DOI: 10.7860/JCDR/2023/60810.17365

Original Article

Anaesthesia Section

Comparison of Analgesic Efficacy of Nalbuphine and Fentanyl as Adjuvants to Intrathecal Hyperbaric Bupivacaine in Patients undergoing Lower Limb Orthopaedic Surgeries: Randomised Clinical Trial

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ABSTRACT

Introduction: Postoperative pain management poses a major challenge in patients who undergo lower limb orthopaedic surgeries. Methods that reduce the requirements of systemic analgesics and have minimal adverse effects on haemodynamic stability are the need of the hour. Nalbuphine, a kappa agonist/partial μ antagonist can be utilised in spinal anaesthesia as an auxiliary to local anaesthetic.

Aim: To evaluate the efficiency of intrathecal hyperbaric bupivacaine versus nalbuphine plus fentanyl as adjuvants in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods: This prospective randomised clinical trial comprised 70 American Society of Anaesthesiologists (ASA) grade I and II patients aged between 18 to 60 years who had been posted for elective lower limb orthopaedic operations. Patients were randomly assigned to either Group NB (intrathecal bupivacaine with nalbuphine) or Group FB (Intrathecal bupivacaine with fentanyl). Onset and duration of sensory and motor block, haemodynamic alterations, side-effects, and requirement for systemic analgesics in the postoperative period were examined.

Results: There was no statistically significant difference in beginning of sensory and motor blockage between the two groups. In comparison to group FB, group NB's sensory blockade lasted substantially longer (126.06±6.52 minutes vs. 103.34±3.7 minutes; p-value<0.001). In group NB, the length of the motor block was considerably longer (p-value<0.001). When compared to patients in group FB (230.83±7.98 minutes), patients in group NB experienced analgesia for a mean time of 278.31±9.58 minutes, which was noticeably longer. There was no discernible difference between group NB and group FB (p-value>0.05) in terms of symptoms such as nausea, vomiting, bradycardia, and hypotension throughout the intraoperative period.

Conclusion: In patients scheduled for elective lower limb orthopaedic procedures, intrathecal nalbuphine 1 mg as an adjuvant to 0.5% hyperbaric bupivacaine for subarachnoid block extend the duration of sensory block, motor block, and the postoperative analgesia more successfully than intrathecal fentanyl 25 μg.

Keywords: Central neuraxial block, Haemodynamic stability, Motor block, Sensory block

INTRODUCTION

Spinal anaesthesia is a common modality used for surgeries below the hip. Single-shot spinal anaesthesia though technically feasible and cost-effective, especially in settings of limited resources, comes with the disadvantage of a shorter duration of action of local anaesthetic, which may not suffice in the postoperative period [1,2]. The use of systemic analgesics like opioids, Non Steroidal Anti-Inflammatory Drugs (NSAIDs), and acetaminophen forms part of multimodal analgesia. Still, an effective intrathecal adjuvant to local anaesthetic with minimum adverse effects would be more advantageous. Spinal anaesthesia frequently involves the use of hyperbaric bupivacaine. Action lasts between two and four hours. Adding intrathecal opioids to local anaesthetics prolongs the time that postoperative analgesia lasts [2]. An opioid with a rapid onset of effect following intrathecal injection is fentanyl. It does not diffuse to fourth ventricle with enough concentration when administered intrathecally to cause delayed respiratory depression. Without influencing sympathetic block, it generates synergistic analgesia for somatic and visceral pain [3]. Nalbuphine is a lipophilic semisynthetic opioid with a relatively potent μ-antagonist and κ-agonist activity. κ-opioid receptors that regulate nociception are found across the brain and spinal cord. Nalbuphine produces analgesia by attaching to κ-receptors in the brain. Nalbuphine's μ-antagonist characteristics contribute to fewer adverse events such as respiratory depression, itching, nausea, and vomiting [4]. Adding nalbuphine to intrathecal bupivacaine maintain sensory block and better postoperative analgesia, according to studies, without exacerbating adverse effects or untoward complications [3,4].

