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Efficacy of dexmedetomidine and magnesium sulphate as adjuvant to bupivacaine among patients undergoing lower extremity surgeries: A blinded randomized controlled trial

Sangita Padhi

Assistant Professor, Department of Anesthesia, MKCG Medical College
Email: sangitapadhi.1981@gmail.com

Subhasree Ratha

Senior Resident, Department of Anesthesia, MKCG Medical College
Email: subhasree.ratha14@gmail.com

Dr. Manas Nahak

Dept of Pediatrics, MKCG Medical College & Hospital
Email: manas.83.nahak@gmail.com

Ashok Kumar Nanda

Assistant Professor, Dept of Pediatrics, MKCG Medical College & Hospital
*Corresponding author email: ashokumarnanda2011@gmail.com

Abstract---In this prospective randomised double blind study, an attempt was made to compare the effects of adding dexmedetomidine 10 mcg or magnesium sulphate 50mg to 0.5% hyperbaric bupivacaine on subarachnoid block characteristics and postoperative analgesia in patients undergoing elective lower extremity surgeries. Randomization of the participants was done in three equal groups (n=30). A total of 90 patients of age between 18-60 years of either sex and good physical status posted for elective lower extremity surgery were included. Group B received 15 mg hyperbaric bupivacaine(3ml) with 0.5ml preservative free normal saline, Group D received 15 mg hyperbaric bupivacaine (3ml) with 10 mcg dexmedetomidine in 0.5 ml preservative free normal saline intrathecally and Group M received 15 mg hyperbaric bupivacaine (3ml) with 50mg magnesium sulphate (0.5ml) intrathecally for subarachnoid block. Different parameters of sensory block, motor block and analgesia effect were assessed as outcomes. Results showed that the groups were similar in demographic parameters like age, sex, height, weight, physical status. Bupivacaine with dexmedetomidine as adjuvant shows early onset of

sensory and motor block, early onset of peak block height, prolonged sensory block, prolonged two segment regression time. There was no statistical significance in hemodynamic parameters or adverse effects experienced by either group patients. Bupivacaine plus dexmedetomidine group is better than Bupivacaine plus magnesium sulphate group in respect of an earlier onset of sensory and motor block, prolonged duration of sensory and motor block, longer duration of postoperative analgesia and a lesser number of doses of rescue analgesia required.

Keywords---dexmedetomidine, magnesium sulphate, bupivacaine, patients, extremity surgeries.

Introduction

Spinal anesthesia procedures have had a long history of evolution since their inception, over a century ago. It is now the most common anesthesia procedure in the world. Surgical procedures involving the lower limbs are the most common surgeries performed under spinal anaesthesia apart from cesarean surgeries. The distribution of anesthesia and block height depends on multiple factors related to the drug itself, the procedure and the patient. These include factors such as dose of the drug, baricity, spinal anatomy and cerebrospinal fluid (CSF) volume, height and age of the patients etc. (1). Bupivacaine is a commonly used amino-amide long acting local anesthetic drug belonging to the family of n- alkyl substitute pipercoloxylidide that acts by reversibly binding to specific voltage dependent sodium channels. (2,3) Its is frequently used in procedures of surgical anaesthesia such as epidural, intrathecal, brachial plexus block, peripheral nerve block and local infiltration as well as for pain management procedures such as continuous epidural infusion, single or multiple bolus epidural administration for the management of pain especially post- operative pain or labour analgesia. (4)

On the other hand, Magnesium Sulphate (MgSO₄) acts as an antagonist at the N-methyl-D-aspartate (NMDA) receptor and is a calcium channel blocker. It has multiple other effects on nervous, respiratory, and musculoskeletal systems. (5,6) It has been commonly used to prevent & treat seizures of pre-eclampsia & eclampsia, as an antiarrhythmic agent, a bronchodilator in severe asthmatic attack and in replacement therapy for hypomagnesemia. In anesthesia, it is used to reduce the dose requirement of opioids, anaesthetics & muscle relaxants and increase the effect of muscle relaxants etc. In spinal anesthesia, MgSO₄ produces a state of general sedation lasting about an hour. Dexmedetomidine hydrochloride is the dextrorotatory S-enantiomer of medetomidine that is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. (7) It is also indicated for sedation of non-intubated patients prior to and/or during surgical and other procedures as it has sedative, analgesic, sympatholytic and anxiolytic effects that blunt many of the cardiovascular responses in the perioperative period. While clonidine has been in use as an adjuvant in regional anaesthesia and local analgesia, there are only a few studies available on such effects of dexmedetomidine.

