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EFFECT OF ADDING NALBUPHINE VS FENTANYL ON BLOCK CHARACTERISTICS OF 0.75% HYPERBARIC ROPIVACAINE IN LOWER LIMB SURGERY: A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background: Fentanyl and Nalbuphine are the commonly used adjuvant drugs in spinal anesthesia. The efficacy of these drugs along with Hyperbaric Ropivacaine remains better but the question remains unsolved that whether Ropivacaine plus fentanyl or ropivacaine plus Nalbuphine, which works better. Hence this study was undertaken to compare the effects of fentanyl and nalbuphine as adjuvants to 0.75% hyperbaric ropivacaine of spinal blockade in terms of onset, duration, hemodynamic parameters, and adverse effects.

Methods: This prospective randomized, control study was conducted among patients undergoing lower limb surgeries in Rohilkhand Medical College Hospital, Bareilly for elective surgical procedures. Sixty-eight patients were included in the study with 34 patients for each group. Group A - 3ml of "Hyperbaric Ropivacaine" with 25 ug Intrathecal Fentanyl and Group B - 3ml of "Hyperbaric Ropivacaine" with 0.8 mg Intrathecal Nalbuphine. Under all aseptic precautions, spinal anaesthesia was given with the study drug injected between L3-L4 or L4-L5 inter vertebral space, using a 25G (Quincke needle) in the Sitting Position. Then the patient would be immediately taken into Lateral or Supine Position for surgery. The patient was evaluated for Motor and Sensory block, immediately after spinal anaesthesia for onset of action of drug and duration of action of the drug. During the surgery the patient's pulse rate, Systolic and Diastolic blood pressure, Mean Arterial Pressure was recorded every 3 mins for 30 minutes and then every 5 minutes until completion of the surgery. Data analysis was done using SPSS version 17.

Results: The time to onset of sensory block, the time to onset of Motor block and the duration of the motor blockade was significantly higher in Group A Fentanyl with Hyperbaric-ropivacaine compared to Group B Nalbuphine with Hyperbaric Ropivacaine group. Although our study showed non-significant results for the duration of the sensory blockade between both the groups. The first rescue analgesia was more in Group B Ropivacaine plus Nalbuphine Group as compared to Ropivacaine plus Fentanyl, reducing the analgesic requirement in the early post-operative period. The hemodynamic parameters were more stable in both the groups.

Conclusion: Fentanyl with hyperbaric ropivacaine provides better blockade time and duration but Nalbuphine shows better rescue analgesia with no difference between both the groups in terms of hemodynamic stability.

Key Words: Hyperbaric Ropivacaine, Fentanyl, Nalbuphine, Spinal anesthesia

INTRODUCTION:

"Pain is an unpleasant emotional and sensory experiences associated with actual and potential tissue damage or described in terms of such damages". The main aim of anesthesia is to relieve pain during surgery. The expertise acquired in this field is extended into the postoperative period.[1]

Spinal Anaesthesia is the most Popular technique performed in the field of Anaesthesiology. It is easy to perform, reduces stress response to surgery and provides effective post-operative analgesia. Since spinal anesthesia by itself only provides shortterm postoperative analgesia, intrathecal adjuvants to local anesthetic have been developed to improve the duration and clinical efficacy of analgesia after orthopedic surgery.

Postoperative analgesia is effectively prolonged by intrathecal opioids. Opioid analgesics activate the opioid receptors on the primary afferent neuron, which activates the painmodulating systems.[2] Their activation may have the impact of either directly lowering neurotransmission or inhibiting the synthesis of excitatory neurotransmitters. Incorporating adjuvant medications with intrathecal local anesthetics extends postoperative pain relief and improves both the quality and length of the sensory blockade. It is easily affordable or comfortable to administer and it is commonly used technique for lower limb surgeries. The advantages of awake patient and early recovery earlier have made this method of choice for ambulatory surgery.

Comparing the effects of fentanyl and nalbuphine as adjuvants to 0.75% hyperbaric ropivacaine of spinal blockade in terms of onset, duration, hemodynamic parameters, and adverse effects is the aim of this study. As most of the studies have been done with isobaric ropivacaine or hyperbaric bupivacaine, we conducted this study with hyperbaric ropivacaine.

