

Intrathecal Nalbuphine as an Adjuvant to Spinal Anaesthesia: What is Most Optimum Dose?

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Abstract

Background: To find out the most effective dose of nalbuphine as an adjuvant to spinal anesthesia. To compare the three different doses and find out most optimum dose of nalbuphine with minimal side effects and maximum analgesic effect.

Materials and Methods: We conducted prospective randomized double-blinded controlled study with 120 American Society of Anesthesiology I and II patients who were undergoing lower limb orthopedic surgery under spinal anesthesia. We randomly allocated four Groups A, B, and C to receive 0.4, 0.6, and 0.8 mg nalbuphine made up to 0.5 ml with distilled water, and Group D receive 0.5 ml of plain distilled water added to 2.5 ml of 0.5% hyperbaric bupivacaine (3 ml), respectively. The onset of sensory block and motor block, duration of surgery, duration of motor blockade and analgesia, visual analog scale score, vital parameters, and adverse effects compared between these groups.

Findings: No difference was noted in the onset of sensory and motor blockade among the four groups. Duration of two-segment regression time of sensory block, duration of motor blockade, and duration of analgesia time were prolonged in Groups B (0.6 mg) and C (0.8 mg) and found to be significant. The incidence of adverse effects was frequently higher in Group C ($P < 0.005$) compared to other groups.

Conclusion: Nalbuphine is effective adjuvant in spinal anesthesia, in a dose of 0.6 mg to prolong the duration of analgesia without increased adverse effects.

Key words: Hyperbaric bupivacaine, Nalbuphine, Spinal anesthesia

INTRODUCTION

Patients undergone orthopedic procedures have significant pain in post-operative period, if we used bupivacaine alone in spinal anesthesia. Hence, various adjuvants are used along with local anesthetics in neuraxial blockade to prolong the post-operative analgesia. Most commonly used adjuvants are opioids, alpha-2 adrenergic agonist, ketamine, midazolam, etc., but certain side effects such as pruritis, respiratory depression, nausea, vomiting, and urinary retention were observed with opioids.^{1,2} Hemodynamic changes also occur significantly in alpha-adrenergic agonists.

Nalbuphine is semi-synthetic opioid with mixed kappa agonist and μ antagonist properties.³ Nalbuphine bind to kappa receptors distributed in spinal cord and brain and produce analgesia. Nalbuphine bind to μ receptor helps to dispute to other μ agonist properties, so it produces very minimal side effects.^{4,5} Our study is aimed to find out the optimum dose of nalbuphine to produce significant prolongation in the duration of analgesia without adverse effects.

MATERIALS AND METHODS

Ethical Committee approval and written informed consent were obtained from all patients before going for study. About 120 patients of American Society of Anesthesiology (ASA) I and II, aged 20-60 years, both sexes posted for elective lower limb orthopedic surgery under spinal anesthesia included in the study. Patients were allocated randomly to four groups ($n = 30$). They received nalbuphine 0.4 mg (Group A), nalbuphine 0.6 mg

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(Group B), and nalbuphine 0.8 mg (Group C) made up to 0.5 ml with distilled water added to 2.5 ml (12.5 mg) 0.5% hyperbaric bupivacaine (total volume 3 ml) and plain 0.5 ml distilled water added to 2.5 ml (12.5 mg) 0.5% hyperbaric bupivacaine (total volume 3 ml) is Group D. This study was double-blind study. Patients with h/o allergy to bupivacaine or ASA III and IV, contraindication to spinal anesthesia, are excluded from the study.

All patients are secured with 18/20 G intravenous cannula. ECG, SPO₂, noninvasive blood pressure (BP) monitor attached before giving anesthesia. Patients preloaded with ringer lactate 15 ml/kg over 10 min. Under aseptic precaution, spinal anesthesia was performed in sitting position at L3-L4/L4-L5 space using 25 G quincke spinal needle. Then, the patient placed in supine position.

