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Comparison of intrathecal dexmedetomidine and intrathecal fentanyl as an adjuvant to bupivacaine during spinal anaesthesia for lower limb orthopedic surgery

Dipty Agrawal[1], Niyati Sinha[2], Shiv Kumar Singh[3]

[1,2]Assistant Professor, [3]Professor and Head, Department of Anaesthesia, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India

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ABSTRACT

Background: In this study, we have compared the addition of fentanyl 25 mcg and dexmedetomidine 5 mcg to 15 mg of 0.5% hyperbaric bupivacaine for spinal anesthesia separately for patient undergoing lower limb orthopedic surgery. Dexmedetomidine is an α-2 adrenoreceptor agonist and it can prolong the motor and sensory block for long spinal anesthesia. It act by binding to presynaptic C-fiber and postsynaptic dorsal horn neurons. The analgesic action is a result of depression of release of C-fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons. **Aims and Objectives:** The present study compares the onset, duration of sensory and motor block, postoperative analgesia, hemodynamic changes, and adverse effects of intrathecal dexmedetomidine and intrathecal fentanyl as an adjuvant to bupivacaine during spinal anesthesia for lower limb orthopedic surgery. **Materials and Methods:** Patient was randomly grouped by close-envelope technique into the three equal group of 30 in each group. Total 90 patients were including in this study. The blind nature of the study was maintained and the study drug is given according as, Group-1: 15 mg of 0.5% hyperbaric bupivacaine. (Control group), Group-2: 15 mg of 0.5% hyperbaric bupivacaine with 25 mcg of fentanyl, and Group-3: 15 mg of 0.5% hyperbaric bupivacaine with 5 mcg dexmedetomidine for spinal anesthesia. **Results:** Patients in dexmedetomidine Group-3 had a significantly longer sensory (160 ± 18.5 min) and motor block (242 ± 22 min) time as compared to patients in fentanyl and control group ($P < 0.001$). The time to first request of analgesic in the post-operative period was also longer in dexmedetomidine group (245 ± 3.6 min) when compared to bupivacaine and fentanyl in which it was 125 ± 1.0 min and 220 ± 2.5 min, respectively ($P < 0.001$). **Conclusion:** We concluded that intrathecal dexmedetomidine with bupivacaine for spinal anesthesia is associated with prolong motor and sensory block then fentanyl 25 μg with bupivacaine and bupivacaine alone.

Key words: Dexmedetomidine; Fentanyl; Bupivacaine; Spinal anesthesia

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INTRODUCTION

Spinal anesthesia is the most commonly used technique for lower limb orthopedic surgery as it is very economical and easy to administer. However, post-operative pain control is a major problem because spinal anesthesia using only local anesthesia is associated with relatively short duration of action, and early analysis intervention is needed in the postoperative period. A number of adjuvants such as midazolam and clonidine and other have been studied to prolong the effect of spinal anaesthesia.[1,2] A common problem during lower limbs surgery under spinal anesthesia is visceral pain, nausea and vomiting.[3] The addition of dexmedetomidine and fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early post-operative spinal block.[4] The addition of opioids to local

Address for Correspondence:
Dr. Dipty Agrawal, Assistant Professor, Department of Anaesthesia, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India. **Mobile:** +91-9910179925. **E-mail:** drjugalkishore@gmail.com

anesthetic solution has disadvantage such as vomiting and respiratory depression. Dexmedetomidine a newly highly selective α-2 agonist is under evolution as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative, and prolong post-operative analgesia with minimal side effects.[5,6] It has been approved by food and drug administrations a short-term sedative for mechanically ventilated intensive care init patients. Based on earlier human studies, it is hypothesized that spinal anesthesia with 5 mcg dexmedetomidine would produce more post-operative analgesic effect with hyperbaric bupivacaine with minimal side effect[5,6] It acts on the alpha 2 receptors on the dorsal horn cells and reduce the sympathetic neurotransmitter release. The duration of motor block may be increased when it binds to the motor neurons in the spinal cord.[7] In our study, we have evaluated the effect of adding dexmedetomidine and fentanyl to hyperbaric bupivacaine separately for spinal anesthesia.

Aims and objectives

1. To assess efficacy and safety of intrathecal dexmedetomidine and fentanyl as an adjuvant to bupivacaine for the lower limb surgery.
2. To compare post-operative analgesia and complication of intrathecal dexmedetomidine and fentanyl as an adjuvant to bupivacaine.
3. To assess the duration of analgesia and time of rescue analgesia for intrathecal dexmedetomidine and fentanyl as an adjuvant to bupivacaine.

