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Comparison of Efficacy of Intrathecal Fentanyl versus Nalbuphine with Ropivacaine in Spinal Anesthesia for Postoperative Analgesic Effect following Lower Segment Caesarean Section- A Randomized Comparative Study

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Abstract
Background and Aims: *The aim of current study is to compare the analgesia efficacy & hemodynamics following the use of intrathecal fentanyl and nalbuphine as adjuvants to 0.5 % isobaric ropivacaine in LSCS.*
Materials and Methods: *A prospective, randomized double blind comparative study was conducted on 60 patients undergoing LSCS following spinal anesthesia. Patients were randomly allocated into two groups with 30 patients in each group. Group I received ropivacaine (0.5%) 10 mg + 20 μg fentanyl and group 2 received ropivacaine (0.5%) 10 mg + 0.8 mg nalbuphine. Hemodynamics at baseline, immediately after spinal (T0), 5 min. (T5), 10 min. (T10), 15 min. (T15), 20 min. (T20), 25 min. (T25), 30 min. (T30), and 45 min. (T45) were recorded.*
Results: *Patients in group 1 had significantly rapid onset of sensory and motor blockade, (P<0.001), however duration of blockade was comparable in both groups (P>0.05). The mean duration of effective analgesia (VAS<3) was significantly higher in group 2 (235.67±52.96 vs. 413.00±40.24, OR=1.04, 95% CI= 1.02-1.07, P<0.001). The requirement of rescue analgesics were less in group 2 (2.63±1.40 vs. 1.87±1.04, OR=0.62, 95% CI=0.39-0.97, P=0.019). Both groups had comparable baseline hemodynamic parameters. Systolic BP was maintained in both groups (P>0.05). Group 2 had significant decrease in diastolic and mean BP at 15, 20, 25, 30, and 45 minutes (P<0.05), but mean BP was maintained above the desired level (>60 mm Hg) throughout surgery in both groups.*
Conclusion: *We conclude that both intrathecal fentanyl 20 μg and nalbuphine 0.8 mg are effective adjuvants to 0.5% ropivacaine in LSCS.*
Keywords: *Fentanyl, nalbuphine, ropivacaine, lower segment cesarean section.*

Introduction

International Association for the Study of Pain defines PAIN as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] The most important concern of a

patient preoperatively is "postoperative pain." It remains grossly underrated and untreated leading to high degree of patient dissatisfaction.

Currently, regional anesthesia techniques (spinal) are used in many elective and emergency surgeries due to their higher level of safety. It is easier to perform by injecting anesthetic drug into the subarachnoid space with rapid onset of anesthesia, which provides analgesia both intra- and post-operatively. Since spinal anesthesia provides postoperative analgesia for a short time, many intrathecal adjuvants to local anesthetics have been addressed to augment the clinical efficacy and duration of analgesia. Among various adjuvants, intrathecal opioids have provided an effective prolongation of postoperative analgesia after surgical procedures.

Both fentanyl and nalbuphine are opioid analgesics. Fentanyl is an opioid agonist and acts on μ- opioid receptors.[2] Nalbuphine is a synthetic opioid analgesic with agonist–antagonist activity and acts as antagonist at μ- receptors and agonist at κ- receptors to provide reasonably potent analgesia. Nalbuphine, when used as adjuvant to hyperbaric bupivacaine, has improved the quality of perioperative analgesia with fewer side effects.[3]

Bupivacaine is extensively used and produces an adequate sensory and motor blockade.[4] Although intrathecal bupivacaine has low incidence of postoperative complications, it has selective cardiac effects which are more pronounced with R-isomer than S isomer.

These adverse effects have prompted a search for drugs with lesser toxicity. Newer long-acting local anesthetics (ropivacaine, levobupivacaine) have been introduced for clinical use. Ropivacaine is a long-acting, enantiomerically pure (S enantiomer) amide local anesthetic, with a low lipid solubility which blocks sensory nerve fibers (Aδ and C fibres) to a greater degree than those controlling motor function (Aβ fibers).[5]

Due to this property, ropivacaine has consistently demonstrated an improved safety profile over bupivacaine, with a reduced central nervous system (CNS) and cardio toxic potential.[6]

Ropivacaine is an amide type of local anesthetic. It differs from bupivacaine in that it is prepared as a pure S- enantiomer and it provides more differential sensory- motor block and has less CNS and cardiovascular toxicity.