Patients undergoing elective lower limb orthopaedic procedures, the current study compared the effectiveness of intrathecal nalbuphine and fentanyl as adjuvants to hyperbaric bupivacaine. Main aim was to evaluate the effectiveness of 25 μg of fentanyl and 1 mg of nalbuphine as adjuvants to intrathecal 0.5% hyperbaric bupivacaine. Onset and duration of the sensory and motor blockage were the outcome measures. Studying intraoperative haemodynamic changes and adverse effects such pruritis, nausea, vomiting, respiratory depression, bradycardia, and hypotension was the secondary goal.

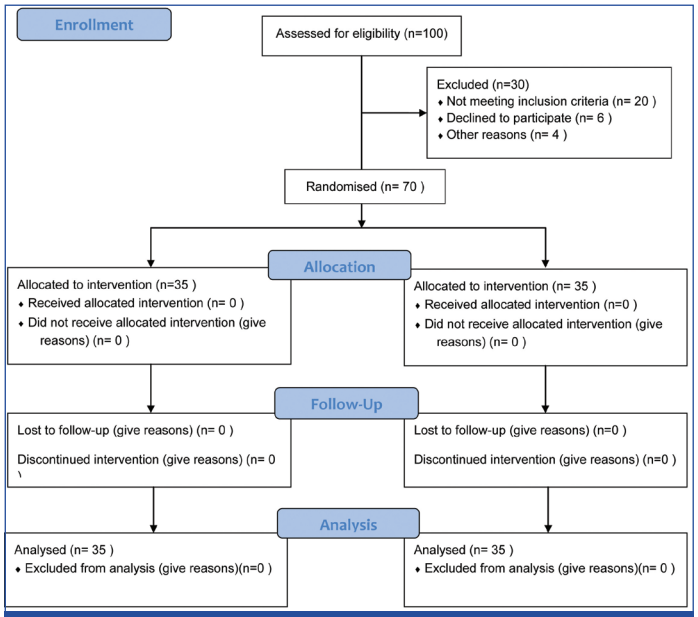
MATERIALS AND METHODS

The present randomised clinical trial was carried from January 2020 to September 2021 at the BLDEDU Shri BM Patil Medical College Hospital and Research Centre, Vijayapur, Karnataka, India. Approval was obtained from the Institutional Ethical Committee (IEC) (IEC/No-131/2019). The study was entered into the CTRI/2021/05/033463 clinical trial registry in India. The participants gave their informed consent to be a part of study.

Inclusion criteria: A total of 70 patients with ASA grades 1 and 2 between ages of 18 and 60 who were scheduled to have elective lower limb orthopaedic procedures under the subarachnoid block were included in the study.

Exclusion criteria: Patients with known allergies to study medicines or contraindications to spinal anaesthesia were excluded from in the trial.

Sample size calculation: The formula used to determine sample size was $n = f(\alpha/2, \beta) \times 2 \times \sigma 2 / (\mu 1 - \mu 2)^2$,where μ1 and μ2 were the mean outcome in the study groups respectively, σ is standard deviation. To achieve a two-tailed significance level of 5% and 80% power of detection of an increase in analgesic duration, a sample size of 60 was estimated.



[Table/Fig-1]: CONSORT flow diagram chart.

A computerised randomisation method was used to allocate patients into two groups of 35 patients each. The patients were blinded to the group allocation. Group NB received intrathecal 0.5% hyperbaric bupivacaine (15 mg; 3 mL)+1 mg of nalbuphine. Patients in group FB received intrathecal 0.5% hyperbaric bupivacaine (15 mg; 3 mL)+25 μg of Fentanyl [Table/Fig-1].

