

## COMPARATIVE EVALUATION OF NALBUPHINE AND FENTANYL INTRATHECALLY WITH BUPIVACAINE IN ORTHOPEDIC SURGERIES. “OUR EXPERIENCE OF 120 CASES”

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### ABSTRACT

**Background & Objective** - This study aimed to compare efficacy of nalbuphine and fentanyl as adjuvant to bupivacaine in providing intra-operative anesthesia and post-operative analgesia in lower limb orthopedic surgeries, and to compare the characteristic of sensory and motor block, hemodynamic parameter, time of first rescue analgesia and adverse effects between two groups.

**Method**- In this clinical trial, 120 patients undergoing elective lower limb orthopedic surgeries under spinal anesthesia were randomly allocated in two groups. In group BN, the patients received 0.5% 3ml (Heavy Bupivacaine + 800 mcg Nalbuphine. In group BF patients received 0.5% 3ml (Heavy Bupivacaine + 25mcg Fentanyl).

**Result & interpretation**- In group BF Onset of motor block, maximum level of block and time to reach a peak level of the block was significantly faster, whereas in BN group duration of motor block and time for first rescue analgesia was significantly prolonged. However, there was no significant difference in time for two segment regression=0.157 (NS) and hemodynamic changes.

**Conclusion**- We conclude that fentanyl as an adjuvant to bupivacaine provides higher segmental level sensory blockage, faster sensory and motor blockage than nalbuphine. Postoperative analgesia more in the Nalbuphine group than fentanyl.

**Keywords**- Analgesia, Bupivacaine, Fentanyl citrate, Nalbuphine

### INTRODUCTION

A control of postoperative pain relievers leads to earlier rallying, smaller pulmonary and cardiac complications, lower chances of deep vein thrombosis, with lower likeliness of the progression of

neuropathic agony, drop cost of care and enhance patient satisfaction.<sup>1</sup>

A multi-disciplinary way to deal with pain management by providing regional anesthesia, centrally acting analgesics like paracetamol, peripheral nonsteroidal anti-inflammatory drugs and opioids leads to enhance pain relief, better patient outcomes, improved efficacy and reduced drawbacks, including the long-term satisfaction of reduced risk of developing chronic pain.<sup>2</sup> Spinal anesthesia is defined as “the regional anesthesia by blocking nerves in subarachnoid space” is a leading and customary technique. It is simple to perform, offers quick onset of action and relatively less drawbacks. So, choice of technique for lower limb surgeries.<sup>3</sup> There is numerous profits of neuraxial anesthesia over general anesthesia like decline incidence of strain reaction to surgery with post-operative analgesia. but only one local anesthetic drug given in spinal anesthesia provide brief period of analgesia post-operatively.<sup>4</sup>

Eklblom and Widman (1966) employed bupivacaine for spinal agony and reported its low toxicity and extended duration of action. It was later used by many workers for conduction of epidural block and they perceive that the potency and duration of bupivacaine was three to four times more than lignocaine.<sup>5</sup> Adjuvants such as (morphine, midazolam, dexmedetomidine, clonidine etc) have been practiced with local anesthetic in regional anesthesia to nullify intra-operative visceral and somatic agony and to offer prolonged duration of post-operative agony.<sup>6</sup>

A lipophilic narcotic like fentanyl ( $\mu$ agonist) turned into the adjuvant of decision due to its fast beginning, and brief length of activity with a lower incident of respiratory depression.

Dosages of 10–25 mcg of fentanyl is usually utilized intrathecally. Focal neuraxial narcotics are known for their incidental effects, like pruritus, urinary incontinence and respiratory depression.<sup>6,7</sup>

Nalbuphine is combined  $\mu$  antagonist and  $\kappa$  agonist. It can possibly keep pace with or even upgrade  $\mu$ -narcotic based analgesia while at the same time limiting the  $\mu$ -opioid related incidental effects. Therefore, while giving great absence of pain, it is without narcotic related adverse impacts that is (sickness, emesis, pruritus, bothersome sedation, respiratory discouragement and the advancement of tolerance/reliance) and improve the absence of pain by  $\kappa$ -opioid receptors.<sup>7-9</sup>

In this study, we compared effect of nalbuphine and fentanyl as adjuvant to hyperbaric bupivacaine in spinal anesthesia in attempt to prolong spinal anesthesia and analgesia.

## METHOD

This prospective, randomized, and comparative, interventional study was conducted from September 2021 to May 2021, after receiving approval from the institutional ethical committee. Written and informed consent was obtained from all the patients.