This prospective randomized double- blind study was aimed to compare the clinical efficacy of intrathecal fentanyl (20 μg) with nalbuphine (0.8 mg) as adjuvant to 0.5% isobaric ropivacaine following spinal anesthesia in lower segment cesarean section (LSCS).

Subjects and Methods

This trial was registered with the clinical trial registry-India (CTRI), hosted at the ICMR's National Institute of Medical Statistics (www.ctri.nic.in), under the registration number CTRI/2019/06/019827. Following the approval by the institutional research ethics board and obtaining written informed patient consent, a double blind randomized prospective comparative study was conducted on 60 patients of ASA I and II of age group 20–40 years with normal coagulation profile undergoing LSCS under spinal anesthesia. Patients were randomly allocated (computer generated random numbers) into two groups with 30 patients in each group.

Group I received 10 mg (2.0 ml) of 0.5% ropivacaine with 20 μg (0.4ml) fentanyl.

Group 2 received 10 mg (2.0 ml) of 0.5% ropivacaine with 0.8 mg (0.4 ml) nalbuphine.

Patients with contraindication for spinal anesthesia were excluded from this study.

All patients following evaluation & relevant laboratory investigations were taken up for spinal anesthesia. All Patients vital parameters were monitored by using multichannel monitor having pulse oximetry, electrocardiogram, and non-invasive blood pressure. Intravenous line was secured with 18-gauge IV cannula and preloading was done with Ringer lactate 7 ml/kg IV. The patient was positioned in the sitting position and under all aseptic precautions, lumbar puncture was

performed at the level of L2-L3 or L3-L4 inter-space through a midline approach using 25G spinal needle and study drug was injected after confirmation of needle tip in the subarachnoid space by free and clear flow of CSF. Syringe preparation and drug administration was done by an independent anesthesiologist (not involved in the study). After the injection, patients were immediately aligned into a supine position.

All operations were performed in the similar operation theater conditions, which maintained a constant humidity and an ambient temperature of around 22°C ± 1°C. Oxygen was administered to all patients at a rate of 4 L/min with venturi mask (FiO2 = 0.28) and patients were covered with drapes, but not actively warmed. Intravenous (IV) fluids and anesthetic drugs were administered at room temperature.

Sensory and motor block characteristics were assessed at every minute interval. Sensory block was assessed by pinprick method and motor block by Modified Bromage Scale.[7] Sensory level was determined by pinprick method using sterile 24 gauge hypodermic needle. Sensations of pinprick were tested every minute from time 'Zero', which corresponded to the time of intrathecal injection. The onset of sensory blockade, time to reach maximum sensory blockade and duration of sensory blockade (two segment regression from highest level of sensory blockade and S1 regression) were recorded in each patient. The loss of discrimination to pinprick at T10 dermatome was taken as the time to onset of sensory block. Time to reach maximum sensory blockade was defined as absence of pinprick sensation at T6 dermatome or above. The onset of motor blockade (Bromage's Grade 1 motor block), onset of complete motor blockade (Bromage's Grade 3 motor block) and duration of motor blockade [time required for motor blockade to return to Bromage's Grade 0 from the time of onset of motor blockade) were noted.

Blood pressure (BP) (systolic, diastolic, and mean BP), heart rate and SpO$_2$ were continuously monitored and recorded at 5, 10, 15, 20, 25, and 30 min after the injection, and subsequently every 15 min till the end of surgery. Hypotension (defined as systolic BP of <90 mmHg or a decrease of systolic pressure of >20% from baseline value) was treated with intravenous fluid initially (250 ml boluses repeated twice) and intravenous mephentermine 6 mg, if required. Bradycardia (defined as heart rate of <60) was treated with 0.6 mg of intravenous atropine sulfate.

Grades of sedation during surgery were assessed by the Modified Ramsay's sedation scale.[8]

Patients were also assessed for side effects such as respiratory depression, nausea, vomiting, hypotension, pruritis, and bradycardia.