Onset of sensory block (time of injection to loss pin prick sensation), onset of motor block (time of injection to complete grade IV block), higher level of sensory block, duration of two-segment regression of sensory block (time of higher level of sensory block to two-segment regression time), duration of motor block (time required for grade IV block to grade I motor block in Bromage scale (6), duration of analgesia (time of injection subacromial bursa to visual analog scale [VAS] score >3 or first rescue analgesia requirement) were noted. Intraoperative sedation score by Ramsay sedation score observed. SPO₂, PR, and BP monitor at 0, 2, 5, 10, and 15 min and thereafter every 10 min to end point of the study were noted. Any adverse effects such as hypotension, bradycardia, nausea, vomiting, pruritis, and respiratory depression (SPO₂ <90%) or RR <10/min were noted. Post-operative sensory level, motor block was assessed every 30 min for first 2 h then everyone hour up to end of the study. Pain intensity assessed by VAS scale. All data are analyzed statistically by Student's *t*-test, one-way ANOVA and Fisher's test. $P < 0.005$ was considered statistically significant.

RESULTS

All groups were comparable in all demographic data such as age, sex, weight, sex ratio, and duration of surgery (Table 1); $P > 0.05$.

There was statistically insignificant ($P > 0.005$) in all four groups in the onset of sensory and onset of motor block (Table 2). The Higher sensory block was achieved by all groups was between T6 and T8. Two-segment regression time of sensory blockade was progressively prolonged in Groups A, B, and C compared to Group D (Table 2). Group C recorded with a mean of 190.4 min compared with 180.2 min in Group B, in Group A 152.4 min and

Group D 116.6 min. The duration of motor blockade also prolonged progressively in Groups A, B, and C compared to Group D (Table 2). Group C recorded with the longest duration of motor blockade with a mean of 220.5 min compared to Group B 202.4 min, Group A 188.12 min, and Group D 142.18 min (Table 2). The duration of analgesia was prolonged progressively in Group A, B, C compared to Group D (Table 2). Group C recorded with the longest duration of analgesia with a mean of 280.2 min compared to Group B 260.5 min, Group A 229.5 min, and Group D 168.2 min (Table 2).

The adverse effects of hypotension, bradycardia, pruritis, nausea, vomiting, and respiratory depression are more common in Group C compared to other groups (Table 3).

DISCUSSION

Intrathecal opioids used as adjuvants to neuraxial anesthesia for prolonged the duration of analgesia but intrathecal opioids have some disadvantages such as respiratory depression, pruritis, nausea, and vomiting.^{6,7} To overcome these adverse effects opioids with partial agonist-antagonist action have been studied extensively. Nalbuphine is semi-synthetic opioid having agonist activity at kappa receptors and antagonist activity at μ receptor.^{8,9} Analgesic action of nalbuphine produced by kappa receptor, it is present throughout the brain and spinal cord area of involved in nociception.³ Hence, nalbuphine acts primarily at the level of the first synapse in the nociceptive system in producing analgesia. There are few studies suggest that neuraxial administration of nalbuphine has minimal side effects such as respiratory depression, pruritis, nausea, vomiting, and significant prolonged duration of analgesia.¹⁰

Culebras *et al.* are first study used intrathecal nalbuphine for cesarean section patients. In this study, they compared morphine 0.2 mg added to hyperbaric bupivacaine with different dose of intrathecal nalbuphine 0.2, 0.8, and 1.6 mg added to hyperbaric bupivacaine and concluded that nalbuphine 0.8 mg have significant prolonged duration with minimal side effects, but nalbuphine 1.6 mg did not increase efficacy but increased incidence of adverse effects.¹¹

Fournier *et al.* compared between intrathecal nalbuphine 0.4 mg morphine 160 μ g in old patients undergoing THR. They concluded that nalbuphine produce faster onset of pain relieving but duration of analgesia shorter than morphine.¹⁰

