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Original Research

To Compare the Efficacy of Intrathecal Nalbupine Versus Fentanyl as Adjuvant to 0.5% Hyperbaric Bupivacaine in Parturients Undergoing Elective LSCS

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ABSTRACT

BACKGROUND: Neuraxial opioidsare widely used for providing intraoperative and postoperative analgesia without prolonging motor and sympathetic block. The commonly used opioid adjuvants are fentanyl and nalbupine. The aim of the study was to evaluate and compare the anesthesia characteristics between Nalbuphine and Fentanyl when added as an adjuvant to Intrathecal Hyperbaric bupivacaine in parturients undergoing elective LSCS.

METHODOLOGY: After obtaining informed written consent, 60 parturients posted for elective cesarean section under subarachnoid block were randomly allocated into two groups GROUP F (n = 30) received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.5ml Fentanyl (25µg) whereas GROUP N (n = 30) received 2.5 ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.1 ml nalbuphine (1mg) diluted with normal saline to make total volume 3 ml. The primary objective was to note the time of onset of sensory and motor blockade. The secondary objective was to determine the total duration of analgesia and the hemodynamic effects.

RESULTS: The time of onset of sensory blockade was similar in both the groups (2.13 ± 0.51 min in Group F and 2.20 ± 0.61 min in Group N, p = 0.647). The time of onset of motor block was also similar in both groups (3.20 ± 0.66 min in Group F vs. 3.07 ± 0.74 min in Group N, p = 0.466).The duration of complete postoperative analgesia was significantly longer in Group F (175.83 ± 31.84 min) compared to Group N (140.0 ± 15.25 min) (p < 0.001).The duration of effective analgesia was also significantly longer in Group F (222.0 ± 27.95 min) compared to Group N (179.00 ± 11.17 min) (p < 0.001).There was no significant difference in Visual Analog Scale (VAS) pain scores. At 0, 2, 4, 6, 12, and 24 hours between the groups, indicating comparable pain relief efficacy.

CONCLUSION: Both nalbuphine and fentanyl serve as effective adjuvants to intrathecal hyperbaric bupivacaine for cesarean deliveries. While fentanyl provides rapid-onset analgesia, nalbuphine offers prolonged postoperative pain relief with fewer opioid-related side effects. nalbuphine may be a preferable alternative to fentanyl in clinical scenarios where extended postoperative analgesia is a priority.

KEYWORDS: Bupivacaine, Adjuvants, Cesarean Section, Fentanyl, Nalbuphine, Subarachnoid Block.

INTRODUCTION

Subarachnoid block is the most commonly administered neuraxial anesthetic for caesarean delivery because of its simplicity, speed of onset, and reliability. Blockade to the T4 dermatome is necessary to perform caesarean delivery without maternal discomfort. The most common complication of neuraxial anesthesia is hypotension, bradycardia, and the attendant risk of decreased uteroplacental perfusion.[1]

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Bupivacaine, a long-acting amide local anesthetic that is used most commonly for spinal anaesthesia, has a slow onset, high potency and relatively short postoperative analgesia. The intrathecal dose of hyperbaric bupivacaine for CS ranges from 12 to 15mg. peritoneal traction and handling of intraperitoneal organs during cesarean delivery led to intraoperative visceral pain. Increasing the dose of hyperbaric bupivacaine leads to a decrease in the incidence of intraoperative visceral pain at the expense of possible risk of higher blockade and its adverse effects. Therefore, adjuvants are added to avoid these drawbacks.

Neuraxial opioids are widely used for providing intraoperative and postoperative analgesia without prolonging motor and sympathetic block. The commonly used opioid adjuvants are fentanyl and nalbupine. Fentanyl is probably the most widely used opioid in patients undergoing cesarean section, improves the quality of spinal anaesthsia, reduces dose of local anaesthetics, but has a little impact on prolonging postoperative analgesia, intrathecal dose ranges from 15-25mcg with a wide range of 2.5-50mcgs for cesarean delivery has been investigated. Nalbupine, a synthetic agonist-antagonist opioid used in the range of 200mcg -1600mcg, provides complete and effective analgesia.