MATERIALS AND METHODS:

This prospective randomized controlled trial was conducted among patients undergoing lower abdominal and lower limb surgeries, in Rohilkhand Medical College Hospital, Bareilly during for elective surgical procedures. Sixty-eight patients between the age group of 19-65yrs either sex patient posted for elective lower limb surgeries, who belongs to American Society of Anesthesiologists (ASA) grade I and II were included in the study. Patients who were allergic or intolerant to local anesthetics, Infection at the site of injection, any abnormality of spinal anatomy and Coagulopathy or Bleeding disorder were excluded from the study. The study was approved by the ethical committee of this institution. Informed consent was obtained from the study participants before starting the study. The study patients were randomized and divided into two groups with 34 patients for each group. Group A had 3ml of "Hyperbaric Ropivacaine" with 25 ug Intrathecal Fentanyl and Group B had 3ml of "Hyperbaric Ropivacaine" with 0.8 mg Intrathecal Nalbuphine. Detailed history and the observations were documented in a proforma by the principal investigator. In the preoperative room, baseline recording of heart rate, respiratory rate, systolic blood pressure and conscious levels of the patients were noted. Spinal anesthesia was performed under all aseptic precautions, spinal anaesthesia was given with the study drug injected between L3-L4 or L4-L5 inter vertebral space, using a 25G (Quincke needle) in the Sitting Position. Then the patient was immediately taken into a Lateral or Supine Position for surgery. The patient was evaluated for Motor and Sensory block, immediately after spinal anaesthesia for onset of action of drug and duration of action of the drug. During the surgery the patient's pulse rate, Systolic and Diastolic blood pressure, Mean Arterial Pressure was recorded every 3 mins for 30 minutes and then every 5 minutes until completion of the surgery.

Observation was made as Time to Onset of Sensory Blockade Onset - Measured as the interval between the end of the injection, and the lack of pinprick feeling at (T -10) dermatome. Time to onset of Motor block by Modified Bromage Score -time from intrathecal injection to achievement of Bromage 3. Duration of sensory block- The time between the completion of the injection and the loss of pin prick sensation at the (T -10) dermatome is the beginning of sensory blockade. Duration

of motor block- time from intrathecal injection to Bromage 1. Rescue analgesia was given when VAS > 4 and the time for first rescue analgesia was noted as duration of analgesia.

Table1: Modified Bromage scale for lower limb [3]

Grade	Criteria	Degree of Block
0	Free movement of legs and feet	Nil (0%)
I	Knee flexion decrease but full flexion of feet and ankle	Partial (33%)
II	Unable to flex knee, flexion of ankle and feet present	Partial (66%)
III	Unable to flex knee or ankle or move toes	Complete paralysis (100%)

All statistical analysis was performed using SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA). *T*- test for independent samples was used to compare two groups for data with a nrmal distribution. Yates's continuity correction test (Chi-square test) and Fisher's exact test were used for comparison of qualitative data. All data were summarized as Mean± standard deviation for continuous variables/numbers and as percentages for categorical variables. $P < 0.05$ was considered statistically significant.

RESULT:

A total of sixty-eight patients completed the study. Demographic data including age, height, weight, and ASA status was statistically comparable in both the groups. [Table 2]

Table 2: Demographic profile of the study participants

VARIABLES	GROUP A	GROUP B	p-value
Age	42.44 ± 12.96	44.15 ± 10.11	0.426#
Height	164.41 ± 3.69	163.44 ± 4.37	0.326#
Weight (in Kg)	58.0 ± 5.64	57.41 ± 5.33	0.660#
ASA GRADE	1.41 ± 0.5	1.5 ± 0.51	0.473#

* Statistically significant # statistically insignificant

The Mean onset of sensory blockade of patients in Group A (Fentanyl) was less as compared to Group B(Nalbuphine) and there was significant difference in mean onset of sensory blockade. Mean time of onset of motor blockade of patients Group A (Fentanyl) was less as compared to Group B(Nalbuphine) and there was significant difference in mean time of onset of motor blockade (P=0.000). There was significant difference in mean time of the onset of motor blockade of patients in between Group A (Fentanyl) and Group B (Nalbuphine)(P=0.012). But there was no significant difference in mean time of duration of sensory block between in Group A(Fentanyl) and Group B(Nalbuphine)(P=0.079). [Table 3]

Table 3: Onset of sensory and motor blockade, Duration of sensory and motor blockade.

