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A COMPARATIVE STUDY OF INTRATHECAL NALBUPHINE HYDROCHLORIDE WITH HYPERBARIC BUPIVACAINE 0.5% AND HYPERBARIC BUPIVACAINE 0.5% ALONE IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERY

Anaesthesiology

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ABSTRACT

Introduction: Spinal anesthesia is the most commonly used regional anesthesia technique today. It offers several advantages over general anesthesia. Intrathecal opioids are synergistic with local anesthetics and intensify the sensory block without increasing the sympathetic block. They are commonly added to local anesthetics for potentiating their effects, reducing their doses, and thereby reducing their complications and side effects and offer hemodynamic stability. Nalbuphine is a mixed agonist–antagonist opioid. It has a potential to attenuate the mu opioid effects and to enhance the kappa opioid effects.

Materials and Method: Randomized double blind study done on 120 patients undergoing lower abdominal surgeries under subarachnoid block. Patients were randomly allocated to two groups receiving either 17.5 mg of bupivacaine with 0.4ml of nalbuphine (0.8mg) in Group N or intrathecal 17.5 mg of bupivacaine +0.4 mL normal saline alone IN Group B.

Result: the onset of sensory and motor blockade, highest level of sensory blockade, duration of motor blockade and analgesia, VAS score, hemodynamic and respiratory changes, side effects were recorded, tabulated, and analyzed. Onset of sensory and motor blockade was faster in group N. The VAS scores showed that post-operative analgesia lasted significantly in patients in group N than in group B. No significant side effects were observed in either of the two groups.

Conclusion: Thus we conclude that intrathecal nalbuphine improved the quality of intraoperative and postoperative analgesia, with minimal side effects.

KEYWORDS

Hyperbaric Bupivacaine, nalbuphine hydrochloride

INTRODUCTION

Spinal anesthesia is the most commonly used regional anesthesia technique today. It offers several advantages over general anesthesia, like, reduced morbidity, ability to use fewer drugs, ease of technique, having an awake patient and above all, avoidance of complications related to general anesthesia.

Cocaine was the first spinal anesthetic used by August Bier and his assistant August Hildebrandt in 1898[1]. Procaine and tetracaine soon followed.[2] Spinal anesthesia performed with lidocaine, bupivacaine, tetracaine, mepivacaine, and ropivacaine has been successful. Among them bupivacaine is one of the most widely used agent and provides adequate anesthesia and analgesia for intermediate to long duration surgeries.[3]

There are several adjuvant drugs used to improve the quality and duration of spinal anesthesia; opioids such as morphine, fentanyl, sufentanil, hydromorphone, diamorphine and meperidine have been well studied, as are some non-opioid drugs such clonidine, ketamine etc.

Intrathecal opioids are synergistic with local anesthetics and intensify the sensory block without increasing the sympathetic block. They are commonly added to local anesthetics for potentiating their effects, reducing their doses, and thereby reducing their complications and side effects and offer hemodynamic stability. They also prolong the duration of postoperative analgesia.[4]

Nalbuphine, a mixed agonist–antagonist opioid[5].It has a potential to attenuate the mu opioid effects (respiratory depression, sedation, pruritus, nausea, vomiting and urinary retention) and to enhance the kappa opioid effects (sedation and spinal analgesia).

Intrathecal nalbuphine acts synergistically to potentiate bupivacaine induced sensory spinal block, which in terms reduced the analgesic requirement in the early postoperative period without prolonging motor block recovery.[6]

There are very few studies of intrathecal nalbuphine for postoperative analgesia. Hence, we have tried to study the effect of intrathecal nalbuphine for postoperative analgesia and its side effects. In this study we compare the duration and quality of post-operative analgesia and any side effects by the addition of intrathecal nalbuphine with bupivacaine compared with bupivacaine alone.

METHODS:

After the institutional ethical committee approval and written informed consent, 120 patients of either sex with physical status ASA grade I and II, aged 20 to 50 years, scheduled for elective lower abdominal surgeries under spinal anaesthesia were included in the study. Patient's refusal, emergency surgeries, coagulation abnormalities and bleeding disorders and patients with active skin lesions over the lumbosacral area were the exclusion criteria in the study.

The patients were randomly assigned into two groups including 60 patients in each group.

1. Group N(n=60) – Hyperbaric 0.5% Bupivacaine 3.5ml + 0.4ml(0.8 mg) of Nalbuphine (total volume 3.9 ml) was given.
2. Group B (n=60) - Hyperbaric 0.5% Bupivacaine 3.5ml + 0.4 ml of Normal saline (total volume 3.9 ml) was given.

All patients were thoroughly evaluated preoperatively. All routine investigations were taken into consideration. Patients were explained about preoperative procedure of spinal anaesthesia, intraoperative management and postoperative management. VAS (Visual Analog Scale) consisting of a 10 cm line with 0 - no pain and 10 cm - maximum imaginable pain, was explained to patients at preoperative visit.