Because there was relatively limited published data on the comparison between the effects of the addition of nalbupine and fentanyl as adjuvant to hyperbaric bupivacaine, the present study is undertaken.

The aim was to evaluate and compare the anesthesia characteristics between Nalbuphine and Fentanyl when added as an adjuvant to Intrathecal Hyperbaric bupivacaine in parturients undergoing elective LSCS.

METHODOLOGY

This prospective, randomized comparative study was performed after obtaining institutional ethics clearance. After obtaining informed written consent, 60 parturients were randomly allocated into two groups based on random numbers generated by www.randomization.com.

- Group F (n = 30) received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.5ml Fentanyl (25μg).
- Group N(n = 30) received 2.5 ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.1 ml nalbuphine (1mg) diluted with normal saline to make total volume 3 ml.

The primary objective was to note the time of onset of sensory and motor blockade. The secondary objective was to determine the total duration of analgesia and the hemodynamic effects. After the preoperative assessment and the explanation of the procedure, all patients were instructed to fast for 8 hours for solid food and 4 hours for clear fluids. Baseline investigations like haemoglobin, blood sugar, urea, creatinine, ECG, urine analysis for albumin and sugar were checked. Vital parameters like pulse rate, blood pressure, and respiratory rate were recorded. Thorough examinations of all the systems and airway assessments was being done. The patients were educated about the Visual analogue scale (VAS) and its interpretations. All patients received Inj. Ranitidine 50mg IV and Inj. Metoclopramide 10mg IV for aspiration prophylaxis before surgery. Patients were shifted to the operating room. In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked, and the patient was placed on it. The non-invasive blood pressure monitor, pulse oximeter, and electrocardiogram leads were connected to the patient. In the anaesthesia chart, proper recording of preoperative baseline systolic and diastolic blood pressure, pulse rate, respiratory rate, and oxygen saturation were documented. An 18G intravenous cannula was secured to the patients, and preloaded with 1000ml of Ringer's lactate. The patient was placed in a left lateral position. Under aseptic precautions, lumbar puncture was performed at the level of L3-L4/L2-L3 interspace through a midline approach using 25 G Quincke's spinal needle, and the study drug was injected after confirmation of needle tip in the subarachnoid space by clear and free flow of cerebrospinal fluid. The surgeon, patient, and observing anesthetist were blinded to the patient group. Intrathecal injection was given over approximately 10-15s. Patients was made to lie supine immediately. Patients was monitored with ECG, NIBP, SPO2, heart rate, and respiratory rate at regular intervals of every two minutes for the first 10 mins and every 5 mins till the end of surgery and every 30 mins in the post-operative period until the VAS Scale of >4, where rescue analgesia is given.

Parameters recorded were time for onset of sensory and motor block, Maximum level of block attained and the time taken for the same, Total duration of sensory and motor block, and time for two segments sensory regression. Sensory blockade was tested bilaterally with a blunt 27 G hypodermic needle every 15 seconds till the onset of sensory blockade and thereafter at 2-minute intervals till the maximum level of sensory blockade was achieved and subsequently at 5-minute intervals during first 30 mins intervals until complete recovery.

The quality of motor blockade was assessed by the modified Bromage scale. The blockade was assessed every 5 minutes until maximum motor block was achieved and then every 30 minutes until the return of normal motor function. Visual analogue scores for pain were recorded immediately post op, then 2nd hourly for first 6 hrs and at 12 and 24 hrs postoperatively. Sedation was assessed every 15 minutes intraoperatively and hourly in the post-operative period for the first 6 hours using the Ramsay sedation score. Neonatal APGAR scores in 1 and 5 mins and Analgesic requirement for first 24 hours postoperatively.

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Sample Size

The Sample size was calculated based on a previous study, conducted by Ahmed FI, A randomized double-blind study in parturient undergoing elective LSCS.

