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Research Article

COMPARISON OF INTRATHECAL NALBUPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE IN SPINAL ANESTHESIA IN PATIENTS UNDERGOING LOWER LIMB SURGERIES

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ABSTRACT

Objective: The objective of this study is to compare nalbuphine 0.5 mg and fentanyl 25 µg when used as an adjuvant to 0.5% bupivacaine heavy in spinal anesthesia for their effect on the sensory block, motor block, and post-operative analgesia.

Methods: After fulfillment of inclusion criteria and after obtaining informed written consent from patients, a group of a total of 80 patients was enrolled and divided in GRP-F and GRP-N equally. (1) Group F: Patients received diluted 25 µg of fentanyl with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine. (2) Group N: Patients received diluted 0.5 mg of nalbuphine with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine.

Results: The duration of sensory block and motor block was significantly longer in GRP-F than GRP-N. Post-operative analgesia was comparable in both groups with minimal side effects.

Conclusion: Intrathecal fentanyl in post-operative period was found to be significantly better than nalbuphine when used as an adjuvant therapy with 0.5% hyperbaric bupivacaine in elective lower limb surgeries with insignificant adverse effects like hypotension, nausea, and vomiting.

Keywords: Spinal anesthesia, Fentanyl, Nalbuphine, Sensory block, Motor block.

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INTRODUCTION

The central neuraxial blockade is a commonly employed technique in contemporary anesthesia. Spinal anesthesia offers optimal surgical conditions for procedures performed below the umbilicus.

The procedure is simple to execute and has a faster onset, providing both effective sensory as well as motor block [1]. Bupivacaine, broadly utilized amide local anesthetic, results in a profound sympathetic blockade, a sustained sensory along with the motor block, and hence excellent surgical relaxation [2].

Arthur Barker [3], in 1907, University of London surgery professor reported improved spinal techniques, including hyperbaric spinal sterility, local anesthetic, and midline over paramedian dural puncture. The method has been improved, resulting in superior intrathecal spinal or subarachnoid block.

To extend the duration of anesthesia, a variety of adjuvants is administered intrathecally with the local anesthetics. Adjuvants not only offer adequate blockade but also prevent the undesirable hemodynamic impacts of spinal anesthesia by reducing the dosage of local anesthetic.

Intrathecal opioids were first utilized to treat acute pain by Wang *et al*. [4] in 1979. Since then, intrathecal opioids have been used extensively to treat trauma and chronic cancer pain, as well as to improve the "quality of intraoperative anesthesia as well as extend post-operative analgesia.

Nalbuphine is a synthetically manufactured opioid which has both κ agonist and µ antagonist properties. Analgesia and sedation are produced by kappa receptors," resulting in no negative effects from µ receptors. Fentanyl, a synthetic opioid µ receptor agonist, is structurally similar to meperidine and is derived from phenylpiperidine. Numerous studies have shown that intrathecal fentanyl as an adjuvant to the local anesthetic reduces visceral and somatic pain quickly [5].

Aims and objectives

The aim of the study was to assess and compare the following factors in two groups – Intrathecal nalbuphine and fentanyl as adjuvants to bupivacaine heavy in spinal anesthesia in patient undergoing lower limb surgeries with respect to:

1. Sensory and motor blockade – onset and duration
2. Duration of analgesia.

METHODS

After approval by the institutional ethical committee and from the CTRI (CTRI/2024/01/062089), all included participants gave a written well-informed consent before being in the study. The study was conducted in Silchar Medical College and hospital for the duration of 12 months from March 2023 to February 2024 on 80 patients with patients placed randomly into two groups (Groups N and F), each containing 40 patients. The study population selected from patients posted for the lower limb surgeries during our study period using inclusion and exclusion criteria of our study after taking informed consent from patient and relatives.

Inclusion criteria

a. American Society of Anesthesiologist (ASA) Status I and II
b. Age 25–65 years
c. Both genders (posted for surgeries of lower limb).

Exclusion criteria

a. Patients with contraindication to spinal anesthesia
b. Pre-existing neurological deficits
c. Patients with allergy history to study drugs
d. Pregnant patients.

