paravertebral block versus peritubular infiltration and Zehra Hatipoglu et al comparatively studied ultrasound- guided paravertebral block versus intravenous tramadol for postoperative pain in percutaneous nephrolithotomy inboth these studies found that paravertebral block has better postoperative VAS and DVAS scores and longer duration of analgesia than other techniques.[16,17]

Paravertebral block preferred using ultrasound guidance to avoid inadvertent complication such as pleural puncture, intrathecal injection, intravenous placement, block failure and pneumothorax.[18] In our study no complication was encountered in any patients during ultrasound guided paravertebral block.

Paravertebral block being a regional anaesthesia technique, have less effects on hemodynamic variables. In our study there was no significant changes in HR, MAP, in postoperative period between groups. Zehra Hatipoglu et al andBaidya DM et al in both these studies no change in hemodynamic variablesin postoperative period following paravertebral block and control group

similar to our study.[17,19]

In our study demand for first rescue analgesiatime were lower in paravertebral block group compared to peritubular infiltration group and total consumption of tramadol were low in paravertebral block. Yayik et alstudied ultrasound –guided low thoracic paravertebral block versus peritubular infiltration in their study also showed that first demand of rescue analgesia time and fentanyl consumption both are lower in paravertebral block compared to control group.[20]

In recent years regional anaesthesia techniques were used increasingly in postoperative period under ultrasound guidance because they are simple, safe and give good analgesia without any side effects. We tried paravertebral block and peritubular infiltration for percutaneous nephrolithotomy surgeries. In both techniques better pain relief in postoperative period was observed but longer duration was observed in patients receiving paravertebral block under ultrasound guidance seems to be an advantage.[21]

Conclusion

Hence paravertebral block under ultrasound guidance with increased duration, minimal adverse effects, reduction in consumption of rescue analgesia make it suitable technique of choice for postoperative analgesia in percutaneous nephrolithotomy. Peritubular infiltration may be a simple alternative technique.

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Conflicts of interest: Nil

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Original Article

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Comparative Evaluation of Bupivacaine and Bupivacaine with Dextmedetomidine in Subarachnoid Block

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Abstract

Introduction: Since the introduction of spinal anaesthesia in 1898 by Dr. August Bier, who described the intrathecal administration of cocaine, spinal anaesthesia is preferred over general anaesthesia, particularly in surgical procedures of lower abdomen and lower limbs[1] (D C Simon et al 2008). The aim of intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for all below umbilical surgeries. Hyperbaric Bupivacaine is the most commonly used intrathecal local anaesthetic. Various adjuvants have been added to Bupivacaine to shorten the onset of block and prolong the duration of block. A number of adjuvants such as clonidine, Midazolam, opioids have been studied to prolong the effect of spinal anaesthesia[3,4] (Elia N.et al 2008, Boussofara et al 2006). Clonidine has side effects like bradycardia, hypotension, dryness of mouth, nausea, respiratory depression, itching, and neurological toxicity. Dexmedetomidine is a new highly selective α_2 agonist. It is α_2 agonist drug, when given intrathecally, significantly prolongs the duration of spinal block. Intrathecal α_2 receptor agonists have been found to have antinociceptive action for both somatic and visceral pain[5] (Al Ghanem SM et al 2009). It is hypothesized that intrathecal 5 µg Dexmedetomidine would produce more postoperative analgesic effect with hyperbaric Bupivacaine in spinal anaesthesia with minimal side effects[5-7] (Al Ghanem, Al Mustafa et al 2009 & Kanazi GE). To see whether the Dexmedetomidine alleviates the side effects of clonidine & Midazolam, we decided to study the efficacy and safety profile of Dexmedetomidine in combination with local anaesthetic in subarachnoid block for below umbilical surgeries.

Keywords: Spinal Anaesthesia; Bupivacaine; Dexmedetomidine.

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Introduction

Intrducation not provided.

Aims & Objectives:

1. To compare the onset & duration of sensory block.
2. To compare the onset & duration of motor block.
3. To evaluate total duration of analgesia.
4. To evaluate incidence of intraoperative and postoperative complications.

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Material and Methods

Hundred patients were included in this study after getting approval from ethical committee and informed consent from patients. Each group included 50 patients, Group B & Group BD. Group B patients were anaesthetized with hyperbaric Bupivacaine 0.5% 3cc (15mg) + 0.5 cc normal saline and Group BD patients were given hyperbaric Bupivacaine 0.5% 3cc (15mg) + 5 µg Dexmedetomidine. All the basic investigations were done including complete blood count (CBC), Urine exam. 12 lead ECG, Random blood sugar, Blood urea & Sr. Creatinine, LFTs.

The procedure was explained to each patient a day prior to surgery and patients were kept nil per oral after 10 pm on previous night.

On the day of surgery, patient's basic PR & BP was recorded. Patients were secured with IV line and preloaded with 1 l RL. Patients were connected to multiparameter. Under all aseptic precautions lumbar puncture was done with Quincke's spinal needle in L3-4 space. Group B patients were given Inj. Bupivacaine 0.5% (3cc) + 0.5 cc Normal saline and Group BD patients were injected Inj. Bupivacaine 0.5% (3cc) + 5µg Dexmedetomidine. The study was double blinded.

All the vital parameters were recorded at 0,3,5,10,15,20,25,30 minutes after spinal anaesthesia and every 10 minutes for one hour, then every 30 min for first two hours and then every 60 min for 9 hours in postoperative period.

Sensory blockade was assessed using 22G needle. Analgesia is defined as loss of sensation to pinprick and anaesthesia as loss of sensation to touch.

Motor blockade was assessed by straight leg raising while lying supine and was graded according to Modified Bromage Scale.[17]

Grade 0 – No Paralysis

Grade 1 - Inability to raise extended legs

Grade 2 - Inability to flex knee, able to move feet only

Grade 3 - Complete paralysis

Onset of motor block was taken as time to achieve Bromage score 1 from the time of intrathecal injection of drug. After 20 min of block the Bromage score was considered as the maximum degree of motor block.

Intraoperatively and postoperatively complications viz. hypotension, variations in the heart rate, nausea, vomiting were noted & treated.

Postoperatively the patients were observed for the duration of analgesia by using VAS score (0 to 10). Zero being no pain and 10 being the most severe pain. Patients were given rescue analgesics once the VAS score exceeds.[5]

The onset of sensory blockade, Maximum sensory blockade, Motor onset, Maximum motor blockade, duration of sensory & motor block and duration of analgesia were noted.

The results of the study were statistically analyzed between the groups using unpaired t test.

$P < 0.05$ - statistically significant

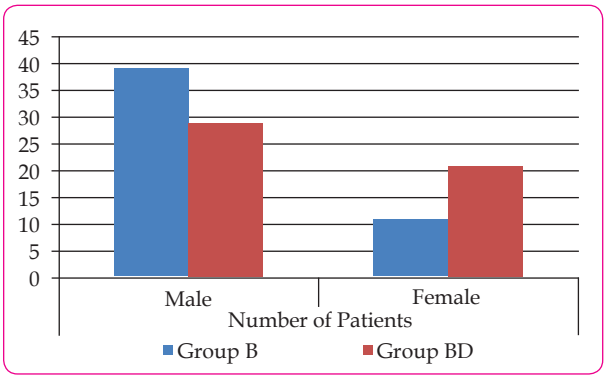
$P < 0.01$ - statistically highly significant

$P > 0.05$ - statistically not significant

Observations and Results

Table 1: Sex wise distribution.

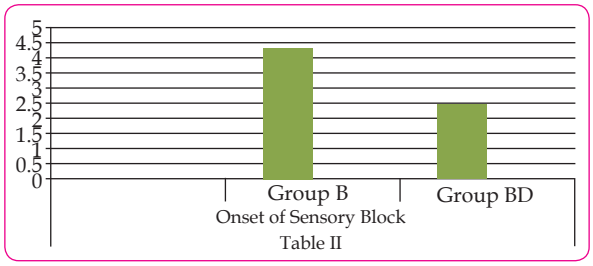
Gender	Number of Patients		Chi Square Test	P value
	Group B	Group BD		
Male	39	29	2.71	>0.05
Female	11	21		
Total	50	50		



Sex wise distribution was statistically compared using chi square test and found to be non significant i.e. $P > 0.05$. (Table 1)

Table II: Onset of Sensory Block.

	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Onset of Sensory Block in minutes	4.32	±0.61	2.47	±0.29	< 0.05; Significant

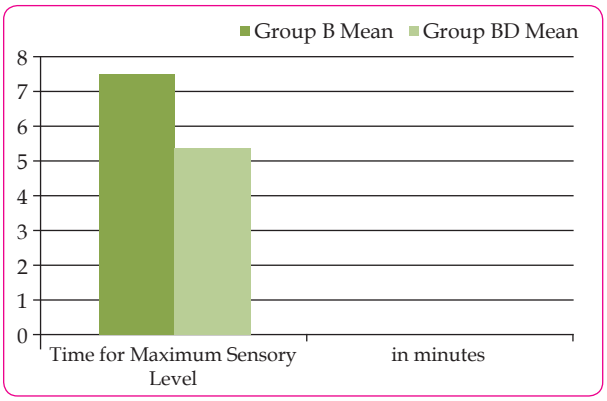


We can see that there is statistically significant difference in the mean duration of onset of sensory block between two groups. (P < 0.05) (Table 2)

Onset of sensory block was significantly faster (P < 0.05) in study group compared to control group.

Table III: Time for Maximum Sensory Level.

	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Time for Maximum Sensory Level in minutes	7.51	±0.27	5.39	±0.31	< 0.05; Significant

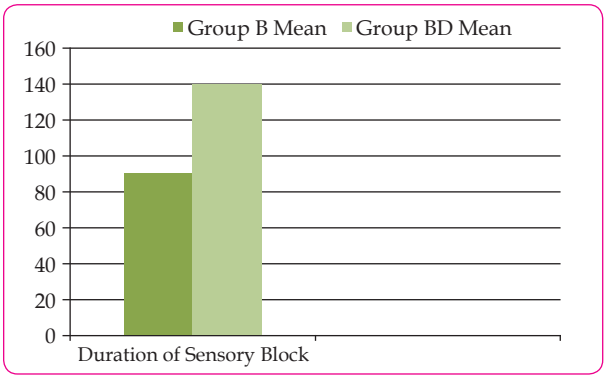


We can see that there is statistically significant difference in the mean duration of maximum sensory level between two groups. (P < 0.05) (Table 3)

It indicates cephalic spread of sensory block occur faster when Dexmedetomidine was added to intrathecal Bupivacaine.

Table IV: Duration of Sensory Block.

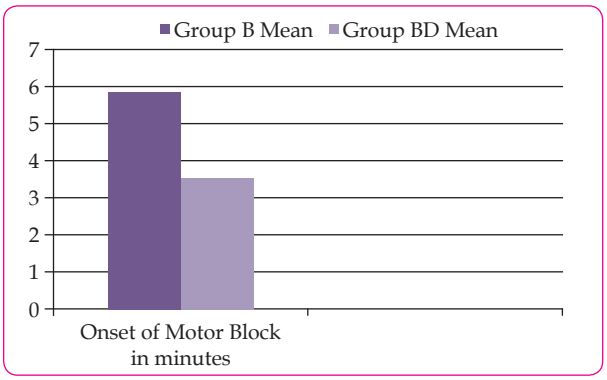
	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Duration of Sensory Block	90.21	±6.09	139.86	±6.18	< 0.001; Highly Significant



From above graph we come to know that there is statistically significant difference in mean duration of time for regression of two segment sensory blockade between two groups (P < 0.001). It means regression of sensory block was slower in patients those who received intrathecal Dexmedetomidine. (Table 4)

Table V: Time for Onset of Motor Block.

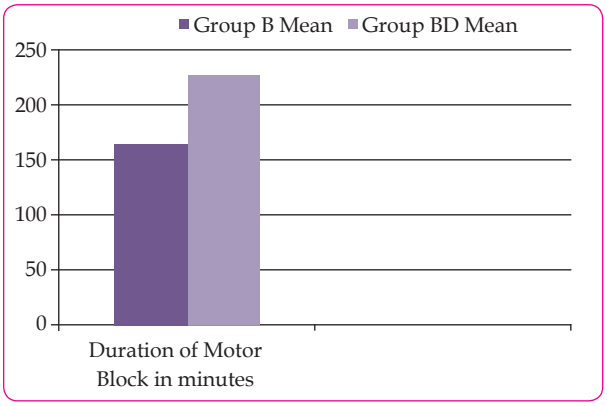
	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Onset of Motor Block in minutes	5.87	±0.29	3.53	±0.27	< 0.05; Significant



There is statistically significant difference in mean duration of onset of motor block between two groups (P< 0.05). Thus from above results it is clear that onset of motor block is quicker in patients received intrathecal Dexmedetomidine. (Table 5)

Table VI: Duration of Motor Block.

	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Duration of Motor Block in minutes	164.32	±3.45	227.1	±1.76	< 0.001

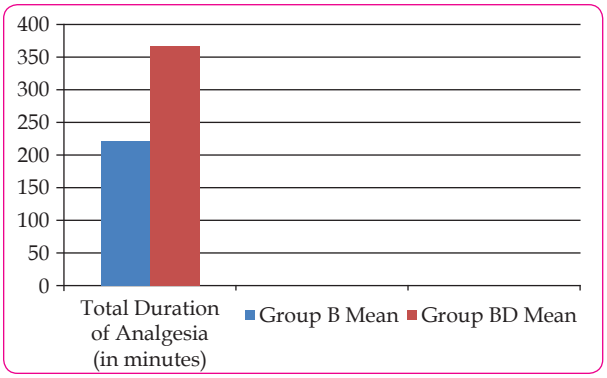


In present study, the mean duration of motor block i.e. time for regression to Bromage 0 in Group BD (Dexmedetomidine group) was 227.1±1.76 min as compared with Group B in which it was 164.32±3.45 min. (Table 6)

There is statistically significant difference in mean duration of time for regression to Bromage 0 i.e. duration of motor block between the two groups (P <0.001).