$n = 2 \times (Z_{\alpha} + Z_{(1-\beta)})^2 \times \sigma^{2} / d^2$

Where

n= no. of sample size

Z_{α}=Standard table value for 95% confidence interval (CI)

$Z_{(1-\beta)}$ =for 80% power

σ= mean standard deviation= (62.6+34.4) ÷2=48.5

d= expected mean difference on substituting,

$n = 2x (1.96+0.84)^2 \times 48.5^2 / 41.2^2$

n = 21.72

By adding 10% dropout to attrition, 21.72+2.17=23.89 approx. 25

Therefore, the final sample size was rounded off to 30 in each group.

RESULTS

The demographic parameters such as age, weight, and gender were comparable between both groups, and there were no significant differences **(table 1)**. The time of onset of sensory blockade was 2.13 ± 0.51 min in Group F and 2.20 ± 0.61 min in Group N, with no significant difference (p = 0.647).The time to achieve maximum sensory block was significantly longer in Group N (3.63 ± 1.03 min) compared to Group F (3.13 ± 0.51 min) (p = 0.021).The time for two-segment regression was comparable between groups (45.83 ± 2.65 min in Group F vs. 45.50 ± 1.52 min in Group N, p = 0.553).The time of onset of motor block was similar in both groups (3.20 ± 0.66 min in Group F vs. 3.07 ± 0.74 min in Group N, p = 0.466). The time to achieve maximum motor block was significantly longer in Group N (5.93 ± 1.36 min) compared to Group F (4.30 ± 0.70 min) (p < 0.001).The duration of motor block was significantly longer in Group F (141.33 ± 33.08 min) compared to Group N (127.83 ± 12.91 min) (p = 0.042) **(table 2)**.

Postoperatively, the duration of complete postoperative analgesia was significantly longer in Group F (175.83 ± 31.84 min) compared to Group N (140.0 ± 15.25 min) (p < 0.001).The duration of effective analgesia was also significantly longer in Group F (222.0 ± 27.95 min) compared to Group N (179.00 ± 11.17 min) (p < 0.001).The total 24-hour paracetamol consumption was significantly higher in Group N (2733.33 ± 520.83 mg) compared to Group F (2200.00 ± 664.36 mg) (p = 0.001) **(table 3).**

Neonatal APGAR scores at 1 and 5 minutes were comparable between the groups, with no statistically significant differences (p = 0.869 at 1 min, p = 0.350 at 5 min) **(table 4).**

Visual Analog Scale (VAS) pain scores. At 0, 2, 4, 6, 12, and 24 hours, there was no significant difference in pain scores between the groups, indicating comparable pain relief efficacy **(table 5).**

Parameters	Group F		Group N		t-value	p value
	Mean	SD	Mean	SD		
Age(yrs)	24.93	2.7	25.60	3.3	0.842	0.304
Weight(KG)	70.70	5.91	69.13	6.05	1.01	0.58
Height (mts)	1.60	0.06	1.57	0.43	2.44	0.42
BMI(kg/m^2)	27.20	2.56	27.90	2.33	-1.01	0.83

Table 1: **Comparison of demographic data between Study Groups**

Parameters		Group F		Group N		P-value (student t test)
		Mean	SD	Mean	SD	
Intra-OP	Time of onset of sensory blockade (min)	2.13	0.507	2.20	0.61	0.647
	Time for Max Sensory Block (min)	3.13	0.507	3.63	1.03	0.021
	Time for 2 Segments Regression	45.83	2.65	45.50	1.52	0.553
	Time of onset of motor block (min)	3.20	0.66	3.07	0.74	0.466
	Time for max Motor Block (min)	4.30	0.70	5.93	1.36	< 0.001
	Duration of motor block (min)	141.33	33.08	127.83	12.91	0.042