PRE-OPERATIVE PREPARATION

After collecting a "complete medical history from the patient and their family, a thorough physical examination was performed. Patient height (cms), weight (kg), and body mass index were measured. Airway and spine examinations were done. Complete blood count, renal function test, blood grouping and typing, random blood sugar, electrocardiography, coagulation profile, and chest X-ray which have been properly analyzed before surgery. The procedure was explained to the patients and their relatives using language that they could easily comprehend, and their consent was obtained after providing them with all the necessary information. All patients who have been kept fasting for a duration of 6hrs and were premedicated with alprazolam 0.5 mg and ranitidine 150 mg on night before surgery.

Preparation on the day of surgery

Anesthesia machine circuits were checked and resuscitation drugs as well as equipment which have been ready when entering the operating room. Initial values were recorded for non-invasive blood pressure (NIBP), electrocardiogram (ECG), and SpO_2 monitors. Using an 18G cannula, an intravenous (IV) line was started. Once the IV line was secured, the patients have been pre-loaded with" 10 mL/kg of Ringer's lactate (RL) solution containing premedication including 40 mg pantoprazole and 4 mg ondansetron.

The preparation of study drug

Fentanyl (50 µg/mL) was taken in insulin syringe up to 5 markings, that is, 0.5 mL (25 µg). And added to the 5 mL syringe containing 3 mL of 0.5% hyperbaric bupivacaine.

Nalbuphine (10 mg/mL) was diluted in 10 cc syringe, and from that drug was taken in insulin syringe up to 5 markings, that is, 0.5 mL (0.5 mg), and added to another 5 mL syringe containing 3 mL of 0.5% hyperbaric bupivacaine.

Group F who has been received 25 µg fentanyl and 3 mL (15 mg) of 0.5% hyperbaric bupivacaine, while Group N received 0.5 mg nalbuphine and 3 mL (15 mg) of 0.5% hyperbaric bupivacaine. The drug volume for both groups was 3.5 mL.

Technique

After entering the operation theatre, the patient has been described about the process of spinal anesthesia. The patient has been placed in sitting position with the head down, hands folded forward, and wrapped around a pillow. A well-trained assistant has been asked for supporting the patient from the front. The patient was asked to "push out" the lower back to open up lumbar vertebral spaces. Draping of back was done with povidone-iodine, followed by spirit, and all the aseptic precautions were taken. Sterile spinal sheet for performing spinal anesthesia was placed on back. L3-L4 intervertebral space was chosen. Lignocaine 2% 2–3 mL (40–60 mg) was given at the "site of lumbar puncture subcutaneously. A lumbar puncture was conducted at the L3-L4 intervertebral space using a 25 G Quincke's needle, employing the midline approach. The unobstructed movement of transparent CSF was" verified, followed by the administration of the medication at a rate of 0.2 mL/s. Subsequently, the patient was positioned in a supine posture. The administration of IV fluid was initiated, and oxygen has been given at a rate of 4L/min through face mask.

Monitoring

The injection administration completion is recognized as the time zero (T0) and from this point all measurements have been observed.

The sensory block evaluation was conducted using the pinprick technique and tested for the highest level. The duration needed to reach the highest level, that is, time from drug (T0) administration to the greatest sensory level was recorded.

The time required to attain the T12 (highest level) level has been considered as the onset of the sensory block, while motor blockade has been evaluated every 2 min according to the modified Bromage scale [6].

0: No motor block
1: Lack of ability to elevate the leg fully; capable of flexing the knees and moving the feet
2: Lack of ability to extend the leg and flex the knee; capable of moving the feet 3: Complete motor block of limb.

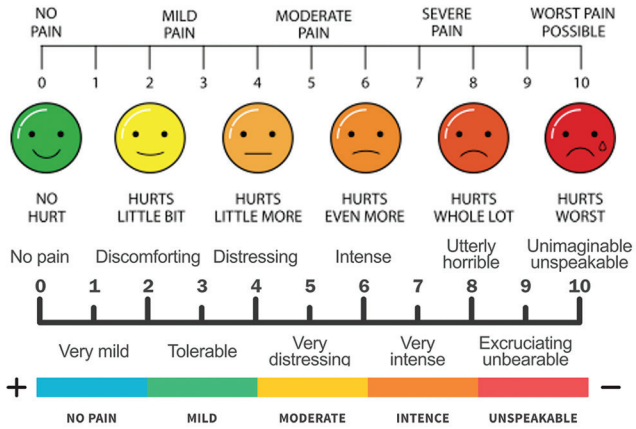
The motor blockade assessment was conducted for 20 min initially, followed by subsequent assessments every 5 min until the maximum level of the block has been achieved. The duration of the block's 2-segment regression was recorded. The motor block initiation was classified as modified Bromage Grade III.

