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Comparison of Efficacy of Intrathecal Isobaric Ropivacaine-Fentanyl and Ropivacaine-Nalbuphine for Post-Operative Analgesia in Lower Limb Orthopaedic Surgery

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Abstract

Background: Spinal anesthesia is a common widely used technique in lower limb orthopedic surgeries for effective pain relief. Adding intrathecal adjuvants like opioids can prolong the effects of analgesia. This study is done to compare the efficacy of fentanyl citrate and nalbuphine hydrochloride as adjuvants for spinal anesthesia.

Methods: The present study included 100 patients undergoing elective lower limb orthopedic surgeries under spinal anesthesia. We randomized the patients into two groups: Group RF (fentanyl 25mcg + ropivacaine 22.5mg) and Group RN (nalbuphine 1mg + ropivacaine 22.5mg). The factors for assessment were Intraoperative hemodynamics, onset and duration of sensory and motor block, analgesia duration, and post-operative pain scores (VAS).

Results: We observed that the Group RF had a statistically significant faster onset of sensory and motor block as compared to the Group RN ($p < 0.05$). Sensory block and motor block durations were shorter in Group RF compared to group RN (254.22 ± 7.89 mins vs. 296.98 ± 8.31 mins) and (153.18 ± 4.76 mins vs. 190.2 ± 5.82 mins) respectively. Longer post-operative analgesia was observed in Group RN (299.7 ± 7.72 mins) than in Group RF (274.38 ± 9.79 mins) ($p < 0.0001$) which was statistically significant.

Conclusions: Both fentanyl and nalbuphine, combined with ropivacaine for spinal anesthesia, provided effective pain relief. Nalbuphine offered longer analgesia, while fentanyl had a quicker onset and shorter motor block.

Nalbuphine may be preferred for prolonged analgesia, while fentanyl is better for faster motor recovery.

Keywords: Fentanyl, Nalbuphine Hydrochloride, Isobaric Ropivacaine, Lower Limb Orthopedic Surgeries, Isobaric Ropivacaine**.**

Introduction

Spinal anesthesia is often preferred over general anesthesia due to its ability to reduce stress responses and provide effective postoperative pain relief. However, spinal anesthesia offers temporary analgesia, which is why intrathecal adjuvants like opioids are used to extend pain relief duration. Opioids can enhance the sensory block effect without increasing the sympathetic block, thus can improve the quality of spinal anesthesia.[1]

Ropivacaine, a long-acting local anesthetic, is considered safer than bupivacaine due to its lower cardiotoxicity and neurotoxicity. It also provides better sensory-motor differentiation, allowing for faster motor recovery. Fentanyl, a synthetic opioid, primarily acts on mu-receptors to provide potent analgesia with fewer side effects compared to morphine. Nalbuphine, a synthetic opioid with agonist-antagonist properties, mainly acting on kappa-receptors with a favorable safety profile, has less opioid related side effects of nausea and pruritus[2].

The aim of our study is to compare the efficacy of fentanyl citrate and nalbuphine hydrochloride as an adjunct to isobaric ropivacaine intra-thecal injection for lower limb orthopedic surgeries. Outcome factors assessed are: hemodynamic stability during the surgery, postoperative pain, rescue analgesia requirements and the side effects. Both fentanyl and nalbuphine are expected to provide prolonged analgesia, maintain stable vital signs, and reduce opioid-related side effects compared to traditional anesthetic techniques[3].

By examining these drug combinations, the study will help identify the most effective adjuvant to improve patient outcomes and minimize complications during and after spinal anesthesia.

Methods

The present prospective observational study included 100 participants at our institute from May 2019-May 2021. The study was approved by our Institutional Ethical Committee with no concerns. Informed consents were taken from all patients. In the inclusion criteria, patients with American Society of Anaesthesiologist's Physical Status (ASA PS) I and II with age between 18 to 65 years who were scheduled to undergo Elective Orthopaedic Surgery of lower limb under Subarachnoid Block were selected.

Patients having the allergy to Local Anaesthetic drugs and opioids or having contraindication for Spinal Anaesthesia or Pregnant patients or those who don't give consent were excluded from study. All the patients were kept NBM overnight for 8 hours. Pre-medications were given in the form of Tablet Lorazepam 1mg at 10 pm the night before surgery. No intravenous fluid was given till arrival to operating theatre. Psychological counselling was done and procedure explained to all the patients in advance. All the patients were made familiar with the concept of Visual Analogue scale for pain (VAS), which consisted of 10cms line, with 0 suggesting No pain and 10 suggesting the Worst possible pain.