During the preoperative evaluation patient's detailed history and general physical and systemic examinations were carried out. The airway, respiratory system and cardiovascular system were assessed. Before performing the subarachnoid block, 500 mL of ringer's lactate solution was administered intravenously with an 18G intravenous cannula to establish intravenous access. Standard monitors were connected, and baseline vital values for Pulse Rate (PR), Blood Pressure (BP) and Oxygen Saturation (SpO_2) were recorded, including Non Invasive Blood Pressure (NIBP), pulse oximeter, and Electrocardiography (ECG).

26G Quincke spinal needle in L3-L4 intervertebral space, a lumbar puncture was carried out in the sitting position under strict aseptic guidelines. The study drug was injected intrathecally after confirming clear free flow of Cerebrospinal Fluid (CSF). An Anaesthesiologist blinded to the group allocation of the study drug carried out a recording of the study parameters. A hypodermic needle was used to test sensory blockade, and time of onset, the highest intensity of blockade, and length of the block was recorded. Onset of analgesia was defined as interval between intrathecal injection of study drug and achievement of T8 sensory level. Modified Bromage scale was used for assessment of motor blockade. Time of onset, degree of motor blockade and duration were noted. The period of time between the onset of analgesia and the administration of rescue analgesia was used to characterise the duration of analgesia.

Haemodynamic parameters noted at 0, 5, 10, 15, 30, 60 and 120 minutes.

Modified Bromage Scale [1]:

- Able to raise leg straight, full flexion of knees and feet.
- Inability to raise the leg, just able to flex knees, full flexion of feet.
- Unable to flex knees, but some flexion of feet possible.
- Unable to move the legs or feet.

Visual Analogue Scale (VAS) was used to measure the pain. Patients were given a scale with numbers ranging from 0 to 10 and asked to indicate on the scale how much pain they are currently feeling, from 0 (no pain) to 10 (worst pain possible). When VAS was greater than 3, diclofenac sodium 1.5 mg/kg IV infusion was administered to provide rescue analgesia, and the duration of the rescue analgesia was recorded. Side-effects like pruritis, nausea, vomiting, respiratory depression, bradycardia and hypotension were monitored. Atropine injections of 0.6 mg intravenously were to be used to treat bradycardia, which was defined as a 20% reduction in PR from the baseline PR. A bolus dose of 3 mg of injectable mephentermine was to be used to treat hypotension, which defined as a 20% drop in BP from basal values.

STATISTICAL ANALYSIS

Frequencies and proportions served as the representation for categorical data. Mean and standard deviation used to depict continuous data. For qualitative data, the Chi-square test was utilised. To determine mean difference between the variables, the independent t-test was employed as a measure of significance. Statistics were considered significant if p-value<0.05.

RESULTS

Both groups were compared on various demographic variables like age, gender distribution, body mass index and ASA grades. There was no significant difference observed [Table/Fig-2].

Variables (years)		Group NB	Group FB	p-value
Age		38.97±12.43	40.26±11.06	0.649
Sex (M:F)		27:8	24:11	0.420
Body Mass Index (kg/m^2)		22.91±1.98	22.37±2.16	0.285
ASA	1	21	24	0.454
	2	14	11	

[Table/Fig-2]: Demographic profile distribution.
M: Male; F: Female; ASA: American society of anaesthesiologists

There was no statistically significant difference between patients in group NB and group FB regarding the time at which sensory blockade began (onset; 178±14.97 vs. 174.4±12.57 seconds; p-value=0.28). There was no statistically significant difference between the two groups in the average time from the commencement of motor block to Bromage grade 3 (318.09±13.36 seconds in group NB and 322.23± 16.29 seconds in group FB). It was statistically significant that mean time for sensory block in groups NB and FB was 126.06± 6.52 minutes and 103.34± 3.7 minutes, respectively. With a p-value of <0.001, patients in group NB had a motor block for a mean time that was substantially longer than those in group FB (135.43± 6.63 minutes) [Table/Fig-3].