Hemodynamic parameters such as NIBP, mean arterial pressure (MAP), heart rate (HR), and SpO_2 have been calculated at 2-min intervals during the first 10 min of the surgery and after then at 10-min intervals thereafter until the surgery was completed.

Patients who have been monitored for adverse effects such as vomiting, nausea, and low blood pressure for a maximum of 24 h following the surgical procedure and received appropriate medical intervention as needed.

Patients who experienced surgical complications such as excessive bleeding, the need for re-exploration, or conversion to general anesthesia have been eliminated from the research.

The post-operative period utilized a visual analog scale to evaluate pain, while also recording the duration required to administer rescue analgesic.



Rescue analgesia which has been administered in the form of a 75 mg intramuscular injection of diclofenac. This was given if the patient's pain score exceeded 4 or if the patient requested it, and could be repeated if necessary.

An analgesic was not administered immediately after the surgery until the patient specifically asked for pain relief, and the time at which the first analgesic was given has been observed. The duration of post-operative analgesia has been determined as the interval from the spinal injection administration to the administration of rescue analgesic.

Observation and analysis

Comparison of baseline hemodynamics (Systolic blood pressure [SBP], Diastolic blood pressure [DBP], MAP, and HR)

In our study, we observed that there has been no statistical variation among Group N and Group F for baseline hemodynamics like SBP, DBP, MAP, and HR. p-value was insignificant.

Comparison of sensory onset among Groups N and F

The sensory block onset was comparable in Groups N and F with onset of sensory block 3.805±3.931722 min in Group N and

Table 1: Baseline hemodynamics

Variable	Group N		Group F		p-value
	Mean	SD	Mean	SD	
Systolic blood pressure	127.7	9.552017	125.95	7.792008	0.3720
Diastolic blood pressure	74.95	9.290055	74.8	8.543103	0.9402
Mean arterial pressure	74.85	6.701171	74.83333	7.117029	0.9914
Heart rate	84.2	14.62208	79.825	10.81046	0.1321

Table 2: Sensory onset

	Group N		Group F		P value
	Mean	SD	Mean	SD	
Sensory onset(min)	3.805	3.931722	3.685	0.21903	0.8477

Table 3: T peak motor

	Group N		Group F		P value
	Mean	SD	Mean	SD	
T peak motor(min)	5.405	0.19735	6.1575	0.266879	< 0.0001

Table 4: Duration of motor block

	Group N		Group F		P value
	Mean	SD	Mean	SD	
Duration of motor block(min)	132.65	2.991869	151	6.034091	< 0.0001

Table 5: Time to regression to L2

	Group N		Group F		P value
	Mean	SD	Mean	SD	
Time to regression to L2(min)	170.675	9.199742	177.7	7.317699	0.0003

3.685±0.21903 min in Group F which was statistically insignificant by having the p=0.8477.

Comparison of T peak motor among Groups N and F

The mean of time to attain peak motor block has been higher in group F (6.1575±0.266879) than Group N (5.405±0.19735) which was statistically significant by the p<0.0001.

Comparison of duration of motor block among Groups N and F

The motor block's mean duration was higher in Group F (151±6.034091) than Group N (132.65±2.991869) that has been statistically significant by having the p-value p<0.0001.

Comparison of time to regression to L2 (2 segment regression) among Group N and Group F

Comparison for mean time for two segment regression of the sensory level is higher for Group F (177.7) than Group N (170.675) which was statistically significant. p=0.0003 (p<0.05).