MATERIALS AND METHODS

The study was conducted in Rama Medical College Hospital and Research Centre, Hapur, after approval of ethical committee of the institution. Written and informed consent was obtained from all patients. Total 90 patients male and female who were in the age group between 20 and 60 years belonging to the American Society of Anaesthesiologists (ASA) Class I and II scheduled for lower limb orthopedic surgery under spinal anesthesia were enrolled.

Exclusion criteria

Patients with contraindication to the spinal anesthesia as ischemic heart disease, heart blocks, hypertension, renal disorder, liver disorder, and pregnant patient were excluded from the study. The anesthesia technique, the visual analog scale (VAS) scale for pain, and other relevant things were explained to the patients in the pre-operative room and in the operation theatre. A18 Gauge intravenous cannula was inserted in the hand and preloaded with 10 mL per kg Ringer lactate solution. Electrocardiogram pulse oximeter and non-invasive arterial pressure monitor were applied. Patients were randomly grouped by close envelope technique into the three equal group of 30 in each group. The blind nature of the study was maintained and the study drug is given according as below.

Group 1: 15 mg of 0.5% hyperbaric bupivacaine. Group 2:15 mg of 0.5% hyperbaric bupivacaine with 25 microgram of fentanyl for spinal anesthesia. Group 3: 15 mg of 0.5% hyperbaric bupivacaine with 5 mg intrathecal dexmedetomidine for spinal anesthesia. Lumbar puncture was done under aseptic precaution in the sitting position. First skin was anaesthetized with local anesthetics and then a 25 G Quincke type spinal needle was inserted at L3-l4 space. The study drug was injected after confirming free flow of cerebrospinal fluids. After the procedure, the subjects were placed in the supine position. Oxygen @ 5 L/min by face mask was given to all the patient. After the surgery, all the patients were taken to the post-operative room where the patient was monitored and later on discharged to the ward after spinal block effect faded up to level S1. The demographic data of the patient's age in years, sex, weight, height, and ASA physical status were noted. Hemodynamic parameters, heart rate, and mean arterial blood pressure were recorded before the spinal anesthesia. After spinal anesthesia, the heart rate and mean arterial blood pressure were measured every 5 min for the first 20 min and then every 10 min intraoperatively till the patient is shifted from the recovery room. Hypotension was said to have occurred when systolic blood pressure decreased by more than 20% from baseline measurement or a fall below 90 mmHg. It was treated with bolus intravenous fusion of normal saline 300 mL. Bradycardia was said to have occurred if heart rate <50 beats/min. It was treated with 0.6 mg of intravenous atropine. Total number of patient who required atropine or vasopressure in the intraoperative period were recorded. Sensory block level was tested by pinprick test every min for the first 10 min or until T10 level was obtained. Time for regression of sensory blockage to S1 level was recorded. The motor block was assessed and recorded using modified Bromage (MB) Scale score 0, 1, 2, and 3 and time to reach MB score 3 was recorded.

MB Score 0=the subject is able to move the hip, knee and the ankle, MB Score 1=the subject is unable to move the hip, but not knee and ankle.

MB Score 2=the subject is unable to move the hip and knee, but not ankle. MB Score 3=the subject is unable to move the hip, knee, and ankle. Time to regress of motor blockage to MB score 0 was assessed and recorded in the post-operative period.

The post-operative pain scores were recorded for 24 h at 1, 6, 12, 18, and 24 h using VAS. The time to the first

request for analgesia was recorded. For statistical analysis, SSPS 21.0 software was used. Data were given as means and standard deviation medians and range. Chi-square and Fisher exact tests were used for categorical data like (sex, ASA class, nausea/vomiting, analgesia, hypotension and bradycardia). ANOVA test was used for continuous data. P<0.05 is taken as significant in the limit of 95% confidence interval.

RESULTS

There was no significant difference with respect to the patient's demographic data, ASA status, and duration of surgery among the three groups (Table 1). Among the spinal block characteristics, the time to regress sensory block a level of S1 was longer in Group 3 when compare with the Group 1 and Group 2 which is strictly highly significant (<0.001) (Table 2). The time of the motor block regression to MB 0 was significantly longer in Group 3 when compares with Group 1 and Group 2. Time to the first request for analgesia was longer in Group 3 then Group 1 and 2 which is strictly highly significant (P<0.001) There was no significant difference in variation of heart rate of patient in all three group observed. With regards to intraoperative mean blood pressure, respective study groups showed no significant difference. Hence, hemodynamic parameters were stable in all the groups and there was no complication in any patient among the three group (Table 3). No statically significant difference was seen among the study groups in the number of patient who required atropine, diclofenac, and tramadol in 24 h. The VAS score was higher in Group 1 and 2, as compared to Group 3 at any time interval but which was statically non-significant (P<0.0712) (Table 4).