Postoperative recordings and pain assessment:

For recovery of block, time to two dermatome regressions, time to S1 regression and time to complete motor recoveries were recorded.

Preoperatively, all patients were educated in detail about grading of pain using a visual analog scale (VAS) pain score (0 – no pain and 10 – worst imaginable pain) and to request supplementary analgesics if needed.

The duration of effective analgesia was taken as the time from the completion of spinal injection to the time of administration of the first rescue analgesic reflected on VAS 10 scoring. The VAS score was serially assessed every 30 min till patients complain of pain (VAS>3) and Intramuscular diclofenac (75 mg) was administered as rescue analgesic. In other words, the duration of postoperative analgesia will be measured from the time of spinal drug injection to the next complaint of pain or VAS >3 or the VAS score of >3 constituted the end point of the study. The total number of rescue analgesics required postoperatively over 24 hour was recorded. Patients were also assessed for side effects such as any respiratory depression, nausea, vomiting, hypotension, pruritis, and bradycardia.

Statistical analysis was performed with SPSS Statistics 24 for Mac (IBM). The sample size was calculated according to the time to initiation of pain, and it was estimated that a group sample size

of 21 patients for each group would be sufficient to detect a difference of 180 min between group 1 and group 2, with a significance level of <0.05 and power of study (1- β) as 80% (β=0.2). Continuous variables were expressed as mean±standard deviation (SD). Continuous variables were compared with the Student's t-test and Mann–Whitney U-test as appropriate. Differences between proportions derived from categorical data were compared with chi-square or Fisher's exact test. For all tests, a P < 0.05 was considered significant and P < 0.001 was considered highly significant.

Results

A total of 62 patients were enrolled for the study. Finally 60 patients meeting the inclusion criteria (randomly assigned to the treatment groups) completed the trial, were analyzed [Figure 1].

The demographic, baseline, and surgical characteristics were comparable among the groups [Table 1].

Sensory Block characteristics were illustrated in Table 2. For sensory block both the onset (3.03±0.51 vs. 4.27±0.57, OR=13.39, 95% CI =1.28-139.51, **P<0.001**) and time to reach a maximum level (5.47±1.66 vs. 7.97±0.69, OR= 1.79, 95% CI= 0.75-4.29, **P<0.001**) were statistically significant among the groups (*P* < 0.001). Median level of peak sensory block was T5 in both groups. Time of two segment sensory regression (90.23±6.51 vs. 93.17±5.16, OR=1.09, 95% CI=0.91-1.32, P=0.058) and regression to S1 level were comparable between groups (P>0.05).

Motor block Characteristics were also illustrated in Table 2.

There was a significant difference in onset time of motor blockade (Bromage 1) (3.25±0.64 vs. 4.84±0.54, OR=12.08, 95% CI= 2.73-53.36, P<0.001) and complete motor blockade (Bromage 3) (8.01±0.90 vs. 10.15±1.40, OR=2.75, 95% CI=1.01-7.52, P<0.001) among groups. Also, Table 2 is 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. (111.00±10.53 vs. 108.83±8.57, OR= 1.01, 95% CI= 0.91-1.13, P = 0.386).

Sedation: The Modified Ramsay sedation score was recorded at 30 min interval from subarachnoid injection till 120 min. The score was comparable among both groups at 30, 60, 90 and 120 min (P>0.05).

Analgesia

As illustrated in Table 2, the mean duration of effective analgesia (VAS<3) was statistically highly significant between group 1 and 2 (235.67±52.96 vs. 413.00±40.24, OR=1.04, 95% CI= 1.02-1.07, **P<0.001**) (Figure 2A). The requirement of rescue analgesics, over 24 hour, in terms of total number of doses of intramuscular diclofenac were significantly less in group 2 when compared to Group 1 (1.87±1.04 vs. 2.63±1.40, OR=0.62, 95% CI=0.39-0.97, **P=0.019**) (Figure 2B).