The patients were pre-medicated with oral alprazolam 0.25 mg on the night before surgery & were advised to have light meals and remain nil orally from 10 p.m. onwards.

Intraoperatively, intravenous line was secured with 18/20 Gauge cannula. Monitors were attached before giving spinal anaesthesia. All the patients preloaded with 10 ml/kg Ringer's lactate solution. Ranitidine (50 mg) Glycopyrrolate (0.2 mg) and Metoclopramide (10 mg) were given intravenous to all patients. Intrathecal block under strict aseptic conditions performed in sitting position at L3-4 or L4-5 interspinous space with 25G Quinckes spinal needle. Patients were received 3.9ml out of a mixture of 3.5ml of 0.5% hyperbaric bupivacaine and 0.4ml of nalbuphine (0.8mg) in group N and 3.9ml out of mixture of 0.5ml of 0.5% isobaric bupivacaine and 0.4ml of normal saline in group B. Patients were placed in the supine position with 10-20 degree tilt.

The time of injection was noted and patients were placed in supine position immediately. Onset of sensory block was checked by loss of sensation to pinprick. Sensory testing was performed using a blunted needle. Dermatome level was tested every 2 minutes until the level was stabilized for 3 consecutive tests. A sensory blockade at T8 was recorded. The time taken from intrathecal injection to the attainment of highest level of sensory block was recorded. Later, the time taken for two segment sensory regression from the highest sensory level and time for first rescue analgesia were also noted.

Motor block in the lower limbs was assessed as per Modified Bromage scale: 0 - No paralysis 1 - Inability to raise extended legs 2 - Inability to flex the knee 3 - Inability to flex the ankle Duration of motor blockade was recorded from the onset upto the cessation of grade I block.

Patient's pain was assessed on 10cm linear visual analogue scale (VAS). Any patient with VAS score > 3 was administered Diclofenac sodium (75 mg) intramuscularly.

Hemodynamic variables such as systolic arterial pressure, diastolic arterial pressure and heart rate were recorded at baseline, at 5 min., 10 min., 15 min., 30 min., 45 min., 60 min, 90 min, 120 min. and 180 min.. Hypotension was taken as a fall in baseline systolic arterial pressure by 20%. Hypotension was then treated with bolus doses of intravenous ephedrine 5mg. Bradycardia was taken as heart rate less than 60 beats per minute. Bolus doses of intravenous atropine 0.5mg were injected to treat the episodes of bradycardia.

Ramsay sedation scoring was done and noted for each patient in both the groups.

Ramsay Sedation Scale

1 Patient is anxious and agitated or restless, or both
2 Patient is co-operative, oriented, and tranquil
3 Patient responds to commands only
4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6 Patient exhibits no response

Respiratory depression was defined as decrease in respiratory rate <10/minute and decrease in O_2 saturation (SpO_2) less than 90%.

Side effects like nausea, vomiting, pruritus, shivering, urinary retention, neurological deficit etc. were recorded.

In the recovery room, time from injection until block regression to L5, duration of grade I motor blockade, voiding and ambulation (i.e. time at which the patients have normal sensation of their buttocks and feet and are able to stand and walk without support) was checked to rule out any adverse motor or neurological deficits and bowel or bladder dysfunction. Throughout the period pulse, blood pressure and oxygen saturation was monitored.

RESULTS:

Both groups were comparable in all demographic data such as age, sex, weight, height, type of surgery and duration of surgery (Table 1); *P* > 0.05.

The difference in heart rate (beats/minute)systolic blood pressure, diastolic blood pressure between the two groups at baseline, 5 min., 10 min., 15 min., 30 min., 45 min., 60 min.,75 min., 90 min.,120 min., and 180 min.. were statistically insignificant (p-value > 0.05).

There was early onset of sensory block in group N 118.91±6.83 sec. than group B 148.00±9.21sec. (table 2). The Higher sensory block was achieved by all groups was between T4 and T6.There was statistically significant prolonged two segments regression time and requirement of first rescue analgesia time in group N than group B (table 2). The onset of motor block was earlier in group N p<0.05 (Table 2). Mean Visual Analogue Score (VAS) during postoperative period was statistically significant at various time intervals. The pain intensity at the time of administration of rescue analgesic and thereafter was less in group N as compared to group B.

The duration of motor block was 141.16 ± 10.34 min in group N and 150.75± 9.28 min. in group B. Most of the patients in group N had sedation score 3 followed by sedation score 4 and then sedation score 2, but in group B most of the patient had sedation score 2 followed by 1 which was desirable.

Hypotension, bradycardia and fall in SpO_2 were observed more in group as compared to group B because of intraoperative sedation. Nausea/vomiting and shivering were observed more in group B as compared to group N. Headache and neurological complications were not seen in any patient of either group.