VARIABLES	GROUP A	GROUP B	p-value
Onset of sensory blockade(min.)	3.12 ± 0.73	4.26 ± 0.67	**0.000***
Onset of motor blockade(min.)	4.35 ± 0.6	4.88 ± 0.41	**0.000***
Duration of sensory blockade (min.)	3.12 ± 0.69	2.82 ± 0.67	0.079#
Duration of motor blockade(min.)	2.75 ± 0.69	2.32 ± 0.67	**0.012***

* Statistically significant # statistically insignificant

The mean VAS score at different time intervals in between Group A (FENTANYL) and Group B (NALBUPHINE)**.** At hour 1, hour 2, hour 3, hour 4, hour 5, hour 6, hour 12, hour VAS score in Group

B was more as compared to Group A (P= <0.001). VAS score at 18 hour and 24 hours between Group A and Group B was statistically not significant (P=0.506, 0.308 respectively) [Table 4]

Table 4: Comparison of Mean VAS SCORE at different time interval between Group A (Fentanyl) and Group B (Nalbuphine)

Variables	GROUP	N	Mean	Std. Deviation	P-Value
VAS Score at 1hr	GROUP A	34	2.15	0.99	<0.001*
	Group B	34	1.00	0.00	
VAS Score at 2hr	Group A	34	3.32	1.25	<0.001*
	Group B	34	1.56	0.50	
VAS Score at 3hr	Group A	34	4.12	0.88	<0.001*
	Group B	34	3.56	0.70	
VAS Score at 4hr	Group A	34	5.09	0.90	<0.001*
	Group B	34	4.12	0.88	
VAS Score at 5hr	Group A	34	5.03	0.67	<0.001*
	Group B	34	4.64	0.90	
VAS Score at 6hr	Group A	34	5.82	0.94	<0.001*
	Group B	34	5.03	0.67	
VAS Score at 12hr	Group A	34	5.86	0.94	<0.001*
	Group B	34	5.18	0.94	
VAS Score at 18hr	Group A	34	5.26	0.94	0.506#
	Group B	34	5.12	0.88	
VAS Score at 24hr	Group A	34	5.19	0.84	0.308#
	Group B	34	5.08	0.81	

* Statistically significant # statistically insignificant

DISCUSSION:

Spinal anesthetic offers a longer length of post-operative analgesia. Faster and more efficient onset of sensory and motor block, it is a commonly used technique for lower limb surgeries. The central neuraxial obstruction is determined by the drug's distribution and the patient's characteristics. Patient-related parameters include age, height, posture, spinal column anatomy, and CSF volume. Among the factors affecting the drug's spread are its amount, volume, specific gravity, density, baricity of solution, and potency.[1] The rate of drug delivery, the amount of drug administered, and the barbotage technique all influence the spread in addition to the previously listed variables.

In our study the mean onset of sensory blockade was 3.12 ± 0.73 in Group A Fentanyl and 4.26 ± 0.67 in Group B Nalbuphine with p value of **0.000** which is statistically significantly higher in Group A Fentanyl as compared to Group B Nalbuphine which was delayed. The study conducted by **Bisht S** compared intrathecal fentanyl with nalbuphine. The start of sensory block was quicker in the fentanyl Group than in the nalbuphine group. in the fentanyl group, the time to reach maximal sensory blockage was qucker.[4] **Parekh KM et al** did an analytic study between Nalbuphine and Fentanyl as Adjuvants to Bupivacaine in Spinal Anesthesia in Lower Limb Orthopedic Surgeries observed that the time to reach peak block level was faster in the Fentanyl Group (7.83 ± 2.22 min) than in the Nalbuphine Group (10.50 ± 2.26 min). This finding is similar to our study.[5]

In our study both groups showed statistically significant results in onset of motor block (p value **0.000**). It was 4.35 ± 0.6 in Group A Fentanyl and 4.88 ± 0.41 in Group B Nalbuphine. The study done by **Mavaliya V *et al*** where they compared Nalbuphine Versus Fentanyl as an Adjuvant to 0.75% Isobaric Ropivacaine in Subarachnoid Block found that the mean time for onset of motor block was statistically comparable in fentanyl and nalbuphine. (P-0.457)[6] **Khatri N *et al*** observed the onset of motor blockade (Bromage 1 & 3) was significantly more rapid with Group Fentanyl than Group

Nalbuphine in their study and this can be due to high lipid solubility and rapid tissue uptake of fentanyl than nalbuphine.[7]