Table VII: Total Duration of Analgesia.

	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Total Duration of Analgesia in minutes	222.54	14.68	368.74	11.72	< 0.001



In present study we found that mean duration of sensory analgesia was 222.54 ±14.68 min in Group B as compared to 368.74 ±11.72 min in Group BD. (Table 7)

There is statistically significant difference in mean duration of analgesia between two groups (P < 0.001).

Thus there was significant prolonged duration of sensory analgesia in Dexmedetomidine group i.e. in Group BD as compared to control group (P<0.001).

Intraoperative and postoperative complications

In our study, intraoperative and postoperative complications were observed such as inadequate level of analgesia, bradycardia, tachycardia, hypotension, high level of block etc.

Only two patients in Group B and 4 in Group BD had bradycardia. Two patients in Group B and 3 patients in Group BD had hypotension .

There was no statistically significant difference of intraoperative & postoperative complications between both the groups with p value as >0.05.

Discussion:

Dexmedetomidine Hydrochloride, a newer agent within the class of α_2 adrenoreceptor agonist delivers clinically effective sedation with analgesic property for use in intensive care unit setting. Additionally it has ability to eliminate or reduce the need for other analgesic medications. There is no evidence of respiratory depression with Dexmedetomidine. Because of its selective α_2 receptor activity, use of Dexmedetomidine has modest and predictable haemodynamic effects, making it a popular sedative and analgesic drug in intensive care unit.[18]

Dexmedetomidine is now being used outside the ICU in variety of clinical settings including sedation and adjunct analgesia in the operating room, sedation in diagnostic procedures and for other applications such as withdrawal / detoxification amelioration in adult and paediatric patients.[19]

Animal studies have been used intrathecal Dexmedetomidine at a dose ranged 2.5 – 100 µg. The largest dose of intrathecal Dexmedetomidine 100 µg was used in a sheep model, where a 7 day follow up showed no neurological deficit in the studied animals.[20] In human studies, dose ranged 3-5 µg 5,8,9,10,21. The dose of Dexmedetomidine used in subarachnoid block ranged 3-5 µg in various studies showing effective clinical & safety profile. Hence, in this study, we used 5 µg preservative free Dexmedetomidine with 15 µg hyperbaric Bupivacaine intrathecally in Group BD.

Present study was undertaken to evaluate the effect of addition of Dexmedetomidine in subarachnoid block along with 0.5% Bupivacaine (H) on sensory, motor, haemodynamic and analgesic parameters both intraoperatively and postoperatively. It was compared with routine standard technique using 0.5% Bupivacaine (H) for spinal anaesthesia.

Our study included 100 patients between 15-45 years of either sex with ASA grade I and II posted

for elective surgeries below umbilicus. The patients having contraindications were excluded from study. Patients were divided into two groups (each 50) i.e. control group (Group B) and study group (Group BD) depending upon drugs used.

Group B received Inj. Bupivacaine 0.5% (heavy) 15mg (3cc) + Normal saline 0.5 cc

Group BD received Inj. Bupivacaine 0.5% (heavy) 15mg (3cc) + Inj. Dexmedetomidine 5µg (0.5cc)

In present study, in Group B 39 patients were males and 11 were females while in Group BD 29 were males and 21 were females.

Sensory Block parameters: (Table no. II, III & IV)

Time of onset of sensory block:

In present study mean time for onset of sensory block was 2.47±0.29 min in Group BD, which was quicker as compared to 4.32±0.61 min in Group B. Onset of sensory block was significantly faster ($p<0.05$) in study group as compared to control group.

Regarding onset of time our findings are similar to study conducted by R. Brinda et al.,[16] who carried out study on 100 patients who were undergoing elective lower abdominal surgery. Group A(n=50) received hyperbaric Bupivacaine 0.5% + normal saline and Group B was given 0.5% Bupivacaine 15mg + 5 µg Dexmedetomidine. Time to sensory block to reach T10 dermatome was 4.60(0.70 min in Group A and 2.07(0.47) min in Group B. Quicker onset of sensory block in patients of Dexmedetomidine group in present study is also comparable with studies carried out by Nazima Memon et al 15, Veennah Chatrath et al.[13] Our findings were also similar to Sunil B.V. et al.,[22] who studied 90 patients in three groups of each.[30] Each group received intrathecally either 15mg hyperbaric Bupivacaine alone (Group B) or 10 µg (Group D10) or 5 µg Dexmedetomidine added to 15 µg hyperbaric Bupivacaine. The sensory block onset time to reach T10 in group B was 4.7±1.1 min, group D5 3.5±0.8 min and group D10 3.1±0.5 min.

In conclusion, addition of Dexmedetomidine prolonged the sensory block significantly when used with hyperbaric Bupivacaine intrathecally in a dose dependent manner. It supports the addition of Dexmedetomidine up to 10 µg with Bupivacaine in spinal anaesthesia.

Our findings were contradictory to study conducted by Feroz Ahmad Dar et al.,[14] Sangeeta Agrawal Bansal et al.,[12] who found no difference in time of onset using 5 µg Dexmedetomidine.

Time for Maximum Sensory Block and Maximum Sensory Level achieved: (Table III)

In our study time to achieve maximum sensory block was 5.39±0.31 min in Group BD as compared to 7.51±0.27 min in Group B. Time to achieve maximum sensory block was significantly lower ($p<0.05$) in Dexmedetomidine group as compared to control group. It indicates cephalad spread of sensory block occur faster when Dexmedetomidine was added to intrathecal Bupivacaine. This finding was similar to that of study carried out by R. Brinda et al.,[16]

However our finding was contradictory to finding of Sangeeta Agarwal Bansal et al.,[12] and Feroz Ahmad Dar et al.,[14] who found no such difference regarding time to achieve maximum sensory block.

In present study maximum sensory block achieved was T4 in both groups, Group BD & Group B. This finding was comparable to study conducted by Veena Chatrath et al.,[13] found similar dermatomal level of maximum sensory block achieved in patients who received intrathecal Dexmedetomidine.

Duration of Sensory Block (Time for Two Segment Regression): (Table IV)

In our study, mean time for two segment regression from maximum sensory dermatomal level in Group BD was 139.86±6.18 min which was much significantly longer ($p<0.001$) than that of Group B in which it was 90.21±6.09 min.

It means regression of sensory block was slower in patients those who received intrathecal Dexmedetomidine.

Our result is comparable with the study conducted by Nazima Memon et al.,[15] and Hala E A Eid et al.,[11]

Motor Block Parameters: (Table No. V & VI)

Onset of Motor Block: (Table No. V)

In present study mean time of onset of motor block was significantly quicker ($P<0.001$) i.e. 3.53±0.27 min in Group BD as compared to 5.87±0.29 min in Group B.

This result was comparable to R. Brinda et al.,[16] who found mean time of onset of motor block 2.30±0.45 min in Dexmedetomidine group (5 mcg) as compared to 6.57±0.49 min in control group.

Thus from above results it is clear that along with faster onset of sensory block, onset of motor block is also quicker in patients who received intrathecal Dexmedetomidine.

Duration of Motor Block: (Time for regression to Bromage 0): (Table No. VI)

In present study the mean duration of motor block in Group BD was 227.1±1.76 min which was significantly prolonged (P<0.001) as compared to Group B in which it was 164.32±3.45 min.

Results of our study are comparable with the study carried out by R. Brinda et al.[16] The mean time for regression of motor block to Bromage 0 was 141.56±15.29 min in control group and 229.98±14.26 min in Dexmedetomidine group.

Our results were also comparable with the study carried out by Veena Chatrath et al13 who found that the mean duration of motor blockade was 318.36±9.374 min in Dexmedetomidine group as compared to only 146.94±9.713 min in control group(P<0.05). Similar results were observed by Sunil B.V. et al22 in which mean duration of motor block was 225±23.3 min in Dexmedetomidine group (5mcg) as compared to 149.4±17.5 min in control group.

Duration of Analgesia: (Table No. VII)

In present study we found that the mean duration of sensory analgesia was 222.54±14.68 min in Group B as compared to 368.74±11.72 min Group BD.

The mean duration of sensory block was prolonged in our study comparable to most of the previous studies carried out by R. Brinda et al.,[16] Nazima Memon et al.,[15]

Our findings are similar to that of study conducted by Veena Chatrath et al.,[13] who studied 'comparative evaluation of Bupivacaine alone versus Bupivacaine and Dexmedetomidine for spinal anaesthesia in infraumbilical surgeries'. They concluded that addition of Dexmedetomidine to Bupivacaine leads to early onset of sensory and motor block with prolonged duration and patient remained pain free for longer period with decreased demand for rescue analgesia in the postoperative period as compared with Bupivacaine.

Intraoperative and postoperative complications

In our study, intraoperative and postoperative complications observed were inadequate level of analgesia, bradycardia, tachycardia, hypotension, high level of block.

Intraoperatively two patients had bradycardia in Group B and 4 in Group BD which was treated by Atropine. Hypotension found in 2 patients in Group B and 3 patients in Group BD, treated with Ringer's Lactate solution and Mephenteramine.

There was not a single patient with inadequate level of analgesia, tachycardia and high level of block. Our findings were similar to findings of Sunil B.V. et al.,[22] R.Brinda et al.,[16] Nazima Memon et al.,[15] who also found minimal intraoperative complications.

There was no statistical difference of intraoperative and postoperative complications between both the groups (p>0.05). Results of our study are similar with the studies carried out by Sunil B.V. et al.,[22] Veena Chatrath et al.,[13] Nazima Memon et al.,[15] R.Brinda et al.,[16] in respect of onset of sensory block, onset of motor block, duration of sensory block, duration of motor block, duration of analgesia, intraoperative and postoperative complications.

Summary

The present study titled 'Comparative evaluation of Bupivacaine and Bupivacaine with Dexmedetomidine in subarachnoid block' was prospective, randomized, double blind study included 100 patients belonging to ASA grade I or II of either sex with age between 15-45 years posted for elective for below umbilical surgery.

Control group Group B received Inj. Bupivacaine 0.5% 15mg + Normal Saline 0.5cc while Study group Group BD received Inj. Bupivacaine 0.5% 15mg + Inj. Dexmedetomidine 5mcg (0.5cc).

Pulse rate, systolic and diastolic blood pressure, respiratory rate and SpO2 were monitored intraoperatively and in postoperative period for 9 hours after spinal anaesthesia. Other parameters observed i.e. sensory and motor block parameters, analgesia time and VAS score and subjected to statistical analysis.

The demographic data such as age, sex, height and weight were comparable in both groups and has no influence on outcome of the study.

1. There was no significant difference in mean duration and type of surgery between both groups (p<0.05).
2. Mean time for onset of sensory block was significantly less 2.47±0.29 min in Group BD as compared to that of Group B 4.32±0.61 min (p<0.05).
3. Mean time for onset of motor block was significantly less 3.53±0.27 min in Group BD as compared to that of Group B 5.87±0.29 min (p<0.05).
4. Maximum sensory dermatomal level achieved

was equal i.e. T4 in Group B & BD.

5. Mean time for two segment regression was significantly longer (p<0.001) i.e. 139.86±6.18 min in Group BD compared to 90.21±6.09 min in Group B.
6. Mean duration of motor blockade in Group BD was 227.1±1.76 min which was significantly prolonged (P<0.001) as compared to Group B in which it was 164.32±3.45 min.
7. Mean duration of sensory analgesia was significantly prolonged (P<0.001) i.e. 368.74±11.72 min in Group BD than in Group B i.e. 222.54±14.68 min.
8. There was minimal variation in mean pulse rate during intraoperative and postoperative period in both groups from baseline readings (P>0.05).
9. Fall in systolic and diastolic blood pressure was not more than 15% of baseline readings in both the groups with haemodynamic stability.
10. There were minimal intraoperative and postoperative complications in both the groups and difference was statistically not significant (P>0.05).

Conclusion

After this study we came to the following conclusion that 0.5% hyperbaric Bupivacaine (15mg) with Dexmedetomidine (5mcg) in subarachnoid block.

1. leads to significantly quicker onset of sensory block as compared to 0.5% hyperbaric Bupivacaine.
2. leads to significantly quicker onset of motor block as compared to 0.5% hyperbaric Bupivacaine.
3. leads to prolonged duration of sensory block as compared to block as compared to 0.5% hyperbaric Bupivacaine.
4. leads to prolonged duration of motor block as compared to block as compared to 0.5% hyperbaric Bupivacaine.
5. leads to prolonged duration of analgesia as compared to block as compared to 0.5% hyperbaric Bupivacaine.
6. leads to minimal intraoperative and postoperative complications as compared to block as compared to 0.5% hyperbaric Bupivacaine.
7. leads to favourable haemodynamic stability without any significant side effects making patients more comfortable in postoperative period.

Therefore addition of 5mcg Dexmedetomidine to 15 mg of 0.5% hyperbaric Bupivacaine in subarachnoid block can be considered safe and as effective as higher doses, minimizing the complication. It is useful in subarachnoid block for below umbilical surgeries where prompt onset and prolonged duration of postoperative analgesia is needed.

Result of our study matches with the result of studies of Nazima Memon et al.,[15] Sunil B.V. et al.,[22] R.Brinda et al.,[16] & Veena Chatrath et al.[13]

Dexmedetomidine produces early onset of prolonged duration of sensory and motor block as well as prolonged postoperative analgesia with minimal side effects. Hence it can be used as an adjuvant to Bupivacaine in subarachnoid block for below umbilical surgeries requiring long time with excellent quality of spinal anaesthesia in postoperative period.

