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Characteristics of Block and Post-Operative Analgesia of Low Dose Intrathecal Fentanyl and Midazolam Combined With Hyperbaric 0.5% Bupivacaine in Patients Undergoing Lower Limb Orthopaedic Surgeries

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ABSTRACT

Aim: To investigate characteristics of block and post-operative analgesia of low dose intrathecal Fentanyl and Midazolam combined with hyperbaric 0.5% bupivacaine in patients undergoing lower limb orthopaedic surgeries.

Material and method: Selected consented 60 patients scheduled for orthopaedic surgeries under subarachnoid blockade were randomized into two comparable equal groups of 30 patients each i.e. Group A(Sub arachnoid block with addition of 25 µg (0.5 ml available preservative free) fentanyl to 3ml of 0.5% Bupivacaine hydrochloride (hyperbaric) and Group B: (Sub arachnoid block with addition of 1 mg (0.2 ml preservative free) midazolam (+ 0.3 ml normal saline) to 3ml of 0.5% Bupivacaine hydrochloride (hyperbaric).The motor block of the lower extremities was evaluated bilaterally by modified Bromage scale (0-3). Duration of sensory analgesia was taken from onset of spinal anesthesia to time of administration of first rescue analgesic, reflected on visual analogue scale (VAS).

Results: The mean time required to achieve Complete Sensory blockade was 142.77±8.73 sec in patients of Group A and 138.57±7.65 sec in patients of Group B. Sedation score was recorded every 30 min for 90 mins (using Ramsay sedation score) considering the time of study drug given as zero in both groups. The mean sedation score at 30 mins in patients of Group A was 2.10±0.31 and in patients of Group B it was 2.27±0.45.

Conclusion: It can be concluded that intrathecal midazolam can be used as an adjuvant to local anesthetics if fentanyl is not available or contraindicated.

Keywords: Sedation, Spinal Anaesthesia, VAS

INTRODUCTION

The concept of spinal anesthesia is unique and unparalleled in a way that a small mass of drug, virtually devoid of systemic pharmacological effects can produce profound surgical anesthesia. A single intrathecal injection with local anesthetic is used for effective sensory and motor blockade. It is particularly advantageous for surgery of the lower limbs, pelvic organs, genitals and perineum, lower abdomen and most urological procedures.

Spinal anaesthesia is advantageous because it uses a small dose of the anaesthetic, is simple to perform and offers a rapid onset of action, reliable surgical analgesia and good muscle relaxation is achieved. These advantages are sometimes offset by a relatively short duration of action and complaints of post-operative pain when it wears off[1].

Spinal anaesthesia with hyperbaric bupivacaine hydrochloride is popular for longer procedures due to its prolonged duration. But there is a need to intensify and increase duration of sensory blockade without increasing the intensity and duration of motor blockade, and thus prolong the duration of postoperative analgesia. Many

adjuvants like clonidine, fentanyl, midazolam, ketamine, etc. are used to prolong the effect of spinal analgesia for post-operative pain relief[2].

Thus, in our study we have used intrathecal midazolam and fentanyl as adjuvants with heavy bupivacaine and compared their pharmacological effects in terms of onset and duration of motor and sensory blocks, duration of post-operative analgesia, side effects and changes in hemodynamics. This study is aimed to establish or refute whether these adjuvants are ideal drugs for the purpose of extending post-operative analgesia without compromising the patient's safety or any other unwanted complications.

MATERIAL AND METHOD

The study was conducted at Chhatrapati Shivaji Subharti tertiary Hospital, affiliated to Subharti Medical College and Swami Vivekanand Subharti University, Meerut over a period of 24 months from July 2017 to June 2019.After obtaining approval from the Ethical Committee of the hospital, a clinical study was designed enrolling 60 patients.

The selected adult consented 60 patients scheduled for orthopaedic surgeries under subarachnoid blockade, were randomized into two comparable equal groups of 30 patients each, according to computer generated randomized number table.

Group A: Sub arachnoid block with addition of 25 µg (0.5 ml available preservative free) fentanyl to 3ml of 0.5% Bupivacaine hydrochloride (hyperbaric).

Group B: Sub arachnoid block with addition of 1 mg (0.2 ml preservative free) midazolam (+ 0.3 ml normal saline) to 3ml of 0.5% Bupivacaine hydrochloride (hyperbaric).

