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Original Research Article

A Comparative Randomised Double-Blinded Study of Fentanyl versus Nalbuphine as an Opioid Adjuvant to Hyperbaric Bupivacaine in Spinal Anaesthesia for Lower Limb Orthopaedic Surgeries

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Abstract:

Introduction: Many adjuvants like opioids are added to the local anaesthetic agents for better and prolonged postoperative analgesia for orthopaedic surgeries done under spinal anaesthesia. In our study, we compared the efficacy of Fentanyl versus Nalbuphine as intrathecal adjuvant to hyperbaric Bupivacaine in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods: A randomized double-blinded study was conducted at a Tertiary care center on 100 ASA grade I and II adult patients divided into two groups, A and B, having 50 patients each, scheduled for lower orthopaedic surgeries under spinal anaesthesia. Group A received 3 ml Bupivacaine with 25 mcg Fentanyl, whereas Group B received 3 ml Bupivacaine with 0.5 mg Nalbuphine intrathecally. The onset and duration sensory and motor blockade, duration and quality of analgesia, hemodynamic changes and adverse effects were studied statistically, using Graph pad prism version 3.0. The quantitative variables were compared using unpaired t-test whereas qualitative variables were compared using Chi-square test.

Results: The differences between onset of sensory and motor blockade between two groups is significant ($p < 0.05$). The duration of sensory blockade, motor blockade and analgesia were significantly prolonged in Group B compared to Group A ($p<0.05$). Not a single patient from Group B required rescue analgesia whereas 15 patients from Group A required rescue analgesia. No complications seen in both the groups.

Conclusion: Nalbuphine is better intrathecal adjuvant to hyperbaric bupivacaine than Fentanyl, having faster onset of sensory and motor block with better analgesia, with hemodynamic stability and without any side effects.

Keywords: Nalbuphine, Fentanyl, Bupivacaine, Spinal anaesthesia.

Introduction

Spinal anaesthesia has always been considered better over General Anaesthesia as it is easy to administer having quick onset of action, safe with reduced stress response to surgery and having additional benefit of postoperative analgesia. In lower limb orthopaedic surgeries done under spinal anaesthesia, effective postoperative analgesia is very challenging as the effect of only local anaesthetic agents lasts for a short duration. For enhancing the duration and efficacy of spinal anaesthesia for achieving better postoperative analgesia, with reduced requirements of local anaesthetic agents and maintaining hemodynamic stability, various opioids are added as an adjuvant to the local anaesthetic agents used for spinal anaesthesia [1,2].

Fentanyl, a 4-anilido-piperidine compound is a highly lipid soluble opioid agonist that acts on μ receptor and principally responsible for supraspinal and spinal analgesia along with side effects like nausea, vomiting, pruritus, sedation and respiratory depression. It has been proved that it prolongs the duration of spinal anaesthesia with better postoperative analgesia [2,3}. Nalbuphine, a synthetic opioid agonist-antagonist drug of phenanthrene series. It acts as a partial kappa receptor agonist and μ receptor antagonist to provide analgesia. Nalbuphine administered intrathecally to produce analgesia without any μ agonist side effects like respiratory depression, excessive sedation, nausea, vomiting and urinary retention [4].

Nalbuphine is easily available whereas other opioid agonists like morphine, fentanyl are limited and needs licensing as they come under Narcotic Act. Though, few studies compared the effect of intrathecal nalbuphine versus fentanyl, with hyperbaric Bupivacaine as an adjuvant in caesarean section, there is relatively dearth of published data of such comparison in lower limb orthopaedic surgeries [5,6,7]. Therefore, this study was conducted to compare the effects of 25 mcg fentanyl and 0.5 mg nalbuphine when used as opioid adjuvants along with hyperbaric bupivacaine in terms of onset and duration of sensory and motor blockade, duration and quality of postoperative analgesia, hemodynamic changes, and adverse effects in patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia**.**

Method

A comparative randomised double-blinded study was conducted at a tertiary care center on 100 ASA grade I and II adult patients of both genders, aged between 18 to 55 years (both inclusive) divided into two groups, A and B having 50 patients each, scheduled for lower limb orthopaedic surgeries under spinal anaesthesia from September 2022 to September 2023. Patients with any contraindication to Central neuraxial blockade and with known hypersensitivity to any of the study drugs were excluded.

