E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.01.143

Research Article

Comparison of Nalbuphine V/S Fentanyl as Intrathecal Adjuvant to Hyperbaric Bupivacaine in Orthopedic Lower Limb Surgeries

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Received: 07.03.25, Revised: 30.04.25, Accepted: 26.05.25

ABSTRACT
Aims: To compare intrathecal nalbuphine v/s fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and postoperative analgesia in patients undergoing lower limb orthopaedic surgery.
Settings and Design: Single centre, prospective, randomized double blind controlled interventional study in patients posted for lower limb orthopaedic surgery.
Methods and Material: 90 patients posted for elective orthopaedic lower limb surgeries under spinal anaesthesia were randomly divided into three groups of 30 each. Group B with 0.5ml saline, group F with 50 microgram fentanyl and group N with 1 mg nalbuphine as adjuvants to 0.5% hyperbaric bupivacaine. Block characteristics, hemodynamic parameters, duration of analgesia and advesre effects were monitored.
Statistical analysis used: The collected data were analysed by one- way ANOVA and results were obtained in form of mean and standard deviation. The probability value $p < 0.05$ is considered as statistically significant.
Results: Onset of sensory blockade in group N, F and G was 305.67 ±19.42, 292 ± 14.48 and 290 ± 18.36 seconds respectively. Duration of motor block Group N is higher than the Group F & Group B & it is statistically significant (191±19.31, 164.37±7.05 and 161.6 ±6.07 minutes respectively). Regression of sensory level is prolonged in Group N in comparison to Group F and B (300.13 ± 14.69, 181.37±7.92 and 178.97±7 minutes respectively). Duration of analgesia was 408 ± 21.44 and 391.93 ± 25.37 and 383.27 ± 19.75 minutes in group N and group F and group B respectively.
Conclusion: Nalbuphine providing longer duration of motor block and analgesia compared to fentanyl can act as an effective alternate adjuvant in spinal anaesthesia.

Keywords: Nalbuphine, Fentanyl, Bupivacaine, Spinal Anaesthesia.

INTRODUCTION

One of the most commonly performed technique in modern anaesthesia is central neuraxial blockade. In lower limb orthopaedic surgeries the most preferred regional anaesthesia is spinal anaesthesia. It is easier to perform by injecting anaesthetic drug into the subarachnoid space & with rapid onset of anaesthesia, produces dense motor, sensory[1] and sympathetic blockade also provides analgesia both intra and post-operatively with decreased stress response to surgery and intra operative blood loss. Most commonly used amide local anaesthetic bupivacaine produces prolonged intense sensory and motor block with significant sympathetic blockade[2].

Addition of adjuvant along with local anaesthetic prolong sensory-motor block, also have synergistic anti-nociceptive effect along with intrathecal local anaesthetic both during intra operative and post-operative periods by extending analgesia duration[3] and also limit the side effects of altered hemodynamics due to usage of higher dose of local anaesthetic[4,5]. Among the adjuvants opioid group of drugs are used most commonly.

Fentanyl is a lipophilic μ receptor opioid agonist and has a rapid onset of action and significantly reduces visceral and somatic pain [6,7] . Nalbuphine is synthetic opioid which has both agonist and μ antagonist properties[8]. It produces analgesia and sedation via kappa receptors thus side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride. It also reaches ceiling effect at lower intrathecal

dosage thus avoiding the need to increase the dosage.

In this study we compared the effectiveness of the two adjuvants nalbuphine and fentanyl added to 0.5% hyperbaric bupivacaine in patients undergoing lower limb surgeries as Group A and Group B respectively, along with a control group C of intrathecal bupivacaine alone with normal saline.

MATERIALS AND METHODS

Approval was obtained from the institutional Ethics Review Committee, the study was conducted in the department of anaesthesiology at the Jhalawar medical college, Jhalawar on 90 patients of age group 18-55 years of ASA I or II and undergoing elective lower limb orthopaedic surgeries under subarachnoid block. Patients with infection at the subarachnoid block injection site, significant co-existing conditions like neurological and musculoskeletal disease, patients with bleeding disorders or on anticoagulants, patients with history of allergy to local anaesthetics or opioids were excluded.

After obtaining written informed consent eligible patients were randomly divided into three groups either nalbuphine group(N) or fentanyl group (N) or bupivacaine group (B) based on computer generated random number by anaesthetist not invovled in the study.

