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ORIGINAL RESEARCH

STUDY OF POST OPERATIVE ANALGESIC EFFICACY OF INTRATHECAL FENTANYL COMPARED TO NALBUPHINE WITH BUPIVACAINE IN SPINAL ANAESTHESIA FOR LOWER LIMB SURGERIES

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ABSTRACT:

Background:
Subarachnoid block or spinal anesthesia is the commonly used technique for lower abdominal and lower limb surgeries. Local anaesthetic bupivacaine is the commonly used cost-effective drug which gives satisfactory analgesia for about 90–120 min. Intrathecal opioids and α2 agonists were found to extend the analgesia in the postoperative period. The present study aimed to compare the postoperative analgesic efficiency of intrathecal fentanyl with nalbuphine as adjuvant to 0.5% hyperbaric bupivacaine for orthopedic lower limb surgeries.
Methods: Seventy-two adult patients of American Society of Anesthesiologist physical status I and II of both gender aged 25–65 years were randomized into two groups of 36 each to receive either fentanyl 25 μg (Group I) or nalbuphine 2 mg (Group II) with 3.5 mL 0.5% hyperbaric bupivacaine, making intrathecal drug volume to 4 mL in each group. Sensory and motor block characteristics and time to first rescue analgesic (intravenous tramadol 100 mg) were recorded. Drug-related side effects of pruritus, nausea/vomiting, and respiratory depression were also recorded.
Results: it was revealed that both groups were comparable regarding the onset and cephalic extension of block. The time to two dermatome regressions and time for complete motor recovery were significantly longer in patients of Group II with statistical significant difference ($P < 0.05$). Duration of analgesia was also extended in patients of Group II as compared to Group I with highly significant difference ($P < 0.001$). No drug-related side effects were observed in either group.
Conclusion: Hence, Intrathecal nalbuphine 2 mg as adjuvant to 0.5% bupivacaine was clinically more efficient than fentanyl for enhancing the postoperative analgesia for lower limb surgeries.
Keywords: Fentanyl, intrathecal, Nalbuphine, Orthopedic surgery, spinal.

INTRODUCTION

The most common surgical technique for lower abdominal and lower limb is subarachnoid bloackade. The surgical procedure is performed by simply injecting the anaesthetic solution inside the subarachnoid space and it provides a rapid onset of relief which inturn provide dual

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intra and post operative anaesthesia. [1] The drug named as nalbuphine hydrochloride is primarily a kappa agonist/partial mu antagonist analgesic. The mu agonist, fentanyl, aids in its action by opening K+ channels and thereby reducing Ca++ influx, which results in inhibition of transmitter release.[2]

The local anaesthtetic drug named Bupivacaine hydrochloride which is an amide type was synthesized by Ekenstam in 1957 and came into practice in 1963. The mechanism of bupivacaine acts by blockading the voltage-gated Na+ channels in the axonal membrane and possibly has an effect on presynaptic inhibition of calcium channels.[3] Thus the use of adjuvants such as nalbuphine with bupivacaine has shown to decrease its dose requirements in spinal anesthesia thereby minimal incidence of side effects is observed and aids in minimal induction analgesia dose. There are various studies on higher dose of nalbuphine (0.8 µg). This study compare the lower dose of nalbuphine inorder to know the efficacy and incidence of its side effects.[4]

The intrathecal injection of fentanyl which is a lipophilic opioid has a rapid onset after injecting the drug. This drug does not migrate to the 4th ventricle in adequate concentration to cause respiratory depression. It is most commonly in addition to intrathecal bupivacaine in cesarean delivery by many anesthesiologists.[5] It was found to improve the quality of anesthesia without any significant side effects and helps to improve post-operative analgesia and hemodynamic stability.[6] The aim of the study was to compare post operative analgesic efficacy of intrathecal fentanyl compared to nalbuphine with bupivacaine in spinal anaesthesia for lower limb surgeries.