Table 6: Duration of analgesia

	Group N		Group F		P value
	Mean	SD	Mean	SD	
Duration of analgesia(min)	273.8	6.081498	276.675	11.92646	0.1783

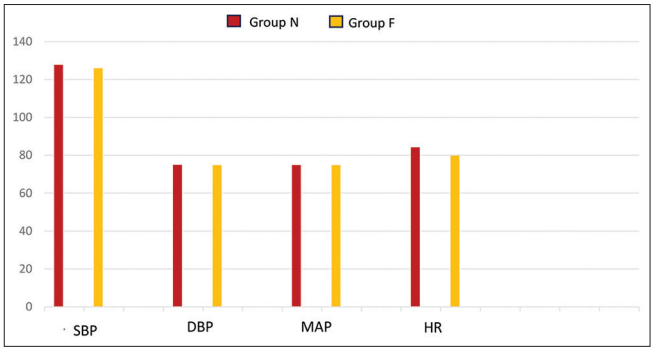


Fig. 1: Baseline hemodynamics

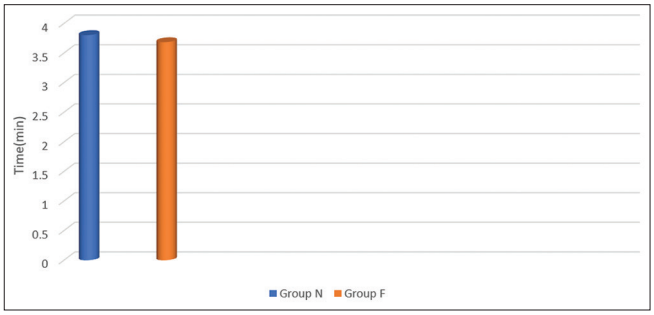


Fig. 2: Sensory onset

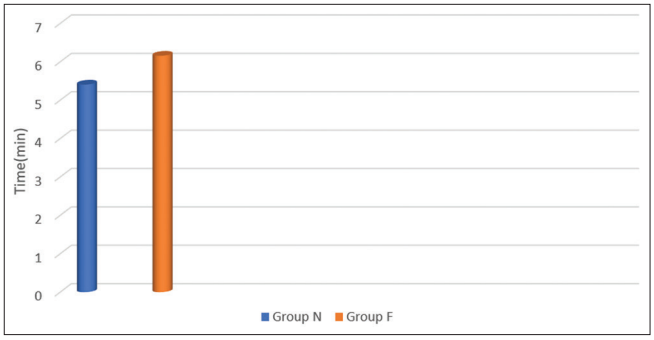


Fig. 3: T peak motor

Comparison of duration of analgesia among Group N and Group F

This is comparable in Groups N and F with duration of analgesia 273.8±6.081498 min in Group N and 276.675±11.92646 min in Group F that has been statistically insignificant with p=0.1783 (>0.05).

DISCUSSION

Regional anesthesia is the preferred method in most of the infraumbilical surgeries as it avoids many likely risks associated with general anesthesia such as difficult intubation, aspiration, post-operative pulmonary complications, surgical stress, and delayed recovery. Intrathecal adjuvants are usually administered for prolonging the spinal anesthesia duration and better hemodynamic stability by ultimately decreasing the total dosage of local anesthetics used in spinal anesthesia with additional benefit of decreasing post-operative