120 Patients were randomly divided into two groups of 60 in each with the help of a computer-generated table of random numbers. Both the patient and the observer were blinded. The observer recruited all the patients and collected the data. Spinal anaesthesia was performed by an experienced anesthesiologist.

### INCLUSION CRITERIA:

Patients with ASA CLASS I/II

Lower limb surgery

Age between 18 to 65 years

Patients giving written & informed consent

#### EXCLUSION CRITERIA:

Patient refusal for the procedure.

with bleeding diathesis,

Local infection at injection site, allergic to study drugs,

Any neurological disease, spinal deformity.

A detailed pre-anaesthetic evaluation of the patient was performed a day before surgery. Patient was kept NPO for 8 hours. Standard five lead ECG, non-invasive blood pressure (NIBP) and pulse oximetry (SpO<sub>2</sub>) were noted in operating room. Intravenous (IV) access was secured using a 20G cannula on nondominant hand.

Under all aseptic precautions, subarachnoid block was given after local infiltration of skin with 2% lignocaine using 25G Quincke's spinal needle at the level of L3-4 or L4-5 inter- space via the midline approach in sitting position: After Free flow of CSF following combination was given:

Group N received 3 ml of 0.5% heavy Bupivacaine with 800mcg Nalbuphine (diluted in normal saline to make total volume 3.5 ml) was injected intrathecally.

Group F received 3 ml of 0.5% heavy Bupivacaine 0.5 ml (25 mcg) with fentanyl (total volume 3.5 ml) was injected in subarachnoid space.

Following subarachnoid block, patients were positioned supine and evaluated for sensory and motor block characteristics. Sensory block was checked using a pin prick method in mid- axillary line every 2 minutes for 15 min, then every 15 minutes until the completion of surgery.

Using modified Bromage scale assessment of motor block was done.

0=able to flex whole lower limb at hip

1=able to flex the knee but unable to raise leg at hip

2=able to flex the ankle but unable to flex knee 3=no movement of lower limb.

Sensory and motor block was assessed every 2 minutes for 15 min and then every 15 minutes until complete regression. Hemodynamic changes Pulse rate, Blood pressure was monitored.

Bradycardia was treated with inj. Atropine sulfate 0.6mg iv. Hypotension was treated with Inj. mephentermine as per requirement

Pain rating scale was from 0 to 10. No pain was considered when score was 0 and first rescue analgesia was considered when score was more than 4. Injection paracetamol was given as first rescue analgesia and time was noted.

Duration of pain relief defined as the time from intrathecal injection to first request for supplemental (rescue) analgesia. HR, BP, respiratory rate, and Sedation score was recorded. Patients were assessed using a 10-point VAS.

#### Statistical analysis

Statistical analysis was done with the SPSS, version 21 (SPSS inc., Chicago, IL, USA). The Categorical variables were presented as numbers (percent) and were compared using the Chi-square test. The quantitative variables were presented as mean and standard deviation and were compared by

student t-test. Results are considered to be significant if the P-value was less than 0.05.

Sample size was calculated based on previous study done by Farahat et al.<sup>12</sup> Duration of post-operative complete analgesia was considered as primary outcome and previous studies showed that it was significantly longer in BN group (Bupivacaine and nalbuphine) than BF group (Bupivacaine and fentanyl) with (p value < 0.001).

Based on previous study with confidence interval of 95% and power of 80%. 52 patients in each group were required as sample size. To compensate possible dropout, we include 120 total patients (60 in each group) as sample size.

## RESULT

Demographic data includes age, sex, ASA grading is comparable. The highest level of sensory block level achieved in both the group was T6. But in group F more number of (70%) patients achieve level T6 compared to group N (25%). and in group N more number of patients achieve level T8 (53.3%). The difference was statistically significant between groups. (P value < 0.001).

The mean time to reach peak block level was 7.84±2.21 minutes in group F and 10.51±2.25 minutes in group N. (Table 1) The difference was significant between groups as time to reach peak level was more in group N than group F. (P value < 0.001)

Table 1. Characteristics of sensory block

Sensory block Characteristics	BN Group	BF Group	P-Value
Peak Sensor Block Level, n (%)			
T6	15(25)	42(70)	
T8	32(53.3)	16(26.6)	
Time to reach peak level(min), mean±SD	10.51±2.25	7.84±2.21	<0.001(S)
Time to two-segment regression(min), mean±SD	97.91±11.86	94.02±12.41	0.157(NS)

The mean time for two-segment regression for group F was 94.02 ±12.41 minutes and for group N was 97.91 ±11.86 minutes. (Table 1)) There was no significant difference found between two groups for two-segment regression. (P value 0.157)

