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A RANDOMIZED COMPARATIVE STUDY OF THREE DIFFERENT DOSES OF INTRATHECAL NALBUPHINE AS AN ADJUVANT TO 0.5% HYPERBARIC BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES UNDER SPINAL ANAESTHESIA

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ABSTRACT **Introduction:** Adjuvant drugs added to intrathecal agents improves the quality and duration of the sensory blockade and hence prolongs postoperative analgesia. Intrathecal opioids are synergistic with local anaesthetics, thereby intensifies the sensory block without increasing the sympathetic block. Nalbuphine has been used intrathecally as an adjuvant in previous studies, but none clearly stated the most effective dose of nalbuphine. The purpose of our study was to establish the effectiveness of intrathecal nalbuphine as an adjuvant, compare three different doses and determine the optimum dose with prolonged analgesic effect and minimal side-effects. **Materials and Methods:** In this prospective, randomized, double-blind, controlled trial, 90 ASA I and II patients undergoing lower limb orthopedic surgery under subarachnoid block (SAB), were randomly allocated to three groups: group A received 15 mg of 0.5% hyperbaric bupivacaine with 0.4 mg of nalbuphine, group B received 15 mg of 0.5% hyperbaric bupivacaine with 0.6 mg of nalbuphine and group C received 15 mg of 0.5% hyperbaric bupivacaine with 0.8 mg of nalbuphine. The primary outcome was the duration of post operative analgesia, while secondary outcomes included onset, duration of sensory and motor block and side effects. **Results:** The onset time of the sensory block was 3.7 ± 1.2 minutes, 3.3 ± 1.5 minutes, and 3.0 ± 1.0 minutes in groups A, B and C respectively. The onset time of the motor block was 8.3 ± 1.0 minutes, 8.2 ± 1.1, and 8.1 ± 1.0 minutes in groups A, B and C respectively. The onset of sensory and motor block was comparable among the three groups but statistically insignificant ($p > 0.05$). Mean duration of post operative analgesia was 326.83± 16.00, 379.67± 10.74 and 387.33± 13.69 minutes in group A, B and C respectively which was statistically significant ($p<0.001$). **Conclusion:** Intrathecal nalbuphine is a useful adjuvant in SAB and in a dose of 0.8 mg prolongs the duration of postoperative analgesia without increasing the side-effects.

KEYWORDS : Intrathecal Nalbuphine, Three different doses, Lower limb orthopaedic procedure.

INTRODUCTION

Subarachnoid block is the commonest anaesthesia technique used for below umbilical surgeries. It allows the patient to remain awake and minimizes or completely avoids the problems associated with airway management. The technique is simple, easy to perform, economical and also provides postoperative analgesia. Intrathecal opioids are used as adjuvants to local anaesthetics because of its synergistic effect with local anaesthetics thereby intensifying the sensory block and also prolong postoperative analgesia without increasing sympathetic block.[1],[2]

Nalbuphine is a synthetic highly lipid soluble opioid which posses an agonist action at the κ-opioid receptor and antagonist action at the μ-opioid receptor to provide reasonably potent analgesia.[3] It is used in almost all types of general and regional anesthetic techniques. Nalbuphine binds to kappa receptors distributed in the spinal cord and brain to produce analgesia. When used as an adjuvant to hyperbaric bupivacaine, it also improves the quality of perioperative analgesia with fewer side effects.[4],[5]

Systemic Nalbuphine has a lesser incidence of respiratory depression and other adverse effects because of its μ-opioid receptor antagonistic activity as compared to Morphine.[6],[7],[8]

This study was designed to evaluate three different intrathecal dosages of nalbuphine on subarachnoid characteristics of 0.5% hyperbaric bupivacaine. The primary outcome was the duration of post operative analgesia, while secondary outcomes included onset, duration of sensory and motor block and side effects.

METHODS

This prospective, randomized, double-blind, controlled trial was conducted in a tertiary care hospital after clearance from institutional ethical committee and written informed consent obtained from patients involved in the study between November 2018–April 2020. 90 patients between 20 and 60 years of age belonging to American society of anaesthesiologists (ASA) physical class I and II posted for lower limb orthopaedic procedure under spinal anaesthesia were included in the study. Patients with cardiovascular or cerebrovascular disease, pulmonary disease, renal or hepatic disorder, deformities of the spinal column/cutaneous infection at the lumbar puncture site, bleeding/coagulation disorder and known hypersensitivity to local anaesthetics/opioids were excluded from the study.