Multiple studies have established the neurological safety profile of various doses of dexmedetomidine for different indications. (8,9) There have also been studies that have shown the beneficial effect of adding dexmedetomidine (5 mcg and 10 mcg) to spinal bupivacaine (12.5 mg) in urological surgeries. (10,11) This benefit is surgery type and dose dependent and has not been proven conclusively. While there are a few studies exploring the role of dexmedetomidine in various types of surgeries, the results are dose dependent and far from conclusive. (12–14). Therefore, with this background, the following study was planned with an objective to compare the efficacy of adding 10 mcg of dexmedetomidine & 50 mg of magnesium sulphate as adjuvant to 0.5% hyperbaric bupivacaine(15mg) on Time to reach T10 dermatome, peak block height and other anesthesia/analgesia outcomes among patients undergoing lower extremity surgeries under spinal anaesthesia.

Methodology

Design and setting

This was a prospectively randomised, blinded study that was carried out in the department of anaesthesiology and orthopedics at M.K.C.G Medical College & Hospital, Berhampur, Odisha from 2018 to 2020.

Study population

Patients of good physical status (I and II), scheduled for elective lower limb surgeries conducted under subarachnoid block were selected using the following eligibility criteria: healthy adult patient of age group 18-60 years with a height of 150 cm or more and weight between 60- 100kg who gave informed consent were included in the trial. Those with a known hypersensitivity to local anaesthetics, in shock, on anticoagulants/ bleeding diathesis/thrombolytic/ fibrinolytic therapy, those having septicemia / bacteraemia/infection at local site, those with gross kyphosis, lordosis or scoliosis or a significant abnormality of laboratory values, patients with patients with raised intracranial pressure and progressive neurological diseases or Pregnancy were excluded from our study.

Sample size, randomization and allocation

A required sample size of 45 was calculated to be sufficient to measure a 30% improvement in the primary outcome of interest (with a type-1 error of 20% and type 2 error < 0.05%). Therefore, 90 adult patients were recruited in total for this study who were randomized using computer generated random numbers and were and were allocated into 3 groups (n = 30 each):

- Group B(n=30): They received 15mg of 0.5%hyperbaric bupivacaine(3ml)+0.5ml of preservative free normal saline. [Control]
- Group D (n=30): They received 15 mg of 0.5% hyperbaric bupivacaine (3ml) +10 mcg dexmedetomidine in 0.5 ml of preservative free NS intrathecally.
- Group M (n=30): They received 15 mg of 0.5 % hyperbaric bupivacaine (3ml) and 50 mg of magnesium sulphate in 0.5 ml of preservative free NS intrathecally.

Patients were randomly allocated into two groups using a sealed envelope technique.

Blinding of the study

This was a double blinded study where the patients were unaware of the study groups. Study drugs were prepared in 5 ml syringe by a single anaesthesiologist and were handed over to the anaesthesiologist performing the spinal block. The anaesthesiologist performing spinal block was blinded to the study drugs and groups and recorded the intraoperative and post-operative data.

Ethical concerns

The study was approved by the institutional ethical clearance committee of MKCG medical college, Berhampur. Written informed consent was obtained from all participants prior to enrolment and the decision to participate did not influence their treatment.

Preoperative assessment

The patients included in this study had a thorough preoperative evaluation, that included a detailed medical history, physical examination, airway assessment, and laboratory investigations as per our institutional protocol.

