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ORIGINAL ARTICLE

Comparative study of different doses of dexmedetomidine as an adjuvant to intrathecal hyperbaric bupivacaine in lower limb orthopedic surgeries

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ABSTRACT

Background and Aim: Spinal anesthesia is most preferred anesthesia for lower limb orthopedic procedures. The present study was designed to compare the effect of two different doses of dexmedetomidine to hyperbaric bupivacaine in spinal anesthesia for lower limb orthopedic surgeries to find out the suitable dose of dexmedetomidine.

Material and Methods: Seventy five patients of ASA I & II status were randomly divided into three groups of 25 patients each. The study drug was diluted to 0.5 ml of normal saline along with 2.5 ml hyperbaric bupivacaine. Group A received 5 µg dexmedetomidine, Group B received 10 µg dexmedetomidine and Group C (control group) patients received only 0.5 ml of normal saline along with 2.5 ml hyperbaric bupivacaine. Time for onset of analgesia (pin prick method), time to achieve T10 sensory level, onset of motor block, duration of analgesia and duration of motor block and frequency of any complications were noted.

Results: Time for onset of analgesia in Group C was 3.18 ± 0.30 min but in Group A was 2.33 ± 0.14 min and in Group B was 2.24 ± 0.06 min. Duration of motor block was significantly higher in study group; 279.36 ± 14.54 min and 344.21 ± 9.19 min in Group A and B respectively, whereas it was 169.39 ± 6.96 min in control group. Duration of analgesia was also significantly higher in study Group A (342.62 ± 13.06 min) and in Group B (398.24 ± 12.31 min) compared to control group which was 204.95 ± 8.54 min.

Conclusion: 10 µg dexmedetomidine is preferred adjuvant to hyperbaric bupivacaine in spinal anesthesia with early onset of analgesia and motor block, longer duration of motor and sensory block with hemodynamic stability and minimum side effects.

Key words: Bupivacaine; Dexmedetomidine; Motor block; Spinal anesthesia

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INTRODUCTION

Pain is inevitable to all surgeries causing significant postoperative morbidity. Perioperative pain management is a major challenge for anesthesiologist. Attenuation of the postoperative pain may decrease perioperative morbidity and mortality.[1] By optimizing postoperative analgesia, we can reduce postoperative complications and facilitate recovery during immediate postoperative period and early discharge of the patients.

Spinal anesthesia is the preferred technique for lower abdominal, perineal and lower limb surgeries due to its rapid onset of action, less failure rate and superior level of blockage.[2] Relatively short duration of action of local anesthetic injected intrathecally needs early analgesic intervention in postoperative period or use of intrathecal adjuvant to local anesthetic.[3]

Many drugs like fentanyl, midazolam,[4] neostigmine, ketamine, clonidine, have been used as an additive to local anesthetic in spinal anesthesia to prolong the duration of action and to provide adequate postoperative analgesia. Fentanyl is commonly used opioid to prolong the effect of bupivacaine. But it's use is associated with side effects like pruritus, nausea, vomiting, constipation and respiratory depression.[5-7] Neostigmine an anticholinesterase is also useful for prolonging the duration of action of bupivacaine but it is also associated with side effects like vomiting and bradycardia.[8] Clonidine, an alpha-2 agonist is also used as an adjuvant to local anesthetic but it is associated with side effects like hypotension and bradycardia.[9,10] Most clinical studies about intrathecal α2 adrenergic agonist are related to clonidine. The literature on intrathecal use of dexmedetomidine is relatively scarce.

Dexmedetomidine, highly selective α2 adrenergic agonist was approved by FDA in 1999, for use in humans as a short term medication for sedation and analgesia in ICU. It has hypnotic, sedative, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression.[11-12] It acts by inhibiting release of norepinephrine in locus ceruleus .It produces anti-nociceptive action for both somatic and visceral pain. It has 10 fold greater affinity to α2 adrenergic receptors than clonidine and lesser α1 effect which leads better analgesia with minimal side effects. It seems to be a useful adjuvant to intrathecal hyperbaric bupivacaine for prolonging sensory and motor block which provides adequate postoperative analgesia along with stable hemodynamics without respiratory depression.[13-15]

The aim of the study was to compare two different doses of dexmedetomidine 5 μg and 10 μg along with 2.5 ml hyperbaric bupivacaine intrathecally, for elective lower limb orthopedic surgeries. We studied the onset and duration of sensory and motor block, adequacy of analgesia and associated side effects if any.