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Effect of Ondansetron on QTc Interval during Sevoflurane Anaesthesia: A prospective Randomized Double-Blind Study

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Abstract

Aim and objectives: Serious drug interactions are amongst the common problems encountered by the anaesthesiologists in their practice that compells them to understand the effects of individual drugs and their combinations. One such drug interaction is the effect of sevoflurane and ondonsetron on QT interval when administered individually and also when combined together.The aim of the study is toevaluate the effects of Ondansetron and Sevoflurane and theirpossible synergistic effectson QT interval. The effects on QT interval were observed whenOndansetron was administered on patients undergoing Sevoflurane anesthesia using corrected QT interval (QTc) by Bazett's formula.

Methodology: Our study was a prospective randomized double blinded study which was done to evaluate QTc interval in 150 patients, aged between 20-60 years. QT interval was corrected by using Bazett's formulato the heart rateand are noted at various interval period such as base line(Preoperative period), 10min, 15min, and 20 mins after the administration of ondansetron using 5 lead ECG in Lead II.

Results: There was significant prolongation of QTc interval in Sevoflurane + ondansetron group (477.92 ± 11.44) when compared with placebo (448.93 ± 8.21) with p value of <0.00001.

Conclusion: Ondansetron when administered with sevoflurane significantly prolonged theQTc intervalthat was not significant enough to produce arrhythmias. Though this combination seems to be safe, one must consider caution when administering these drugs to patients with long QT syndrome or any arrhythmia along with continuous ECG monitoring.

Keywords: Ondansetron; Sevoflurane; QT interval.

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Introduction

Anaesthesiologists administer medications routinely in combinations. It is a challenge to the anaesthesiologist to reach an optimal conditions and maintenance of anaesthesia while maintaining minimal side-effects during perioperative period.

In daily practice Anaesthesiologists encounter

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a variety of medications some of which can possibly cause arrhythmias and it is a prime responsibility to understand every detail of these medications. Some of the common drugs delivered to the patients such as antihistamines, antiemetics, inhalational agents and some antibiotics etc are arrhythmogenic individually and synergistic when combined causing significant morbidity and mortality perioperatively. One of the arrhythmias that are caused by these drugs is prolongation of QT interval which is more frequent than usually thought.

In 1920 drug induced syncope was encountered for the first time with Quinidine. Quinidine at that time was used as an antiarrhythmic. After that time occassional fatal syncopes were seen after the usage of other medications. Quinidine characteristic polymorphic arrhythmia was first observed by Dessertenne in a patient with atrio-ventricular block.[1] He reported his observations, changes in QRS complex around the isoelectric line on the surface ECG and coined the term "torsades de pointes".Since then there is an extensive research on understanding the mechanism of drug induced QT prolongation. QT prolongation may lead to polymorphic ventricular tachycardia known as "torsades de pointes" a fatal arrhythmia that can cause ventricular fibrillation and cardiac arrest. QT interval acts as a surrogate marker of proarrhythmic potential of the drugs used.

QT interval represents the Starting point of QRS complex that represents ventricular depolarization to the end of 'T" wave indicating ventricular repolarisation. It approximately estimates the duration of average ventricular action potential, a major part of the cardiac cycle. A smooth ventricular repolarisation is essential for the conductance of next electrical impulse along the myocardial fibres. QT interval prolongation can become a fatal life threatening polymorphic ventricular tachycardia which may lead to sudden cardiac death when associated with major risk factors such as electrolyte imbalance, congenital QT syndrome or associated with any medication which has the potential to increase QT interval. It is considered an independent risk factor for sudden death due to cardiac arrest especially in older adults and in general population.[2,3] It is the point where scrutiny should be highest and focused for further study.

Furthermore, situation of acquired QT prolongation is complicated by polypharmacotherapy used regularly in daily practice. It is relatively risky in patients receiving two or more drugs which might affect the QT interval.

It is a common practice in anaesthesiology to use multiple drugs. Drugs used in perioperative setup such as halogenated inhalational agents, antiemetics, anticholinergics etc. The drug that is used commonly for induction and maintenance of anaesthesiasuch as sevoflurane has the tendency to prolong the QT interval.[4,5] Moreover, the most commonly administered antiemetic, ondansetron also have the potential to cause increase in QT duration individually. Especially when administered in patients who are prone to long QT syndrome, it can cause torsade de pointes. There have been many reports of SCD (sudden cardiac death) in the intraoprative and postoperative period because of various ventricular dysrrhythmias in patients to whom ondansetron has been administered.[6,7] In addition when these drugs are used in combination they have collegial effect in increasing the duration of QT.We used corrected QT interval (QTc) using Bazett's formula[8] to measure the accurate QT interval which helps to compare the interval at different heart rates[9] and increses the identification of potential arrhythmias.

This study was done to analyze drug-drug interaction, betweenondansetron and sevoflurane on QT interval during intra-operative period.

Methods

This is a prospective randomized double blind comparative study conducted between May 2014 to May 2015 after institution Ethical committee approval in Vinayaka Mission's Medical College and Hospital, Karaikal, India. Written informed consent from all patients enrolled in our study was taken.

Sample size was calculated based on previous studies and 95% confidence level with a margin of error of 5% and 7.5 confidence interval using sample size calculator. We found out that the sample size required for our study is 124 patients and then we added 26 patients in order to cover the fallouts. 150 ASA I and II patients of both sexes, 20-60 years old, with BMI 21-26 kg/m2, undergoing elective surgery with expected duration of >90mins, were randomly divided into 2 groups (group 1, group 2) of 75 patients each. Randomized into groups using computer generated randomization (using rand between function on Microsoft Excel 2010).

Patients with baseline ECG abnormalities, who are on drugs implicated in prolonging QT interval, renal /hepatic dysfunction, severe cardiac disease, electrolyte abnormalities and who require change

in concentration of sevoflurane were excluded from the study.

Measuring QTc interval is an important aspect in our study. The most universally adopted method is Bazett's formula (QTc = QT/√RR in seconds) that provides an adequate correction for heart rate ranging anywhere between 60 and 100 beats/min. Nonetheless, it underestimates and overestimates the QT interval at low and high heart rates, respectively.

Based on Bazett's corrected QTc value, in adult males a QT interval greater than 450 ms is considered prolonged and between 430 and 450 ms is considered borderline. For females, a QT interval greater than 470 ms is considered prolonged and between 450 and 470 ms is considered borderline [Goldenberg et al. 2006].

All participants received Diazepam 5mg as anxiolytic premedication. Two syringes labelled A & B were prepared for the study by an investigator not involved in the drug administration or monitoring of the patients. The contents of syringe A were administered in the preoperative holding area, syringe B intraoperatively during sevoflurane anesthesia.

In group 1, syringe A contained ondansetron and syringes B contained normal saline placebo.

In group 2, syringe B contained ondansetron and syringes A contained normal saline placebo.

Patients were assessed one day before surgery and their ECGs taken,their QT intervals were calculated and corrected using Bazett's formula as it is widely used and accepted within the range of physiological heart rate.

A baseline ECG is obtained and the contents of syringe A were administered in the preoperative holding area for all patients. ECG was recorded after 10mins, 15 mins, 20 mins monitoring the QTc interval with a 5 lead ECG. The patients were then taken to the Operation theatre and induced with Inj. fentanyl 2.0 mcg/kg, propofol 2 mg/kg, vecuronium 0.1mg/kg and intubated with appropriate size ET tube and airway secured. Anaesthesia was maintained throughout the surgery using nitrous oxide (66%), oxygen (33%) and with 1 MAC concentration of Sevoflurane. After one hour of anaesthesia, patients received drug from syringe B and thereafter ECGs were recorded at 10 mins, 15mins and 20 mins. After the surgery the patients were reversed from the effect of muscle relaxant with neostigmine of 0.04mg/kg and glycopyrolate 0.01mg/kg. Hemodynamic changes were noted from the start of administration of syringe A to 4 hours after surgery.

All the ECG recordings obtained were immediately noted by using inbuilt QTc interval monitor, and recorded QTc interval as per study. Bazett's formula was used to correct the QT interval and the measured QTc interval was taken routinely a day before surgery and during the assessment period.

The QTc changes with preoperative IV ondansetron were evaluated from ECG obtained from patients in group 1 after syringe A. ECG from Group 2 after syringe A provides data on saline placebo control for preoperative QTc.

The QTc changes with administration of ondansetron during sevoflurane anesthesia were obtained from group 2 patient's ECG, after administration of syringe B. ECG from Group 1 after syringe B provides data on QTc changes during sevoflurane anesthesia in patients on preoperative ondansetron.The primary outcome wassynergistic interactions between ondansetron and sevoflurane on QTc interval.

Statistical Analysis

The statistical analysis was performed using SPSS version17. As per Shapiro-Wilk test normality of the groups confirmed and both groups were comparable(Table1) .The continuous data with normal distribution was described as mean and 95% confidence interval for mean (95%C.I). The continuous variables were compared between the groups using Student t-test. Categorical data was compared using Chi-square test. The changes in the QTc from baseline were compared with ANOVA for repeated variables. A two-sided p value of < 0.05 was considered significant for all tests.

After administration of syringe A and syringe B in group 1 there was a significant increase in QTc comparing with base line mean 434.58(±8.45) ms at 10 min after ondansetron administration of intravenously mean 448.93(±8.21) and maximum difference is observed at 10 min after giving of ondansetran with the mean of 14.3466(±2.63) when compared to baseline (p=0.).

After administration of contents of syringe A and B in group 2 the change in QTc interval after 10min of ondansetron intra-operatively showed significant prolongation of mean 477.92(±11.44)ms compared with baseline mean 438.41(±8.99)ms with significant p=0.0018. The maximum raise of QTc (mean ± SD 39.46±5.96 ms) interval is seen at 10min after intravenous ondansetron during sevoflurane anesthesia in the intra-operative period.

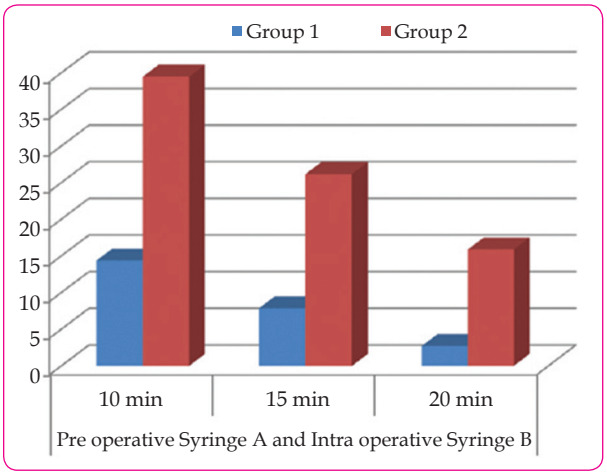
After administration of content of syringe B, patients receiving ondansetron intraoperatively during sevoflurane anesthesia (group 2) had a significant prolongation of QTc when compared to patients who are receiving ondansetron preoperatively (group 1). The mean QTc was more than 450 m sec immediately 10 mins after the drug administration and continued after 15 and 20 mins. The maximum (mean ± SD) difference between these groups are 25±12 ms with P value 0.00089.

Table 1: As per Shapiro-Wilk test normality is confirmed in the groups and both groups are comparable.

Parameter	Group I	Group II
Mean:	434.580	438.413
Standard Deviation:	8.45	8.996
Variance:	45.134	80.921
Kurtosis:	0.769	-0.354
Calculated Shapiro-Wilk statistic W:	0.910462	0.017746
Calculated Shapiro-Wilk p-value:	0.000059	0.01774
Critical value of W (5% significance level):	0.947	0.947
P value	0.00342	0.947

Table 2: Group 1 syringe A (ondansetron only) & Group 2 syringe B (ondansetron + sevoflurane)

Time	Group 1 A (ondansetron only)	Group 2 B (ondansetron + sevoflurane)	P value
Baseline	434.58±8.45	438.41±8.99	0.115(not significant)
10 min	448.93 ± 8.21	477.92 ± 11.44	0.0031 (significant)
15 min	442.44 ± 8.25	464.45 ± 10.32	0.0047 (significant)
20 min	436.97 ± 8.56	454.28 ± 9.30	0.007 (significant)



Graph 1: Observed QTc Prolongation after syringe B (ondansetron with sevoflurane) in Group 2 (intraoperative) compared with Syringe A (ondansetron only) in Group 1 (preoperative).

Discussion

The Surgical patients under general anesthesia with inhalational agents are simultaneously exposed to several intravenously administered drugs, several of which are known to cause QT prolongation.[10] Typical drug classes include antibiotics, antiemetic medications (ondansetron or droperidol) and antihistamines. In addition, conditions conducive for QT prolongation such as stress, hypothermia, and electrolyte disturbances, particularly hypokalemia and hypomagnesemia, are common during major surgery.

The introduction of the 5HT3 receptor antagonist, ondansetron, in the early 1990s was a significant breakthrough in treating nausea and vomiting. Apart from minor side effects like constipation, ondansetron is also known to cause major changes in electrical rhythm of heart (QT interval prolongation) especially when administered in patients who are prone to long QT syndrome, it can cause torsade de pointes in these patients.[11] There have been many reports of SCD (sudden cardiac death) in the intraoprative and postoperative period because of various ventricular dysrrhythmias in patients to whom ondansetron has been administered. FDA black label warning for its use with caution in patients with cardiovascular abnormalities has also been issued.

Sevoflurane, Halogenated volatile anaesthetic agent with low pungency, a non-irritant odour and a low blood: gas partition coefficient replaced many of the standerd inhalational agents for induction and maintainance of anesthesia. It can be rapidly and conveniently administered without discomfort, and its low solubility facilitates precise control over the depth of anaesthesia and a rapid and smooth induction of, and emergence from, general anaesthesia. Sevoflurane though considered as one of the best induction agents is also implicated in increasing the QT intervaland are sometime arrhythmogenic in susceptible individuals.