Study procedure and measurements of outcomes

In the operating room, Boyle's anaesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure. Emergency drug tray containing atropine, adrenaline, mepheteramine, phenylephrine, dobutamine, dopamine, and vasopressin were kept ready. The patients were advised to take tab Alprazolam 0.5 mg and ranitidine 150 mg at bed time on previous night before surgery. They were kept nil orally 8 hour prior to surgery. In the operation theatre, lumbar puncture was performed in all subjects in sitting position at L3 — L4 intervertebral space through a midline approach using 25 G Quincke spinal needle under strict aseptic precaution. After confirming free flow of CSF, the study drug was administered intrathecally at rate of 0.2 ml/sec. At the end of injection, a small sterile dressing was applied and the patient immediately turned into horizontal supine position with a pillow under the head & neck and the vital recording were taken , this is labelled as time zero(0) reading.

Sensory block was assessed by 20 gauge hypodermic needle prick along midclavicular line in bilaterally over S1, L3,T12,T10,T8,T6,T4 or higher dermatomes till sensory block scale by 4 by needle protrusion 2mm through a guard and we used C5-C6 baseline point for normal sensation. Sensory block was assessed at one minute interval (after administration of study drug) in intraoperative period and at 30 minutes interval in postoperative period upto 6 hours. We used a visual analogue pain scale where patients marked a circle around a point (0,1,2,3 etc..) on a 10 point-scale indicating their level of pain.

Motor block was assessed at 1 minute interval (after giving spinal anaesthesia) in preoperative period and motor block regression is assessed at 30 minutes interval in post operative period upto 6 hours, using the Bromage score. Hemodynamic variables were assessed at 5 minutes before giving subarachnoid block and studied at 5 minutes interval in intraoperative period and at 30 minutes interval upto 6 hours in post operative period. Perioperative and postoperative side effects were recorded at 5 minutes interval in intraoperative period and at 30 minutes interval postoperatively upto 6 hours.

Statistical analysis of data

Collected data were analysed using an intention to treat analysis method with the help of Microsoft Excel and Statistical Package for the social Sciences version 16. Numerical parametric data were presented as mean (\pm SD). Ordinal and nominal data were expressed in cross tables as number (percent) of patients in each ordinal or nominal category. Numerical parametric data were compared by Students t-test (independent sample t test) and analysis of variance (ANOVA) test. P value < 0.05 was considered statistically significant.

Results

The mean age of the participants was 42.2 years (SD=8.5 years), the mean height was 164.8 cm (SD=4.6 cm) and the mean weight was 66.0 kg (SD=6.2 kg). While 37% of the participants were females, the rest were males. The demographic profile of all the participants across the three groups were comparable as shown in table-1 below. Our study reports a significant benefit in terms of outcomes of anesthesia assessed in groups that used adjuvants. Significantly better statistics for time to reach T10 dermatome, peak block height, time to reach peak block height, Duration of sensory block at T10, two segment regression time & Time to reach VAS-4 (in minutes) were reported in the groups that received adjuvants as shown in table-2 and figure-1 below.

Table 1
Comparison of the Demographic profile of the three groups

	Group B	Group D	Group M	P-Value	Statistically Significant difference
Age (Year)	39.16+10.12	43.6+10.51	41.63+9.85	0.245	Non significant
Height(Cm)	166.47+6.40	164.43+5.91	163.6+5.62	0.168	Non significant
Weight(Kg)	66.86+7.20	66+7.81	67.2+7.56	0.816	Non significant
ASA (I /II)	I-21 II-9	I -21 II -9	I -26 II -4		Non significant
Sex (M/F)	M-19 F-11	M-19 F-11	M-18 F-12		Non significant

Outcome variable	Group B	Group D	Group M	P-Value	
Time to reach T10 dermatome(min)	4.40 ±1.61	3.60+0.89	5.1 ± 1.06	<0.01	
Peak block height	T4	0	4	2	<0.01
	T5	0	11	10	
	T6	6	13	15	
	T7	8	2	1	
	T8	16	0	2	
Time to reach Peak block height (min)	7.33 ± 0.80	9.13+2.80	9.80 ± 1.97	<0.01	
Duration of sensory block at T10(mini)	138.0± 9.70	246.33+10.35	208.66±13.26	<0.01	
Two segment regression time (mini)	84.16+9.19	177.40±5.99	139.40± 4.03	<0.01	
Time to reach VAS -4 (mini)	153.66±27.88	316.60±22.10	290.50±19.53	<0.01	