The study was initiated only after institutional Ethics committee permission was obtained. The study was performed in accordance of the ethical principles specified in the declaration of Helsinki and as per the guidelines of good clinical practice. The spinal block and perioperative information record keeping were performed by an anaesthesiologist who was blinded to the opioid adjuvant used and the group of patients.

After doing thorough pre-anaesthetic evaluation day prior to surgery and counselling for the spinal anaesthesia, patients were kept fasting overnight and scheduled for the procedure after obtaining informed consent from them. In the operation theatre, the multipara monitor was attached and the basal pulse rate (HR), non-invasive arterial systolic and diastolic blood pressure (SBP & DBP), Electrocardiogram (ECG), oxygen saturation (SpO2) were recorded.

A 20 G intravenous cannula was inserted in the suitable arm and Ringer Lactate solution was infused 10 ml/kg as preloading. Patients were premedicated with Inj. Ondansetron 0.1 mg/kg IV. Under all aseptic precautions subarchnoid block was given by using 25 G Quinkes needle at L3-L4 intervertebral space in sitting position using midline approach.

Patients belonging to Group A were injected with 0.5% hyperbaric Bupivacaine with 25 mcg Fentanyl and those belonging to Group B were injected 0.5% hyperbaric Bupivacaine with 0.5 mg Nalbuphine intrathecally. After completion of injection patients were made supine and end point of injection was considered as time zero.

Parameters evaluated:

1. **Sensory block:** Sensory blockade was assessed by using pin prick method on each side. Onset of sensory block was defined from the end of intrathecal injection till the sensory loss at T10 level and its duration was defined as the period between the end of intrathecal injection and recovery of sensation at L1 level.
2. **Motor block:** Motor blockade was assessed by Modified Bromage Scale as follows-

Score 0 = Patient is able to move hip, knee and ankle

Score 1= Unable to move hip but able to move knee and ankle

Score 2 = Unable to move hip and knee but able to move ankle

Score 3 = Unable to move hip, knee and ankle

Onset of motor block was the time duration from the intrathecal injection to achievement of Modified Bromage Score 3 and its duration was defined as regression of the motor blockade to Modified Bromage Scale 0.

3. Vital Parameters: Vital parameters were monitored continuously for every minute for the first 10 minutes and then every 5 minutes till the end of the surgery and then every 15 minutes till complete regression of the block. Fall in baseline. Hypotension was treated with fluid bolus and subsequently titrated doses of Inj. Mephenteramine 3 mg IV if needed. Heart Rate less than 60 is considered as bradycardia and treated with Inj. Atropine 0.01 mg/kg intravenously.

4. Quality of Analgesia: It was assessed with the help of visual analogue scale (VAS – 0 to 10 where 0 means no pain to 10 means worst pain). No analgesic was given in the immediate postoperative period until the patient requested for analgesia. Duration of effective analgesia was taken as the time from the completion of subarachnoid block to the first rescue analgesic requirement of intramuscular Inj. Diclofenac 75 mg, at VAS score of > 3.

5. Side effects: Incidence of side effects such as nausea, vomiting, respiratory depression, shivering was noted. Nausea and vomiting was treated with inj. Ondansetron 4 mg IV and pruritus with Inj. Pheniramine maleate 2 ml. IV. Respiratory

depression if any was treated with oxygen supplementation.

Statistical Analysis: Categorical variables were presented in number and percentage and continuous variables were presented as mean ± SD and median.

Normality of data was tested by Kolmogorov-Smirnov test. If the normality is rejected then non-parametric tests were used.

Statistical tests applied as follows

- Quantitative variables were compared using unpaired t-test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.
- Qualitative variables were compared using Chi-Square test /Fisher's exact test.

A p value of < 0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Graph pad prism version 3.0.

Results

Table 1: Demographic Details and ASA grading in study groups

Parameter	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
Demographic Details			
Mean Age (years)	45.2 ± 12.95	42.24 ± 14.16	0.27*
Number of Males	36	42	0.22 †
Number of Females	14	8	
ASA grading			
ASA Grade I	49	50	1.00 †
ASA Grade II	1	0	

***Comparison by Unpaired t - test, p value not significant (p > 0.05), † Fisher's test indicates no significant difference (p > 0.05)**

The demographic parameters and ASA grading were comparable between both the groups as shown in the Table 1 (p>0.05).