Variables	Group NB	Group FB	p-value
The onset of sensory block (seconds)	178±14.97	174.4±12.57	0.28
The onset of motor block (seconds)	318.09±13.36	322.23±16.29	0.249
Duration of sensory block (minutes)	126.06±6.52	103.34±3.7	<0.001
Duration of motor block (minutes)	156.66±9.31	135.43±6.63	<0.001
Two segment regression time (minutes)	132.4± 5.82	100.2±6.81	<0.001
Duration of Analgesia (minutes)	278.31±9.58	230.83±7.98	<0.001

[Table/Fig-3]: Block characteristics of two groups.

Haemodynamic parameters like Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in group NB and group FB at 0, 5, 10, 15, 30, 60 and 120 minutes intervals during intraoperative and postoperative, periods were comparable. There were no significant changes between the two groups. Occurrences of side-effects like nausea, vomiting, bradycardia and hypotension during the intraoperative period were minimal, and there was no significant difference (p>0.05) between group NB and group FB [Table/Fig-4].

Side-effects	Group NB	Group FB	p-value
Nausea	8	7	0.771
Vomiting	4	4	1.000
Bradycardia	4	4	1.000
Hypotension	13	13	1.000
Pruritus	0	0	-
Respiratory depression	0	0	-

[Table/Fig-4]: Comparison of side-effects between two groups.

In this study, there was no significant difference in mean VAS score between the two groups from 0 to 2 hours, but at 4 hours, the mean VAS score was higher in group FB than in group NB [Table/Fig-5].

Time	Group NB	Group FB	p-value
0	0	0	-
2 hours	0.4	0.49	0.572
4 hours	1.29	2.86	<0.001
6 hours	3.63	3.71	0.702

[Table/Fig-5]: Mean VAS score comparison.

DISCUSSION

Subarachnoid block has been used extensively in lower limb procedures. Subarachnoid block with local anaesthetics alone has a shorter duration of postoperative analgesia. To enhance postoperative analgesia, opioid additives such as fentanyl, morphine and buprenorphine have been explored [5-7]. Intrathecal opioids can give longer-lasting postoperative analgesia, causing fewer negative effects than systemic opioids [8,9]. The commonly administered opioids are agonist agents with extremely good analgesic efficacy but with a variety of μ accompanying adverse effects. Later, it was found that significant analgesia may get induced interacting with κ-binding sites without having any adverse effects associated with it [10,11]. The main benefit is selective pain blockade without considerable sympathetic and motor block, allowing for greater haemodynamic stability. There were studies on opioids like nalbuphine, a κ agonist/partial μ antagonist analgesic [12], as an adjuvant in spinal anaesthesia. The goal of the current randomised comparative trial was to evaluate the effectiveness of 0.5% hyperbaric bupivacaine and intrathecal nalbuphine 1 mg and fentanyl 25 μg as adjuvants in patients posted for elective lower limb surgeries. In patients scheduled for elective lower limb orthopaedic surgeries, it was found that intrathecal nalbuphine 1 mg as an adjuvant to 0.5% hyperbaric bupivacaine for subarachnoid block prolongs the duration of sensory block, motor block, and the postoperative analgesia more effectively than intrathecal fentanyl 25 μg.

Nalbuphine was compared to intrathecal morphine at doses of 0.2 mg, 0.8 mg, and 1.6 mg by Culebras X et al., [13], who found that intrathecal nalbuphine 0.8 mg provide more effective intraoperative and early pain relief with no side-effects. Additionally, they found that increasing the intrathecal nalbuphine dose in this group to 1.6 mg did not improve analgesic effects but did increase unfavourable effects. It asserts that increasing the dosage of nalbuphine only slightly improves its analgesic effects upto a point and then has no further effect. Nalbuphine 1 mg was used in this study to compare to fentanyl 25 μg.