Anesthesia technique/Methodology: All patients enrolled underwent the pre-anaesthetic check-up which included a detailed medical and surgical history and any previous anaesthetic exposure and its outcomes and physical examination. The routine and relevant investigations were done. They were premedicated with tab alprazolam 0.25 mg and tab ranitidine 150 mg the night before surgery. On arrival to Operation theatre, standard monitors were attached and baselines reading for all vital parameters were recorded. The observations for these parameters were cycled at three-minute interval. The lumbar puncture was performed at L3-L4 intervertebral space with a 25 G Quincke's spinal needle through midline approach. If the spinal block failed at the level of L3-L4, the intervertebral level was changed to L2-L3. After identification of correct placement by free flow of spinal fluid from the needle, 3.5 ml of study drug solution was injected slowly into the subarachnoid space and the spinal needle was withdrawn. Immediately after the intrathecal injection, the patient was placed in supine position on operation table and 10^0Trendelenberg tilt of table was done to achieve the blockade up to T10 segment and then the table was straightened. All patients received supplemental oxygen at rate of 3 L/min via face mask throughout the surgical procedure. Time at the completion of intrathecal injection was noted as zero time. Then hemodynamic and subarachnoid blockade variables were recorded sequentially as per pre-determined time intervals. Another anesthesiologist, who was blinded to the study protocol, assessed the sensory and motor block characteristics after the intrathecal injection of 3.5 ml of study drug solution at 2 min intervals till the adequate surgical anesthesia was achieved. The segmental level of sensory block to pin prick was assessed bilaterally along the mid-clavicular line by using short beveled 26 G hypodermic needle. The motor block of the lower extremities was evaluated bilaterally by modified Bromage scale (0-3) and graded as follows:

0 = full movement and able to raise straight leg against resistance,

1 = unable to raise extended leg at the hip but able to flex knee,

2 = unable to flex the knee but able to move ankle joint and
3 = unable to move hip, knee or ankle (no motor activity).

Duration of sensory analgesia was taken from onset of spinal anesthesia to time of administration of first rescue analgesic, reflected on visual analogue scale (VAS): 0 where 0= no pain to 10= worst possible pain. Patients with VAS score of 4 or more received Tramadol 100 mg intravenously as rescue analgesia. Time taken to achieve complete motor blockade (modified Bromage Scale 3) and time to complete recovery from motor blockade (modified Bromage Scale 0) was observed. All sedation scores were recorded considering the time of giving the study drug as zero. Side effect of nausea, vomiting, sedation, itching and shivering were also noted and were managed accordingly.

Statistical analysis: The results obtained in the study were presented in a tabulated manner as Mean and Standard deviation (SD) and were analysed using Microsoft Excel and SPSS software version 23.0 for windows. Statistical analysis in mean difference among the two groups was done by using unpaired t-test. The demographic data for the categorical variables were compared using chi-square test and unpaired t-test. Block characteristics were also compared using unpaired student t-test and Z proportion test. A 'p' value of <0.05 was considered to indicate statistical significance.

RESULTS

For Group A, mean age was 34.20±11.75 years, mean weight was 59.33±7.75 kgs. The corresponding values of these parameters for Group B were 39.17±10.35 years and 58.63±8.90 kgs (table 1).

The mean time required to achieve Complete Sensory blockade was 142.77±8.73 sec in patients of Group A and 138.57±7.65 sec in patients of Group B. Mean maximal cephalic dermatome level was similar, 7.47 ± 0.86 for Group A and 7.47 ± 1.28 for Group B, was comparable and not statistically significant (p>0.05) as depicted in Table 2.

The preoperative mean arterial pressure (MAP) was 96.00±5.05 mm Hg in patients of Group A and 95.4±9.36 mm Hg in patients of Group B. The values of mean heart rate(HR) were 81.07±14.18 and 80.13±10.53 beats/min for Group A and B respectively as shown in Table 3.

Table 1: Showing demographic profile in all sixty patients

Demographic data	Group A (N=30)	Group B (N=30)	p value
Age(years)	34.20±11.75	39.17±10.35	0.0875
Weight(kg)	59.33±7.75	58.63±8.90	0.7464
ASA (I/II)	27/3	28/2	0.6404
Duration of surgery (mins)	85.27±21.25	86.77±19.73	0.7779