METHODOLOGY

After approval from the institutional ethical committee a prospective, double blind, randomized study was conducted from July to December2018. Seventy Five patients of American Society of Anesthesiologist physical status I/ II, of either sex, aged between 18 to 60 years, presenting for lower limb orthopedic surgeries were taken for study. Patients having history of uncontrolled hypertension, cerebrovascular diseases, ischemic heart disease, arrhythmia, COPD, local skin site infection, previous spine surgeries, any kind of bleeding disorders, height <150 cm were excluded from the study. The patients were advised overnight fasting. Informed and written consent was taken from all the patients participating in study. Patients were explained about procedure and how to express degree of pain on visual analogue scale (VAS), 0-10 scale, (0=no pain, 10 = most severe pain). Study participants were selected randomly by using chit method in which a box was made having 3 chits of each groups with 1:1:1 ratio. Total 75 patients admitted for elective lower limb orthopedic surgery were recruited for the study. Patients were randomly assigned into Group A, Group B and Group C. Patients in Group A received 5 μg dexmedetomidine in 0.5 ml of distilled water with 2.5 ml of 0.5% hyperbaric bupivacaine. Patients in Group B received 10 μg dexmedetomidine in 0.5 ml of distilled water with 2.5 ml of 0.5% hyperbaric bupivacaine. Patients in Group C received 2.5 ml of 0.5% hyperbaric bupivacaine with 0.5 ml of distilled water. The preparation of the drugs was carried out by the anesthesiologist not involved in the study and both patient and the anesthesiologist collecting data were remained blind from the preparation of drug.

In the operating room all patients were monitored for ECG, NIBP and SpO_2. Baseline vitals were recorded. An intravenous line was established with 18/20G cannula and preloading with 10 ml/kg of Ringers lactate solution was done. Inj ranitidine 1 mg/kg and inj ondansetron 0.08 mg/kg was given intravenously as premedication. Ranitidine given is more effective than proton pump inhibitors in reducing volume of gastric secretion and increasing gastric pH. Ranitidine is useful to reduce the volume of gastric content and increase gastric pH Spinal anesthesia was given in sitting position under strict aseptic and antiseptic precaution with 25G spinal needle in L3-L4 or L2-L3 intervertebral space. Patients were given total volume of 3 ml of the drug of either study group. After intrathecal injection patients were placed in supine position. Vital signs (heart rate, blood pressure and SpO_2) were recorded at 2 min, 5 min, 10 min, 15 min and thereafter at every 15 min interval till the end of surgery and every 30 min for 2 hours in postoperative period. Sensory block was assessed by loss of pinprick sensation to 24G hypodermic needle till T10 level was established. Time for onset of analgesia and complete sensory block at T10 level were recorded. Motor block was assessed by modified Bromage scale. Time of complete motor blockade, defined as the time from intrathecal drug injection to time to attain modified Bromage scale 3 was recorded. Duration of motor block, defined as time interval from complete motor blockade to regain of motor activity (modified Bromage scale 0) was recorded.

Assessment of analgesia was done by Visual Analogue Scale (VAS), 0 to 10 cm score (0=no pain, 10 = most severe pain) on marked paper strip intraoperatively every 15 min and postoperatively every half hourly till first rescue analgesic was needed. Rescue analgesic was given if VAS was more than 3. Time of giving

Table 3: Characteristics of motor and sensory block (min)

Observation	Group A	Group B	Group C	p-value		
				C&A	C&B	A&B
Time for onset of analgesia	2.33 ± 0.14	2.24 ± 0.06	3.18 ± 0.30	0.001*	0.002*	0.20
Time for complete sensory block	5.32 ± 0.13	5.23 ± 0.06	7.45 ± 0.15	0.05*	0.001*	0.02*
Time for complete motor block	6.38 ± 0.09	6.24 ± 0.05	9.11 ± 0.40	0.001*	0.01*	0.11
Duration of motor block	279.36 ± 14.54	344.21 ± 9.19	169.39 ± 6.96	0.03*	0.01*	0.04*
Duration of analgesia	342.62 ± 13.06	398.24 ± 12.3	204.95 ± 8.54	0.01*	0.001*	0.02*