In this current study, the onset of sensory block was comparable in group NB (178±14.97 seconds) and group FB (174.4±12.57 seconds), and there was no significant difference between the two groups in terms of reaching the T8 sensory block level (p-value=0.280). In the Gomaa HM et al., study there was hardly any significant variation in the initiation of the sensory block between the fentanyl and nalbuphine groups compared to intrathecal nalbuphine 0.8 mg and fentanyl 25 μg [14]. Similarly, Gupta K et al., also reported no statistically difference among nalbuphine and fentanyl groups [15]. Mean time for motor block development in group NB was found 318.09±13.36 seconds compared to 322.23±16.29 seconds in group FB, which was not statistically significant (p-value=0.249). Both Gupta K et al., [15] and Bindra TK et al., [16] found hardly any statistically significant differences in two groups in the start of motor blockage. However, Gomaa HM et al., [14] found that onset of motor block with fentanyl was noticeably quicker than with nalbuphine.

In present study, the mean duration of sensory block was longer (126.06±6.52 minutes) in patients of group NB than in patients of group FB (103.34±3.7 minutes), and it was statistically significant (p-value <0.001). Gupta K et al., and Gurunath BB and Madhusudhana R in their study discovered that time of two-segment sensory regression test in nalbuphine group was much longer than in the fentanyl group [15,17]. Duration of motor block in patients of group NB (156.66±9.31 minutes) was more than that of group FB (135.43 ±6.63 minutes), which was statistically significant (p-value <0.001). Ahluwalia P et al., also found that the nalbuphine group had a prolonged duration of motor block compared to the fentanyl group [18].

Duration of analgesia was substantially longer for patients in this trial who had received intrathecal nalbuphine 1 mg as an adjuvant than for the individuals who received intrathecal fentanyl 25 μg (p-value<0.001). In group NB, mean time of analgesia was 278.31± 9.58 minutes; in group FB, it was 230.83±7.98 minutes. Tiwari AK et al., observed that nalbuphine was statistically significant and had a longer analgesic duration than fentanyl [19]. Gomaa HM et al. Study on comparison of postoperative analgesia between intrathecal fentanyl 25 μg and nalbuphine 0.8 mg found that the nalbuphine group's analgesia was prolonged but that there was no statistically significant difference between the two groups.

At intervals of 0, 5, 10, 15, 30, 60, and 120 minutes, there was no statistically significant difference between the two groups in vital signs such heart rate, systolic blood pressure, and diastolic blood pressure. In this study, there was no any significant difference in mean VAS score between two groups from 0 to 2 hours. At 4 hours mean VAS Score was higher in group FB compared to group NB. Bindra TK et al., found that in the nalbuphine group, the mean VAS score for postoperative pain was lesser than in the fentanyl group [16]. Mostafa MG et al., and Naaz S et al., found patients who received intrathecal nalbuphine required a much smaller amount of rescue analgesics [20,21].

Side-effects such as pruritis, nausea, vomiting, respiratory depression, bradycardia and hypotension following administration of spinal anaesthesia with the above intrathecal opioids were minimal in both the groups and did not differ much among the two groups and were statistically not significant. In a study by Singh N et al., by combining nalbuphine with intrathecal bupivacaine, were able to maintain sensory block, postoperative analgesia without any negative side-effects or problems [22]. When Gurunath and Madhusudhana R compared intrathecal nalbuphine to fentanyl as a good spinal adjuvant, they discovered that nalbuphine users experienced less side-effects than fentanyl [17].

Limitation(s)

Since the present study was done in only elective lower limb orthopaedic surgeries, the observations and results of the study cannot be generalised for emergency surgeries.

CONCLUSION(S)

Patients scheduled for elective lower limb orthopaedic procedures, intrathecal nalbuphine 1 mg as an adjuvant to 0.5% hyperbaric bupivacaine for subarachnoid block prolongs duration of sensory block, motor block, and postoperative analgesia more successfully than intrathecal fentanyl 25 µg.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 15, 2022
- Manual Googling: Nov 22, 2022
- iThenticate Software: Dec 02, 2022 (12%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 14, 2022**
Date of Peer Review: **Nov 17, 2022**
Date of Acceptance: **Dec 06, 2022**
Date of Publishing: **Jan 01, 2023**