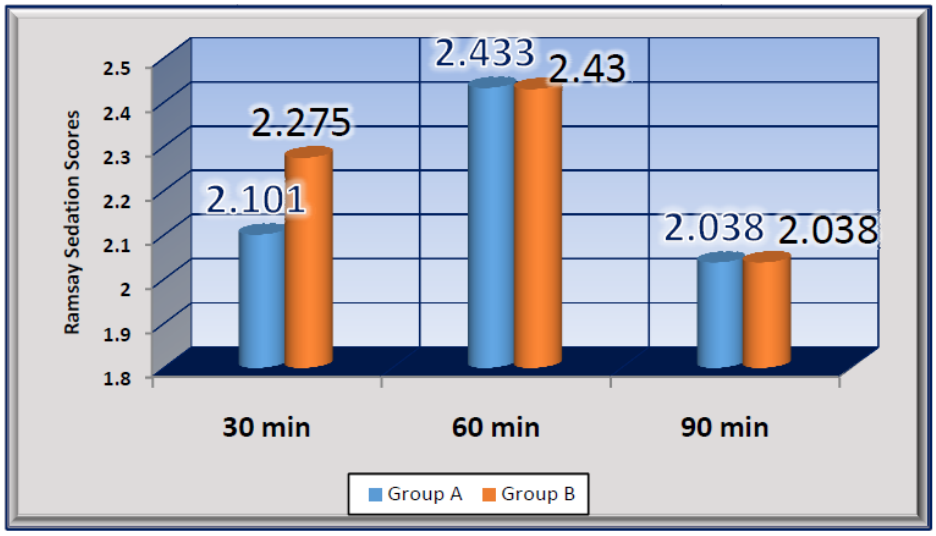
Table 2: Sensory and motor blockade profile comparison among the study groups

Parameters	Group A	Group B	p value
	Mean±SD	Mean±SD	
Time required to complete Sensory blockade (sec)	142.77±8.73	138.57±7.65	0.05
Maximal Cephalic dermatome level (T)	7.47 ± 0.86	7.47 ± 1.28	1
Mean time of Two segment regression (min)	153.90 ± 11.02	152.27 ± 10.93	0.57
Duration of sensory analgesia (min)	341.63±37.41	356.50±21.66	0.07
Onset of complete motor block (sec)	223.40±23.76	219.60±16.10	0.47
Duration of motor blockade (min)	228.17±19.27	232.67±31.48	0.51

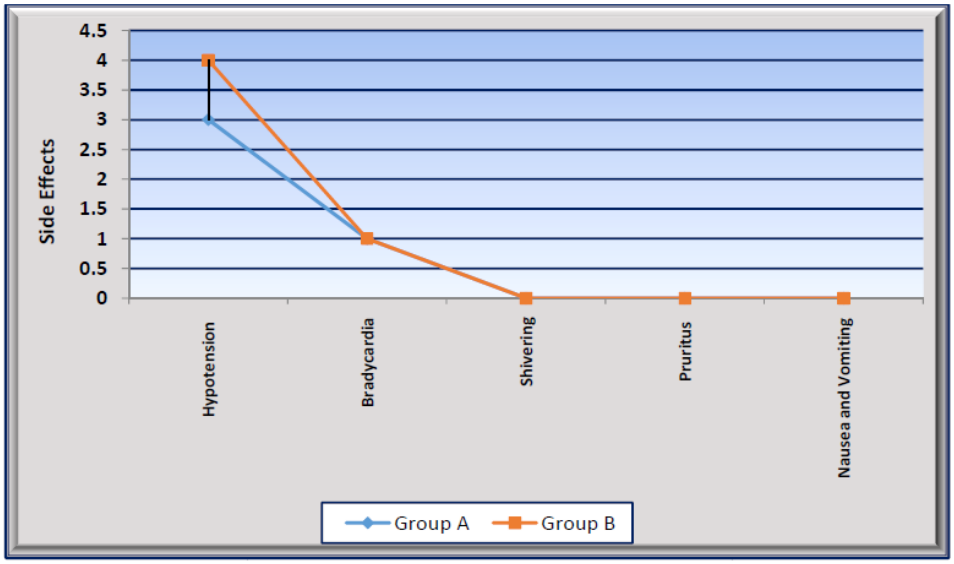
p Value <0.05 is statistically significant

Table 3: Preoperative mean hemodynamic parameters comparison among the study groups

Hemodynamic Parameter	Group A	Group B	p value
	Mean±SD	Mean±SD	
Mean Systolic blood pressure (mmHg)	125.17±8.55	127.6±12.60	0.39
Mean Diastolic blood pressure (mmHg)	81.40±5.70	79.47±9.07	0.33
Mean arterial pressure (mmHg)	96.00±5.05	95.4±9.36	0.76
Mean Heart rate (beats/ min)	81.07±14.18	80.13±10.53	0.77



Graph 1: Sedation score comparison among the study groups



Graph 2: Side effects comparison among the study groups

Sedation score was recorded every 30 min for 90 mins (using Ramsay sedation score) considering the time of study drug given as zero in both groups. The mean sedation score at 30 mins in patients of Group A was 2.10±0.31 and in patients of Group B it was 2.27±0.45. All patients were calm and comfortable. The sedation score remained comparable till 90 mins of giving study drug in both groups. The variation in the Sedation score values at time intervals between Group A and B was statistically insignificant as $p>0.05$ (graph 1).