DISCUSSION

In this study, we have compared the intrathecal addition of 25 μg fentanyl and 5 μg dexmedetomidine to 15 mg of 0.5% hyperbaric bupivacaine for spinal anesthesia separately for patient undergoing lower limb orthopedic surgery. Dexmedetomidine is a highly selective α-2 adrenoreceptor agonist that prolongs the motor and sensory block for a spinal anesthesia. It acts by binding to presynapti C- fiber and postsynaptic dorsal horn neurons. The analgesic action is a result of depression of release of C-fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons.[5,8,9] The prolongation of effect may result from synergism between local anesthetic and alpha-2 adrenoreceptor agonist while the prolongation of motor

Table 1: Comparison of demographic and surgical duration

Variables	Group-1	Group-2	Group-3	P-value
Age	42.21±3.6	44.3±4.06	44.3±3.8	0.904
Sex (M/F)	19/11	21/9	20/10	0.936
Height	157±2	156±1.8	158±1.01	0.986
ASA grade I and II	20/10	21/9	18/12	0.931
Weight	19/11	64.4±1.3	65.23±1.01	0.952
Duration of surgery	165±20	175±10	170±15	0.005

Table 2: Spinal block characteristics of patients

Block characteristics	Group 1	Group 2	Group 3	P-value
Time to reach highest sensory level (min)	12.5±1.7	13.2±1.6	11.9±1.8	P<0.001
Sensory block time to regression to S1(min)	80±20.3	92±22.2	120±23.5	P<0.001
Total analgesic dose in first 24 h (drug % in mg)	210±65	174±70	84±60	P<0.001
Time to rescue analgesia (min)	135±18.9	170±22.22	255±29.69	P<0.001
Motor block- time to reach modified bromage 3 (min)	7±1.6	10±1.6	5±1.6	P>0.05
Motor block- regression to modified bromage 0 (min)	110±20.2	196±16.2	242±22	P<0.001
Time to first request of analgesic (min)	125±10	220±2.5	245±3.6	P<0.001

Table 3: Complications

Variables	Group-1	Group-2	Group-3	P-value
No complication	18	26	26	P>0.05
Hypotension	2	1	1	P>0.05
Bradycardia	1	0	1	P>0.05
Hypotension+bradycardia	5	3	2	P>0.05
Shivering	1	0	0	P>0.05
Nausea+vomiting	2	0	0	P>0.05
Pruritus	1	0	0	P>0.05
Total	30	30	30	

Table 4: Post-operative visual analog scale

Variables	Group-1	Group-2	Group-3	P-value
1 h	0	0	0	0
6 h	5	3	3	>0.05
12 h	5	5	3	>0.05
18 h	5	4	3	>0.05
24 h	5	4	2	>0.05

block of spinal anesthesia may result from the binding of alpha-2 adrenoreceptor agonist to motor neurones in the dorsal horn[10] Intrathecal alpha-2 receptor agonist has been found to have antinocioceptive action for both somatic and visceral pain[6] Fentanyl is a lipophilic mu receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opoid receptors in the dorsal horn of spinal cord and may have to a supraspinal spread and action.[11] In our study, patient demographic characteristics and the duration of surgery were comparable. There were no significant differences with respect to hemodynamic characters (heart rate and blood pressure) among the groups and there was also no significant side effect (sedition, hypotension, etc.). Kanazi et al.,[5] concluded that the 3 mcg dexmedetomidine when added to the intrathecal bupivacaine for spinal anesthesia resulted in rapid onset of motor block, prolongation of the duration of motor and sensory block, no hemodynamic derangements, and no sedation.

Similarly to our results, the study by Mahendru et al.,[12] showed that dexmedetomidine 5 mcg with 12.5 mg bupivacaine prolong the duration of motor and sensory block, preserved hemodynamic, and decreased post-operative analgesic requirement compared to clonidine 30 mcg, fentanyl 25 mcg, or 12.5 mg hyperbaric bupivacaine alone in patients undergoing lower limb surgery. In this study, addition of intrathecal 5 μg dexmedetomidine of 15 mg of 5% heavy bupivacaine for spinal anesthesia significant prolong the time for the spinal regression to S1 level when compared to the other groups. Our study showed that the motor regression to MB score 0 and time for request of first analgesia was significantly longer in dexmedetomidine group than other group.