Table 1: Demographic data and duration of surgery

	Group N	Group B
Age(yrs)	37.60±8.05	36.48±7.52
Sex(M:F)	23:37	22:38
Weight(kg)	54.91±6.05	54.50±7.50
Height(cm)	156.40±4.43	156.01±4.56
Duration of surgery(min)	107.00±20.05	109.16±22.03

Table 2: Duration of sensory and motor block and first rescue analgesia

	Group N	Group B	P value
Onset of sensory block(sec.)	118.91±6.83	148.00±9.21	0.032
Two segment regression time (min.)	153.75 ± 9.28	115.75 ± 11.74	0.001
Time for 1st rescue analgesia (min.)	295.33±20.88	186.91±16.52	0.019
Onset of motor block(sec.)	304.16 ± 42.58	349.41 ± 12.28	0.027
Duration of motor block (min.)	141.16 ± 10.34	150.75± 9.28	0.321

Table 3: Adverse effects

	Group N	Group B
Hypotension	15	9
Bradycardia	7	2
Fall in SpO_2	7	0
Nausea vomiting	2	3
Shivering	2	5
Headache	0	0
Neurological complication	0	0

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. Partial agonist-antagonist has been studied extensively to overcome these adverse effects opioids. Nalbuphine binds avidly to kappa-receptors to produce analgesia. The pattern of binding and effects of nalbuphine is as a mixed agonist—antagonist having agonist activity at kappa receptors and antagonistic activity at mu receptors. Analgesic action of nalbuphine produced by kappa receptor, it is present throughout the brain and spinal cord area of involved in nociception. 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.

In our study we used nalbuphine 0.8 mg as an adjuvant to intrathecal bupivacaine(0.5%) heavy for lower abdominal surgeries and compared its block characteristics, hemodynamics, post-operative analgesia, and adverse effects with intrathecal bupivacaine (0.5%) alone.

The principle finding of this study is that addition of 0.8mg of intrathecal nalbuphine to spinal anaesthesia in patients undergoing lower abdominal surgery with hyperbaric 0.5% bupivacaine early onset of sensory block, prolonged two segment regression time and increases the duration of first rescue analgesia time without μ related side effects.

Mukherjee et al[7]studied the duration of analgesia with different dosages of intrathecal nalbuphine (0.2, 0.4, and 0.8 mg. They observed onset time of sensory block was 1.59±0.18 min with bupivacaine with 0.8mg.of intrathecal nalbuphine; this was in commensurate with the present study. They observed onset time of complete motor block was 5.9±0.57 min in group with bupivacaine alone and 5.6 ± 0.53min in group with intrathecal bupivacaine and Nalbuphine (0.8mg) (p=0.396) and duration of motor blockade was 138.8±5.84 min in group with bupivacaine alone and 141±5.83 min in group with bupivacaine and Nalbuphine(0.8mg) intrathecally (p=0592). The mean time for onset of sensory block, the mean time for onset of motor block & the mean duration of motor block in our study were similar to those observed by Mukherjee et al[7].

In our study mean duration for two segments regression from highest level of sensory block was 153.75 ± 9.28 min in group N and 115.75 ± 11.74 min in group B. Mukherjee et al[7] also observed similar result in their study. It was 118.2±6.80 in group bupivacaine alone patients and 153.3±6.05 in group of bupivacaine with 0.8mg of intrathecal nalbuphine.

In our study mean duration of time of request for first analgesia was 295.33±20.88 min. in group N and 186.91±16.52 min. in group B. Shehla Shakooh et al[8] also concluded similar result. The mean duration of time of request for analgesia was 298.00±51.02. min.. in group with 0.5% bupivacaine heavy (3cc) with 0.8mg nalbuphine and 161.00±16.68min.. in group with 0.5% bupivacaine heavy (3cc) (P<0.001).

Jyothi B et al[9] observed onset time of sensory block as 3.3±0.8 min., two segment regression time as 122.2±5.5 min. and duration of analgesia as 322.4±31.1 min.. Duration of analgesia was similar to our study but onset time of sensory block and two segment regression time were more in their study most probably due to smaller sample size(n=25).

Tarangini Das et al[10] observed that onset time of sensory block was 2.24±0.68 min., time of onset of motor block was 4.1±0.7 min., and duration of sensory block was 205.14±5.4 min. with 0.75mg of intrathecal nalbuphine as an adjunct, which was similar to our study. Manjula R et al[11] observed that the mean time of onset of sensory block was 1.69±0.20 min., the mean time of onset of motor block was 5.8±0.64 min., two segment regression time was 133.5±5.85 min., duration of motor block was 140.7±6.01 min. and duration of effective analgesia was 260±5.64 min.. The findings were similar to our study.

CONCLUSSION:

From the present study it may be concluded that Nalbuphine(0.8mg) when used in conjunction with hyperbaric 0.5% bupivacaine(3.5ml) intrathecally is safe and effective in providing prompt onset, adequate anaesthesia and prolonged analgesia. It provides excellent post-operative pain relief and increases the duration of request for analgesia without affecting the early recovery from anaesthesia. It also provides intraoperative sedation, which to an extent is beneficial intraoperatively. Adverse effects are minimal with 0.8mg of nalbuphine.

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