On the day of surgery, patients were kept fasting for 8 hours prior to surgery,all the patients were premedicated with inj glycopyrrolate 0.2mg, inj midazolam 1mg, inj ranitidine 50mg, Inj metaclopramide 10mg, 30min before the subarachnoid block. Upon arrival to the operating room, standard monitors like noninvasive blood pressure (NIBP), Electrocardiography(ECG) and pulseoximetry (SPO2) were connected and baseline values were recorded. An intravenous line was secured with 18G cannula and patients were preloaded with Ringer Lactate (RL) solution at 10ml/kg.

The patient was placed in the right lateral decubitus position/sitting position. Under strict aseptic precautions, lumbar puncture was performed at L3- L4 intervertebral space using 25 G quincke's needle using the midline approach. After confirming free flow of clear cerebrospinal fluid (CSF), drug was injected slowly.The drug was prepared by resident and anaesthetist performing the procedure was blinded to the group allocation.

Spread of sensory block was assessed by using sterile hypodermic needle pricked from the unanaesthesized to the anaesthesized zones using hollmen scale. Onset of sensory blockade was defined as the time interval between the end of anesthetic injection to loss of sensation to pinprick at T10 level. The quality of motor block was assessed by modified Bromage scale. Onset of complete motor blockade was defined as the time interval taken between the completion of study drug injection until Bromage Scale 3 was achieved. Duration of analgesia was defined as time from onset of sensory block till the patient had complained of pain.

Intraoperatively oxygen at 4l/min was administered through face mask. Hemodynamic parameters like peripheral oxygen saturation (spo2), non invasive blood pressure (NIBP), pulse rate were recorded at regular intervals. Hypotension was defined as systolic blood pressure less than 90mmHg or less than 20% from baseline, which was treated with Ringer's lactate or IV boluses of Mephentermine 6mg. Bradycardia was defined as heart rate less than 60 beats/min, whichwas treated with - Inj. Atropine 0.6mg iv bolus.Nausea & vomiting was treated with IV ondansetron. Post operatively patients were periodically evaluated in the postoperative ward using visual analog scale and rescue analgesia (iv Tramadol) was given at a VAS score of 4 or more.

Interpretation of data was carried out using SPSS 22. The collected data were analyzed by one- way ANOVA and results were obtained in form of mean and standard deviation. The probability value $p < 0.05$ is considered as statistically significant.

RESULTS

No patients were excluded from the study.

Table 1: Demographic Data of Patients

Characteristics	Group F n= 30	Group N n= 30	Group B n= 30	P value
Age(yrs)	37.07±10.42	39.13±6.78	34.33±10.38	0.721 (NS)
Gender (m:f)	26:4	25:5	22:8	0.39(NS)
ASA (I & II)	I-23, II- 7	I-23, II-7	I-28, II-2	0.15(NS)
Height (cm)	165.03 ± 7.09	161.43 ± 6.37	166.23 ± 7.25	0.217(NS)
Weight (kg)	63.47 ± 9.73	67.87 ± 8.63	62.77 ± 8.33	0.129(NS)

Demographically all patients were comparable with regards to age, weight, height and ASA status between the study groups.

Table 2: Onset of sensory block and motor block

Parameter	Group F	Group N	Group B	Result (p value)
Onset of sensory block (sec)	292.00 ± 14.48	305.67 ± 19.42	290.10 ± 18.36	0.001 (S)
Onset of motor block (sec)	600.00±36.86	603.00 ± 26.02	580.33 ± 27.60	0.009 (S)

Comparison of mean time of onset of sensory block is statistically significant among three groups (p value = 0.001). Onset of sensory block is earlier in Group B than Group F and it much earlier in Group B as compared to Group N.

Comparison of mean time of onset of motor block is statistically significant among three groups (p value = 0.009). Onset of motor block is earlier in Group B than Group F and it is much earlier in Group B as compared to Group N.

Table 3: Duration of motor and sensory block

Parameter	Group F	Group N	Group B	Result (p value)
duration of sensory block/regression to S1 level (mins)	181.37 ± 7.92	300.13 ± 14.69	171.89 ± 7.00	<0.001 (S)
Duration of motor Block (mins)	164.37±7.05	191.13 ± 19.31	161.60 ± 6.11	<0.001 (S)

Comparison of mean for regression of sensory level (Duration of Sensory Block) among three groups is statistically significant (p value < 0.001) and it is prolonged in Group N in comparison to Group F & B.

When we compare all the three groups the mean duration of motor block of Group N is higher than the Group F & Group B & it is statistically significant (p value=0.001) .

Table 4: Total duration of analgesia

	Group F	Group N	Group B
Total duration of analgesia(mins)	391.93 ± 25.37	408.00 ± 21.44	383.27 ± 19.75
Result (p value)	0.0001 (S)		

Comparison of mean of duration of analgesia among all three group is Group N > Group F > Group B & its statistically significant (p value=0.0001) and it is highest (408 min) in Group N in comparison to Group F & B.