** indicates statistically significance at p ≤ 0.05 Test applied one way ANOVA*

first rescue analgesic was noted. Intravenous infusion of 1.5 mg/kg diclofenac was given if VAS > 3. It was repeated after 8 hours. The incidence of side effects like hypotension, bradycardia, nausea, vomiting, sedation, respiratory depression was recorded. Bradycardia (HR < 50 beats / min) was treated with intravenous atropine 0.6 mg. Hypotension (SBP < 20% of baseline value or < 90 mmHg)was treated with additional Ringer's lactate solution IV or injection mephentermine 6 mg. Inj ondansetron was given to treat intraoperative nausea-vomiting. Respiratory depression (RR<10 bpm) was noted and treated with oxygen supplementation and respiratory support if needed.

Statistical analysis:

Data were analyzed using open EPI info software. Considering mean onset time of motor block and standard deviation of previous study, calculated sample size at 95% confidence interval and 80% power(α=0.05 and β=0.8)was 25 in each group. Results were expressed as mean and standard deviation (SD) or number or percentage. Analysis of data between groups were performed using one way analysis of variance (ANOVA) followed by Tukey's multiple post-hoc test. The p value<0.05 was considered statistically significant and p < 0.001 was considered highly significant.

RESULTS

A total of 75 patients were enrolled in our study. All three groups of our study were comparable with respect to age, sex, body weight and ASA physical status as shown in Table 1. Hemodynamic parameters (heart rate, blood pressure and SpO_2) were comparable among all three groups at all time intervals as per Table 2 and Figures 1 and 2.

Onset of analgesia was earlier in Group B than Group A but both Group A and Group B had earlier onset of analgesia than Group C which was statistically highly significant (p = 0.000) as per Table 3. There was statistically highly significant difference in Group A and B as compared to Group C for time to achieve maximum sensory level T10 (Table 3). Time to achieve complete motor block was highly significantly higher (p = 0.000) in Group C than Group A and Group B. Duration of motor block was also statistically highly significant in all 3 groups (p = 0.000). Duration of analgesia was the longest in Group B (398.24 ± 12.31 min), than Group A (343.62 ± 13.06 min) and Group C (204.95 ± 8.41 min). There was highly significant difference in duration of analgesia between 3 groups (p = 0.000). Table 4 shows the incidence of perioperative adverse effects. All 3 groups were comparable with respect to side effects. Group B had

Table 1: Comparativr demographic data

Variable	Group A	Group B	Group C	p-value		
				C&A	C&B	A&B
Age(years)	38.44 ± 11.20	42.6 ± 7.5	40.8 ± 6.5	>0.05	>0.05	>0.05
Gender(M/F)	20/5	18/7	17/8	>0.05	>0.05	>0.05
Weight(Kg)	54.55 ± 8.20	55.7 ± 7.10	53.68 ± 7.82	>0.05	>0.05	>0.05
ASA I/II	21/4	19/6	20/5	>0.05	>0.05	>0.05

Table 2: Comparativr baseline vital signs

Parameter	Group A	Group B	Group C	p-value		
				C&A	C&B	A&B
HR (/min)	83.1 ± 4.24	82.9 ± 4.17	83.6 ± 3.80	>0.05	>0.05	>0.05
MAP (mmHg)	93.3 ± 2.89	93.8 ± 2.50	94.2 ± 2.13	>0.05	>0.05	>0.05
SpO_2 (%)	99.0 ± 0.00	99.0 ± 0.00	99.0 ± 0.00	>0.05	>0.05	>0.05