In our study Blockade was significantly more in Group A Fentanyl which was 2.75 ± 0.69 as compared to Group B Nalbuphine which was 2.32 ± 0.67 (p value **0.**012). **Khatri N et al** who did Comparison of Efficacy of Intrathecal Fentanyl versus Nalbuphine with Ropivacaine in Spinal Anesthesia, results indicative of no significant difference in duration of motor blockade (time required for motor block to return to Bromage's Grade 0 from the time of onset of motor block) between two groups. The dose of Fentanyl used were 20 mcg with Isobaric ropivacaine therefore their study had non-significant finding.[7]
Sathapathy S et al where fentanyl was compared with nalbuphine in hyperbaric bupivacaine found that the motor block regression to Bromage 0 was significantly lesser in the fentanyl Group than in the nalbuphine Group ($p<0.001$)[2]
Unfamiliar result showed by **Bisht S.** concludes that the duration of motor block in Group Fentanyl with bupivacaine was comparable to that in Group Nalbuphine plus bupivacaine ($p = 0.096$). The time to first analgesic requirement was significantly prolonged in Group Nalbuphine plus bupivacaine as compared to Group Fentanyl with bupivacaine ($p < 0.001$)[8]

Our study showed statistically non- significant result in mean duration of sensory blockade (p value 0.079). It was 3.12 ± 0.69 in Group A Fentanyl and 2.82 ± 0.67 in Group B Nalbuphine. **Khatri N et al** observed that the time of two segment sensory regression and regression to S1 level were comparable between groups ($P>0.05$) and their study did not corresponds to our study.[7]
Sathapathy S et al where fentanyl was compared with nalbuphine in hyperbaric bupivacaine found that the sensory block regression to S2 was significantly lesser in the fentanyl Group than in the nalbuphine Group ($p<0.001$) as Fentanyl was used along with Bupivacaine in their study significant parameters were observed.[2]
Analogous study by **Bisht S.** where comparison of intrathecal fentanyl and nalbuphine: A prospective randomized controlled study in patients undergoing total abdominal hysterectomy remarked that the duration of sensory block- the time to two segment sensory level regression was longer in Group Nalbuphine, than Group Fentanyl ($p < 0.001$).[8]
When compared, effective analgesia was significantly in patients receiving intrathecal nalbuphine Higher than in intrathecal fentanyl at 5, 6 and 12 hours and was non-significant at 1-4 hour, 18 hour and at 24 hr. Our study findings are consistent with those of other studies, which reported a considerable lengthening of the duration of spinal analgesia with Group B nalbuphine.
The mean duration of analgesia (time to first rescue analgesia) was longer in Group *N* (318.2 ± 14.14 vs. 152.42 ± 11.96 min), this study was conducted by **Mavaliya V et al** which showed similar finding to our study.[10]
The study done by **Khatri N et al** showed similar result as our study where they found the duration of postoperative analgesia was significantly more in the nalbuphine Group (Group B) than fentanyl Group (GROUP A). If we consider the 24-hour analgesic consumption, Patients who received intrathecal nalbuphine required significantly lesser number of rescue analgesics than fentanyl group.[7]
In our study, we observed that there were no such wide changes in Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure and SpO_2. Ropivacaine is hemodynamically stable and produces less cardiovascular toxicity because it has lipophilic property and because of its stereoisomerism, it has higher threshold for cardiovascular toxicity.
According to a study by **Mehdi I *et al*** the heart rate significantly decreased but other measurements such as mean arterial pressure, diastolic blood pressure, and systolic blood pressure stayed same after administration with Nalbuphine.[10]
In research by **Sapate S *et al***., patients who received nalbuphine showed higher mean heart rate, systolic blood pressure, and diastolic blood pressure compared to the control group, suggesting a significant change in hemodynamic profile.[11]

According to a study by **Prabharkaraiah UN *et al*** fentanyl and nalbuphine hydrochloride as an adjuvant to bupivacaine for spinal anesthesia in lower abdominal surgeries did not show a statistically significant difference in the incidence of bradycardia and hypotension between the groups.[12] This demonstrates that both opioids improved the spinal cord's antinociception rather than having any discernible sympatholytic effects.

CONCLUSION:

Based on our research findings, it can be inferred that the administration of Ropivacaine with fentanyl intrathecally results in a increased duration of motor and sensory blockade, a lower level of motor blockade, and a reduced time until the first rescue analgesia seen with Nalbuphine group, when compared to the use of Fentanyl. Furthermore, it exhibits greater hemodynamic stability. Therefore, the utilization of Hyperbaric Ropivacaine in conjunction with fentanyl for Spinal Anaesthesia presents a more favorable option for lower limb surgeries due to its ability to expedite the initiation of ambulation.

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