Fukushima et al.,[13] administrated 2 μg/kg epidural dexmedetomidine for post-operative analgesia in humans but did not report neurological deficits. Our study has shown that the addition of 5 mcg dexmedetomidine with hyperbaric bupivacaine significantly prolongs both sensory and motor block. Both fentanyl and dexmedetomidine provided good quality intraoperative analgesia and hemodynamic stability. The analgesia was clinically better in Group 3 as compared to Group 1 and Group 2 but it was not statistically significant. Small dose of intrathecal dexmedetomidine used in combination with bupivacaine in human have been shown to shorten to onset of motor block with hemodynamic stability and lack of sedition.[5] Al-Ghanem et al., had studied the effect of addition of 5 μg dexmedetomidine or 25 μg fentanyl intrathecal to 10 mg isobaric bupivacaine in vaginal hysterectomy and concluded that 5 μg dexmedetomidine produce more prolonged motor and sensory block as compared to 25 μg fentanyl.[6] In our study too, the Group 3 we found longer duration of both sensory and motor blockade, stable hemodynamic condition, and good patient satisfaction. Al-Mustafa et al.,[14] studied effect of dexmedetomidine 5 and 10 μg with bupivacaine in urological procedures and found the duration of spinal anesthesia in a dose dependent manner. Similarly, Elnabtity and Ibrahim[15] compared the post-operative pain when intraperitoneal bupivacaine (0.025%) is administrative alone versus the addition of dexmedetomidine 1 μg/kg in 52 children undergoing laparoscopic appendectomy in a prospective and randomized trial. Post-operative VAS score was lower in the dexmedetomidine group at 2, 4, and 6 h compared with the plain bupivacaine group (mean=4,5,4,respectively) ($P<0.05$) but had more sedation scores at 0, 2, and 4 h ($P<0.05$) longer time to first rescue analgesia ($P<0.03$), lesser rescue analgesia consumption, shorter length of hospital stay, and higher patient satisfaction. They concluded that adding dexmedetomidine to intraperitoneal bupivacaine provides adequate post-operative analgesia in children undergoing laparoscopic appendectomy. The study results were accordance with our study.

It was observed that the addition of dexmedetomidine or fentanyl to bupivacaine was not associated with post-operative nausea and vomiting in the present. Bakhamees et al.,[16] 2007 in a similar study compared intraperitoneal installation of 50 mL of bupivacaine 0.25% (12 5 mg) + 1 μg/kg of dexmedetomidine the observed that the incidence of post-operative nausea and vomiting was comparable in both groups.[17] Similarly, in our study, the incidence of the PONV was insignificant. The present study finding suggests that both dexmedetomidine can be safely and effectively used as an adjuvant to intrathecal bupivacaine for the spinal anesthesia. Both drugs achieved a similar level of blockage and produce almost similar side effects profile. However, dexmedetomidine at a dose of 5 μg showed a better profile for duration of blockade and time to the requirement of post-operative rescue analgesia. Further the hemodynamic profile of patients receiving dexmedetomidine had a faster on-set of sensory action (11.9±1.8 min) which was statistically significant. Our finding is consistent with studies of those of Khosravi et al.,[18] and of Shukla et al.,[19] that also found a better onset of time for 5 μg dexmedetomidine.

In the present study, 5 μg intrathecal dexmedetomidine as an adjuvant has provided a prolong duration of analgesia

in the form of sensory blockade up to 265 min, reducing the need of rescue analgesics and polypharmacy in the post-operative period. Paramasivan et al.,[20] all in a systemic review and meta-analysis on the effect of intrathecal dexmedetomidine group was 363.6 min (range 252.3–824) compared to be placebo group. Gupta et al.,[21] reported increasing the dose of dexmedetomidine from 2.5 μg to 10 μg would show better and longer sensory and motor block with longer duration of anesthesia and comparable hemodynamic and side effect profile.

Limitations of the study

Sample size is very small for this study. So further studies on larger sample sizes needs to be done to reach a general conclusion.

CONCLUSION

Instillation of bupivacaine in combination with 5 μg intrathecal of dexmedetomidine or with 25 μg fentanyl significantly reduces post-operative pain score and provides longer duration of sensory and motor blockage. They also provide hemodynamically stable conditions with minimal side effect in comparison to bupivacaine alone in patients undergoing lower limb orthopedic surgery.

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Author's Contribution:
DA- Concept and design of the study and collection of data; **NS-** Collection of data and interpreted the result; **SKS-** Prepared first draft of manuscript and finalize the manuscript.

Work attributed to:
Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India.

Orcid ID:
Dr. Dipty Agrawal - https://orcid.org/0000-0003-0853-9388
Dr. Niyati Sinha - https://orcid.org/0009-0001-6831-1660
Dr. Shiv Kumar Singh - https://orcid.org/0009-0008-1789-7287

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