All patients were randomized into three equal groups of 30 patients each by a computer-generated random number table. Group A received 15 mg of 0.5% hyperbaric bupivacaine with 0.4 mg of nalbuphine. Group B received 15 mg of 0.5% hyperbaric bupivacaine with 0.6 mg of nalbuphine. Group C received 15 mg of 0.5% hyperbaric bupivacaine with 0.8 mg of nalbuphine. To ensure double blindness of the study, total volume of the study drug solution was kept at 3.5 ml by adding normal saline. The study drug solution was prepared by the resident anesthesiologist who was not involved in the study. Institution of subarachnoid block, intraoperative monitoring and postoperative follow up was done by a different anaesthesiologist who was also not involved in the study.

All participants underwent preanaesthetic evaluation on the day prior to surgery and were prescribed tablet Ranitidine 150 mg and tablet Alprazolam 0.25mg orally and six-hour fasting period.

On the day of surgery, all patients were connected to standard monitoring with non invasive blood pressure, electrocardiogram, and pulse oximetry.

After securing intravenous (IV) access, all patients were pre-hydrated with 10 ml/kg Ringer lactate solution 30 minutes before the initiation of SAB to replenish the fluid deficit.

Under strict aseptic precautions, Subarachnoid Block was performed using 25G Quincke's spinal needle at L3 – L4 intervertebral space with patient in left lateral position. 3.5 ml of study drug solution was injected over 15 seconds into the subarachnoid space. Immediately after the procedure, patients were turned to supine position and oxygen was supplemented at 4L/minute using venturi mask.

Sensory block was assessed by loss of sensation to cold temperature. The onset of sensory block, defined as time to reach sensory block to

T10, the time to reach highest dermatomal level of sensory blockade, time for two segments sensory regression was collected.

Motor block was assessed using Modified Bromage Scale (MBS). Onset of motor block was defined as the time taken to achieve MBS grade 2. Time taken to achieve complete motor blockade (MBS grade 4) and duration of motor blockade (MBS grade 2 to 0) was also collected.

MBS was used as follows. 0=Able to perform a full straight leg raise over the bed for 5 sec. 1=unable to perform a leg raise but can flex knee. 2=Unable to flex knee but can flex ankle. 3=Unable to flex ankle.4=Unable to move toes.

In cases of failure/partial Subarachnoid block, general anaesthesia was administered and such patients were excluded from the study.

Intraoperatively noninvasive blood pressure (NIBP), pulse rate, respiratory rate and oxygen saturation (SpO2) were recorded every minute for first 5 minutes, every 5 minutes for next half an hour and every 15 minutes till the completion of surgery. Postoperatively all patients were followed up every hour for the first 24 hours after surgery.

Hypotension (systolic blood pressure< 100 mmhg) was treated with bolus dose of 100 ml Ringer's Lactate (RL) and 6 mg injection Mephentermine given intravenously. Bradycardia (Heart rate <50 beats/minute) was treated with a bolus dose of intravenous injection Atropine 0.6 mg.

Postoperatively, the total duration of analgesia was noted from the time of intrathecal injection to the first requirement of rescue analgesic by the patient. Intravenous injection Paracetamol 1GM was administered as rescue analgesia (VAS>4). Incidence of other adverse effects such as nausea, vomiting, pruritis and respiratory depression were also noted and treated according to a clinical protocol.

All the statistical analysis was done using the Statistical Package for Social Sciences (SPSS) for Windows software (trial version 22.0; SPSS Inc, Chicago). The results are given as mean and standard deviation (SD) for continuous variables while frequencies and percentages are used for categorical variables. Data were compared using Student's t-test, Fisher's exact test, and chi square test. P-value < 0.05 was considered to indicate statistical significance.

RESULTS

A total of 90 patients were recruited and all patients completed the study. Thirty patients in each group were analyzed. The patient demographics with respect to age, sex, height, weight and ASA physical status were comparable between the three groups. All patients achieved adequate spinal block height above T6 at 5 minutes and the level of dermatomal height achieved was comparable between the three groups. There was no significant difference in the duration of surgery between the three groups. (Table 1)

Table 1. Duration Of Surgery

Variable	Group A	Group B	Group C	P value
Duration of surgery	104.9 ± 8.6	105.7 ± 10.8	106.4 ± 13.4	0.91

Mean values of heart rate, blood pressure, respiratory rate, blood oxygen saturation and visual analogue scale score were comparable between the study groups.