On arrival in the operating room an IV access was secured using an 18G cannula in the forearm vein. Preloading was done with 10ml/kg Ringer's lactate and further fluid adjusted as per the blood loss and maintenance during surgery. Patient is given Inj. Ondansetron 0.15mg/kg IV as Antiemetic medication. A fall of mean arterial pressure to less than 70mm hg was

treated with rapid infusion 0f 500 ml RL and 6 mg of Injection Mephentermine intravenously if there is no response to fluid administration.

Bradycardia (Heart rate less than 50/minute) is treated with intravenous Atropine sulphate 0.6mg**.**

Standard monitoring including continuous electrocardiogram, Heart rate, Oxygen saturation, noninvasive automated blood pressure measurements and visual assessment of Respiratory rate done and baseline values were noted. With strict aseptic and antiseptic precautions, in left lateral position, after injection of local anaesthesia with 24G hypodermic needle, the lumbar puncture was done using a 23 G Quincke's spinal needle with a bevelled tip to separate the fibres of dura at the level of L3-L4 interspace in midline. After getting the free flow of CSF the study drug was injected. After completion of injection, patients were immediately returned to the supine position. O2 with venti-mask 4-6 L/min started with maintenance of IV fluid via intravenous line in both groups.

Monitoring

Vital Parameters like HR, BP, MAP, SPO2 and RR were measured at 0, 5, 10, 20 ,30, 60, 120, 180, 240, 300 and 360 mins. Time to onset of the sensory block and the highest sensory block level were counted. Total 4 consecutive tests were performed with the soft touch & pinprick method using 24G sized hypodermic needle along the bilateral mid-clavicular lines at every 2 minutes till the stabilization of the level of anaesthesia. The time required to achieve Modified Bromage scale III was counted and noted as the time of onset of the motor block. Duration of the motor block was measured as the time from Modified Bromage III to Modified Bromage scale 0. The Modified Bromage Scale is defined as:

- Bromage 0: No motor block.
- Bromage I: Inability to raise extended leg, able to move knees and feet.
- Bromage II: Inability to raise extended leg and move knee, able to move feet.
- Bromage III: Complete block of motor limb.

The **Duration of analgesia** is considered as time interval between the injections of local anaesthetic drug intrathecally for spinal anaesthesia to the first rescue analgesic on patient demand (VAS≥4).

Post-operative Pain assessment was done with the Visual Analogue Scale 0 to 10. The assessment of pain was done immediately after surgery and at every 30 minutes till the rescue analgesia (Injection Diclofenac 75mg IV when the VAS score is ≥ 4) was required (0 = No pain, 10 = Most severe pain).

Patients were monitored for respiratory depression (RR<8) and Oxygen desaturation (SPO2<90%) treated with 100% oxygen supplementation and respiratory support if needed.

Statistical Analysis

Data was compiled using Microsoft Excel. Statistical Analysis was carried out using GraphPad Prism Version 7.03. Results on Continuous measurements are presented on Mean ± Standard Deviation and Categorial measurements in Number (%). Demographic data analysis was done with the Student's t-test assuming equal variance in both the groups. Unpaired t-test has been used to find the significance of HR, SBP, DBP, MAP, RR, Onset, Regression and Duration of Sensory block, Onset and Duration of Motor block, Duration of Analgesia and VAS score. Chi- Square test was used to compare the categorial data. Statistically significant level was noted when the P value was < 0.05.

Results

Total of 100 patients randomly divided into two equal groups with ASA grade I and II, of either sex, with 18 to 65 years of age and posted for an elective lower limb orthopedic surgery under Spinal anesthesia were selected for the study.

Following perioperative parameters were recorded in the study.

- Age, Sex, Weight, Height, ASA Grade, Duration of surgery.
- Intraoperatively: HR, SBP, DBP, MBP, SPO_2, RR.
- Characteristics of sensory blockade.
- Characteristics of motor blockade.
- Intraoperative & Postoperative complications
- Post -Operative Analgesia.

Table 1: Demographic Details

Variables	Group RF (n=50)	Group RN (n=50)	P value
Age (years)	33.3 ± 15.2	33.12± 17.25	0.956
Sex (Male/Female)	33/17	31/19	0.6769
Height (cm)	167.66 ± 4.91	166.02 ± 4.21	0.0765
Weight (kg)	62.82 ± 9.99	62.16 ± 9.63	0.6867
Duration of Surgery (Min)	102.26 ± 29.05	102.3 ± 24.53	0.9941
ASA I/II	33/17	28/22	0.4122

(Data is presented as mean ± SD except for sex distribution and ASA Grading)

Table 1 shows that the mean age of patients in group RF was 33.3 ± 15.2 (Range: 18-65yrs) and in group RN was 33.12± 17.25 (Range: 18-65yrs). Both groups were age matched (p=0.956). Matching with respect to sex distribution(p=0.6769), weight (p=0.6867), Height (p=0.0765), ASA Grading (p=0.4122) and Duration of surgery (p=0.9941) was also noted. Mean heart rate, SBP, DBP, MBP and RR between GROUP RF and GROUP RN is comparable at baseline, 0 min,5 mins,10 mins, 20mins,30 mins,60 mins,120mins,180mins, 240 mins, 300mins and 36 mins and there is no statistical difference between them (p value > 0.05).