DISCUSSION

Extensive research have been done over the years mainly to improve the quality of spinal anaesthesia simply by varying drug regimens

and technical methods. Normally to prolong the anaesthetic effects adjuvants are added to 0.5% hyperbaric Bupivacaine and given intrathecally. Adjuvants produce antinociceptive effect by acting perineurally or by acting at different receptor sites in the spinal cord.

Various studies had been done using 25mcg of fentanyl added to 0.5% hyperbaric Bupivacaine which administered intrathecally for various surgeries. Intrathecal fentanyl and nalbuphine hydrochloride was in practice over many years and was found to be safe and effective and has no neurotoxic side effects when used intrathecally. Mukherjee et al[9] perform a study to determine whether nalbuphine hydrochloride is safe and whether it helps to prolongs analgesia by comparing it with control group and also to determine the optimal dose of intrathecal nalbuphine. They observed that 0.4mg of nalbuphine + 0.5% hyperbaric bupivacaine prolongs the duration of postoperative analgesia without any side effects. Hence we used 1mg of nalbuphine intrathecally.

Patient Demographics:

In our study there was no statistical significant difference between the mean age (p value= 0.721), gender (p value=0.390), height (p value=0.217), weight (p value=0.129), ASA grading (p value=0.150) among the three groups. Thus in our study the mean age, gender, height, weight, ASA grading are comparable in the three groups.

Sensory Blockade:

In our study fentanyl significantly shortens the time of onset of sensory block when compared to nalbuphine. The mean onset of sensory block in the nalbuphine group was found to be 305.67±19.42 (sec) (5.09min), in fentanyl it is 292.00±14.48sec (4.86min) whereas in the control group it is 290.10±18.36sec (4.83).The p value for comparison of onset of sensory block is 0.001among the three groups which denotes it is statistically significant. Sensory block onset time is earlier in group B as compared to group F (p value 0.057)& it is much earlier in group B as compared to group N (p value is 0.002). It is found that onset of sensory block is earlier in group F as compared to group N (p value 0.003) & it is statistically significant. In fentanyl group the mean time of sensory block was 0.23 min earlier than nalbuphine group. It is seen that time to reach highest level of sensory block was much earlier in fentanyl group as compared to nalbuphine group & control group. Early onset & earlier to reach highest level of sensory blockade by fentanyl group may be explained due to high lipid solubility of fentanyl which makes it to cross blood brain barrier easily and also rapid tissue uptake. Similar result was obtained by Gurunath BB et al[10], in 2018 and study conducted by Ravikiran J Thote et al[11], However the study conducted by Hala Mostafa Gomaa et al[12], concluded that there is no significant difference between intrathecal nalbuphine and fentanyl regarding to the sensory blockade.

In our study the patients of nalbuphine group achieved the highest level of sensory blockade than the fentanyl group and prolonged effect in regression of sensory level seen in nalbuphine group as compared to fentanyl group. The mean time for sensory regression to S1 in the nalbuphine is 300.13±14.59mins, it is 181.37±7.92 mins in fentanyl group whereas 178.97±7.00 mins in the control group which was statistically significant (p value <0.001). The p value for comparison of mean for regression of sensory level among three groups is statistically significant (p value <0.001). Mean time for regression of sensory level in group N is higher than group F (p value is 0.010) and it is much higher than group B (p value is 0.001) & it is statistically significant. Mean time for regression of sensory level of group F is higher than group B (p value is 0.002) & it is statistically significant. Higher sensory level and more prolongation of regression of sensory blockade by intrathecal nalbuphine than intrathecal fentanyl has also been noticed in the studies conducted by Ravikiran J Thote[11], Gurunath BB et al[10], Shela Shakooh et al[13] and by Jyothi B et al[14].

Motor Blockade:

The mean time of onset of motor block was found to be 603.00±26.02 sec (10.05min) in nalbuphine group, in fentanyl group it is 600.00±36.86 sec (10min) whereas in control group it is 580.33±27.60 sec (9.6 min) The p value for comparison of motor block is 0.009 among the three groups which denotes it is statistically significant. Onset of motor block is earlier in group B than Group F (p value is 0.022) & it is much earlier in Group B as compared to group N (p value is 0.009)& it is statistically significant. Similar to sensory blockade motor block is much earlier in fentanyl group as compared to nalbuphine group (p value is 0.007) just because of highly liphophilic nature of fentanyl, p value denotes it is statistically significant. Similar results have