Tiwari *et al.* had compared intrathecal nalbuphine 0.2 and 0.4 mg added to hyperbaric bupivacaine with bupivacaine alone. They concluded that prolonged duration of analgesia was seen in nalbuphine 0.4 mg without adverse effects.¹²

Table 1: Demographic data and duration of surgery (mean±SD)

Variable	n=30				P value
	Group A	Group B	Group C	Group D	
Age (years)	40.12±12.14	39.8±11.18	40.58±11.58	41.12±10.58	0.766
Weight (kg)	61.24±8.68	63.68±9.18	61.68±10.18	63.28±10.68	0.856
Gender (M:F)	22:8	20:10	21:9	19:11	0.949
Duration of surgery (min)	128±17.68	130±18.12	126±20.18	132±18.14	0.969

SD: Standard deviation

Table 2: Onset and duration of sensory and motor blockade (mean±SD)

Parameters (min)	n=30				P value
	Group A	Group B	Group C	Group D	
Onset of sensory block	2.67±0.22	2.61±0.24	2.48±0.20	3.04±0.52	0.079
Onset of motor block	5.9±0.66	5.8±0.76	5.6±0.56	6.02±0.58	0.389
Two-segment regression of sensory block	152.4±5.83	180.2±6.02	190.4±6.78	116.6±7.80	<0.001
Duration of motor block	188.12±16.12	202.4±16.18	220.5±18.16	142.18±22.68	<0.001
Duration of analgesia	229.5±18.88	260.5±14.88	280.2±22.52	168.2±16.64	<0.001

Table 3: Adverse effects

Groups	Hypotension	Bradycardia	Respiratory depression	Nausea vomiting	Pruritis
Group A	1	0	0	0	0
Group B	2	0	0	0	0
Group C	6	2	0	2	3
Group D	1	0	0	3	0

Mukherjee *et al.* had compared 100 patients undergoing orthopedic lower limb surgeries under spinal anesthesia. They used different doses of nalbuphine 0.2, 0.4, and 0.8 mg added to 0.5% bupivacaine and they concluded that 0.4 and 0.8 mg have significant prolong the duration of analgesia but adverse effect higher with 0.8 mg dose.

We had excluded the 0.2 mg group and 1.6 mg because 0.2 mg group does not show prolonged duration of analgesia and 1.6 mg have increased the adverse effect, and the duration of analgesia was slightly increased compared to 0.8mg. Hence, in this study, we compare nalbuphine 0.4, 0.6, and 0.8 mg added to 0.5% bupivacaine and 0.5% bupivacaine alone, to find out which is most optimum dose.

This study shows that duration of two-segment regression of sensory block, duration of motor block and duration of analgesia all are progressive increase in Group A, B, and C compared to control Group D (Table 2). Our study results are comparable with the previous studies such as Culebras *et al.*, Tiwari *et al.*, and Mukherjee *et al.*¹¹⁻¹³ Nalbuphine 0.6 mg (Group B) significant prolong duration of analgesia with minimal adverse effects ($P < 0.005$) than nalbuphine 0.8 mg (Group C), while nalbuphine 0.4 mg (Group A) have significant lesser duration of analgesia compared to Group B, C (Table 2). Nalbuphine 0, 8 mg (Group C) have prolonged duration of analgesia (Table 2) but increased

adverse effects (Table 3). As regarding neurotoxicity of intrathecal nalbuphine, it used modern day practice more than 10 years without neurotoxicity.¹⁴

CONCLUSION

We concluded that intrathecal nalbuphine 0.6 mg added to 0.5% hyperbaric bupivacaine for spinal anesthesia in patients undergoing lower limb orthopedic surgeries had prolonged duration of motor block and duration of analgesia without increased adverse effects. Hence, we conclude that 0.6 mg of nalbuphine is better adjuvant to bupivacaine in spinal anesthesia.

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