Table 2: Distribution of intra-op parameters

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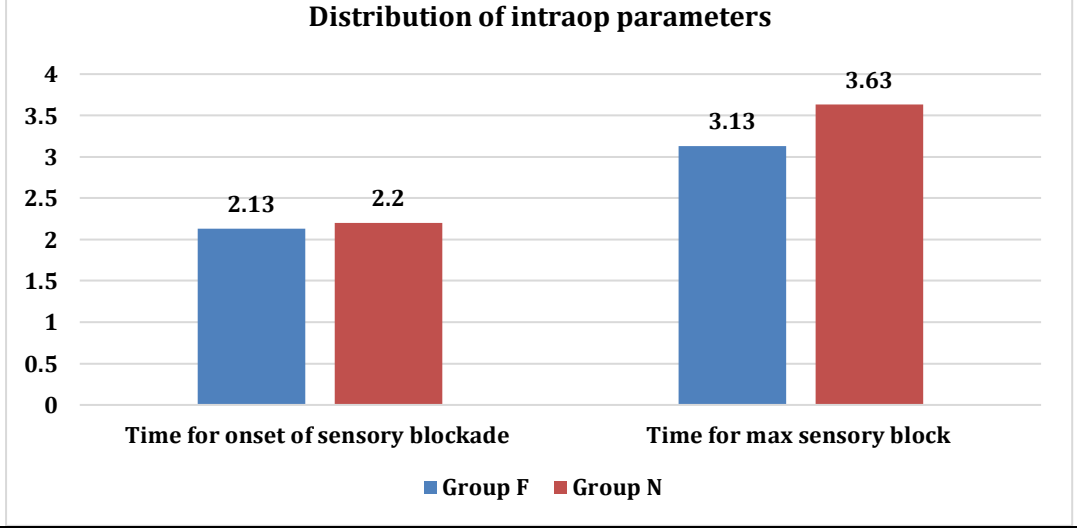
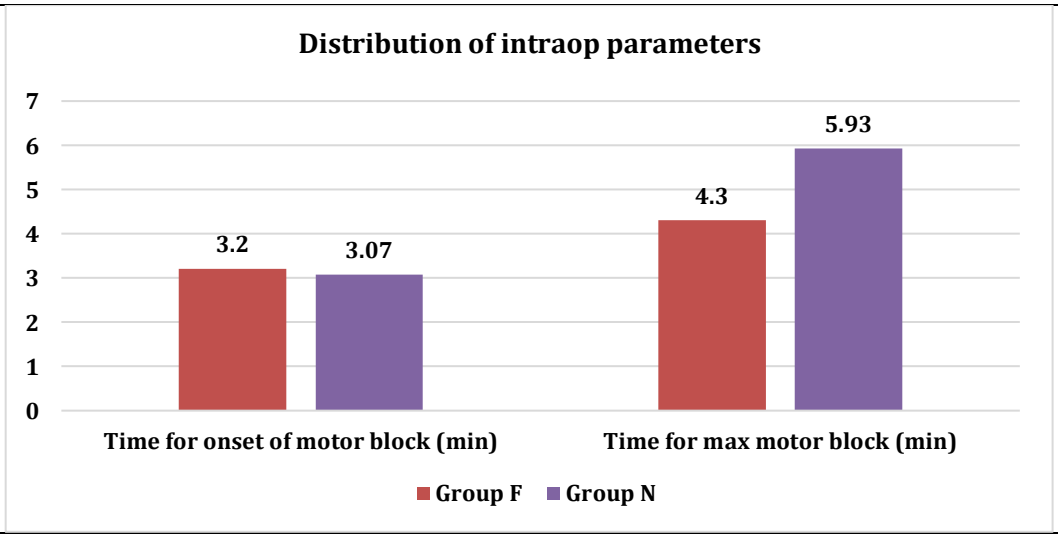