A number of studies were conducted on both sevoflurane and ondansetron for their effects on QT interval.[12] Most of the studies focused on the effect on QT interval prolongation of these drugs when administered independently but their possibility of interaction between the two drugs is not evaluated extensively.

It is important that the anaesthesiologists be aware of the potential arrythmogenicity that results from these drug-drug interactions perioperatively[13,14] and be prepared to manage the complications.[15] It

is seen from this study that two drugs which are in routine usage produce an additive or synergistic effect and produce a complication when least anticipated. Based on the findings of this study, it may be recommended against administration of ondansetron simultaneously with other potential arrythmogenic drugs like isoflurane, sevoflurane and halothane. The results of our study showed that significant prolongation of QTc interval that occurred following administration of ondansetron during sevoflurane anaesthesia even in the absence of potential arrhythmogenic conditions like electrolyte disturbances, metabolic abnormalities and hypothermia. These conditions occur more frequently towards the conclusion of the procedures which coincides with timing of administration of ondansetron. The timing of the ondansteron administration should be re-evaluated in the light of this potential complication.

It is imperative from our study that intravenous ondansetron in clinically administered doses for postoperative nausea and vomiting produces significant prolongation of QT interval. Sevoflurane anesthesia also results in small but statistically not significant prolongation of QT interval. The administration of ondansetron during sevoflurane anaesthesia results in greater prolongation of QTc when compared to either drug administered alone suggesting drug-drug interaction between sevoflurane and ondansetron.

Conclusion

Sevoflurane and ondansetron produce statistically significant prolongation of QTc. Significant number of patients receiving ondansetron along with sevoflurane had QTc exceeding the safe limit although none of the patients had life-threatening arrhythmias. The administration of ondansetron during sevoflurane anesthesia results in greater prolongation of QTc when compared to either drug administered alone suggesting drug-drug interaction between sevoflurane and ondansetron. Caution should be employed when ondansetron is administered in the presence of inhalational agents like sevoflurane. Further studies have to be done to evaluate the effects of these drugs as well as when combined with other commonly used drugs that have the potential to cause increase in QT interval.

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A comparative Study of Epidural Ropivacaine 0.75% Alone and Ropivacaine with Dexmedetomidine for Lower Limb Surgeries

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Abstract

Background: Ropivacaine in epidural anaesthesia provides good analgesia, lesser motor blockade and cardiac stability. Addition of adjuvants like dexmedetomidine provides longer duration of analgesia, prolonged motor blockade with adequate sedation. Our study compares Ropivacaine alone and in combination with dexmedetomidine on block characteristics, postoperative analgesia and sedation.

Methods: Following institutional ethical committee clearance and patients informed written consent Sixty patients (ASA I, II) aged 18 - 60 years of either sex posted for elective lower abdominal and lower limb surgeries were randomized into two groups, Group R and Group RD. The patients in group R received 19ml of 0.75% Ropivacaine with 1ml of normal saline and the patients in group RD received 19ml of 0.75% Ropivacaine with dexmedetomidine (1µg/kg) respectively. Both groups were compared with respect to onset and duration of sensory and motor blockade, intensity of motor blockade using modified bromage scale, maximum level of sensory blockade, sedation score, hemodynamic variations and adverse effects.

Results: The mean onset of sensory and motor block in group R was 11.36±3.03& 16.63±2.70 minutes, in group RD was 6.80±1.30 & 12.10±1.63 minutes respectively. Duration of sensory and motor block in Group R was 199.60±23.4 & 150±17.64 minutes and in group RD was 296.30±21.12 & 235.00±17.64 minutes respectively. The patients in Group RD had rapid onset of action, significant prolongation of motor and sensory block, intense motor block, better sedation score and postoperative analgesia ($p<0.05$).No significant hemodynamic changes in either group.

Conclusion: There is a clear synergism between dexmedetomidine and ropivacaine compared with ropivacaine in epidural anaesthesia without increased morbidity.

Keywords: Epidural; Dexmedetomidine; Motor block; Ropivacaine; Sensory block; Sedation.

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Samudyatha T J, Bhargavi Sanket, Triveni M R et al., / A comparative Study of Epidural Ropivacaine 0.75% Alone and Ropivacaine with Dexmedetomidine for Lower Limb Surgeries. Indian J Anesth Analg. 2021;8(1):117-122.

Introduction

Epidural blockade is a popularized technique to provide anaesthesia and adequate analgesia both during the surgical procedure as well as the post-operative period.[1] Epidural anaesthesia can be used as sole anaesthetic for procedures involving the lower limbs, pelvis, perineum and lower

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abdomen.[2] It has the ability to maintain continuous anaesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration. Epidural anaesthesia will also reduce need for intravenous analgesic agents in the post-operative period. The main advantage of epidural anaesthesia is to provide post-operative analgesia.[1-3]

Ropivacaine, long acting amide local anaesthetic derived from Bupivacaine is claimed to have lesser cardiovascular side effects than bupivacaine.[4,5] Ropivacaine has to be given in larger doses to achieve the analgesic and anaesthetic effects.[6] The addition of adjuvants like α-2 agonists, clonidine and dexmedetomidine can decrease the dose requirement and permit use of more diluted solutions for better analgesia and prevent side effects associated with larger doses of ropivacaine.[7] Dexmedetomidine is highly selective α 2 adrenergic agonist, The stable hemodynamic and the decreased oxygen demand due to enhanced sympathoadrenal stability make it a very useful pharmacological agent.[8-11] In the present study we have compared efficacy of ropivacaine 0.75% alone and ropivacaine with dexmedetomidine (1µg/kg) for lower abdominal and lower limb surgeries.[12]

Objectives of the study

To study the synergistic effect of adding dexmedetomidine to ropivacaine in epidural anesthesia for lower abdominal and lower limb surgeries regarding:[13]

1. Onset & duration of sensory blockade time.
2. Onset & duration of motor blockade.
3. Intensity of motor blockade.
4. Maximum level of sensory blockade.
5. Sedation.

Materials and Methods

After approval from the Institute ethical committee, as well as informed consent from all patients, a prospective double blind randomized clinical study was carried out on 60 adult patients scheduled for various lower abdominal & lower limb surgical procedures belonging to ASA class I and II. Patients were randomly divided into two groups of 30 each using computer generated random numbers, Group "R" (n =30) - 19 ml 0.75% Ropivacaine plus 1 ml normal saline and Group "RD" (n=30) – 19 ml 0.75% Ropivacaine plus dexmedetomidine (1µg/kg).

On the day of surgery patients basal pulse rate and blood pressure (mean), respiratory rate, SpO2 will be recorded, 18 G intravenous line secured. All patients will be preloaded with 20ml/kg of Ringer lactate 30 minutes prior to epidural procedure. Under all aseptic the subject will be given epidural block in sitting position in L2-3 or L3-4 space with 16 gauge Touhy needle and epidural space will be localized and confirmed by loss of resistance technique.[2] Epidural catheter will be secured 3-5 cm into the epidural space and confirmation for correct placement of the catheter done by injecting 3ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200000. After 4-6 minutes of test dose, patients in group "R" will be administered 19ml of 0.75% Ropivacaine with 1ml of normal saline in incremental doses while the patients in group "RD" will receive 19ml of 0.75% Ropivacaine with 1µg/kg dexmedetomidine in incremental doses.[13,14]

Assessment of sensory and motor blockade were done at the end of each minute with the patient in supine position after completion of injection of 19 ml of the study drug, which is taken as the starting time. The onset time for sensory and motor block, the maximum level of sensory block, intensity of motor block will be recorded. The bilateral pin prick method will be used to evaluate and check the sensory level while the modified Bromage scale (Table 1)[2] will be used to measure motor blockade. Analgesia was recorded by using VAS score at 5 min before epidural, at the start of surgery, and then, every 15-min interval till the surgery was over. Sedation score recorded with Ramsay Sedation Score (Table II).

Measurements of blood pressure, heart rate, and oxygen saturation will be recorded every 5 minutes till the end of 1 hour and then every 15 minutes till the end of surgery. Intra-operatively and post-operatively complications like fall in blood pressure, variation in heart rate, dryness in mouth, nausea, vomiting, urinary re-tension , excessive sedation were noted, treated and tabulated.

Onset of sensory blockade

Is taken as the time from the completion of the injection of the study drug till loss of sensation at T 10 level, assessed by loss of sensation to pin prick in the midline using a 22 gauge blunt hypodermic needle.

Onset of motor blockade

Is taken from completion of the injection of study drug till the patient develops modified Bromage scale grade 3 motor blockade.

Duration of motor block

Is taken from the time of injection till the patient attains complete motor recovery (bromage 0).

Duration of sensory block

Is taken from the time of injection till the patient complains of pain at the S1 dermatome.

Statistical Analysis

The results of the study were statistically analyzed between the two groups. A sample size of 25 patients per group was determined through power analysis (α 0.05; β0.80). Considering the drop outs, 30 patients were selected for each group in our study. Statistical analysis was done using SPSS version 22; descriptive statistics was done by calculating mean. Results are expressed as the means and standard deviations. The interferential statistics (test of significance) was done using unpaired t-test and chi square test. 'P' value of >0.05 was considered as statistically insignificant & <0.05 was considered as statistically significant. (Table 5)

Results

Table I: Modified Bromage scale will be used to measure motor blockade.

Score	Patient Response
0	Full movement of legs and feet, with ability to raise extended leg.
1	Inability to raise extended leg, knee flexion is decreased, but full flexion of feet and ankles present
2	Inability to raise leg or flex knees, flexion of ankle and feet present.
3	Inability to raise leg, flex knee or ankle or move toes.

Table II: Ramsay Sedation Score (RSS).

Sedation Level	Description
1	Patient is anxious, agitated or restless, or both
2	Patient is cooperative, oriented, and tranquil
3	Patient responds only to commands
4	Patient responds to light glabellar tap or loud auditory stimulus
5	Patient has a sluggish response to light glabellar tap or loud auditory stimulus
6	No response

Table III: Demographic data.

Variables	Group R (Mean)	Group RD (Mean)	P Value
Age (years)	40.73	32.26	0.49
Sex	21/9	22/8	1.00
Height (cm)	166.9	168.57	0.19
Weight (kg)	63.26	61.06	0.22

Demographic data of both the study groups were comparable and statistically not significant (Table 3)

Table IV: Mean time for onset of sensory and motor block (In minutes).

Sl. No.	Group	Mean time for Sensory Onset	SD	p-Value	Mean time for Motor Onset	SD	p-Value
1	Group R	11.36	3.03	0.001	16.63	2.70	0.001
2	Group RD	6.80	1.30		12.10	1.63	

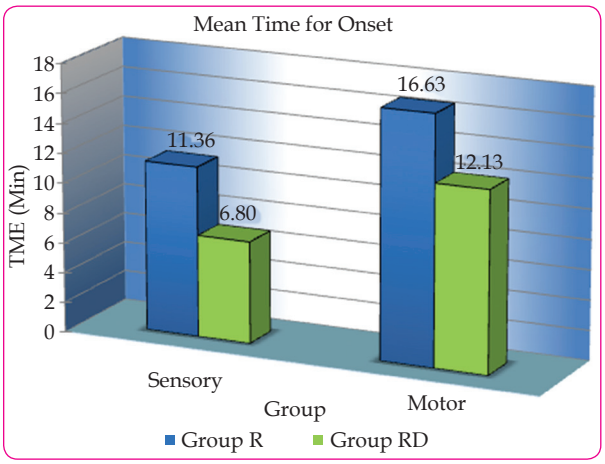

Fig. 1: Graph showing mean time for Onset of Sensory and Motor block (minute).

The mean time of onset of sensory in group R is 11.36 minutes, Group RD - 6.80 minutes. There is highly statistical significant difference between the groups (p=<0.001) (Table 4)

The mean onset time for motor in group R is 16.63 minutes and in Group RD it is 12.13 minutes. There is highly statistical significant difference between the groups (p 0.001). (Fig. 1)

Table V: Maximum level of Sensory Blockade achieved.

Sl. No.	Max. Sensory level	Group R (No. of Patients)	Group RD (No. of Patients)	p-Value
1	T5	0	3	0.52
2	T6	15	17	
3	T8	13	10	
4	T10	02	0	

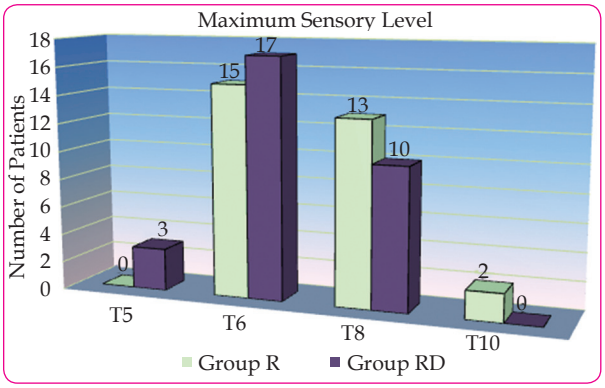

Fig. 2: Maximum level of sensory level achieved.

Maximum level of sensory blockade attained by the two groups, Group RD had the highest level of T5, and highest level in R group was T6. There is no statistical difference between the two groups (p=0.52) (Fig. 2)

Table VI: Grade of Motor Blockade.