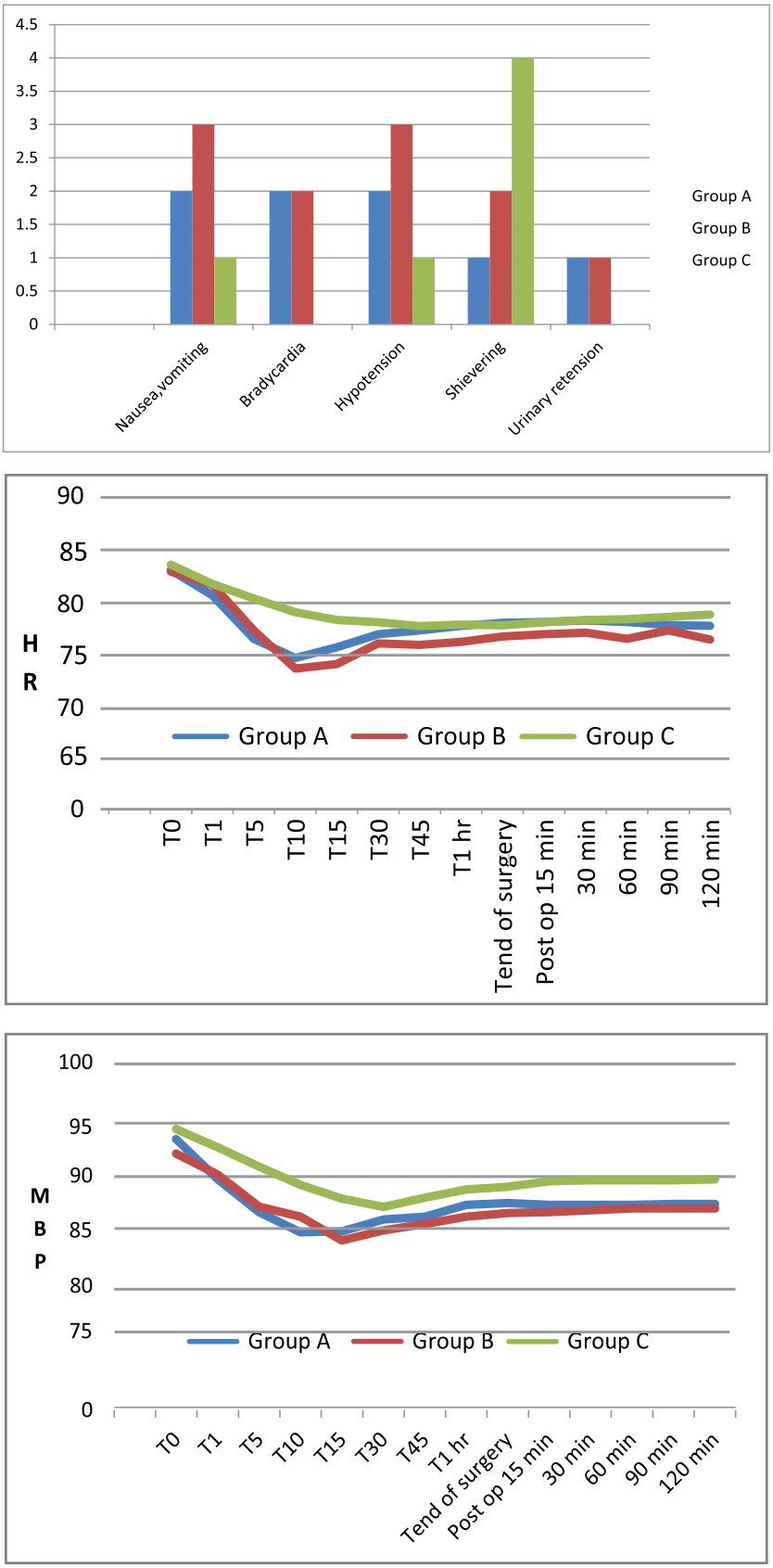

Figure 1: Adverse effects in three groups

more incidence of hypotension, nausea, vomiting but it was not significant statistically ($p > 0.05$).