MATERIALS AND METHODOLOGY

The study was conducted after obtaining clearance from the institutional ethical committee, study was conducted from at the Department of Anaesthesiology and Critical Care. A total of 72 adult patients who come under the criteria of American Society of Anesthesiologist (ASA) physical status I and II. The study includes both genders aged 25–65 years, with a weight of 50–90 kg, and an average height of ≥150 cm, those patients who were scheduled for elective orthopedic surgery of lower limbs under Subarachnoid blockade. A thorough preanaesthetic check-up and investigation was done and those patients with a history of cardiovascular, pulmonary, hepatic, renal, neurologic, psychiatric, or metabolic disease were excluded from the study. Obese patients (BMI >25 kg/m2) with bleeding abnormalities, those with severe spinal deformity, allergic to local anaesthteic drugs or those who are contraindicated to spinal nerve anaesthesia were excluded. Those patients who met the criteria were randomly divided into two groups of 36 patients each using a sampling method through computer-generated random number table. The study patients belonging to Group I were given 17.5 mg (3.5 mL) of 0.5% hyperbaric bupivacaine with intrathecal fentanyl 25 µg and patients of Group II were given 17.5 mg (3.5 mL) of 0.5% hyperbaric bupivacaine with preservative-free intrathecal nalbuphine 2 mg (Nacphin, Neon Laboratories Limited), making intrathecal drug volume to 4 mL for each patient. In this double blinded method, the drug solutions for the study group were prepared by the resident anesthesiologist while SAB was issued by another anesthesiologist. The postoperative data were recorded by postoperative resident, who was unaware of the group I and group II allocation. All enrolled study patients remained fasting overnight before the surgery and all were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg on the night before the surgery.

Before the start of the anaesthetic drug solutions all patients were explained about the methods of sensory and motor blockade assessments. Visual Analog Scale (VAS) scoring system is well explained to all the participants. The VAS consisted of a 10 cm horizontal paper strip with two end points: 0 = no pain and 10 = worst possible pain. In the operation theatre a standard monitoring for heart rate (HR), non invasive blood pressure,

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electrocardiogram, and pulse oximetry (SpO2) was done and was recorded at every 5 min intervals throughout the surgery. A peripheral intravenous (IV) access with 18G IV cannula was secured and lactated Ringer's infusion was stared to replenish the overnight fasting at a rate of 10 mL/kg. Under all aseptic precautions, all the study patients received SAB via midline approach in the sitting position at L3–L4 intervertebral space, using 25-gauge Quincke spinal needle. The study drug solution was administered intrathecally in the supine position with 10° Trendelenburg position immediately after SAB to achieve the desirable level of block. An oxygen supplement was given at a rate of 4 L/min via face mask. All the hemodynamic parameters were assessed. The characteristics of both sensory and motor block were assessed in the normal lower limb at every 2 min interval until there was no pinprick sensation was achieved. The time intervals were calculated at the end of intrathecal injection. Sensory block at T10, maximum cephalic level, time taken to achieve maximum sensory block, and time taken to two dermatome regressions of sensory analgesia were recorded. Motor block was graded according to Bromage scale: 1 - free movements of legs and feet (no motor block - 0%); 2 - able to move knee with free movement of feet (partial motor block - 33%); 3 - unable to flex knee with free movement of feet (near complete motor block - 66%); and 4 - unable to move any part of lower limb (complete motor block-100%).[7]

Patients with VAS score ≥3 received diclofenac 75 mg intramuscularly for rescue analgesia. The VAS score of >3 constituted the end point of the study. Postoperatively, the sensory and motor block levels were assessed at 15 min intervals until normal sensations returned. The parameter like Hemodynamic HR, systolic blood pressure (SBP), and peripheral oxygen saturation (SpO2) were recorded just after spinal injection, then at every 5 min till the end of surgery.

Mostafa et al scale was used to assess the sedation and were graded as: 1 - awake and alert, 2 - awake but drowsy, responding to verbal stimulus, 3 - drowsy but arousable, responding to physical stimulus, and 4 - unarousable, not responding to physical stimulus.[8]

Seventy-two patients were enrolled, accounting for dropout of 5% for better validation of results. The data were collected a mean ± standard deviation (SD), and statistics were calculate using Stat Graphics Centurion (version 16.2). Chi-square test and statistical significance in the mean difference was found using analysis of variance. $P < 0.05$ was considered statistically significant and $P < 0.001$ was considered statistically highly significant.