Figure 1



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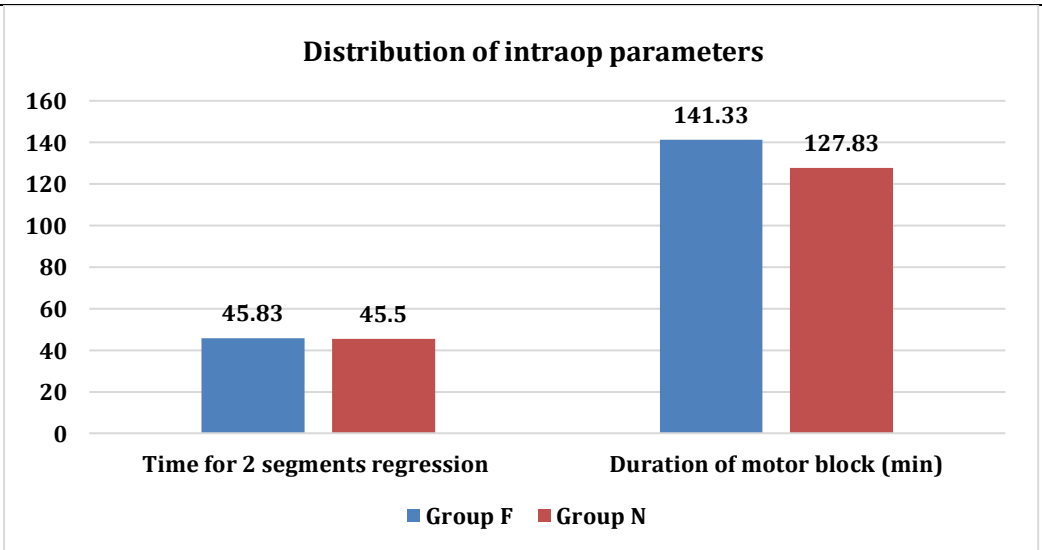

Figure 3

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Parameters		Group F		Group N		P-value (student t test)
		Mean	SD	Mean	SD	
Post-OP	Postop Analgesia complete	175.83	31.842	140.0	15.25	< 0.001
	Post op analgesia effective	222.0	27.95	179.00	11.17	< 0.001
	24hrs PCT Consumption	2200.00	664.36	2733.33	520.83	0.001

Table 3: Distribution of post op parameters

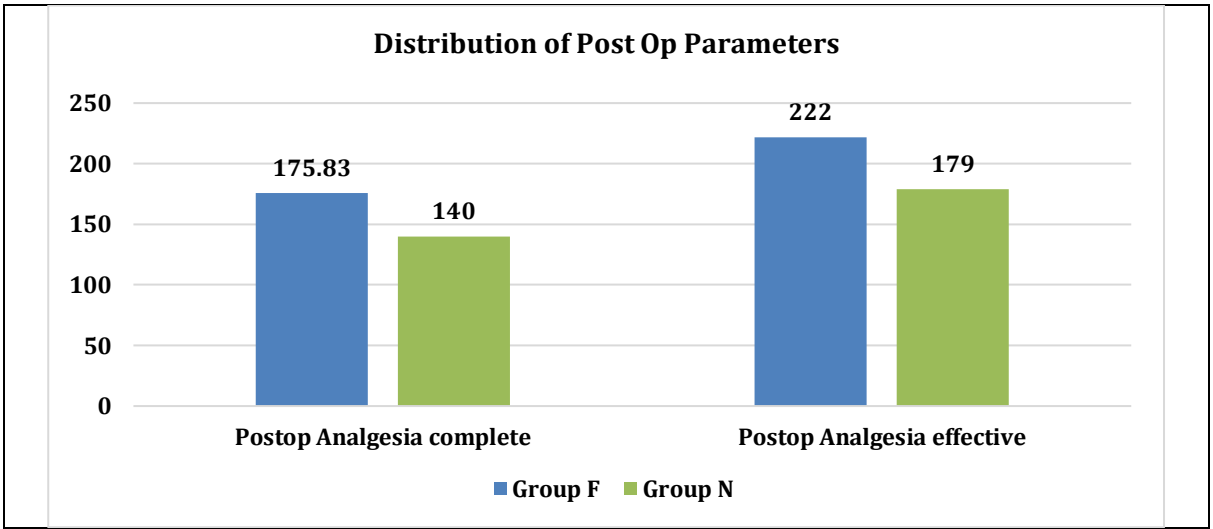

Figure 4

Apgar Score		Group FN (%)	Group NN (%)	Total	p-value (chi-square value)
At 1 min	7	19 (63.3%)	18 (60%)	37 (61.6%)	0.869
	8	10 (33.33%)	11 (36.7%)	21 (35.0%)	
	9	1 (3.4%)	1 (3.3%)	2 (3.4%)	
Total		30(100%)	30(100%)	60 (100%)	
At 5 min	8	12 (40%)	10 (33.3%)	22 (36.6%)	0.350
	9	18 (60%)	20 (66.7%)	38 (63.4%)	
Total		30(100%)	30(100%)	60 (100%)	