Sl. No.	Bromage scale	Group R (No. of Patients)	Group RD (No. of Patients)	p-Value
1	Modified Bromage 1 (M1)	2	0	0.001
2	Modified Bromage 2 (M2)	15	13	1.00
3	Modified Bromage 3 (M3)	13	17	< 0.001

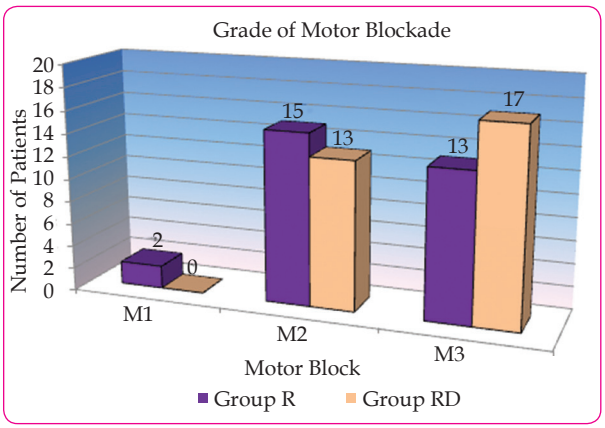

Fig. 3: Graph showing Grade of Motor blockade.

Number of patients with bromage 1 was 2 in group R, and 0 in group RD, where patients with bromage 3 were 17 in group RD, 13 in group R, more intense motor blockade of bromage 3 was found in patients in group RD. more intense motor blockade of bromage 3 was found in patients in group RD compared to patients in group R, the p value being <0.001 is highly significant.(Fig. 3) (Table 6)

Table VII: Sedation Score.

Sl. No.	Sedation Score	Group R (No. of Patients)	Group RD (No. of Patients)	p-Value
1	S1	11	0	< 0.001
2	S2	19	11	
3	S3	0	17	
4	S4	0	2	

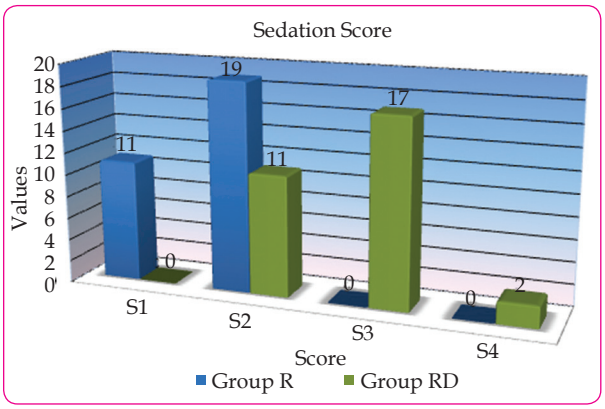

Fig. 4: Graph showing Sedation Score.

Group R the height score of 2, and the highest score in group RD was 4. Dexmedetomidine had highest scores compared to ropivacaine alone. There is highly statistically significant difference between the groups P (< 0.001). (Table 8)

Table VIII: Duration of Sensory and Motor Blocks (In Minutes).

Sl. No.	Group	Duration for Sensory Block	SD	P -Value	Duration for Motor Block	SD	P – Value
1	Group R	199.60	23.40	< 0.001	150.00	15.75	< 0.001
2	Group RD	296.30	21.12		235.00	17.64	

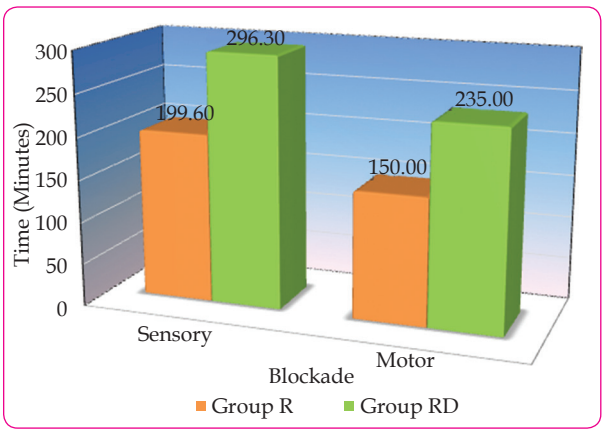

Fig. 5: Duration of Sensory and Motor Blocks (In Minutes).

The mean duration of sensory block in group R-199.60, in Group RD 296.The mean duration of motor blockade in group R 150 minutes, in group RD 235 minutes.There is statistically high significant difference between the groups (p<0.001). (Fig. 5)

Discussion

In our study we used epidural ropivacaine 0.75% alone and ropivacaine plus dexmedetomidine for lower abdominal and lower limb surgeries with major emphasis on onset of blockade, time to maximum sensory blockade, time to complete motor blockade, grade of motor blockade, sedation score, total duration of analgesia, time to complete motor recovery. Dexmedetomidine significantly extends the duration of sensory and motor block with better quality of postoperative analgesia as compared to Ropivacaine given alone.

Dexmedetomidine a novel α2 agonists produce pain relief through an opioid independent mechanism and proves to be a better alternatives to opioid for combination with local anaesthetic for analgesia during surgery.[8,9] Dexmedetomidine appears to exert analgesic effects at the spinal cord level and at supraspinal sites. The selectivity of Dexmedetomidine to alpha-2 receptors compared to alpha-1 receptors is 1620:1, whereas with clonidine it is 200:1. Dexmedetomidine act by binding to the presynaptic C-fibers and post synaptic dorsal horn neurons. They produce analgesia by decreasing the release of C-fiber transmitters and by hyperpolarisation of post synaptic dorsal horn neurons. The combined and synergestic action of local anaesthetics and α2 adrenergic agonists accounts for their prolonged analgesic properties.[10,11] The prolonged motor block may be the result of binding α2 adrenergic agonists to the motor neurons in the dorsal horn. Dexmedetomidine exerts synergistic actions with local anaesthetic agents.

Onset of analgesia (T10)

In our study the mean onset of analgesia in Group R was 11.36 ± 3.03, and in Group RD was 16.63±6.80. This shows that onset of anaesthesia was faster in group RD when compared to Group R (p<0.001); which was highly statistically significant. In a study Bajwa SJ and his colleagues, 2011,[14] a comparative evaluation of dexmedetomidine and clonidine in epidural anaesthesia, they found that onset of analgesia was shorter in RD group along with prolonged duration of analgesia when compared to RC group with mean onset of 8.52±2.36 and in RC group was 9.72±3.44 min.

Maximum sensory level

In our study the maximum level of sensory block in group RD was T5, and group R was T6. The range of block was very wide in both groups (T12-T5). The study conducted by Bajwa SI, Bajwa SK, Kaur J et al.,[15] showed maximum level of sensory block at T5-T6 level in group RD compared to T6-T7 in group RC which compares with our study.

Duration of sensory block

In our study duration of sensory block is longer with group RD compared to group R which is 296.30± 21.12 mins in group RD compared to 199.60 ± 23.40 mins in Group R this is statistically highly significant (p <0.001) Our study concurred with the study conducted by Bajwa SJ, Arora V, Kaur J et al.,[16] who observed the mean duration of analgesia to be 366.62±24.42 mins in group RD compared to 242.16 ±23.86 mins with in group RF which is highly significant

Motor block

The mean onset time for motor in group R - 16.63 minutes, in Group RD - 12.13 minutes. There is highly statistical significant difference between the groups (p 0.001). In our study motor blockade is assessed using modified bromage score and the onset was taken as soon as the patient developed Grade I motor blockade. Our study concurred with the study conducted by Bajwa SJ, Arora V, Kaur J et al.,[16] who observed the mean duration of analgesia to be 366.62±24.42 mins in group RD compared to 242.16 ±23.86 mins with in group RF which is highly significant.

Duration of motor block

In our study mean time to complete motor recovery (in min) was 150.00±15.75 in Group R, and 235.00±17.64 in Group RD. This shows that time to complete motor recovery was significantly longer in Group RD when compared to Group R (P<0.001). In a similar study with Bajwa SJ and his colleagues 2011,[15] mean time to two segment regression with RD group was 136.46 8.12 and 128.08 7.54 with RC group, time for first rescue analgesia was 342.88 29.16 with RD group and 310.76 23.76 with RC group. This shows that duration of sensory blockade was longer with RD group than with RC group. Hence it is highlighted that addition of additives like dexmedetomidine intensifies the motor blockade.

Sedation

Group R the height score of 2, and the highest score in group RD was 4. Dexmedetomidine had highest

scores compared to ropivacaine alone.[17,18] There is highly statistically significant difference between the groups i.e. P (< 0.001). Sedation represents an α2 adrenergic effect, because sedation from epidural clonidine can be reversed by the specific antagonist yohimbine in postoperative patients. The sedative-hypnotic effect of α2-adrenergic agonists is caused by actions on the locus ceruleus. Our results are in agreement with studies by Filos and his colleagues, in which dose-dependent sedation was observed.[19-20]

There was no significant difference in the HR, SBP, DBP, MAP, SPO2 during intraioperative & postoperative period up to 24hrs measured at regular intervals. No patients required any active intervention or had any side effects like nausea/ vomiting.

Conclusion

Dexmedetomedine group had rapid onset of action (p<0.001), prolonged duration of sensory and motor block (p<0.001), better sedation score (p<0.001) and more intense motor block .There was no difference in maximal dermatomal level of analgesia, was associated with side effects like bradycardia and hypotension which were not imposing a major problem in hemodynamic profile.

It can be concluded that Dexmedetomedine given epidurally with Ropivacaine produces synergistic effect of profound and prolonged duration of sensory blockade. Ropivacaine and dexmedetomidine can be a safe and effective agent for epidural blockade in lower abdominal and lower limb surgeries.

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Original Article

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Comparing Dexamethasone and Dexmedetomidine as Adjuvants for Tap Block After Abdominal Hysterectomy Under Spinal Anaesthesia

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Abstract

Background and Aim: Ultrasound guided transversus abdominis plane (TAP) block is a safe, effective analgesic technique for lower abdominal surgeries .This study is designed to compare dexamethasone and dexmedetomidine as adjuvants for TAP block in patients undergoing abdominal hysterectomy under spinal anaesthesia.

Materials and methods: After ethics committee approval and informed written consent ,30 Patients were allocated into 2 groups each by randomized double-blind design using a computer generated randomization posted for abdominal hysterectomy under spinal anaesthesia . Group D1 received Inj Bupivacaine 0.25% 20ml + Inj Dexamethasone 4mg + 1ml normal saline in TAP Block on each side. Group D2 received Inj Bupivacaine 0.25% 20ml + Dexmedetomidine 25mcg+ 1ml normal saline in TAP Block on each side at the end of surgery under ultrasound guidance. Assessment parameters included hemodynamic, post operative VAS score, duration of post operative analgesia, total dose of post operative rescue analgesia and side effects.

Results: There was no significant difference in Heart rate and Mean arterial blood pressure in both the groups. In the first 8 hr post operative VAS score was lower in GROUP D1compared to GROUPD2 ($p < 0.05$).Duration of post operative analgesia was longer in GROUP D1 compared to GROUP D2 ($p<0.05$).Total dose of post operative rescue analgesia consumption in 24hrs was lower in GROUP DI than in GROUP D2 ($p<0.05$) . No significant side effects were noted.

Conclusion: Dexamethasone as an adjuvant to bupivacaine in TAP block has prolonged postoperative analgesia and has reduced requirement of rescue analgesia than dexmedetomidine following abdominal hysterectomy under spinal anesthesia.

Keywords: Dexamethasone; Dexmedetomidine; Post operative analgesia; Transversus abdominis plane block.

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Introduction

Hysterectomy is a frequent surgery performed in women, due to the substantial incision and soft-tissue undermining associated with this operation, it could result in moderate to severe postoperative pain which affects multiple systems and induces physiological, immunological, and psychological

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changes.[1] Successful management of postoperative pain can have an impact on a patient's quality of life. Neuraxial block has many advantages over general anaesthesia like easier to perform, rapid onset of action and good muscle relaxation. One of the main disadvantage is its limited duration of action and hence lack of postoperative analgesia.[2]

Traditionally NSAIDS (non steroidal anti inflammatory drugs) or opioids used for post operative analgesia, however the use of systemic analgesics is confined for short period of time and associated with frequent side effects, including gastrointestinal problems, kidney dysfunction, nausea and vomiting, and reduced bowel mobility.[3]

There are different modalities to reduce the post-operative pain of lower abdominal surgery, including systemic analgesia with non-steroid anti-inflammatory drugs (NSAIDs), opioids, intravenous patient controlled analgesia and regional analgesic techniques like port-site local anesthetic infiltration, patient controlled epidural analgesia, Transversus Abdominis plane block.

Transversus Abdominis Plane[4] containing the thoraco-lumbar nerves originating from T6 to L1 lies between the internal oblique and transversus abdominis. Dexamethasone, tramadol, buprenorphine, clonidine, dexmedetomidine have been used as adjuvants[5] for transverses abdominis plane block for postoperative analgesia for lower abdominal surgeries.

Dexmedetomidine[6], alpha-2(α_2) adrenergic receptor (AR) agonist has been the focus of interest due to sedative, analgesic, and haemodymic stabilizing properties and prolonged postoperative analgesia with minimal side effects. Site of action of dexmedetomidine are prejunctional and postjunctional α_2 receptors present in the dorsal horn of the spinal cord. Activation of presynaptic receptors reduces neurotransmitter release, whereas postjunctional receptor activation results in hyperpolarization and reduction of pulse transmission. It has a relatively high ratio of α_2/α_1 activity (1620;1) and lack respiratory depression, making it a safe adjuvant.

Dexamethasone[7] is also used as an adjuvant.. Steroid induces vasoconstriction,which decreases the absorption of local anaesthetic solution. Alternatively, dexamethasone blocks nociceptive impulse transmission along unmyelinated C-fibers through its anti-inflammatory and/or immunosuppressive effect.[8] After intracellular uptake, glucocorticoids activate cytoplasmatic receptors that bind to their response elements in DNA. Hence decreasing the production of inflammatory proteins (eg, cyclooxygenase-2, inducible nitric oxide synthase, cytoplasmatic phospholipase A2, interleukins, and inflammatory chemokines) and increasing the production of anti-inflammatory proteins (lipocortin-1 receptor antagonist).