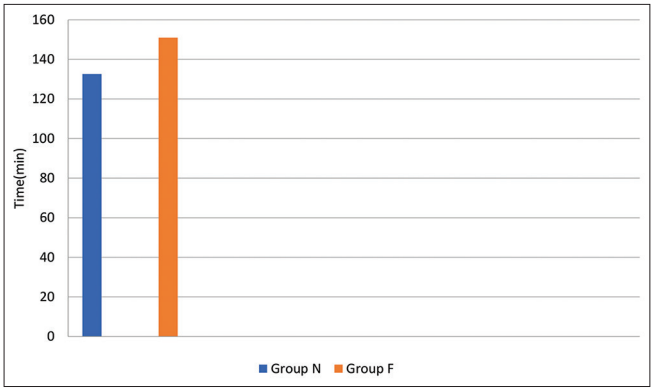


Fig. 4: Duration of motor block

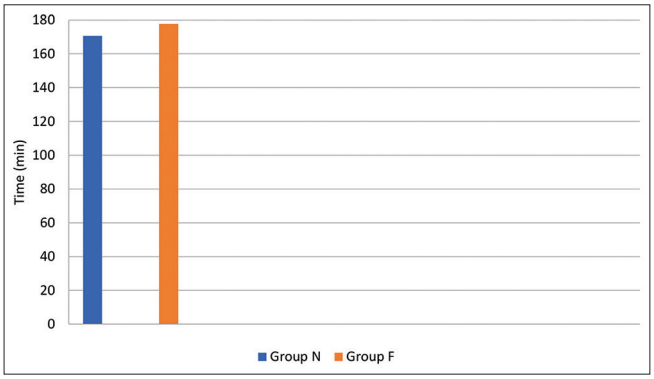


Fig. 5: Time to regression to L2

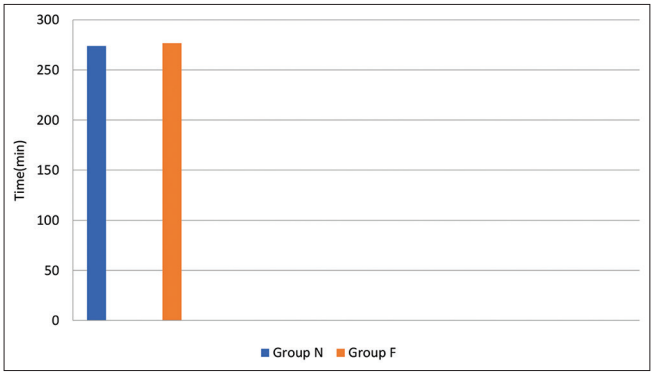


Fig. 6: Duration of analgesia

analgesic requirement significantly. Intrathecal adjuvants like opioids have several advantages like early onset of sensory along with the motor blockade, and early ambulation due to motor and sympathetic sparring properties.

Nalbuphine acts as an agonist at kappa receptor and antagonist at μ receptor. The analgesic potency of nalbuphine is almost equivalent to Morphine. The respiratory depression effect of nalbuphine is almost the same as equianalgesic doses of morphine until 30 mg after which it will not aggravate respiratory depression due to its ceiling effect [7].

Fentanyl is a mu receptor agonist with dose-dependent respiratory depression action. Due to its higher lipid solubility, fentanyl has faster onset of action and also decreases the stress response to the surgery.

This Silchar Medical College and hospital randomized control trial compared the impacts of intrathecal adjuvant to hyperbaric bupivacaine on sensory, along with the motor blockade onset and duration, duration of analgesia, and lower limb surgery patients. Our study randomly assigned 80 patients who have fulfilled the criteria of inclusion to two groups after obtaining informed consent for lower limb surgeries.

- Group N received 0.5 mg of nalbuphine with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine
- Group F received 25 μg of fentanyl with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine.

Time to reach T12 level (highest level) was considered the sensory block onset in our research. The sensory block onset was similar in Groups N and F, with 3.805±3.931722 min in Group N and 3.685±0.21903 min in Group F, statistically insignificant (p=0.8477). These results align with Srinivasaiah *et al.*'s [8] study comparing fentanyl (20 μg) and nalbuphine (0.8 mg) adjuvants to 0.5% bupivacaine heavy in lower limb orthopedic surgery. Our study considered T12 level (highest level) the sensory block onset, while their study considered time to reach T10. Some evidence suggests that fentanyl's high lipid solubility speeds absorption and blood-brain barrier crossing.

Group F had a significantly higher mean time to peak motor block (6.1575±0.266879) than Group N (5.405±0.19735), having the p<0.0001.

The motor block mean duration was higher in Group F (151±6.034091) than Group N (132.65±2.991869) that has been statistically significant with p<0.0001.

Gupta *et al.* [9] observed that intrathecal nalbuphine 2 mg prolongs motor blockade longer than intrathecal fentanyl 25 mcg in 3.5 mL 0.5% hyperbaric bupivacaine. Nalbuphine dosage may increase motor block duration.

Group F (177.7) had a statistically significant longer mean time for 2-segment sensory regression than Group N (170.675). (p=0.0003). Bindra *et al.* [10] found similar results when comparing fentanyl (20 μg) and nalbuphine (0.8 mg) as adjuvants to 0.5% bupivacaine heavy in cesarean section patients. The study found a two-level regression indicating a sensory block duration of 111.46±6.49 min in the fentanyl group and 108.46±5.51 min in the group of nalbuphine.

The duration of analgesia was determined by rescue time. Our study found no statistical variations in analgesia duration between nalbuphine and fentanyl. A study by Srinivasaiah et al. [8] comparing the fentanyl (20 μg) and nalbuphine (0.8 mg) as adjuvants to 0.5% bupivacaine. In patients who have been undergoing orthopedic surgery of the lower limb, nalbuphine, and fentanyl had similar analgesia duration (p=0.453).