Table 4: Comparison of APGAR Score between Study Groups

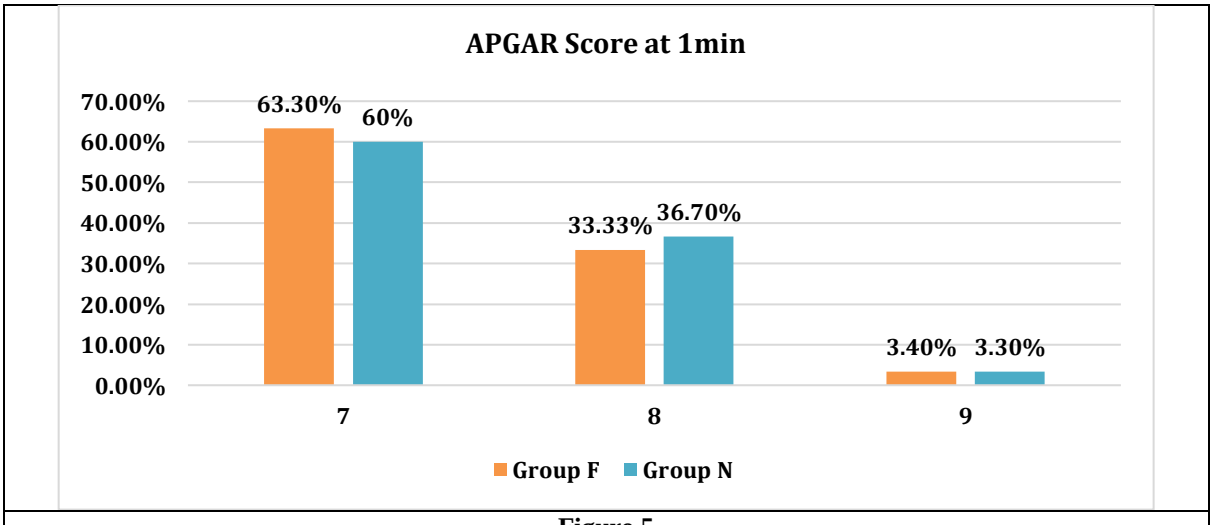

Figure 5

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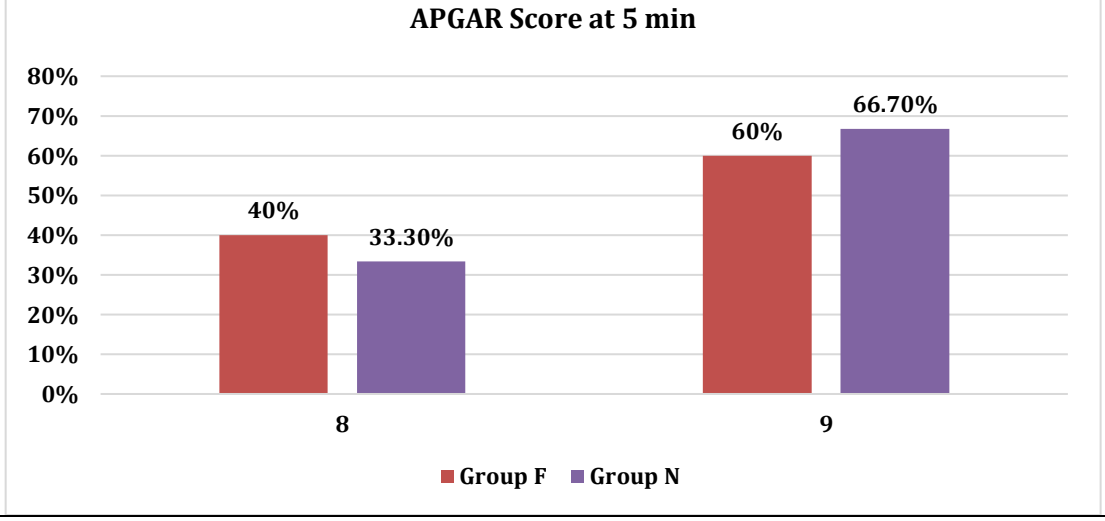