This study is designed to compare dexmedetomidine and dexamethasone as an adjuvant for Transversus abdominis plane block after abdominal hysterectomy under spinal anaesthesia.

Materials and Methods

After approval from the institutional ethical committee and a written informed consent, a prospective randomised double blinded study was conducted in 60 patients , belonging to ASA Classes I or II ,aged between 18- 60years ,weighing 50-80kg posted for elective abdominal hysterectomy under spinal anaesthesia.

Exclusion criteria included patient's refusal, allergy to study drug, contraindication to spinal anesthesia, those who required general anesthesia for surgery, morbid obesity, or chronic analgesic user,patients with cardiac dysarrhythmia, patients using adrenergic receptor blockers, calcium channel blockers and with height less than 140cm.

Patients were allocated into 2 groups in a controlled, randomized double-blind design using a computer generated randomization list to receive either 20ml of 0.25% bupivacaine with dexamethasone 4mg (1ml) making total volume of 22ml using normal saline (GROUP D1) or 20ml of 0.25% bupivacaine with dexmedetomidine 25mcg (0.25ml) making total volume of 22ml using normal saline (GROUP D2).

All patients were evaluated preoperatively on the previous day of surgery. Procedure and the use of visual analogue scale (VAS) for pain was explained to the patient. Tablet alprazolam 0.5mg was given night before surgery. On the day of surgery, an 18G intravenous line was secured. On arrival in the operating room, patient was preloaded with lactated Ringer's solution @15ml/kg. Monitors like automated non invasive blood pressure (NIBP), pulse oxymetry, an eletrocardiogram was connected to the patient in operation theatre and base line parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) were noted. These patients did not receive any intravenous analgesics

or sedatives during the surgery. Under all aseptic precautions, spinal anesthesia was administered with 0.5% bupivacaine 2.8ml intrathecally.

After spinal anaesthesia patient was positioned in supine position and supplemented with oxygen (4L/min) through face mask and surgery was allowed to proceed after confirming the attainment of sensory blockade of T6. Intra operative monitoring of HR, SBP, DBP, MAP was done as usual. Intraoperative hypotension i.e systolic blood pressure (SBP) <90mm of Hg or <20% of the baseline whichever appeared first was treated with ephedrine (3mg aliquots) as and when necessary. Bradycardia was treated with atropine 0.02mg/kg if heart rate (HR) decreased to <60/min.

At the end of surgery, TAP block was administered under ultrasound guidance by in plane technique using Sonosite Nano Maxx USG Machine in both the groups with doses as decribed above. Success of the block was confirmed by the distribution of local anesthetic as a hypoechoic enlargement on ultrasonography.

Pain was assessed postoperatively at 0hr (at the time when patient is shifted to Post anaesthetia care unit-PACU) 2, 4 , 8, 12 and 24 hours using a VAS score. At any time during post operative period if the VAS score is equal to or more than 4, rescue analgesia of tramadol 50mg was administered intravenouslyand time of administration noted. The total consumption of rescue analgesia in first 24hr was recorded.Any side effects (nausea or vomiting) were recorded.

Statistical analysis

Statistical analysis was done using the statistical software system, SPSS

version 18.0 (SPSS Inc., Chicago, IL, USA). Student's t test was used for numerical data . Categorical data were analyzed by Chi square test or fisher's exact test as appropriate. Results were expressed as mean ± standard deviation, number or percentage (%). Results were considered statistically significant if $P < 0.05$.

Pain was assessed post operatively at 0hr (at the time when patient is shifted to Post anaesthetia care unit-PACU) 2, 4, 8, 12 and 24 hours using a VAS score. At any time during post operative period if the VAS score is equal to or more than 4, rescue analgesia of tramadol 50mg was administered intravenouslyand time of administration noted. The total consumption of rescue analgesia in first 24hr was recorded.Any side effects (nausea or vomiting) were recorded(Fig. 3)

Results

The mean age in GROUP D1 was 45.9+4.6 and in GROUP D2 was 46.2+4.3. The mean body weight in GROUP D1 was 58.5+6.2 and in GROUP D2 was 59.5+5.3. The demographic data of the patients in both groups were comparable. (Fig. 1,2)

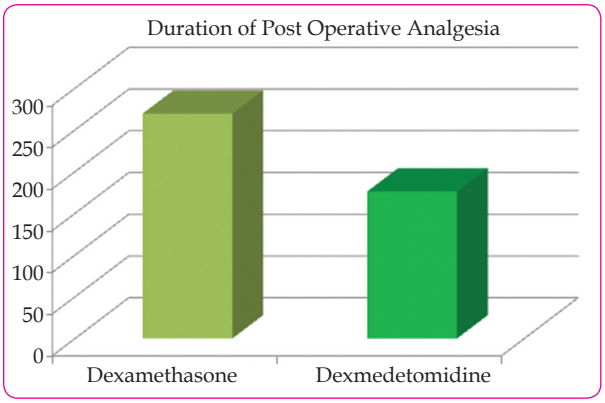

Fig.1: Duration of Post Operative Analgesia.

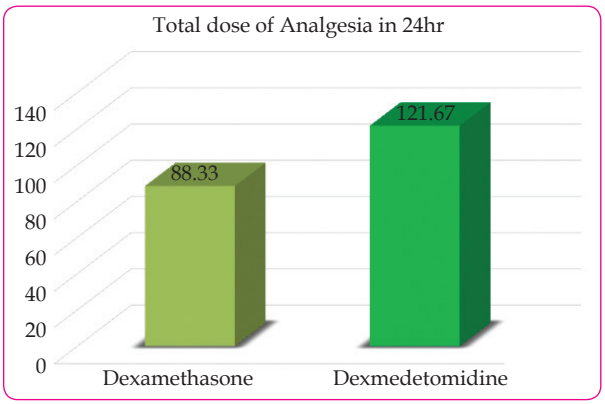

Fig.2: Total dose of Analgesia in 24hr.

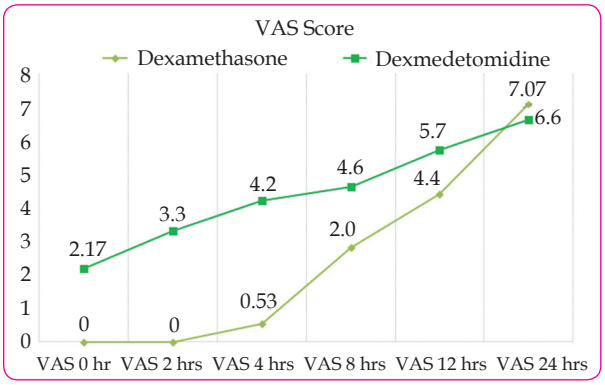

Fig.3: VAS Score.

The duration of post operative analgesia was longer in GROUP D1 than in GROUP D2 (269+79 vs 176+92 , $p < 0.05$). The total dose of consumption of rescue analgesia was lower in GROUP D2 THAN IN GROUP D1 (86.33 vs 121.67, $p < 0.05$) .GROUP

D1 experienced lower post operative pain scores than GROUP D2 especially in first 8hrs ($p < 0.05$). Hemodynamic parameters were comparable between the two groups. No significant side effects were noted within the patients.

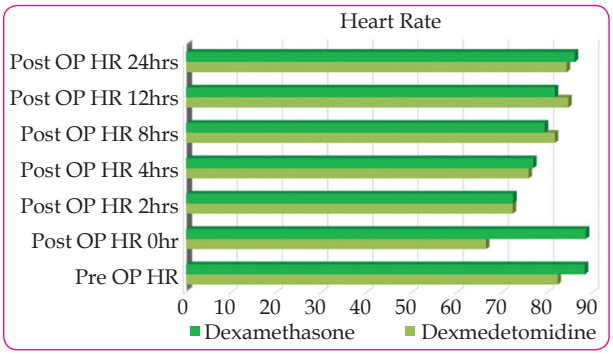

Fig. 4: Heart Rate.

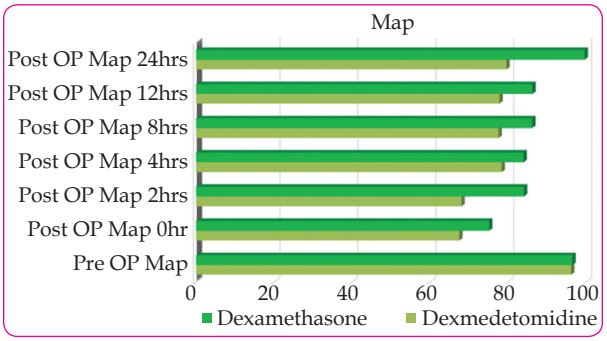

Fig. 5: Map.

Discussion

Abdominal hysterectomy is usually associated with considerable pain during the postoperative period, which may affect multiple systems and induce physiological, immunological, and psychological changes.

Adequate postoperative analgesia causes reduction in the postoperative stress response and postoperative morbidity and in certain types of surgeries postoperative analgesia does yield an improved surgical outcome.[9-11] Other benefits of effective regional analgesic techniques include reduced pain intensity, decrease in the incidence of side effects from analgesics and improved patient comfort.[12]

TAP block as a regional analgesic technique for postoperative analgesia is gaining popularity; it may play a role in major abdominal surgeries. Adjuvants are used to intensify the quality and increase the duration of local anesthetics in different regional block techniques.

A randomised study conducted by G. Niraj, et al., 2009[13] on 52 adult patients undergoing open appendicectomy under general anaesthesia ,a right-sided ultrasound guided TAP block with 20ml of bupivacaine 0.5% was given for post operative analgesia and results were significantly reduced post operative morphine consumption in the first 24 hour.

Deshpande JP et al.,[14] studied the analgesic efficacy of dexamethasone (4mg) added to ropivacaine in transversus abdominis plane block for transabdominal hysterectomy under subarachnoid block. Addition of dexamethasone to ropivacaine TAP block prolonged the postoperative analgesia and reduced post operative analgesic requirement following abdominal hysterectomy under spinal anesthesia. Corticosteroid induces analgesic action by their anti inflammatory or immunosuppressive effects.[15,16] Analgesic action of steroid is by modulation of nuclear transcription.[16] In addition, steroids potentiate the action of local anesthetic through modulation of the function of the K+ channels in excitable cells and also by vasoconstriction which decreases the absorption of the drug.[17] Corticosteroids are also found to have analgesic effect due to their systemic effects.[18] A recent in vivo animal safety models show no adverse event levels and potential neuroprotection and antihyperalgesic effects with clinically relevant dosing of perineural dexamethasone to bupivacaine.[19,20] Many studies have recommended the use of dexamethasone to potentiate analgesia and anesthesia of local anesthetic agents administered through various routes.

Dexmedetomidine, a strong and highly selective α2-adrenoceptor agonist, when added to local anesthetics, it could enhance the analgesic efficacy of local anesthetics.

A study conducted by Rai P et al.,[21] studied the effect of addition of dexmedetomidine (0.5mcg/kg) to ropivacaine (0.25% 20ml) in transversus abdominis plane block on postoperative pain in lower segment caesarean section under spinal anaesthesia. The time for first analgesic dose was longer in dexmetomidine group. VAS score was found to be lower in all post-operative points for the first 6 hrs in dexmedetomidine group. Hence the authors concluded the addition of dexmedetomidine to ropivacaine in TAP block helps achieve better analgesia and decreases the total dose of analgesics required post-operatively without any major side-effects.

Another study conducted by Ramya Parameswari A et al.,[22] to compare the efficacy of 20ml of bupivacaine (0.25%) with 0.5μg/kg of

Dexmedetomidine and 20ml Bupivacaine (0.25%) alone for TAP block for Post-operative Analgesia in Patients Undergoing Elective Caesarean Section under spinal anaesthesia. The addition of dexmedetomidine to bupivacaine in TAP block prolonged the duration of post operative analgesia.

In our study, post operative analgesia with the addition of dexamethasone (GROUP D1) or dexmedetomidine (GROUP D2) to bupivacaine in TAP block was compared. The average VAS score in patients who received TAP with dexamethasone was significantly lower than those who received dexmedetomidine. Further, the duration of analgesia was 269 minutes longer in the first group who received dexamethasone TAP. The total dose of rescue analgesic requirement was lower in group D1 compared to GROUP D2. There were no significant side effects in both the groups.

The limitation of the present study is that the extent of block under spinal anesthesia could not be assessed which can be vital in assessing successful block.

Conclusion

Addition of dexamethasone to bupivacaine in TAP block prolonged the duration of postoperative analgesia and reduced the analgesic requirements compared to addition of dexmedetomidine following open abdominal hysterectomy without any major side effects. We recommend the routine use of a dexamethasone as an adjuvant to bupivacaine in TAP block as part of multimodal analgesic regimen after abdominal hysterectomy to enhance the recovery process and render patient pain free.

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Case Report

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Perioperative Management of a Patient with Prosthetic Mitral Valve Posted for Ankle Surgery

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Abstract

Introduction: Patients with prosthetic valves pose a specific challenge to the anesthesiologist due to their increased predisposition to thrombo embolic events, infective endocarditis and hemolysis.

Case Report: Here we describe the anaesthetic management of a 50 year old female with prosthetic mitral valve posted for wound debridement and external fixation for open type III right ankle bone fracture. She is a known case of Rheumatic heart disease and has underwent mitral valve replacement with tricuspid annuloplasty 5years back and is on oral anticoagualtion which was stopped 7days prior to surgery. Pre operative ECG showed AF with recent ECHO finding of concentric LVH with EF of 60%. Pre operative coagulation profile was normal. Antibiotic prophylaxis was given 2hours prior to incision. Case was done under general anaesthesia. Patient was induced with etomidate and maintained with intermittent doses of propofol and isoflurane with adequate analgesics. Intra operative blood loss was around 100ml.Patient was extubated and shifted to ICU for observation.