The onset time of the sensory block was 3.7 ± 1.2 minutes, 3.3 ± 1.5 minutes, and 3.0 ± 1.0 minutes in groups A, B and C respectively. The onset time of the motor block was 8.3 ± 1.0 minutes, 8.2 ± 1.1, and 8.1 ± 1.0 minutes in groups A, B and C respectively. The onset of sensory and motor blocks was comparable among the three groups but statistically insignificant (p > 0.05)

The time for two-segment regression was 110.4 ± 23.1, 137.2 ± 20.1 and 152.7 ± 21.9 in Group A, B and C respectively and found to be statistically significant among the three groups with p value < 0.001. Mean duration of post operative analgesia was 326.83± 16.00, 379.67± 10.74 and 387.33± 13.69 minutes in group A, B and C respectively which was statistically significant (p<0.001). However the total duration of motor block was comparable but statistically insignificant among the study groups. (Table 2, Chart 1)

Table 2: Characteristics Of Sensory And Motor Block.

Parameter	Group A	Group B	Group C	P value
Onset of sensory block (min)	3.7 ± 1.2	3.3 ± 1.5	3.0 ± 1.0	0.58
Onset of motor block (min)	8.3 ± 1.0	8.2 ± 1.1	8.1 ± 1.0	0.6
Time for two segment regression (min)	110.4 ± 23.1	137.2 ± 20.1	152.7 ± 21.9	<0.001
Mean duration of postoperative analgesia (minutes) (min)	326.83 ± 16.00	379.33 ± 10.74	387.33 ± 13.69	<0.001
Total duration of motor block (min)	126.6 ± 10.2	143.2 ± 13.6	153.6 ± 10.5	0.11

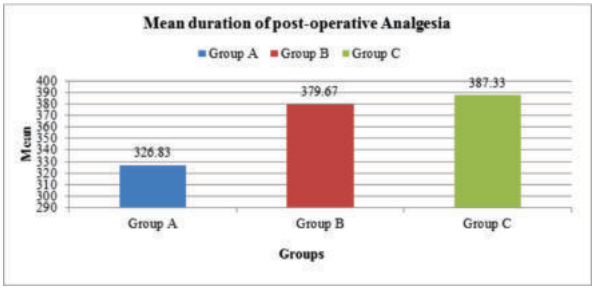

Chart 1: Mean Duration Of Postoperative Analgesia.

None of the study subjects experienced pruritis, sedation, nausea, vomiting and respiratory depression.

DISCUSSION

Spinal anaesthesia has been commonly used for lower abdomen and lower limb surgeries because of its simplicity, rapid onset, cost effectiveness and minimal exposure to depressant drugs.[9]

Good postoperative analgesia aims at long duration of continuous effective analgesia with minimum side effects. Adding adjuvant drugs such as Opioids, Benzodiazepines and Alpha 2 agonists to intrathecal local anaesthetics forms a reliable method to prolong the duration of postoperative analgesia. However intrathecal opioids can produce dose dependent side effects such as nausea, vomiting, pruritis and respiratory depression.[10]

Fournier R et al compared intrathecal morphine and nalbuphine in patients undergoing orthopaedic procedure. They concluded that morphine not only prolongs the duration of postoperative analgesia but also increases nausea, vomiting and pruritis significantly as compared to nalbuphine. Our study also not reported any side effects with the use of intrathecal nalbuphine. [9] The findings of our study were also supported by similar results found in Culebras X et al.[3]

Mukherjee A et al demonstrated the prolongation of postoperative analgesia with intrathecal nalbuphine without altering the duration of motor block. The results of our study also support the similar findings with increased mean duration of postoperative analgesia with minimal effects on motor block.[10]

Intrathecal nalbuphine was compared to fentanyl in a study by Bindra TK et al[11]. It was found that nalbuphine produced longer postoperative analgesia than fentanyl, while contradictory findings were demonstrated in a study done by Prabhakaraiah UN et al[12] with lower pain scores during postoperative period in fentanyl group as compared to nalbuphine group. However similar duration of postoperative analgesia was also reported in a study by Gomaa HM et al.[13].

Thus, there is an irreconcilable opinion between nalbuphine and fentanyl for duration of postoperative analgesia with a recent meta-analysis also showing no difference in duration of postoperative analgesia and block characteristics.[14]

The optimal dose of nalbuphine required for spinal anesthesia has been studied in various trials. Mukherjee A et al. compared doses of 0.2, 0.4, and 0.8 mg of intrathecal nalbuphine and concluded that a dose of 0.4 mg provides adequate analgesia without side effects.[10] But the results of our study demonstrated nalbuphine dose of 0.8 mg produced statistically significant longer duration of postoperative analgesia without any adverse effects. Borah TJ et al. studied doses of 0.4, 0.8, and 1.6 mg of intrathecal nalbuphine and found out that both 0.4 and

0.8 mg provide good quality analgesia, while a dose of 1.6 mg produced adverse effects like nausea, vomiting, bradycardia, and hypotension. [15] The findings of this study were similar to our study results and supports the dose of 0.8 mg intrathecal nalbuphine for prolongation of postoperative analgesia without any adverse effects.