Figure 6

VAS Scoring		Group F		Group N		P value
		Mean	SD	Mean	SD	
Post-op	0th	7.67	0.46	7.60	0.49	0.599
	2nd hour	6.77	0.72	6.60	0.56	0.325
	4th hour	5.20	0.71	5.20	0.71	1.00
	6th hour	5.00	0.74	5.00	0.74	1.00
	12th hour	4.23	0.43	4.23	0.43	1.00
	24th hour	3.70	0.65	3.60	0.65	0.561

Table 5: Comparison of VAS scoring between Study Groups

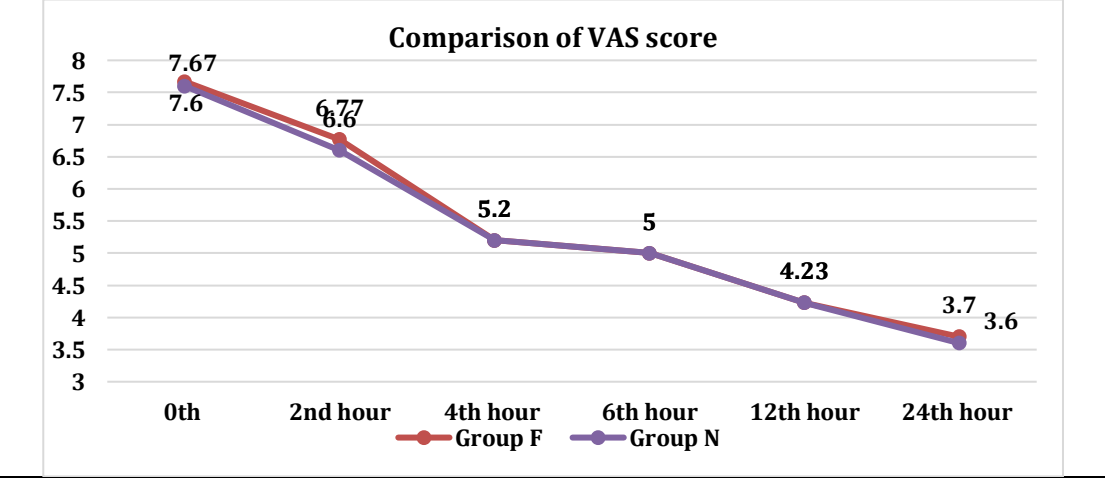

Figure 7

DISCUSSION

The present study aimed to compare the efficacy of intrathecal nalbuphine versus fentanyl as adjuvants to 0.5% hyperbaric bupivacaine in parturients undergoing elective lower-segment caesarean section (LSCS). The key parameters assessed included sensory and motor blockade characteristics, total duration of analgesia, hemodynamic effects, maternal and fetal outcomes, and associated side effects. The findings of the study indicated that both nalbuphine and fentanyl, when used as intrathecal adjuvants, enhanced the quality of spinal anesthesia. However, there were notable differences in their pharmacodynamic properties. While fentanyl is a lipophilic opioid with a rapid onset and short duration of action, nalbuphine, a mixed agonist-antagonist opioid, has been reported to provide longer-lasting analgesia.[2,3] The time of onset of sensory and motor blockade was comparable between the two groups. However, nalbuphine demonstrated a longer duration of sensory blockade compared to fentanyl, suggesting its potential advantage in prolonging intraoperative and postoperative analgesia. Additionally, nalbuphine was observed to provide a more sustained motor blockade duration, though this did not interfere significantly with postoperative recovery.[4,5] Several