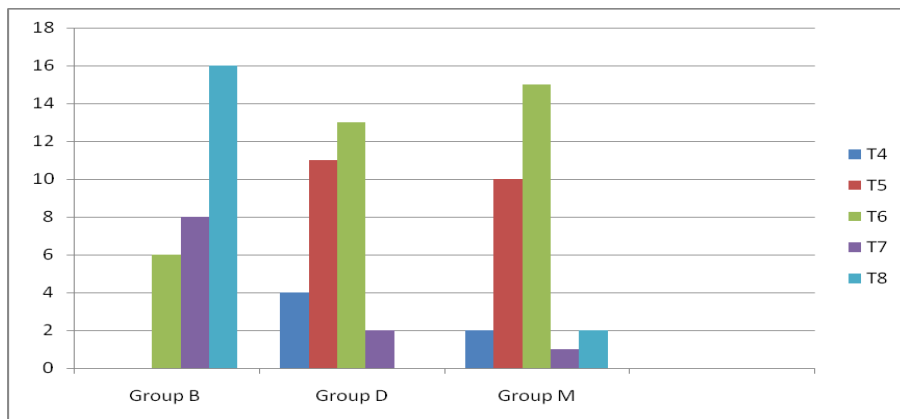


Figure 1. Comparison of Peak Block Height among the groups

The mean time for transition from Bromage-0 to Bromage-3 stage was 6.56 (± 0.72), 5.6 (± 1.49), 6.73 (± 0.82) minutes for group-B,D and M respectively, which was statistically significantly different. Similarly, the mean time for transition from Bromage 3 to Bromage 0 was 156.5 (± 15.71), 283.9 (± 11.7) and 245.7 (± 8.8) minutes for group-B,D and M respectively, which was also significantly different. Figure-2 shows the mean heart rates of each group at 5 minute intervals and figure-3 shows the systolic blood pressure changes over the same period.