The onset of motor block was 2.59±0.85 minutes in Group F and in group N was 5.41±1.31 minutes. The results show that the onset of motor block was faster in group F than in group N and statistically significant. (P value < 0.001) (Table 2)

The duration of motor block was statistically significant between groups. It was significantly shorter in group F compared to group N (178.70±11.31 min vs. 189.82 ±10.36 min in group F and group N respectively). The P-value was significant (P < 0.001, S) (Table 2)

Table 2. Characteristics of motor block&amp; Time for first rescue analgesia

Motor block characteristics	BN Group	BF Group	P-Value
Onset of motor block(min), mean±SD	5.47±1.31	2.59±0.85	<0.001(S)
Duration of motor block(min), mean±SD	189.82±10.36	178.70±11.31	<0.001(S)
Time for first rescue analgesia(min), mean±SD	221.15±15.08	206.43±11.14	<0.001(S)

The mean time for first rescue analgesia was 206.43±11.14 minutes in group F, compared to 221.15±15.08 minutes in group N (P < 0.001, S) (Table 2)

Statistical analysis reveals no significant difference in mean heart rate between group F and group N at different time intervals (P > 0.05).

Difference in the systolic blood pressure at different time intervals was comparable between group F and group N. There was decrease in systolic blood pressure in nalbuphine group was more just after subarachnoid block and up to 10 minutes with significant difference between two groups. (Figure 1).

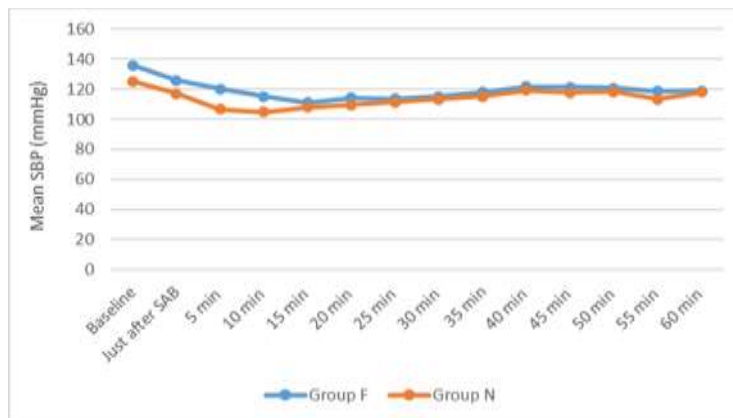


Figure 1: Systolic blood pressure of patients

The difference in mean arterial pressure at different time intervals was mostly non-significant between group F and group N. (P value>0.05) (Figure 2)

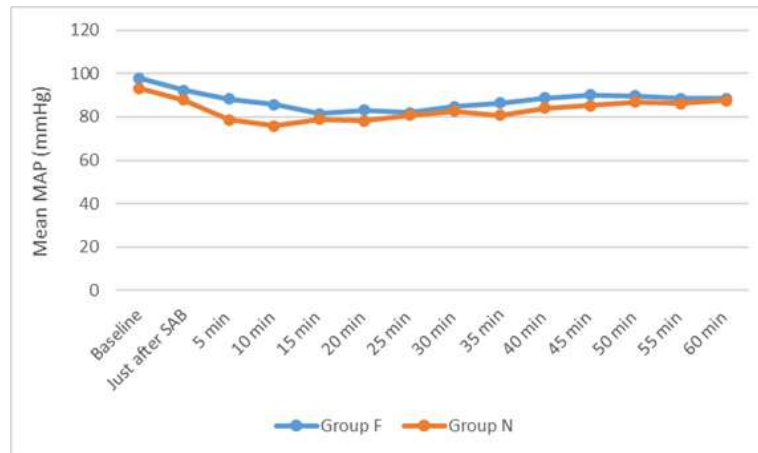


Figure 2: Mean blood pressure of patients.

## DISCUSSION

Surgeries below umbilicus could be practiced under local anesthesia, neuraxial block, and general anesthesia, although neuraxial block is preferred over all other options. Neuraxial block has benefits like quick onset of action, less fear of infection, and budget friendly.

Borse Y M et al<sup>10</sup> found that addition of Buprenorphine with bupivacaine prolongs duration of sensory blockage (132 min for 2.5ml heavy Bupivacaine alone and 215.4 minutes for 2.5ml heavy bupivacaine with 150 mcg buprenorphine).