Results

72 adult consented patients, who were scheduled for elective lower limb orthopedic surgery under SAB. There was no protocol deviation for any of the patients and all have successfully completed the study protocol. Surgical procedures were performed uneventfully and there were no complications during surgery or anaesthesia. Table 1 represent mean age, weight, height, gender, ASA physical status, and surgical characteristics of both groups' patients.

The onset of sensory block at T10 level was 4.32 ± 0.81 min in patients of Group I and 3.98 ± 2.35 min in patients of Group II with no statistical significance ($P = 0.083$). Time to reach maximal cephalic sensory level was also statistically comparable with median cephalic level of T6 in all patients. Time to sensory regression of two dermatomes was significantly extended in patients of Group II (130.32 ± 15.23 min) as compared to patients of Group I (114.65 ± 10.82 min) with statistically highly significant difference ($P < 0.001$) as listed in Table 2. Onset of motor block was 9.2 ± 1.43 min in patients of Group I and 8.97 ± 2.29 min in patients of Group II and was comparable with no statistically significant difference ($P = 0.37$). Duration of motor block was significantly extended in patients of Group II (192.26 ± 22.63 min) as compared to patients of group II (150.63 ± 16.05 min) with statistically significant difference ($P = 0.003$) [Table 2]. The total duration of analgesia was 280.74 ±

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27.47 min in patients of Group I and 315.64 ± 18.42 min in patients of Group II with statistically highly significant difference (P < 0.001) [Table 2]. The parameters such as mean HR and SBP at baseline with intraoperative changes were comparable and there was no statistically significant difference in HR, SBP, and SpO2 during intra- and post-operative periods between both the groups (P > 0.05) [Tables 3]. Out of 72 no patient suffered from postspinal shivering, nausea, vomiting, or respiratory depression.

Table 1: Demographic profile of patients (n=72)

Parameters	Group 1	Group 2
Age (years)	54.4±4.8	56.9±2.2
Weight (kg)	60.56±8.37	63.36±8.54
Height (cm)	160.43±2.7	158.04±4.1
Gender Male: female	30:6	14:22
ASA grade I/II	20/14	22/12
Duration of surgery	110.68±20.74	111.89±24.22

Table 2: Sensory and motor blockade profile

Parameters	Group I	Group II	P value
Onset time of sensory block at T10 level (min)	4.32 ± 0.81	3.98 ± 2.35	0.083
Mediancephalic sensory level	T6 (4–8)	T6 (4–7)	0.076
Time taken to achieve sensory blockade at most cephalic level (min)	7.4±2.72	7.13±3.81	0.069
Time taken to achieve complete motor block (min)	9.2 ± 1.43	8.97 ± 2.29	0.37
Time taken for two regressions of sensory block (min)	114.65 ± 10.82 min	130.32 ± 15.23	0.001**
Duration of motor block (min)	150.63 ± 16.05	192.26 ± 22.63	0.003*
Time to administer first rescue analgesia (min)	280.74 ± 27.47	315.64 ± 18.42	0.000**

Table 3: Changes in heart rate (beats/min)

Parameters	Group I	Group II	P
Preoperative	94.3±9.16	100.2±4.95	0.72
5 min after SAB	82.7±4.34	87.3±2.78	0.89
10 min	79.8±9.21	81.5±3.43	0.68
15 min	79.5±2.28	79.9±4.45	0.51
20 min	78.5±1.45	82.7±1.98	0.67
25 min	70.2±2.67	80.4±2.76	0.50
30 min	67.5±2.38	72.7±6.57	0.67
45 min	69.3±2.47	75.2±7.21	0.76
60 min	70.3±6.61	71.6±5.89	0.58
75 min	66.6±7.36	74.4±2.38	0.82
90 min	70.7±2.93	72.3±2.78	0.84
Postoperative	73.9±4.69	76.9±4.18	0.49