Comparison of Sensory Block Characteristics

Table 2: Comparison of Sensory Block Characteristics Between Both Groups

Time in minutes (min)	Group RF (n=50)	Group RN (n=50)	P value
Time of onset of the sensory blockade (min)	4.41±0.63	4.93 ± 0.95	0.0018
Time from injection to highest Sensory level(min)	7.52 ± 1.11	8.36 ± 1.04	0.0002
Duration of sensory block (min) (REGRESSION TO S2)	254.22 ±7.89	296.98 ± 8.31	<0.0001*

Data is presented as mean ± SD (* p < 0.05)

Table 2 shows that the mean onset of sensory block in Group RF and Group RN were 4.41±0.63 mins and 4.93

± 0.95 mins respectively with the P value of 0.0018. This suggests an early sensory onset in RF group than RN group with statistically significant difference. The mean onset of sensory block to highest sensory level was also significantly early in Group RF (7.52 ± 1.11 mins) as compared to Group RN (8.36 ± 1.04 mins) with the P value of 0.0002. The time duration of sensory block (sensory regression to S2 level) was 296.98 ± 8.31mins in Group RN and 254.22±7.89 mins in Group RF, which was significantly longer in Group RN with a P value of <0.0001.

Table 3: Comparison of Motor Block Characteristics Between Both Groups

Time in minutes (min)	Group RF (n=50)	Group RN (n=50)	P value
Time to Onset of Motor blockade (Min)	6.58 ± 1.12	7.06 ± 1.15	0.0376
Duration of Motor blockade (Time to Reach Grade 0 Bromage (Min)	153.18 ± 4.76	190.2 ± 5.82	<0.0001

(Data is presented as mean ± SD)

Table 3 shows that the mean time to onset of motor blockade in Group RF and in Group RN were 6.58 ± 1.12 mins and 7.06 ± 1.15 mins, respectively with a P value of 0.0376. The duration of motor blockade was significantly longer in Group RN (190.2 ± 5.82 mins) than in Group RF (153.18 ± 4.76 mins) with a P value of <0.0001. Thus, Group with Fentanyl have early onset of motor block and also shorter duration of block compared to Nalbuphine group.

Table 4: Comparison of Postoperative VAS Score Between Both Group

VAS Score	Group RF (n=50)	Group RN (n=50)	P value
0 min	0	0	N/A
30 mins	0	0	N/A
90 mins	0	0	N/A
60 mins	0	0	N/A
120 mins	0	0	N/A
150 mins	0	0	N/A
180 mins	1.2±0.8	1.14±0.81	0.8992
210 mins	1.5±0.8	1.66±0.63	0.3916
240 mins	2.7±0.8	2.52±0.61	0.2060
270 mins	4.2±0.9	3±0.61	<0.0001
300 mins	2.4±0.7	4.24±0.87	<0.0001
330 mins	2.8±0.6	2.9±0.54	0.4848
360 mins	3.3±0.7	3.08±0.75	0.0914

Table 4 shows that the difference in VAS scores was statistically significant after 300 mins (VAS >4) for RN group and after 270 mins (VAS >4) for RF group. Till 300 mins, patient receiving Nalbuphine had lower VAS pain scores than patients who received fentanyl.

Table 5: Comparison of Total Duration of Analgesia Between Both Groups

Time in minutes (min)	Group RF (n=50)	Group RN (n=50)	P value
Total Duration of Analgesia	274.38 ± 9.79	299.7 ± 7.72	<0.0001*

Table 5 shows that the patients in the Fentanyl group requested rescue analgesia at 274.38 ± 9.79 mins and patients in the Nalbuphine group requested at 299.7 ± 7.72 minutes. Thus, the total duration of analgesia was significantly more in Nalbuphine group than Fentanyl group with a P value of <0.0001.

Table 6: Intraoperative and Post-Operative Side Effects

Side effects	Group RF (n=50)	Group RN (n=50)
Nausea	5(10%)	4(8%)
Vomiting	0	0
Hypotension	4 (8%)	3(6%)
Bradycardia	0	0
Pruritus	3(6%)	0
Respiratory Depression	0	0
Shivering	1(2%)	1(2%)
Sedation	0	0
Urinary retention	0	0

Table 6 shows the intra-operative and post-operative side effects.