Conclusion: In patients with prosthetic heart valves the most common complication is thromboembolism therefore optimising the coagulation profile before the surgery and subsequent restarting of anticoagulation therapy immediately after surgery is of utmost importance.

Keywords: Perioperative Management; Ankle Surgery; Prosthetic Mitral Valve.

How to cite this article:

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Introduction

All surgeries are associated with some amount of stress leading to hemodynamic changes. Patients with Valvular heart disease are more prone for hemodynamic instability during perioperative period. The most common valvular lesions include Mitral stenosis/Aortic stenosis.[1]

The problems associated with management of patients with prosthetic heart valves for non cardiac surgeries are

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- Assessment of valvular function and residual pathology
- Infective endocarditis
- Risk of bleeding and preparation for reversal of anti coagulants
- Thromboembolism

We present the successful management of a case with prosthetic mitral valve and atrial fibrillation posted for lower limb surgery.[2]

Case Report

A 50yr old female patient sustained injury to her right ankle following a RTA. She was posted for elective surgery- CRIF with external fixator for ankle fracture dislocation. Preanaesthetic evaluation of the patient showed that she had undergone mitral valve replacement along with tricuspid annuloplasty 5yrs back. She was currently on tablet warfarin 5mg OD Patient had no other co-morbid conditions

On physical examination, she was afebrile and pulse was 106/ min and rhythm irregularly irregular, blood pressure was 110/60mm Hg and RR is 14/min. Systemic examination showed no abnormalities.Airway assessment did not show any predictors of difficult airway. The routine pre-operative blood investigations were done and the reports were within normal limits. ECG showed Atrial fibrillation. ECHO findings were - prosthetic mitral valve, post tricuspid annuloplasty, trivial MR, no clots/vegetations, Dilated LA, atrial fibrillation and ejection fraction -60%. Warfarin was stopped 5days prior to surgery and bridged with enoxaparin(LMWH) 40mg once a day. The day prior to surgery coagulation profile was done and the reports showed PT-18.6sec, APTT-46.7, INR-1.6.Patient was on Tab. Atenolol 25mg OD. Plan of anaesthesia- General anaesthesia (As patient was not willing for regional anaesthesia).

Patients consent for surgery was obtained and the following preoperative instructions were given

1. NPO as per guidelines
2. Stop LMWH 12 hours before surgery
3. Continue Tab atenolol till surgery
4. On the day of surgery Tab atenolol 25mg orally 2 hrs before surgery
5. Tab alprazolam 0.5mg HS, Tab ranitidine 150mg 2hours prior to surgery
6. Inj. Ampicillin 1.5gms I.V 2hours prior to surgery(ATD), infective endocarditis prophylaxis.

After shifting to operation theatre, patient was premedicated with Inj.Fentanyl 2µg/kg IV. Monitors connected- ECG, Pulse oximeter, NIBP, ETCO2 and temperature. Patient was induced with IV Etomidate 0.2mg/kg. After confirming bag mask ventilation, Injection vecuronium 5mg IV was given to facilitate endotracheal intubation. 90 seconds before laryngoscopy, Injection Lignocaine (2% preservative free) 60mg was given. Anaesthesia was maintained with O2 : N2O : Isoflurane mixture (40:60: 0.4%).Inj. Vecuronium 1mg bolus given intermittently(Total 7mg). Inj. Paracetemol 1gm IV infusion given. Blood loss was minimal and correction was done with crystalloids. Duration of surgery was 2hrs.

At the end of surgery, patient was extubated after giving Inj. Neostigmine 2.5mg, Inj.Glycopyrrolate 0.4mg and Injection Lignocaine (2% preservative free) 60mg IV. Extubation was smooth and patient was shifted to recovery for observation.The patient had stable haemodynamics in the Recovery Room. Low molecular weight heparin was started 12 hours after surgery and later bridged on with warfarin. The patient was shifted to the ward and discharged on 14thpost operative day.

Discussion

It is important to note that patient with prosthetic valves will be on multiple medications such as anti coagulants, digitalis, beta blockers and diuretics which may affect their response to anaesthetics. These medications have to be titrated or changed to injectable medications before surgery. Our patient was on Tab Atenolol(Beta blocker) which was continued till the day of surgery. Main threat associated with mechanical prosthetic valves is thromboembolism and the patients are on anticoagulants.Our patient was on tab warfarin which was stopped and bridged with LMWH. Acidosis, hyper ventilation and tachycardia in the intraoperative period may lead to complications like new onset arrhythmias.[3]

Our patient had adequate ventilation as shown by ETCO2 readings between 30 – 35 mmHg and stable hemodynamics in the intraoperative period. Our patient had no clinical signs of IE and the ECHO showed no vegetation. Prophyalactic antibiotics as per guidelines were given to prevent infective

endocarditis .As we did not expect major blood loss and fluctuating vitals during the surgery, we did not place an arterial line and measure IBP.[4-5]

Conclusion

Patients with prosthetic valves are more sensitive than others to hemodynamic changes. They need careful preoperative assessment and clinical evaluation. Bridging of anti coagulants is the major concern in the patients with prosthetic mechanical valves along with antibiotic prophylaxis for Infective endocarditis.

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Case Report

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Anaesthetic Challenges in a Child Presenting with A Large Epiglottic Cyst for Excision

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Abstract

Laryngeal cysts are relatively rare benign lesions that represent approximately 5% of benign laryngeal lesions.1 Though benign, they can present with severe respiratory obstruction. We present one such rare case in a child aged 6yrs presenting with a large epiglottic cyst highlighting the anaesthetic challenges related to management of the airway in this age group. Fiberoptic intubation was planned in our case keeping all the necessary equipments in case of airway crisis.

Keywords: Dysphagia; Loss of appetite; Large epiglotic cyst; Fiberoptic bronchoscopy.

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Introduction

Epiglottic cysts are benign lesions in the larynx. Although benign its size and location may result in airway complications.[1] These cysts are often located on the lingual surface of the epiglottis. The diameter of the respiratory tract is smaller in infants and children, hence an epiglottic cyst may easily obstruct the airway in this age group, and sufficiently large cysts may present with stridor, inability to feed, respiratory distress, and have the potential to be life threatening. We report the anaesthetic management of one such case of a child presenting with a large epiglottic cyst which was planned for surgical removal.

Case Discussion

A 6yr old child weighing 15kgs presented to us with history of odynophagia and dysphagia, resulting in loss of appetite since almost a month child had no other comorbidities parents gave history of occasional snoring when asleep, however there was no history of disturbed sleep for the child due to snoring. There was no history of change of voice or noisy breathing.

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On clinical examination – child was around 15 kgs, there was no pallor, icterus, edema, clubbing, lymphadenopathy, cyanosis. Vitals were stable, room air saturation was normal. On examination of oral cavity the tonsils were enlarged and there was a cystic lesion behind the posterior part of the tongue,uvula and faucial pillars could not be visualized. Blood investigations were within normal limits. CT scan showed a well defined smoothly marginated non-enhancing cystic area in the region of the tongue extending as follows-

1. anteriorly,seen in close relation to the base of the tongue and bulging towards the bilateral vallecular regions(L>R)
2. laterally,in contact with the lateral wall of the pharynx on the left side,with no parapharyngeal extension appreciated.
3. Posteroinferiorly, indenting the epiglottis and reaching till the posterior wall of the oropharynx, with narrowing of the pharyngeal lumen.

Concerns in the above case was airway collapse following anaesthetic induction and chances of rupture of cyst during conventional laryngoscopy and thereby aspiration of the contents of the cyst. Hence fiberoptic intubation was planned. Also an emergency tracheostomy kit was kept standby as a part of difficult airway cart.

22g iv cannula was secured after applying prilocaine local anaesthetic 45 min prior and anaesthetizing the area of iv cannulation. Ringer lactate was started at 50 ml per hour.

Preoperatively child's airway was anaesthetised with lignocaine (2%) 3ml by giving nebulization of the same 15 mins prior to shifting the child to operating room.

Child was premedicated with inj glycopyrolate 0.15mg iv since fiberoptic bronchoscopy was planned.Regarding sedative premedication, care was taken to avoid deep sedation because of anticipated difficult airway. Inj midazolam 0.05mg/kg was given. child was then shifted to operating room.monitors inclusive of pulse oximeter, ECG, NIBP were attached. Oxygen via nasal prongs was started at 2 lts/min. Dexmeditomidine infusion was started at 1 mcg/kg and child was slowly induced with propofol aliquots of 5 mg, maintaining spontaneous breathing. Fiberoptic intubation was performed gently making sure cyst doesn't rupture. The scope was passed beside the cyst gently and the cords were visible, once inside the cords, after confirming the tracheal rings, a 4.5 size flexomettalic endotracheal tube was gently threaded and secured in position after confirming correct placement. Just prior to entering into the cords, a bolus of 15 mg propofol was given intravenously to avoid coughing on the tube. Child was now relaxed with inj atracurium at the dose of 0.1 mg /kg. Sevoflurane was started keeping a MAC of 1,with oxygen and air (1:1). Dexmeditomidine infusion was tapered and stopped. Throat was packed. Warming blanket was put over the child .inj paracetomol at 15mg/kg was given and inj fentanyl at 1mcg/kg aliquots as per the response to incision was given.inj dexamethasone was given in the dose of 0.1mg/kg. Ringer lactate intravenous fluid was continued according to holiday segars formula. The epiglottic cyst was removed in toto,haemostasis was achieved. At the end of the surgery thorough suctioning was done and throat pack was removed, child was reversed after adequate efforts and extubated. Child was put in lateral position and shifted to recovery room where oxygen was started at 5 lts per min and SPO2, ECG, NIBP was attached. The entire procedure went on uneventfully.

Discussion

The challenges encountered in this case was the age of the patient, preparedness for management of airway obstruction on induction of anaesthesia, and the risk of cyst rupture during intubation and soiling of the airway. Hence atmost care was taken taking into consideration the following above aspects. Since the cyst was a huge one obscuring the view of larynx and posterior pharyngeal wall, possibility of passing the fiberoptic bronchoscope across the cyst without rupturing the cyst and visualization of the vocal cords was the biggest challenge. Unlike adults, children donot cooperate for an awake fiberoptic intubation, this was another challenge in this case because induction of anaesthesia would further collapse the already obstructed airway.

There has been a case report of congenital vallecular cyst presenting in a 3 mth old baby in which the airway could not be secured by conventional techniques, thus necessitating tacheostomy.[2]

Laryngeal cysts are relatively rare,benign lesions of the larynx that represent approximately 5% of the benign laryngeal lesions.[1]

Laryngeal cysts are most often located on the lingual surface of the epiglottis and true vocal folds,but also found in the vallecula.[1,3] They are classified as congenital and acquired. Congenital

cysts cause airway obstruction at birth. Acquired cysts can occur at any age but most likely in the 6th decade.[1]

Most of the epiglottic or vallecular cysts are assymptomatic, but common symptoms include globus sensation, voice change and dysphagia.[3]

Cysts of vallecula (space between the base of the tongue and epiglottis) are frequent, often asymptomatic and mostly donot require particular treatment. In contrast epiglottic cyst harvest a bigger risk of impairing the airway, particularly when they are infected and removal is advised.[4]

Large, symptomatic cysts are often treated surgically via direct laryngoscopy or endoscopic visualization and excision with cold instruments, cautery, microdebrider or CO_2 laser.[5] Epiglottic cysts can present from severe airway obstruction in newborns to completely assymptomatic cysts that are incidentally found during induction of anaesthesia causing difficulty to ventilate and intubate. Awareness of structural airway abnormalities (ie, cysts or masses) and prompt direct visualization with prepared anaesthetic and surgical plan is important in treating airway anomalies.

Conclusion

Epiglottic cysts presenting in the paediatric age group is a challenge to the anaesthetist in terms of airway management. Risk increases with increase in size of the cyst, smaller age group and with acute presentation as in the case of an infected cyst. A thorough preoperative evaluation and meticulous planning of anaesthetic management with backup plan for airway crisis management is essential for the success of these cases.

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Case Report

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Management of a Patient with Pheochromocytoma Posted for Right Adrenalectomy

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Abstract

Introduction: Patients posted for adrenalectomy with pheochromocytoma pose major challenge to anaesthesiologist as there may be excess catecholamine release during its removal that leads to severe hypertension and arrythmias intra operatively.

Case presentation: Here we discuss anaesthetic management of 27 year old female with right supra renal mass posted for right adrenalectomy. She came with complaints of abdominal pain and weight gain for which hormonal evaluation and CECT abdomen done and was diagnosed with pheochromocytoma of right adrenal gland. As patient was obese and venous accesibility was difficult central venous catheterisation was done prior to surgery. Case was done under combined epidural with general anaesthesia.

Conclusion: In patients with pheochromocytoma posted for adrenalectomy, pre operative hormonal evaluation, intra operative and post operative hemodynamic stability are important. Intra operative and post operative tachycardia, hypertension prevented by smooth induction, minimise the intubation and extubation response and use of other adrenergic blockade drugs during and after surgery. Effective post operative pain management is necessary.

Keywords: Anaesthetic management; Pheochromocytoma.

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Introduction

Adrenal tumors are classified as hormonal secreting and non-hormonal secreting tumors.[1] Hormonal secreting tumors present to the anesthesiologist unique challenges requiring good preoperative evaluation, perioperative hemodynamic control, corrections of all electrolytes and metabolic abnormalities.[2] Pheochromocytoma presents the biggest challenge to the anesthesiologist compared with the other hormonal secreting

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adrenal tumors. This disease is characterized by excess of catecholamine secretion inducing a sympathetic storm mostly presented by severe hypertension and arrhythmias.[3] Surgical resection of Pheochromocytoma needs a multidisciplinary team including endocrinologist, radiologist, anesthesiologist, and surgeon.[4]

Case Report

A female patient, aged around 27 years, presented with complaint of vague abdominal pain, nausea, generalised fatigue, weight gain and excessive sweating. Ultrasonography showed a right supra renal mass.