Sonia Nahakpam et al<sup>11</sup> compared a three different dose of fentanyl with 7.5 mg 0.5% Bupivacaine and found a significant improvement in duration and quality of analgesia post-operatively with increasing dose of fentanyl from 15mcg to 20 mcg and 25 mcg. ( $129.71 \pm 18.7$ ,  $193.43 \pm 18.46$ ,  $279.43 \pm 31.61$  respectively).<sup>11</sup>

Arghya Mukhrjee et al<sup>12</sup> compared three different doses of nalbuphine with 12.5 mg heavy bupivacaine and 12.5 mg heavy bupivacaine alone shows that nalbuphine prolongs postoperative analgesia significantly. 213.8 min in patients received 0.2 mg, 237.3 min in patients received 0.4 mg, 278.5 min in patients received 0.8 mg nalbuphine and 170 min in patients received bupivacaine alone. Above studies suggest that both fentanyl and nalbuphine both are effective adjuvant with bupivacaine to enhance quality of sensory and motor blockage. So, we have decided to compare quality of nalbuphine and fentanyl in intrathecal route.

### Peak sensory block level

In our study, we observed that the far up level achieved in both groups were T6. But number of patients achieved T6 level were more in Group F (Bupivacaine and fentanyl) and in Group N (Bupivacaine and Nalbuphine) number of patients were more who achieved T8 level as far up level.

Similar data was found by Dr. Rajkumar N Jaisinghani et al<sup>13</sup> They conducted randomized double-blind study in patients undergoing lower limb surgeries and by adding 25 mcg fentanyl or 800 mcg nalbuphine in 15 mg bupivacaine and concluded that more patients achieve T6 level in fentanyl group whereas more number of patients achieve T8 level in nalbuphine group.

Farahat I. Ahmed<sup>14</sup> compared 12.5mg Bupivacaine with 800mcg nalbuphine or 25mcg Fentanyl in spinal anaesthesia in patients undergoing caesarean section. They found that maximum level of

dermatomal block achieved was T3 in fentanyl group and T4 in nalbuphine group.

#### **Time to reach peak sensory block level**

It is the time to attain the highest level of dermatomal block after neuraxial blockade. We observed that the time to reach peak block level was  $7.84 \pm 2.21$  minutes in group F and  $10.51 \pm 2.21$  minutes in group N.

Swati Bisht et al<sup>9</sup> compared a 15 mg 0.5% Bupivacaine and 25 mcg fentanyl in one group and 1 mg nalbuphine in other group, they found that time to reach peak sensory blockage was remarkably quick in fentanyl group ( $6.31 \pm 0.58$  min) compared to nalbuphine group ( $6.76 \pm 0.54$  min) same as our study. Farahat I. Ahmed et al<sup>14</sup> done study to compare effect of 800 mcg nalbuphine and 25 mcg fentanyl as adjuvant to 12.5 mg heavy bupivacaine also found that time to achieve maximum level of sensory blockage was remarkably faster in fentanyl group ( $3.2 \pm 0.7$  min) compared to nalbuphine group ( $3.6 \pm 0.9$  min).

Shagufta Naaz et al<sup>15</sup> compared effect of 12.5 mg hyperbaric Bupivacaine with 25 mcg fentanyl or 0.8 mg Nalbuphine or 1.6 mg Nalbuphine in 3 different groups. They observed that difference was non-significant in all three groups

#### **Time for two segment regression**

The time for two-segment regression and time for regression to T10 in our study in group F was  $94.02 \pm 12.41$  minutes and in group N was  $97.91 \pm 11.86$  minutes. There was no significant difference found between two group for regression up to T10 (P value 0.157).

Our result coincides with Dr. Rajkumar N Jaisinghani et al<sup>13</sup> found that there was no significant difference in two segment sensory regression in patients receiving 25 mcg fentanyl or 0.8 mg nalbuphine with 15 mg of 0.5% Bupivacaine ( $109 \pm 7.06$  min in GF and  $112.6 \pm 11.66$  min in GN).

Manjula R et al<sup>16</sup> done a study and found that there was no significant difference in two segment sensory regression. They did study on patients undergoing lower limb surgeries receiving 1 mg of nalbuphine or 150 mcg buprenorphine as adjuvant to 15 mg 0.5% bupivacaine.

In contrast to our result Swati Bisht et al<sup>9</sup> conducted study on patients receiving 25 mcg fentanyl or 1 mg Nalbuphine with 15 mg of 0.5% Bupivacaine found that nalbuphine takes longer time for two segment sensory regressions ( $88.88 \pm 9.48$  min in GF and  $97.72 \pm 9.50$  min in GN).