been observed in study conducted by Ravikiran J Thote et al[11], Pallavi Ahluwalia et al[15], Bisht et al[16]. Mean duration of motor blockade in the nalbuphine group is 191.13±19.31mins, in fentanyl group it is 164.37±7.05 mins, whereas it is 161.60±6.11mins which was statistically significant (p value <0.001) Mean duration of motor blockade in nalbuphine group is higher than fentanyl group (p value is 0.002) & it is statistically significant. Mean duration of motor block is higher in group F as compared to group B (p value is 0.002) and it is much higher in group N as compared to group B (p value is <0.001), which is statistically significant. Study conducted by Pallavi Ahluwalia et al[15], concludes similar results however Hala Mostafa Gomaa et al[12], concludes that there is no statistically significant difference in the duration of motor blockade between intrathecal nalbuphine and fentanyl.

Duration of Analgesia:

The mean duration of analgesia in the nalbuphine group was found to be 408.00±21.44 mins, it is 391.93±25.37 mins in the fentanyl group whereas it is 383.27±19.75mins in group B which was statistically significant (p value < 0.0001) between the three groups. Comparison of mean of duration of analgesia in our study revealed that duration of analgesia is prolonged in group N as compared to group F (p value is 0.010) & it is more prolonged than group B (p value is <0.001) and it is higher in group F as compared to group B (p value is 0.045), p value indicates that it is statistically significant. The result that obtained in our study reveals that duration of analgesia is much prolonged by intrathecal nalbuphine than fentanyl. Study conducted by Ravikiran J Thote et al[11], also concluded in their study that intrathecal nalbuphine prolongs the duration of analgesia than intrathecal fentanyl which coincides with our results. Mukherjee et al[9] concluded that 0.4mg nalbuphine is the most effective dose that increases post-operative analgesia with no side effects. Gurunath BB et al[10], study also concluded that the nalbuphine group had much prolonged duration of analgesia than fentanyl group. Gupta et al[17] concluded in their study that nalbuphine provides good and prolonged post-operative patients. Bindra TK et al[18] concluded that intrathecal nalbuphine provides good postoperative analgesia when compared to intrathecal fentanyl.

Haemodynamic Parameters:

Comparison of mean systolic blood pressure among Group N, Group B and Group F is statistically significant at 0min, 3min, 5min, 10min and 15min. The mean systolic BP of group N is higher than group B & group F at 0min (p value is 0.001), 3min (p value <0.001), 5min (p value is 0.004), 10min (p value is 0.003) and 15min (p value is 0.005).

Comparing the mean diastolic BP of three groups is statistically significant at 5min (p < 0.001), 30min (p value is 0.005). Mean diastolic BP of group N is higher than the group B & group F and also group B is higher than group F & it is statistically significant.

Comparison of pulse rate of three groups are statistically significant at 3min (p value is 0.0007), 5min (p value is 0.012), 10min (p value is0.004), 15min (p value is 0.003).

Comparing of preoperative vitals in the three groups like systolic blood pressure, diastolic blood pressure, heart rate, SpO2, respiratory rate are statistically non-significant, all the patients were haemodynamically stable in all the three groups. Intrathecal opioids intensifies the sensory block without increasing sympathetic block just because they are synergestic to local anaesthetics. Our results are similar to the results concluded by Hala Mostafa Gomaa et al[12]. Pallavi Ahluwalia et al[15] & Madhusudhana R et al[10] concluded the similar results in their studies.

Adverse Effects:

Bradycardia and Hypotension observed were treatable and it was mainly due to the sympathetic blockade of the local anesthetics itself not by the adjuvants added. Nausea and vomiting is due to the rostral spread of opioid in spinal fluid to intracerebral structures including the vomiting center and chemoreceptor trigger zone. The incidence of post-operative nausea and vomiting ranged from none to 13.33% in group N & group F and 6.67% in the group B. However nausea & vomiting subsided without any treatment. The incidence of nausea & vomiting is increased in postoperative ambulation. Since most of the patients of this study are in plaster of paris immobilization and were not ambulatory so the incidence of nausea & vomiting were low. Side effects observed during our study was very minimal and most of the cases were stable and it is not statistically significant. Xavier Culebras et al[19], Shakooh et al[13], Mukherjee A et al[9] concluded in their studies the safety and effectiveness of nalbuphine and fentanyl when added intrathecally.

CONCLUSION

Comparing between Nalbuphine and Fentanyl concludes that Intrathecal nalbuphine may be a good alternative to fentanyl in orthopaedic lower limb surgeries which provides a prolonged sensory and motor blockade, and prolonged duration of analgesia without any significant adverse effects.

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