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Discussion

This study compared the clinical efficiency of intrathecal fentanyl with nalbuphine as intrathecal as a adjuvant to 0.5% hyperbaric bupivacaine with the assessment of sensory and motor blockade characteristics along with the duration of postoperative analgesia and intraoperative hemodynamic changes, sedation, pruritus, and respiratory depression. Local anesthetics act by inhibiting voltage-gated sodium channels in the spinal cord by interfering with afferent and efferent sensory and motor impulses while intrathecal opioids activate opioid receptors in the dorsal gray matter of the spinal cord (substantia gelatinosa) to modulate the function of afferent pain fibers. Thus the combined effect of adjuvants to local anesthetic aids in prolonged duration without increasing sympathetic or motor blockade thereby declining their systemic side effects. The drug Nalbuphine, is a combined agonist–antagonist which has the potential to maintain and enhance μ-opioid-based analgesia with parallelly mitigating the μ-opioid side effects.

The present study results revealed that there was no statistically significant difference in the onset and cephalic extension of sensory blockade of hyperbaric bupivacaine when intrathecal fentanyl or nalbuphine was used as adjuvant. The period of sensory block and motor block was greatly enhanced by adding the drug nalbuphine by intrathecal injection when compared to intrathecal fentanyl in the present study.

The present study results compared to the other studies observed that addition of nalbuphine or tramadol allowed a significant decrease in pain score.[9,10] The advantages of nalbuphine at doses of 0.2, 0.8, and 1.6 mg compared over intrathecal morphine in ninety obstetric patients undergoing C-section concluded that intrathecal nalbuphine was found to be more effective over morphine to provide better postoperative analgesia without any side effects according to Culbers et al.[11]

A study by Yoon et al. sixty obstetric cesarean section patients scheduled for spinal anaesthesia. All the patients received either morphine 0.1 mg or nalbuphine 1 mg or morphine 0.1 mg with nalbuphine 1 mg along with addition of 0.5% bupivacaine (10 mg) and found that analgesia was prolonged in the morphine group and morphine with nalbuphine group. [12]The study was is in accordance with the results of our study. A study by Ahmed et al. compared the effect of intrathecal nalbuphine with bupivacaine for postoperative analgesia in three different doses such as 0.8, 1.6, and 2.4 mg. It was concluded that the combination of intrathecal bupivacaine with nalbuphine significantly extended the postoperative analgesia as compared to control group and a 1.6 mg dose showed the best results.[13]

The sedation scale was equal in both the groups, but the number of patients rescue analgesia was less in the nalbuphine group.[14] It was found that a statistically significant difference was observed in the duration of motor and sensory block in the present study between fentanyl and nalbuphine groups. Mild pruritus was observed in patients of fentanyl group which was successfully treated with IV injection pheniramine. The incidence of respiratory depression in the study was minimal and comparable. All the study patients were seen to be calm and comfortable during surgery, and no drug-related side effects were occurred. Postoperative analgesic efficacy of intrathecal tramadol (50 mg) with nalbuphine (2 mg) as adjuvant to hyperbaric bupivacaine (12.5 mg) in spinal anesthesia for lower limb orthopedic surgery. The results of there is in accordance to our present study. Verma et al concluded that addition of nalbuphine to hyperbaric bupivacaine was effective in extending the duration of sensorimotor block and enhancing the postoperative analgesia following lower limb orthopedic surgery. Intrathecal tramadol could not make a significant difference in postoperative analgesia as compared to when bupivacaine was used alone.[15]

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Conclusion

It was concluded that when Nalbuphine (2 mg) act as intrathecal adjuvant to 0.5% hyperbaric bupivacaine (17.5 mg) for subarachnoid blockade was found to be clinically more efficient than fentanyl drug for prolonging the duration of sensory motor block and aids in increasing the postoperative analgesia following orthopedic lower limb surgeries with minimal adverse effects.

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