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studies have evaluated the efficacy of intrathecal nalbuphine and fentanyl as adjuvants to hyperbaric bupivacaine. The findings of our study align with those of Ahmed FI, et al[3] who conducted a randomized double-blind study and found that nalbuphine provided a longer duration of analgesia compared to fentanyl in cesarean section patients. Similarly, Bindra TK, et al[4] reported that nalbuphine significantly prolonged postoperative pain relief compared to fentanyl without increasing adverse effects. Gupta K, et al[2] also compared these two opioids in orthopedic surgeries and concluded that nalbuphine exhibited a longer duration of sensory blockade and reduced postoperative opioid consumption. Additionally, Gurunath BB, et al[5] demonstrated that nalbuphine provided superior postoperative analgesia in lower abdominal surgeries compared to fentanyl, supporting the findings of our study. On the other hand, some studies, such as the work by Naaz S et al suggested that fentanyl provided better intraoperative analgesia and hemodynamic stability, albeit with a shorter duration of postoperative pain relief. This highlights the need for individualized opioid selection based on clinical priorities, such as intraoperative pain control versus prolonged postoperative analgesia. One of the primary goals of incorporating adjuvants in spinal anesthesia is to extend the duration of postoperative analgesia without prolonging the motor blockade. This study demonstrated that nalbuphine provided a significantly longer duration of postoperative analgesia compared to fentanyl, as assessed by the visual analog scale (VAS) scores and time to first analgesic request. This finding aligns with previous studies suggesting that nalbuphine has a more prolonged analgesic effect due to its unique receptor activity at kappa and mu opioid receptors.[6,7]

Both nalbuphine and fentanyl groups exhibited hemodynamic stability, with minor variations in blood pressure and heart rate. The incidence of hypotension and bradycardia was comparable between the two groups, and none of the patients required significant pharmacological intervention. This suggests that the addition of either opioid adjuvant does not markedly affect maternal hemodynamic parameters when used in appropriate doses.[8]

Neonatal outcomes, as assessed by the APGAR scores at 1 and 5 minutes, were comparable between the two groups. This indicates that neither nalbuphine nor fentanyl adversely affected fetal well-being. Moreover, maternal sedation levels remained within acceptable limits, with no significant over sedation observed in either group.[9]

Common opioid-related side effects such as pruritus, nausea, vomiting, and respiratory depression were minimal in both groups. However, a slightly higher incidence of nausea was noted in the fentanyl group, consistent with previous literature suggesting an increased propensity for nausea with mu-receptor agonists.[5] Conversely, nalbuphine, due to its kappa agonist and partial mu-antagonist properties, exhibited a lower incidence of pruritus and nausea, making it a favorable alternative in parturients susceptible to opioid-induced side effects.[7,10] The findings of this study have important implications for anesthetic practice in cesarean deliveries. The prolonged analgesic effect of nalbuphine, coupled with its lower incidence of opioid-related side effects, makes it available alternative to fentanyl as an adjuvant in spinal anesthesia. Given the need for optimal postoperative analgesia in LSCS patients, nalbuphine may be preferred in settings where prolonged pain relief is desirable without an increased risk of adverse effects.[6,9]

While this study provides valuable insights into the comparative efficacy of nalbuphine and fentanyl as intrathecal adjuvants, certain limitations must be acknowledged. The sample size, though statistically adequate, could be expanded in future studies to validate the findings. Additionally, long-term maternal and neonatal outcomes were not assessed, which may be an area for future research. Further comparative studies with varying doses of nalbuphine and fentanyl, as well as their effects in different patient populations, could enhance the understanding of their optimal clinical use.[8]

CONCLUSION

In conclusion, this study demonstrates that both nalbuphine and fentanyl serve as effective adjuvants to intrathecal hyperbaric bupivacaine for cesarean deliveries. While fentanyl provides rapid-onset analgesia, nalbuphine offers prolonged postoperative pain relief with fewer opioid-related side effects. Compared to previous studies, our results reaffirm the advantages of nalbuphine in extending analgesia duration and reducing opioid-induced complications. Based on these findings, nalbuphine may be a preferable alternative in clinical scenarios where extended postoperative analgesia is a priority.

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