Patients requiring treatment for hypotension with rapid infusion of IV fluid Ringer Lactate 500ml were 4 in Group RF and 3 in Group RN. Patients requiring treatment for pruritus with Injection Promethazine 25 mg IM were 3 in Group RF and none in Group RN. Patients with complaint of Nausea which was treated with Inj. Ondansetron 0.15mg/kg IV were 5 in Group RF and 4 in Group RN. None of the patients in both groups had Bradycardia, Respiratory depression, Sedation and urinary retention.

Discussion

In the era of modern medicine, the Subarachnoid block is a very well accepted anesthetic technique with a good safety profile and excellent success rate. Hence, the search is for a drug which is safe, efficacious and less toxic with an early recovery profile and a possibly early mobilization. Newer local anesthetic drugs are being investigated for further improvement of the safety concerns. Drugs should provide short acting adequate anesthesia with good post-operative analgesia and a

possibility of early ambulation and discharge to improve the outpatient care[3].

In our study, we compared nalbuphine against fentanyl as an adjuvant to 0.75% isobaric ropivacaine in the subarachnoid block. A total of 100 patients were divided into two groups (n = 50 each) undergoing lower limb elective orthopedic surgeries. Intrathecal fentanyl citrate 25 mcg with 0.75% Isobaric Ropivacaine hydrochloride 22.5 mg was used in Group RF and Intrathecal Nalbuphine 1 mg with 0.75% isobaric Ropivacaine hydrochloride 22.5 mg was used in Group RN. Factors like, Baseline parameters, demographic profile, and duration of operation were statistically comparable between both the groups. The duration of analgesia was measured as the primary outcome and the secondary outcome measures were onset and duration of sensory and motor block, time for regression to S2 from the highest sensory block, hemodynamic parameters, and the adverse effects that need treatment.

Hemodynamic Changes

In the present study there is no statistical difference between Group RF and Group RN with respect to intraoperative Heart rate, Systolic or Diastolic or Mean blood pressures and Respiratory Rate with P values >0.05. Malaviya et al[8] compared intrathecal fentanyl(25mcg) against Nalbuphine (1 mg) with Ropivacaine for lower limb orthopedic surgeries. They observed that the intraoperative hemodynamic parameters were comparable among both the groups which is similar to our study observations. K Vijayendrakumar Babu, G Prasanna Kumar, G Harinath[5] Evaluated Efficacy of Intrathecal Fentanyl Versus Intrathecal Nalbuphine as Adjuvants to 0.75% Ropivacaine for Post-operative Pain Relief in Cesarean Section under spinal anesthesia. They also observed that the Intra operative hemodynamic parameters were comparable between two groups, which is a similar finding to our study. Mostafa et al [6] also compared spinal anesthesia techniques with intrathecal nalbuphine and intrathecal fentanyl with bupivacaine in cesarean section and observed no statistically significant difference in hemodynamics and oxygen saturation. These findings were also relatable to our study.

Onset of Sensory Block

P value of 0.0018 was observed between Group RF and Group RN in terms of Onset of highest level of sensory block with Group RF having faster onset of sensory block (4.41±0.63 mins) than Group RN (4.93 ± 0.95 mins) with a statistically significant difference. Time to reach the highest sensory level was faster in Group RF (7.52 ± 1.11 mins) than in Group RN (8.36 ± 1.04 mins) with a significance level and P value of 0.0002. This in accordance with the study by Naaz et al [7] where Fentanyl 25 mcg plus Bupivacaine 12.5 mg produced early onset of sensory block than Nalbuphine 0.8mg or 1.2mg plus Bupivacaine 12.5mg for spinal anesthesia.

Duration of Sensory Block

In our study, the duration of sensory blockade was recorded as the time to sensory regression to S2 level, which was significantly longer in RN group (296.98 ± 8.31 mins) as compared to RF group (254.22 ±7.89 mins) with a P value of <0.0001. This finding is in accordance with the study of K Vijayendrakumar Babu, G Prasanna Kumar, G Harinath. [5] They observed time required for sensory regression to S2 level was significantly prolonged in Nalbuphine group (263.63 ± 44.88 mins) as compared to fentanyl group (180.75 ± 34.27 mins) for Post-operative Pain Relief in Cesarean Section.