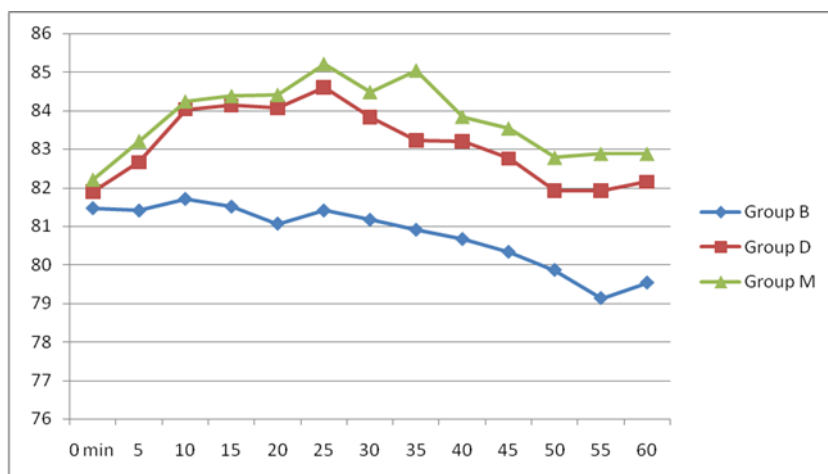


Figure 2. Mean Heart rate of the groups

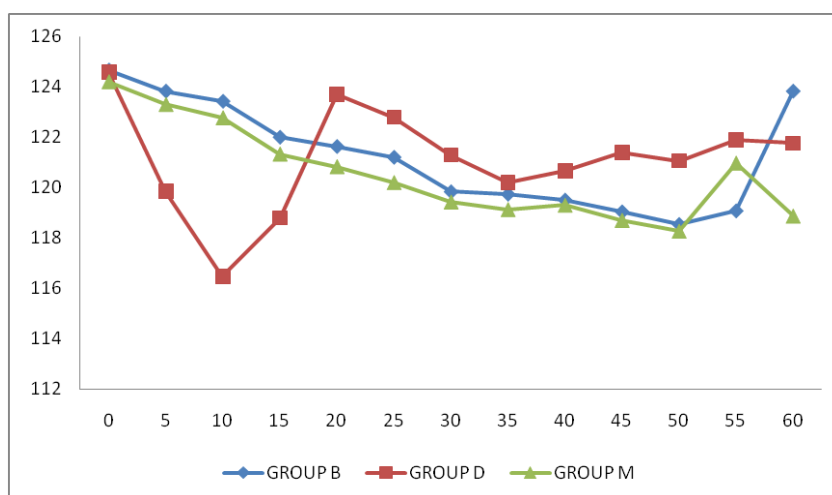


Figure 3. Systolic Blood Pressure of the groups

While no cases across the three groups reported any headache, pruritis or low saturation levels (below 93%), the incidence of nausea/vomiting, tremors, hypotension and bradycardia was equal across the groups, reported in 1 patient from each group.

Discussion

This study to compare the effects of intrathecal dexmedetomidine and Magnesium Sulphate as adjuvants to hyperbaric Bupivacaine shows that the intrathecal administration of 15 mg of hyperbaric Bupivacaine with either Dexmedetomidine (10mcg) or Magnesium Sulphate (50mg) was well tolerated and an adequate level of sensory as well as motor block was achieved for lower extremity surgery in all patients in the three study groups. Bupivacaine with Dexmedetomidine (Group D) showed a faster onset and longer duration of sensory and motor block compared with Bupivacaine with Magnesium Sulphate (Group M). Also, the duration of

analgesia was prolonged in the dexmedetomidine Group compared to Magnesium sulphate. These results are partially in agreement with study results of other investigators who have reported a quicker onset of sensory & motor blockade in Dexmedetomidine as compared to magnesium. (11,15)

There was a significant delay in the time to the first rescue analgesia in group receiving intrathecal dexmedetomidine when compared to magnesium & the mean total dose and times of use of analgesics were also reduced in group with reduction in dexmedetomidine group significantly more than magnesium group. Similar findings are observed by Gupta et al. Al-mustafa et al. (10,12). In our study, it was observed that addition of dexmedetomidine and magnesium both prolonged the duration of sensory as well as motor block when added to bupivacaine intrathecally, but prolongation was more in dexmedetomidine group as compared to magnesium group which was statistically significant. This result showed a similar trend as observed by Shukla et al., which showed the regression time of block both sensory nerves up to T10 dermatome and motor to bromage 3, was prolonged in both groups.

Some studies from India have concluded that dexmedetomidine is a better adjuvant to Bupivacaine for epidural anaesthesia when compared to Nalbuphine as it provides earlier onset of sensory blockade, prolonged duration of sensory block and post operative analgesia with stable vitals and minimal side effects. (14) Others have compared Nalbuphine and Dexmedetomidine as an adjuvant to Ropivacaine for Caudal Block in children undergoing infra umbilical surgeries, and found that caudal Ropivacaine 0.2% with Dexmedetomidine 2 µg/kg resulted in prolongation of duration of analgesia and better quality of analgesia compared with Ropivacaine 0.2% with Nalbuphine 0.2mg/kg without any significant difference in the haemodynamic parameters or increase in the incidence of side effects in children undergoing infra umbilical surgeries. (16)

Conclusion

Addition of dexmedetomidine (10 mcg) prolonged the sensory & motor block significantly when used with the hyperbaric bupivacaine intrathecally, without increasing the incidence of significant adverse effects. Intrathecal magnesium also prolongs the duration of sensory and motor block regression, but lesser than dexmedetomidine group and is associated with a delayed onset. This kind of block may be more suitable for infraumbilical surgeries of longer duration conducted under spinal anaesthesia. Intrathecal dose of dexmedetomidine used in the present study needs further clinical studies to prove its efficacy and safety and to be considered as the suitable dose of dexmedetomidine for supplementation of spinal anaesthetics. Bupivacaine plus dexmedetomidine group is better than Bupivacaine plus magnesium sulphate group in respect of an earlier onset of sensory and motor block, prolonged duration of sensory and motor block, longer duration of postoperative analgesia and a lesser number of doses of rescue analgesia required.

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