Table 2: Comparison of course of Sensory and Motor block with duration of analgesia

Parameter	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
Onset of Sensory block (min)	3.2 ±0.90	2.86 ±0.45	0.04
Onset of Motor block (min)	4.22 ±0.85	3.86 ±0.45	0.02
Time duration of complete resolution of Sensory block (hrs)	4.09 ±0.53	5.03 ±0.43	<0.0001
Time duration of complete resolution of motor block (hrs)	4.51 ±0.48	5.40 ±0.46	<0.0001
Duration of effective analgesia (hr)	4.17 ± 0.48	4.83 ± 0.70	<0.0001

Mann Whitney's Test indicates significant difference (p< 0.05)

Onset of Sensory block and Motor block was significantly earlier among patients in Group B. Time duration of complete resolution of Sensory block as well as Motor block was significantly greater among patients in Group B.

Table 3: Comparison of heart rate among patients in two group

Time (min)	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
0	82.14 ±5.95	80.22 ± 4.86	0.05
2 min	80.14 ±4.67	80.62 ±4.86	0.83
5 min	80.46 ±4.60	81.46 ± 5.04	0.23
10 min	79.72 ±4.24	80.2 ±4.54	0.63
15 min	79.94 ±4.31	80.02 ±4.10	0.51
20 min	79.86 ±4.66	79.74 ±4.76	0.59
25 min	79.44 ±4.21	78.88 ±4.50	0.61
30 min	79.42 ±4.83	79.52 ±4.06	0.84
45 min	79.22 ±4.20	79.5 ±4.06	0.75
60 min	78.48 ±3.91	78.94 ±4.36	0.81
90 min	78.16 ±3.91	79.04 ±4.29	0.36
120 min	77.74 ±3.64	78.48 ±3.49	0.31

No significant difference was seen in the heart rate of patients in both the groups throughout the study period.

Table 4: Comparison of Systolic BP among patients in two group

Time (min)	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
0	118.96 ±11.41	115.8 ±12.85	0.19 (UP)
2 min	117.74 ±11.66	119.2 ±12.68	0.55
5 min	118.88 ±11.55	119.96 ±12.42	0.65
10 min	120.84 ±11.42	121.52 ±12.17	0.59
15 min	119.16 ±12.92	120.08 ±11.85	0.64
20 min	121.12 ±12.18	120.52 ±11.99	0.49
25 min	119.72 ±11.78	118.96 ±11.57	0.68
30 min	120.56 ±10.17	120.2 ±11.86	0.74
45 min	119.16 ±12.92	120.88 ±11.25	0.44
60 min	121.28 ±12.28	121.48 ±10.91	0.84
90 min	120 ±11.66	119.64 ±10.93	0.51
120 min	121.04± 9.94	120.44 ±1.21	0.33

No significant difference was seen in the systolic blood pressure of patients in both the groups throughout the study period.

Table 5: Comparison of Diastolic BP among patients in two groups

Time (min)	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
0	75.96 ±8.60	74.12 ±8.47	0.39
2 min	76.02 ±9.33	80.12 ±8.80	0.02
5 min	77.22 ±8.73	80.44 ±7.97	0.08
10 min	78.36 ±8.16	80.92 ±8.03	0.13
15 min	78.16 ±9.53	79.64 ±8.76	0.36
20 min	78.64 ±8.96	80.28 ±8.83	0.29
25 min	78.36 ±8.06	77.04 ±9.16	0.33
30 min	79 ±7.12	77.4 ±8.57	0.24
45 min	73.82 ±8.34	77.02 ±8.91	0.05
60 min	76.64 ±8.47	78 ±10.15	0.19
90 min	77.56 ±7.96	77.92 ±10.34	0.75
120 min	79.04 ±7.12	76.44 ±0.60	0.11

Diastolic blood pressure was significantly lower among patients in Group A at 2 min. No significant difference was seen in the diastolic blood pressure of patients in both the group in rest of the study period.

Table 6: Rescue analgesic needed

Rescue analgesic	Group A (Fentanyl group) n=50	Group B (Nalbuphine group) n=50	p value
Yes	15	0	<0.0001
No	35	50	(Fisher test)

Significant difference was seen in the number of patients who were given rescue medication.