Onset of Motor Block

In our study, the onset of motor block in Group RF was 6.58 ± 1.12 mins as compared to the Group RN with 7.06±1.15 mins. The onset of motor block was significantly faster in Group RF as compared to Group RN (p value 0.0376). This finding is in accordance with Malaviya et al [8] who stated faster onset of Motor block in fentanyl group (6.97±0.95 mins) than in Nalbuphine group (7.14±1.03 mins) lower limb orthopaedic surgery. Naaz et al [7] found that Fentanyl group took less time to reach complete motor block (5.4±12.96 mins) than Nalbuphine 0.8mg group (7.4±3.13 mins) and Nalbuphine group 1.2mg (10.4±4.5 mins) with Bupivacaine 12.5mg.

Duration of Motor Block

In our study, the duration of motor blockade in RN group was 190.2 ± 5.82 mins, as compared to the RF group with 153.18 ± 4.76 mins, which was significantly longer in Group RN (p<0.0001). In a study done by Gupta K [9] et al, they have found longer duration of motor block in Nalbuphine group (182.26 ± 29.63 mins) than fentanyl group (141.63 ± 18.05 mins), which is comparable to our study. Nirmal A, Singh Y, Mathur SK, Patel S [10] in a prospective, randomized, double blind study, they compared between intrathecal nalbuphine (200mcg) and butorphanol (100mcg) as adjuvants to isobaric ropivacaine (0.75% 2.5 ml) for elective lower limb orthopedic surgeries. The observation they found was the longer duration of motor block (226.63 ± 32.48 mins) in Nalbuphine Group, which was similar to our study.

Duration of Analgesia and VAS Score

Fentanyl and Nalbuphine both provided adequate postoperative analgesia at 30mins, 60mins, 90mins, 120mins, 180 mins and 240 min in our study. The total duration of analgesia in Group RN (299.7 ± 7.72 mins) was significantly longer than Group RF (274.38 ± 9.79 mins) (p<0.0001). Another significant finding was the need for the 1st rescue analgesia, which was earlier in the Fentanyl group than the Nalbuphine group.

The difference in VAS scores was statistically significant after 300 mins (VAS >4) for RN group and after 270 mins (VAS >4) for RF group with a P value of 0.0001. These findings of our study coincide with Malaviya et al[8] who concluded that Nalbuphine group had longer duration of analgesia (318.2 ± 14.14 mins) than fentanyl group with Isobaric Ropivacaine (275.6 ± 18.76 mins). They found VAS score <4 up to 240 mins in both groups, statistically significant difference in the number of patients having VAS ≥4 in Group F versus Group N at 270 mins and 300 mins respectively. (P < 0.001) K Vijayendrakumar Babu, G Prasanna Kumar, G Harinath[5] had observed time to first request of analgesia was significantly prolonged in Nalbuphine group (RF vs RN: 233 ± 36.82 vs. 312.38 ± 65.48 mins) with P value < 0.01, which was considered statistically significant. Sapate et al[11] did a randomized controlled study with intrathecal nalbuphine (0.5 mg) with 0.5% spinal bupivacaine (3 mL) for lower abdominal surgeries in elderly patients and concluded that addition of nalbuphine had better quality of SAB as compared to bupivacaine alone in spinal anesthesia. It also enhanced the postoperative analgesia in the combination group. Opioids can improve the quality of spinal block by enhancing early recovery of the patient and using them intrathecally, along with local anesthetics can improve the effectiveness of intraoperative analgesia and the duration of post-operative analgesia[13,14].

Side-Effects

Regarding the peri-operative side effects in our study, 5 patients in Fentanyl group and 4 patients in Nalbuphine group had Perioperative Nausea requiring immediate treatment. We observed that 4 patients in Fentanyl group and 3 patients in Nalbuphine group had intraoperative Hypotension, while 3 patients in Fentanyl group had developed pruritus and none of the patient's in Nalbuphine group had pruritus as side effect. The incidence of other adverse effects such as shivering, and postoperative sedation were minimal in both the groups without any statistical significance. Malaviya et al[8], Gupta [K9] et al, Gurunath BB[12] and Singh et al[15] also concluded that the addition of nalbuphine to intrathecal bupivacaine has prolonged the duration of sensory block, has improved postoperative analgesia and the requirement of rescue analgesia in the postoperative period is also less without increasing the adverse effects or complications.

Conclusion

We can conclude from our study findings that, by combining the Intrathecal Isobaric Ropivacaine-Nalbuphine, we can significantly prolong the duration of sensory block and motor block along with an improved postoperative analgesia in comparison to Intrathecal isobaric Ropivacaine-Fentanyl for elective orthopedic lower limb surgeries under subarachnoid block in spinal anesthesia, with stable intra-operative hemodynamics and minimal adverse effects.

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