Hypotension was observed in 3 (10%) patients of Group A and 1 (3.3%) patients of Group B. It was treated by increasing the rate of lactated Ringer solution. No vasopressor medication was required to manage the hypotension (graph 2).

DISCUSSION

The drugs commonly used for spinal subarachnoid block are lignocaine and bupivacaine. One disadvantage with spinal anesthesia using local anesthetics alone is that analgesia ends with the regression of the block, which means that there is an early post-operative need for analgesia post-operative pain, apart from reducing discomfort and other deleterious effects involving mainly the cardio-respiratory system.

In our study duration of sensory analgesia was approximately 356 minutes for the intrathecal midazolam group (Group B). The result is comparable to the study conducted by Chattopadhyay A et al in 2013[3].A study by Kim and Lee[4] in 2001 demonstrated a dose-dependent effect of intrathecal midazolam on postoperative analgesia. Midazolam produces spinally mediated analgesia that is different in quality from that produced by the opioid agonist fentanyl. The analgesic effects of intrathecal midazolam have been proposed to be due to its intrathecal spinal receptor interactions affecting the type A gamma-aminobutyric acid receptors[5].

It has also been suggested that intrathecal midazolam is involved in the release of an endogenous opioid acting at spinal delta receptors[6]. This could be the reason for the increased duration of analgesia in the midazolam group (Group B). Mean duration of sensory analgesia was approximately 340 minutes for the intrathecal fentanyl group (Group A). A recent study by Safari F et al[7] in 2012, demonstrated that addition of 1 mg intrathecal midazolam to bupivacaine produces much longer duration of anesthesia (140 min) as compared with 25 μg intrathecal fentanyl (107 min) in opium abusers undergoing lower limb orthopaedic surgery where a double blind, randomized clinical trial was conducted.

The duration of motor blockade was comparable between intrathecal midazolam (approximately 232 mins) and intrathecal fentanyl (approximately 228 mins) in the present study. This is comparable to the comparative study of the effects of intrathecal midazolam and fentanyl as additives to intrathecal hyperbaric bupivacaine (0.5%) for lower abdominal surgeries by Aasim SA et al[8] in 2015.

In the present study heart rates between the groups were comparable throughout the study period. Bradycardia was observed in 1 patient of group A (3.3%) and none in Group B which may be due to the patient's baseline heart rate (65/min) being on the lower side of our consideration for bradycardia in this study, i.e. <60/min. Though fentanyl pharmacologically is known to cause bradycardia, clinically it is not seen in many patients as has been observed in our study also where the incidence was only 3.3% of Group A. One possible site of action is the cardio inhibitory parasympathetic vagal neurons in the nucleus ambiguus (NA), from which originates control of heart rate and cardiac function. Systolic blood pressure was comparable between the groups but was statistically significant at 25 mins and 30 mins, lower in the fentanyl group (Group A) at both occasions. Diastolic blood pressure remained statistically insignificant between both the groups during the entire study period.

Although previous studies[3,4,9] have reported a decreased incidence of PONV with the use of intrathecal midazolam, we did not find any patients in either groups having PONV. None of the patients of either groups had pruritus or urinary retention in our study though these side effects have been seen in other studies[10,11].

The mean sedation score at 30 mins in patients of Group A was 2.10±0.31 Ramsay sedation score and in patients of Group B it was 2.27±0.45 Ramsay sedation score. All patients were calm and comfortable. The sedation scores remained comparable till 90 mins of giving study drug in both groups which is comparable to the study by Bharti N et al in 2015 being 2.06 and 2.15 between Groups BF (bupivacaine + fentanyl) and BM (bupivacaine + midazolam)[12].

Limitations: One limitation of this study can be viewed as not having a control group for comparison, but we didn't want any of the patients to be at a disadvantage of not getting a better quality of postoperative analgesia and decreased doses of analgesics in the post-operative period by not using the intrathecal additives which have been proven to provide far better pain relief, thus we deliberately designed a randomised prospective double-blinded clinical study.

CONCLUSION

Hence, we conclude that the addition of midazolam to intrathecal bupivacaine provides better potentiating of analgesia as compared to intrathecal fentanyl to bupivacaine and both study drugs appear safe in patients undergoing lower limb orthopaedic surgery with minimal hemodynamic changes and fewer side effects. Therefore, intrathecal midazolam can be used as an adjuvant to local anesthetics if fentanyl is not available or contraindicated.

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