DISCUSSION

To prolong the effect of spinal anesthesia additive drugs have been used with local anesthetic drug.[3] Dexmedetomidine is one of them. It is a specific and selective α2 adrenergic agonist and was approved by FDA in 1999 for use in humans for sedation and analgesia in the ICU.[11-12] Dexmedetomidine acts by binding to pre-synaptic C-fibers and post-synaptic dorsal horn neurons. Its analgesic action is a result of depression of the release of C-fiber transmitters and hyperpolarization of post-synaptic dorsal horn neurons. Prolongation of motor block might be caused by direct impairment of excitatory amino acids release from spinal interneurons.[13-15]

Intraoperative administration of dexmedetomidine in lower concentrations has reduced the requirement of other anesthetic agents; fewer interventions to treat tachycardia; and a reduction in the incidence of myocardial ischemia. It is an excellent sedative and analgesic agent, with opioid-sparing properties and minimal respiratory depression; does not decrease gut motility; prevents postoperative nausea, vomiting and shivering; and, at the same time, offers potential benefit towards neuroprotection, cardioprotection and renoprotection Kanazi et al. used a small dose of dexmedetomidine (3 μg) with bupivacaine intrathecally in humans.[16] Shagufta Naaz and colleagues used four different doses of dexmedetomidine like 5, 10, 15 and 20 μg in comparison to placebo as an adjuvant to hyperbaric bupivacaine and found that dexmedetomidine enhances the onset and prolongs duration of sensory and motor block in a dose dependent manner, but with higher doses like 15 and 20 μg there

was higher incidence of side effects like hypotension and bradycardia.[17] Safiya Shaikh and colleagues used 5 μg and 10 μg dexmedetomidine with placebo as an adjuvant to hyperbaric bupivacaine and found that 10 μg dexmedetomidine was a better adjuvant with hyperbaric bupivacaine.[18] In our study we have used similar dose of dexmedetomidine as an adjuvant to intrathecal hyperbaric bupivacaine.

Demographic data were comparable in all three groups of our study which was similar to other studies.[17-19]

A study by Shukla D. and colleagues concluded that there was no significant difference in mean HR and mean MAP between dexmedetomidine and control group.[20] In our study results of mean HR and mean MAP at baseline, intraoperative and postoperative time were comparable between all three groups.

Onset of sensory block, time to achieve T10 sensory level and time to achieve complete motor block were significantly earlier in Group A and Group B than control group. Onset was the earliest in Group B. Our results were similar to those of other researchers.[18,19,21] Similar to our results, some other researchers showed significantly earlier onset of peak sensory block and time to reach Bromage 3 level motor block.[20,22]

Duration of analgesia and motor blockage were prolonged significantly in Group A and Group B than Group C. Duration was earliest in Group B. Our results were similar with various studies in which the researchers found that dexmedetomidine had a dose dependent effect on the regression of sensory and motor block when used as an adjuvant to intrathecal bupivacaine.[23-26] Hala EA Eid and colleagues used 10 and 15 μg dexmedetomidine in spinal anesthesia with 3 ml hyperbaric bupivacaine and found significantly prolonged anesthetic and analgesic effect using higher dose. Their results were similar to that of our study.[27]

Bradycardia, hypotension and nausea, vomiting associated with hypotension occurred due to increased vagal activity after sympathetic block causes increased peristalsis of gastro-intestinal tract. Dexmedetomidine causes activation of central postsynaptic α2 adrenoreceptor resulting in sympatholytic effects leading to bradycardia and hypotension. Shivering developed in 1, 2 and 4 patients in groups. Previous studies showed that dexmedetomidine has anti shivering property.[28] There was no significant differences between study groups regarding side effects.

LIMITATIONS

In our study we included only healthy patients of ASA I and II status. Effect of intrathecal dexmedetomidine in patients of ASA III and IV and those having comorbidities is yet to be studied.

CONCLUSION

Dexmedetomidine, when added to intrathecal hyperbaric bupivacaine, significantly enhances the onset of sensory and motor block, duration of motor block and duration of analgesia. 10 μg dexmedetomidine is preferred than 5 μg as it provides prolonged sensory and motor blockade with hemodynamic stability and minimal side effects. However, hypotension and bradycardia are the most significant side effects. It appears to have minimal respiratory depression and, thus, it can be used safely in both mechanically ventilated and spontaneously breathing patients. It can replace epidural or general anesthesia for long duration surgeries.

Conflict of interest: None

Authors' contribution:

SH: concept, study design, manuscript drafting

DP: data collection, statistical analysis

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