Various studies of intrathecal nalbuphine have used doses ranging from 0.4 to 2.4 mg and most have shown peak analgesic effects with minimal side effects at doses from 0.8 to 1.6 mg.[14] Thus, our study findings also demonstrated nalbuphine dose 0.8 mg as optimal adjuvant dosage for intrathecal injection to prolong postoperative analgesia without any adverse effects.

Our results have shown that nalbuphine can be a useful adjuvant in spinal anesthesia in patients undergoing lower limb orthopaedic surgeries. It significantly prolonged the postoperative analgesia without increasing the duration of motor block or producing any adverse effects. In centers with limited resources, nalbuphine can substitute fentanyl as a valuable intrathecal adjuvant for prolongation of postoperative analgesia.

CONCLUSION

The study concluded that intrathecal nalbuphine in a dose of 0.8 mg is an effective adjuvant to 0.5% hyperbaric bupivacaine in SAB for lower limb orthopaedic procedure. Intrathecal nalbuphine potentiates the subarachnoid block characteristics and enhanced the duration of postoperative analgesia without increasing adverse effects.

REFERENCES

1. Bogra J, Arora N, Srivastava P: Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. BMC Anesthesiol. 2005, 5(1):5.
2. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med. 2008;33:159–67
3. Gupta K, Rastogi B, Gupta PK, Singh I, Bansal M, Tyagi V: Intrathecal nalbuphine versus intrathecal fentanyl as adjuvant to 0.5% hyperbaric bupivacaine for orthopedic surgery of lower limbs under subarachnoid block: a comparative evaluation. Indian J Pain. 2016, 30:90-5.
4. Schmauss C, Doherty C, Yaksh TL: The analgetic effects of an intrathecally administered partial opiate agonist, nalbuphine hydrochloride. Eur J Pharmacol. 1982, 86:1-7.
5. Gunion MW, Marchionne AM, Anderson TM: Use of the mixed agonist-antagonist nalbuphine in opioid based analgesia. Acute Pain. 2004, 6:29-39.
6. Penning JP, Samson B, Baxter AD: Reversal of epidural morphine-induced respiratory depression and pruritus with nalbuphine. Can J Anaesth. 1988, 35:599-604.
7. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA: Advantages of intrathecal nalbuphine, compared with intrathecal morphine, after cesarean delivery: an evaluation of postoperative analgesia and adverse effects. Anesth Analg. 2000, 91:601-5.
8. Tiwari AK, Tomar GS, Agrawal J: Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: a randomized prospective double-blind clinical study. Am J Ther. 2013, 20:592-5.
9. Fournier R, Van Gessel E, Macksay M, Gamulin Z: Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. Acta Anaesthesiol Scand. 2000, 44:940-5
10. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N: Intrathecal nalbuphine as an adjuvant to subarachnoid block: what is the most effective dose?. Anesth Essays Res. 2011, 5:171-5.
11. Bindra TK, Kumar P, Jindal G: Postoperative analgesia with intrathecal nalbuphine versus intrathecal fentanyl in cesarean section: a double-blind randomized comparative study. Anesth Essays Res. 2018, 12:561-5.
12. Prabhakaraiah UN, Narayanappa AB, Gurulingaswamy S, Kempegowda K, Vijaynagar KA, Hanumantharayappa NB, Ramegowda DS: "Comparison of nalbuphine hydrochloride and fentanyl as an adjuvant to bupivacaine for spinal anesthesia in lower abdominal surgeries:" a randomized, double-blind study. Anesth Essays Res. 2017, 11:859-63.
13. Gomaa HM, Mohamed NN, Zoheir HA, Ali MS: A comparison between post-operative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egypt J Anaesth. 2014 , 30:405-10.
14. Yu P, Zhang J, Wang J: Nalbuphine for spinal anesthesia: a systematic review and meta-analysis. Pain Pract. 2022, 22:91-106.
15. Borah TJ, Dey S, Yunus M, Dev P, Karim HM, Bhattacharyya P: Effect of different doses of intrathecal nalbuphine as adjuvant to ropivacaine in elective lower limb surgeries: a dose finding study. Indian J Anaesth. 2018, 62:865-70.