Demographic variables involving height, weight, age, and ASA physical status have been comparable and statistically insignificant.

Two N patients and one F patient developed hypotension in our study. Hypotension was corrected with <12 mg mephentermine, otherwise patient was stable. Three patients in Group F vomited compared to 1 in Group N. There have been no statistical variations in side effects. Patients were stable and comfortable with few side effects.

Ahmed et al. [11] comparing the intrathecal nalbuphine and bupivacaine for post-operative analgesia at 0.8, 1.6, and 2.4 mg. They found that intrathecal bupivacaine and nalbuphine prolonged post-operative analgesia more than the control group, with 1.6 mg being the best dosage.

Summary

An randomized controlled trial has been performed in 80 ASAI and ASAII patients aged 25–65 undergoing lower limb surgeries in Silchar Medical College and Hospital from March 2023 to February 2024 to compare intrathecal fentanyl along with the nalbuphine as adjuvants to 0.5% bupivacaine heavy in spinal anesthesia.

Before starting the study, Institutional Ethical Committee clearance was taken. Based on inclusion criteria, 80 patients were scheduled for the lower limb surgeries which have been randomly assigned to two groups.

- Group N was administered 0.5 mg of nalbuphine along with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine.
- Group F was administered 25 µg of fentanyl along with 3 mL (15 mg) of 0.5% hyperbaric bupivacaine.

After explaining the process to the patient and family, written consent has been taken. A thorough medical history and systemic and general examination were done before surgery. After routine tests, patients fasted for 6 h and were premedicated with the alprazolam 0.5 mg and ranitidine 150 mg the night prior to surgery.

The study measured weight, age, ASA physical status, height, SBP, DBP, MAP, saturation of oxygen, HR, motor onset, peak motor block time, sensory as well as motor duration, two-segment duration regression to L2, analgesia duration, and side effects.

An 18G cannula was used to start an IV line in the operating room. After placing the IV line, patients have been pre-loaded with 10 mL/kg RL solution containing 40 mg pantoprazole and 4 mg ondansetron. Initial values were recorded for NIBP, ECG, and SpO_2 monitors.

The patient has been informed about the spinal anesthesia. The midline approach was used to puncture the L3-L4 intervertebral space with a 25 G Quincke's needle. Injection administration completion is considered time zero (T0), and all subsequent measurements were recorded. Pinprick testing assessed sensory block. The time needed to attain the greatest level (T12) signified the sensory block start, while the duration from drug administration (T0) to the highest level was recorded. The modified Bromage scale assessed motor block. The duration of the 2-segment regression of the block has been recorded. Motor block onset was modified Bromage Grade III.

Hemodynamic parameters, such as NIBP, MAP, HR, and SpO_2, have been analyzed at intervals of 2 min at the time of the first 10 min of the surgery and then at intervals of 10 min until the surgery was completed. A decrease of more than 20% in MAP was addressed by administering a 6 mg IV bolus of mephentermine along with IV fluids. There has been a 20% decline in HR or when the HR fell below 50 beats/min, it has been treated with an IV bolus injection of atropine 0.6 mg.

The demographic variables, including height, age, weight, and ASA status, showed no significant differences ($p>0.05$). The baseline hemodynamic variables in both groups exhibited similar values and which have not statistically significant ($p>0.05$). The SBP, DBP, and MAP exhibited greater stability in group F in comparison to Group N. The time required to reach the max. Motor block, as well as the motor block duration and the sensory level regression two segments, was found to be greater in Group F. Both groups did not exhibit any notable side effects. Additional research is necessary to find out the optimal dosage of nalbuphine for effective post-operative pain relief without an increase in adverse impacts in both study groups.

CONCLUSION

We observed that when 25 µg fentanyl was added as an intrathecal adjuvant in 0.5% hyperbaric bupivacaine, it was more effective than nalbuphine 0.5 mg in prolonging the duration of sensory and the motor blockade. The post-operative pain relief was similar in both the drugs being studied, and there were very few side effects.

We administered nalbuphine at a minimal dosage of 0.5 mg. However, increasing the dosage of nalbuphine is likely to yield more favorable outcomes regarding prolongation of the duration of motor as well as sensory block.

Therefore, further research is necessary involving varying dosages of nalbuphine to find best optimum dose which will prolong both sensory as well as motor block, so that patient gets maximum post-operative pain relief.

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