Discussion

Spinal Anaesthesia is the most suitable anaesthesia technique for lower limb orthopaedic surgeries being a safer technique, with faster onset of action with added advantage of postoperative analgesia. The use of adjuvants especially opioids such as Fentanyl, Nalbuphine with hyperbaric Bupivacaine has shown reduced requirement of local anaesthetic drug, so as to reduce its side effects with better hemodynamic stability and postoperative analgesia enabling early ambulation of patients [1,2,3,4]. Hence, our present randomized double blinded study was conducted to compare intrathecal Fentanyl (mu receptor agonist) with Nalbuphine (kappa agonist-partial mu antagonist) as an adjuvant to 0.5% hyperbaric Bupivacaine in patients undergoing lower orthopaedic surgery under spinal anaesthesia. Various studies conducted earlier proved that intrathecal dose of Fentanyl more than 25 mcg as an adjuvant in spinal anaesthesia, does not show any additional benefit, hence we decided to use 25 mcg Fentanyl for our study [6]. Jyoti B et al concluded from their study that increasing the dose of Nalbuphine more than 0.8 mg does not show any enhanced analgesia but show increased side effects [8,9,11,12]. Moreover, there is not enough data available on 0.5 mg of

Nalbuphine used as an adjuvant to hyperbaric Bupivacaine for spinal anaesthesia, hence we decided to study effects of a very low dose of Nalbuphine (0.5 mg) in present study. Culebras et al., compared intrathecal morphine with intrathecal nalbuphine in different doses of 0.2 mg, 0.8 mg and 1.6 mg and concluded that intrathecal nalbuphine 0.8 mg provides good postoperative analgesia, without any side effects. They found that intrathecal nalbuphine 1.6 mg did not increase the analgesic efficacy, but the side effects increased in this group [9]. It implies that by increasing the dose of nalbuphine, analgesic effect increases only up to a certain point beyond which there is no further increase with the dose enhancement i.e. nalbuphine exhibits a ceiling effect to Analgesia.

In our study, the demographic parameters like age, gender and ASA grading were comparable in both the groups as shown in Table 1($p>0.05$).

The onset of Sensory and motor block was significantly earlier among patients in Nalbuphine group as shown in Table 2, whereas Gurunath et al observed delayed onset in nalbuphine group [22]. However, in a similar study conducted by Monali K et al and Kamal Chandra D et al, no significant difference was found in the two groups with respect to sensory and motor block onset [15,18]. Gomaa et al [19] and Gupta et al [17] compared intrathecal nalbuphine 0.8 mg and fentanyl 25 µg as an adjuvant and found that no statistically significant difference in onset of sensory and motor block between two study groups.

Time of complete resolution of Sensory block was significantly greater among patients in Nalbuphine group (Table 2), which is similar to the results of the studies done by Monali K et al [15], Kamal Chandra et al [18] and Singh N et al [21].

It was also observed that time of complete resolution of motor block was significantly greater among patients in Nalbuphine group (Table 2), similar to the results of Gupta et al [17] and Brinda et al [20].

Duration of analgesia is significantly prolonged in nalbuphine group than fentanyl group (Table 2), like the study conclusions of Kamal Chandra D et al, Bindra et al, where 0.8 mg dose of Nalbuphine was administered [18, 20]. 15 patients in Fentanyl group needed rescue analgesia whereas none of the patients from Nalbuphine group needed it (Table 6). Nath A et al also compared 0.5 mg Nalbuphine with Fentanyl 25 mcg like us but found better analgesia with Fentanyl than Nalbuphine in contrast to our results [23].

Vital parameters like heart rate, systolic and diastolic BP showed statistically insignificant difference except for fall in diastolic BP in Fentanyl group at 2 minutes (table 3,4,5) similar to the results of Gupta et al [17] and Nath A et al [23].

Both groups did not present with any side effects depicting the safety profile of both the drugs similar to the study done by Monali k et al and Nath A et al [15,23].

Conclusion

Nalbuphine (0.5 mg) as an intrathecal adjuvant to hyperbaric bupivacaine increases the duration of sensory block, motor block and the effective analgesia without any significant side effects than that of fentanyl in patients undergoing lower limb orthopedic surgeries under spinal anaesthesia.

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