#### **Time for complete motor blockage**

The onset of complete motor block was  $2.59 \pm 0.85$  minutes in group F and in group N was  $5.41 \pm 1.31$  minutes. The results shows that onset of motor block was faster in group F than in group N and statistically significant. (P value  $< 0.001$ )

Wafaa Zaki AL et al<sup>17</sup> compare 25 mcg fentanyl and 800 mcg nalbuphine as adjuvant to 3.5 ml 0.5% bupivacaine in spinal anesthesia found that nalbuphine took  $57.50 \pm 18.53$  sec and fentanyl took  $51.00 \pm 11.31$  sec for complete motor blockage.<sup>17</sup>

In contrast to our findings M Parvin et al<sup>18</sup> found no significant difference in time to achieve complete motor blockage. They used 25 mcg fentanyl and 2 mg nalbuphine as adjuvant to 15 mg of heavy bupivacaine.

#### **Duration of motor block**

Regression of motor block was assessed using modified Bromage scale, the duration of motor block in

our study was significantly shorter in group F compared to group N ( $178.70 \pm 11.31$  min vs.  $189.82 \pm 10.36$  min in group F and group N respectively). Similar result was noted by M Pravin et al<sup>18</sup> They compared 25 mcg fentanyl and 2mg Nalbuphine as adjuvant to 15 mg heavy Bupivacaine on Patients undergoing perianal surgery. They also found prolonged motor blockage in patient received nalbuphine (190min) than fentanyl (145 min) group.

Kumkum Gupta et al<sup>4</sup> found significant extended duration of motor blockage with 2mg nalbuphine with 3.5 ml 0.5% bupivacaine ( $183.26 \pm 29.63$  min) as compared to 25 mcg fentanyl with 3.5 ml bupivacaine ( $141.63 \pm 18.05$  min).

In contrast to our data Dr Rashmi Bengali et al<sup>8</sup> noted no significant difference in duration of motor blockage ( $163.50 \pm 11.23$  min in group N and  $160.67 \pm 10.31$  mins in group F).

#### **Time for first rescue analgesia**

In our study requirement of first rescue analgesia was significantly earlier in group F compared to group N. The mean time for first rescue analgesia was  $206.43 \pm 11.14$  minutes in group F, compared to  $221.15 \pm 15.08$  minutes in group N.

Kumkum Gupta et al<sup>4</sup> done a study on patients undergoing lower limb orthopedic surgeries compared 25mcg fentanyl and 2 mg nalbuphine as adjuvant to 3.5ml 0.5%

Bupivacaine and evaluated that requirement for first rescue analgesia in nalbuphine group was at  $318.64 \pm 21.92$  mins and in fentanyl group was at  $278.74 \pm 29.67$  mins.

Farahat I. Ahmed et al<sup>14</sup> also found similar results by comparing 800 mcg nalbuphine or 25 mcg fentanyl with 12.5 mg of 0.5% Bupivacaine. They noticed that complete postoperative agony was remarkably longer in nalbuphine group than fentanyl group ( $225.4 \pm 82.3$  min in BN group and  $176.1 \pm 46.4$  min in BF).

Swati Bisht et al<sup>9</sup> noticed that fentanyl group demands early first rescue analgesia than nalbuphine group ( $283.44 \pm 78.97$  mins and  $460.78 \pm 77.98$  min respectively).

#### **Side effects**

In our study side effects like shivering, hypotension, and bradycardia are comparable.

There was no complain of urinary retention, nausea and pruritus.

#### **Hemodynamic changes**

There was mostly no significant difference observed in heart rate, SpO<sub>2</sub>. We observed slight drop of systolic blood pressure, and diastolic blood pressure just after subarachnoid block in nalbuphine group which was easily managed by injection mephentermine.

Shagufta Naaz et al<sup>15</sup> compared three groups who received 12.5 ml heavy bupivacaine and 25 mcg fentanyl or 0.8 mg nalbuphine or 1.6 mg nalbuphine. Only few patients received 1.6 nalbuphine with 12.5 ml bupivacaine experienced hypotension which was easily treated with injection mephentermine.

Dr Rashmi Bengali et al<sup>8</sup> who done study to compare 25 mcg fentanyl and 1 mg nalbuphine as adjuvant to 15mg 0.5% Bupivacaine also observed no statistically significant difference in heart rate, mean blood pressure and SpO<sub>2</sub>.



**CONCLUSION**

We concluded that addition of fentanyl as adjuvant to bupivacaine provides higher segmental level sensory blockage than nalbuphine group. Sensory and motor blockage is faster in fentanyl than nalbuphine whereas longer time of postoperative analgesia is with Nalbuphine.

Thus, we concluded that for lower limb orthopedic surgery addition of nalbuphine is better alternative than fentanyl and provides longer duration of post-operative analgesia.

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**Conflict of interest** None

**Limitation** In our study we compared two drugs for their effectiveness. We did not compare them with control group. After adding of control group we would have more data to study.

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