CECT scan of abdomen revealed heterogeneously enhancing lesion measuring 8.2 × 6.7 × 13.1 cm over right supra renal gland. Left supra renal gland and liver are grossly unremarkable. Hormonal study showed 24-Hr urine Vanillymandelic acid (VMA) was raised (15.2mg/24 hrs). Thyroid and prolactin levels were within the limit. A diagnosis of Pheochromocytoma was made and the patient was started on Tab Phenoxybenzamine 10mg BD and Tab. Metoprolol 25mg BD.

During pre anaesthetic examination, patient was conscious and alert. Morbid obesity noted. (body weight 91.3kg, BMI: 36.5)

Vital signs were heart rate of 106 bpm, BP of 150/90 mmhg and respiratory rate of 18/min. Reviewing the preoperative vital sign chart of the patient since admission(1week) confirmed that the patient had no persistent or episodic increase in blood pressure. Airway assessment was done and Mallampati classification was Grade II. Cardiovascular and Respiratory systems were normal and rest of examination were unremarkable. Routine preoperative blood investigations were done and the reports were normal. Serum electrolytes, Thyroid profile and Serum Prolactin were normal. ECG and ECHO were unremarkable. The plan of anaesthesia was General anaesthesia with lumbar Epidural anaesthesia.

Patient's consent was obtained. The pre operative advice was NPO as per guidelines. Tab. Alprazolam 0.5mg HS. Tab. Ranitidine 150mg HS. Continue Tab.Phenoxybenzamine and Tab.Metoprolol till the day of surgery. A triple lumen central line was placed in left subclavian vein under ultrasound guidance, the previous day of surgery. On shifting to OT non invasive monitors like ECG, NIBP, pulseoximeter, capnograph were connected to the patient. As we were anticipating difficult airway, the difficult airway cart was kept ready. Loaded syringe pumps – NTG and Vasopressin were kept ready. Under aseptic precautions, 20G epidural catheter was placed at L1-2 for intra operative and post operative analgesia. Premedication with 100mcg of IV Fentanyl. Preoxygenation with 100% O2 for three minutes. Induction was done with 180 mg of IV Propofol. Injection Succinyl choline 125mg IV was given to facilitate Endotracheal intubation after confirmation of adequate bag and mask ventilation. Injection lignocaine (2% preservative free) 60mg was given before intubation. After confirming correct placement of ETT, Arterial line was established in Left radial artery. The patient was positioned in the left lateral position and care was taken to pad all pressure points. Invasive monitoring of blood pressure and CVP was started. The patient was catheterised and hourly urinary output was monitored. Anaesthesia was maintained with oxygen, nitrous oxide and isoflurane. Dexmedetomidine infusion was started for maintenance of anaesthesia and to achieve hemodynamic stability. Epidural Top ups of 5ml 0.25% bupivacaine were given every hour during the intraoperative period after the epidural test dose. Patient was transferred fully awake to intensive care unit with stable vital signs. The patient did not have any episodes of hypotension in post operative period. Epidural top ups were continued for two days for post operative pain relief. Patient was shifted to the ward on 3rd post operative day and discharged on 15th day after an uneventful postoperative period. Histopathology of the right adrenal gland confirmed the diagnosis of pheochromocytoma.

Discussion

Pheochromocytoma are tumours of chromaffin tissues which synthesize catecholamines. Pheochromocytoma can be adrenal or extrarenal (paraganglia), and can excessively secrete epinephrine, nor epinephrine, and rarely dopamine.

Pre-operative goals include

- Control of arterial pressure
- Reversal of chronic circulating volume depletion
- Control of heart rate and arrhythmias
- Assessing and optimizing myocardial function
- Managing electrolyte and glucose imbalance.[5]

This tumor can also be associated with multiple endocrine neoplasia. 10% of pheochromocytomas

may be malignant and 10% may be bilateral. Pre-operative assessment of patients with pheochromocytoma is an essential part in management. Treatment with adrenergic blocking agents plays an important role in the operative management of patients with pheochromocytoma.[1] Alpha adrenergic block reduces hypertension preoperatively and modifies responses to high levels of circulating catecholamines. It also expands the intravascular volume in those patients in whom this has been decreased due to intense peripheral vasoconstriction. Beta adrenergic block if used alone in patients with pheochromocytoma, there may be a marked rise in the total peripheral resistance due to vasoconstriction secondary to unopposed alpha adrenergic activity.[4] Our patient was started on Tab Metoprolol (beta blocker) and Tab Phenoxybenzamine (alpha blocker). The efficacy of adequate preoperative alpha blockade were assessed by the Roizen Criteria. The Roizen criteria includes

- Blood pressure not more than 160/90 mmHg for 24hours prior to surgery
- No orthostatic blood pressure
- No ST or T wave changes for 1 week prior to surgery
- No more than 5 premature ventricular contractions per minute.[6]

Our patient had BP of 150/90mmhg, no ECG changes and no orthostatic hypotension which fulfilled all the criteria and the patient was taken up for surgery. Even when patients with pheochromocytoma have been prepared preoperatively with adrenergic blocking agents, episodes of severe hypertension and/or cardiac arrhythmias may occur during excision of the tumor. This is explained by the fact that preoperative adrenergic block is only partial and does not reduce the response to high levels of circulating catecholamines which occur during removal of these tumors. Our patient did not have any episodes of hypertension in the initial period. BP was well controlled with Dexmedetomidine infusion and epidural top ups.[5] Following the removal of pheochromocytoma, the consequent fall in the levels of circulating catecholamines may result in hypotension. In our case, the hypotension was managed with crystalloids, blood products and vasopressin infusion with careful monitoring of central venous pressure and urinary output.[6]

Conclusion

The following points should be considered during the anaesthetic management of a patient with pheochromocytoma.

- Preoperative preparation with adrenergic blocking agents. The adequacy of the block using Roizen criteria.
- Use of an anaesthetic agent which is not associated with release of endogenous catecholamines and does not sensitize the myocardium to high levels of circulating catecholamines.
- Adequate fluid and blood administration, including preoperative transfusion if necessary.[2]

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Case Report

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Anaesthesia for Vertebral Body Tumor in the Pregnant Patient

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Abstract

Introduction: Vertebral body tumors although are rare in pregnancy can cause significant problems like neurological symptoms in the mother and if progressed may cause severe side effects in the fetus.

Case presentation: We present here successful anesthetic management of a 20-year-old pregnant lady with 26 weeks of gestation with a D8 vertebral body tumor posted for excision and spinal fusion in the prone position.

Conclusion: Surgical intervention in pregnant ladies with spinal cord tumors depends on the neurological manifestations and early intervention may be required to prevent harmful effects to both the mother and fetus, hence a multidisciplinary approach between the surgeon, anesthetist and obstetrician is essential in such cases for a safe outcome.

Keywords: Pregnancy; Vertebral body tumors.

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Introduction

Any disease during pregnancy can cause an alteration in the normal functions of other systems. It is imperative to treat the disease based on its emergency. Hence it's essential to report rare diseases and to discuss their pathology, treatment options, and anesthetic management if surgery is deemed necessary.[1] An aneurysmal bone cyst (ABC) is a benign, tumor that is vascular, aggressive, and an osteolytic lesion.[2] The lesions mostly occur in the first two decades of life, usually slightly more in women than men.[3,4] After osteoid osteoma and osteoblastoma, ABC is the third most common benign bone tumor. Primary ABCs represent 1.4 % of primary bone tumors and the vertebral column; particularly the lumbar area and posterior elements are involved in 3–30 % of cases.[5,6] Vertebral body tumors are very less in pregnancy but can cause significant problems like neurological symptoms in the mother and may cause severe effects in the fetus, especially progressive neurological deficits, which require immediate surgical correction.[7] We discuss here the perioperative management of a 20-year-

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old pregnant lady with 26 weeks of gestation with a D8 vertebral body tumor (ABC).

Case Report

A 20-year-old primiparous pregnant woman at 26 weeks of gestation was admitted with para-paresis to the neurosurgical division of R L Jalappa Hospital and Research Center. Her history revealed she had progressive bilateral lower limb weakness for one month associated with decreased power of both limbs. MRI study showed expansile lesions involving the left body, transverse process, and posterior elements of D8 vertebra compressing the spinal cord and left neural elements at that level. Due to increased maternal risk neurosurgical intervention was not delayed.

Pre-operative examination revealed a 55 kg female with a heart rate of 116 bpm, BP of 100/60 mmHg, and respiratory rate of 20/min. Her cardiovascular and respiratory parameters were normal. Abdominal examination showed a uterus size analogous to the period of gestation. Airway examination revealed a Mallampatti Score of I, with intact dentition, good mouth opening, and a full range of neck movements. The patient was given 10 mg intravenous (IV) metoclopramide and 50 mg of ranitidine 30 minutes before induction. Monitoring consisted of continuous ECG, invasive arterial blood pressure, pulse oximetry, capnography. After Preoxygenation with 100% O2 for three minutes, rapid sequence induction was done with 250 mg of thiopentone and 100 mcg of fentanyl. Intubation was facilitated with an injection of succinylcholine 100mg. Anesthesia was maintained with Isoflurane (1%), oxygen, air, and an intermittent boluses of Vecuronium. An arterial line was established and the patient was proned. All pressure points were padded, and the abdomen was made to hang freely. D8 total laminectomy, tumor excision, and posterior instrumentation were performed for about 4 hours. The intraoperative systolic blood pressure and end-tidal carbon dioxide were maintained at ≥100 mmHg and 35-40 mmHg, respectively. Tocolytics were given intraoperatively to prevent preterm labor. Vital parameters were stable. We gave 1500 ml of crystalloids with blood loss of about 350 ml and urine output was 200 ml. After surgery, the patient was supined and awake extubation was done with no complications and transferred to the intensive care unit. The patient had a full neurological recovery by the first postoperative day and the fetus was viable.

Discussion

Vertebral tumor complicating pregnancies are rare and surgery and anesthesia at pregnancy is risky for the mother and pose a significant threat to the fetus also. Knowledge is less regarding the anesthetic management of neurosurgery in parous women. Proper preparation and thorough evaluation must be done based on surgical and anesthetic needs. Several factors must be taken into account for surgery during pregnancy this includes the position of the patient, plan of anesthesia, fetal heart rate monitoring, plans for urgent delivery, aspiration prophylaxis, and tocolysis to prevent preterm labor.[7] Care should be taken to avoid hypoxemia, hypotension, acidosis, and hyperventilation.[8] In this patient, an arterial line was secured to respond immediately to hemodynamic changes. Hypotension reduces uterine blood flow and can cause fetal hypoxia. Urine output should be checked every hour and Isotonic and glucose-free fluids must be given to reduce the risk of cerebral edema and hyperglycemia, crystalloids were given. Spinal surgery in the prone position in pregnant women may improve placental perfusion but monitoring the fetus is difficult and there may be increased epidural venous bleeding. Proning is relatively safe in the first and early second trimester, but a left lateral position is better for the latter part of the second trimester and third trimester.[9] Care must be taken for proper positioning at the time of surgery as excessive pressures can lead to preterm delivery.[10] The main point is to make sure that the abdomen is free, irrespective of the position on the operating table.[11]

Parous women requiring non-obstetric surgery pose a unique challenge where the health of the mother is paramount but equal importance must be given for fetal well-being. A team involving surgeons, anesthesiologists, obstetricians, and intensivists must be involved in the decision regarding surgery. In the first and second trimesters, if the fetus is nonviable, early neurosurgical intervention is better as it improves the outcome and during the later trimesters, priority must be given to cesarean section.[12]

Conclusion

Neurosurgery in pregnant women is very rare. Caring for them is challenging and complicated. A multidisciplinary approach must be followed during that time. The urgent nature of these situations requires respective departments to be accustomed

to managing pregnant patients. Guidelines should be developed for such emergencies with established lines of communication and referrals between specialties.

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Reports of randomized clinical trials should be based on the CONSORT Statement (http:// www. consort-statement. org). When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000 (available at http://www.wma. net/e/policy/l7-c_e.html).

Results

Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Extra or supplementary materials and technical details can be placed in an appendix where it will be accessible but will not interrupt the flow of the text; alternatively, it can be published only in the electronic version of the journal.

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.

References

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. pp 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.

More information about other reference types is available at www.nlm.nih.gov/bsd/uniform_requirements.html, but observes some minor deviations (no full stop after journal title, no issue or date after volume, etc.).

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Tables should be self-explanatory and should not duplicate textual material.

Tables with more than 10 columns and 25 rows are not acceptable.

Table numbers should be in Arabic numerals, consecutively in the order of their first citation in the text and supply a brief title for each.

Explain in footnotes all non-standard abbreviations that are used in each table.

For footnotes use the following symbols, in this sequence: *, ¶, †, ‡‡,

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Graphics files are welcome if supplied as Tiff, EPS, or PowerPoint files of minimum 1200x1600 pixel size. The minimum line weight for line art is 0.5 point for optimal printing.

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Type or print out legends (maximum 40 words, excluding the credit line) for illustrations using double spacing, with Arabic numerals corresponding to the illustrations.

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Standard abbreviations should be used and be spelt out when first used in the text. Abbreviations should not be used in the title or abstract.

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- Conflicts of interest disclosed

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- Middle name initials provided.
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- References according to the journal's instructions

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- Table and figure numbers in Arabic letters (not Roman).
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