Hemodynamics

Both groups had similar baseline Systolic BP, Diastolic BP, Mean BP and heart rate (HR) values. Systolic BP was maintained in both groups (Table 3a and figure 3A). Group 2 had a significant diastolic BP (Table 3a and figure 3B) and mean BP (Table 3b) decrease with respect to the group 1 at 15, 20, 25, 30, and 45 minutes (**P<0.05**). However, Systolic BP was preserved in both groups and Mean BP was maintained above the desired level (>60 mm Hg) in both groups (Figure 3C). Three patients in Group 2 and 1 patient in Group 1 reported hypotension which was mild and easily corrected by giving 6 mg of bolus dose of injection mephentermine. The number of patients requiring mephentermin was higher in group 2, but was statistically insignificant (P >0.05).

Heart rate (HR) were comparable in both groups (P>0.05) (Table 4 and figure 4).

Side Effects

None of the patients experienced respiratory distress & bradycardia at any point of time. All

patients had peripheral oxygen saturation (SpO2) greater than 90% at all the times during surgery. There was no evidence of any respiratory depression in neonates in both the groups. The adverse effects (eg. Nausea/vomiting, pruritis, hypotension and urinary retention) were comparable between both groups (P>0.05).
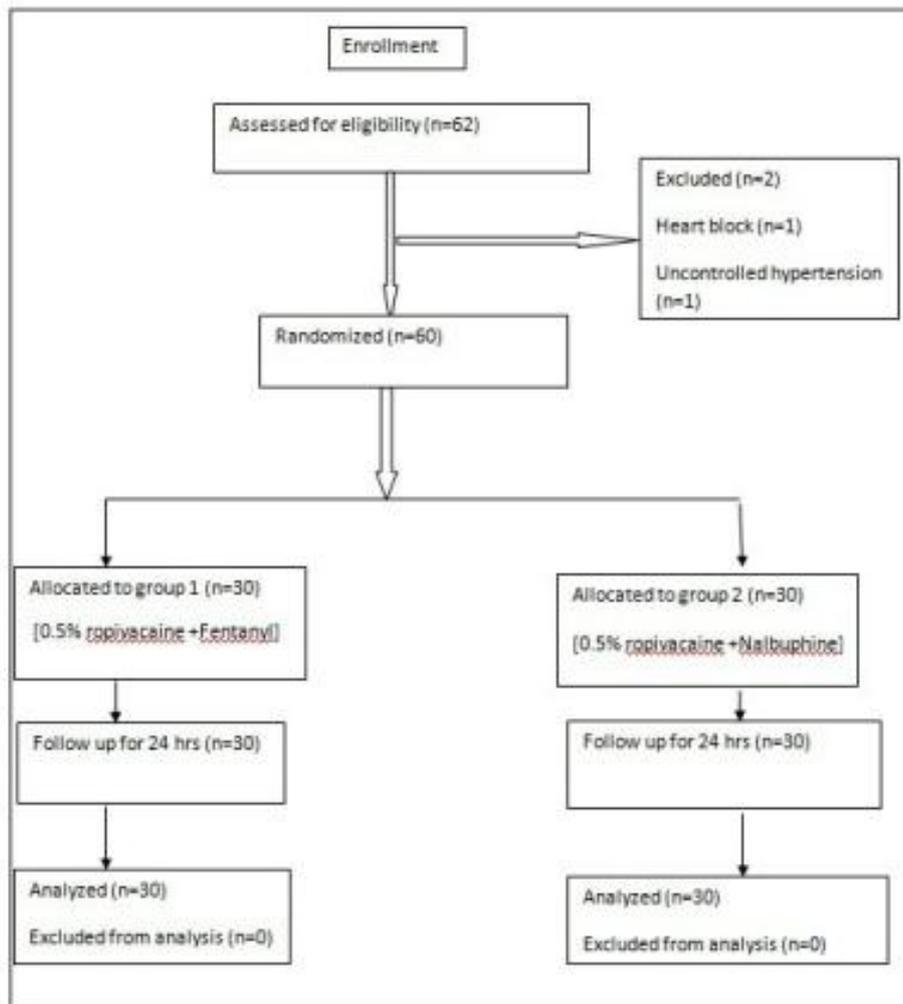

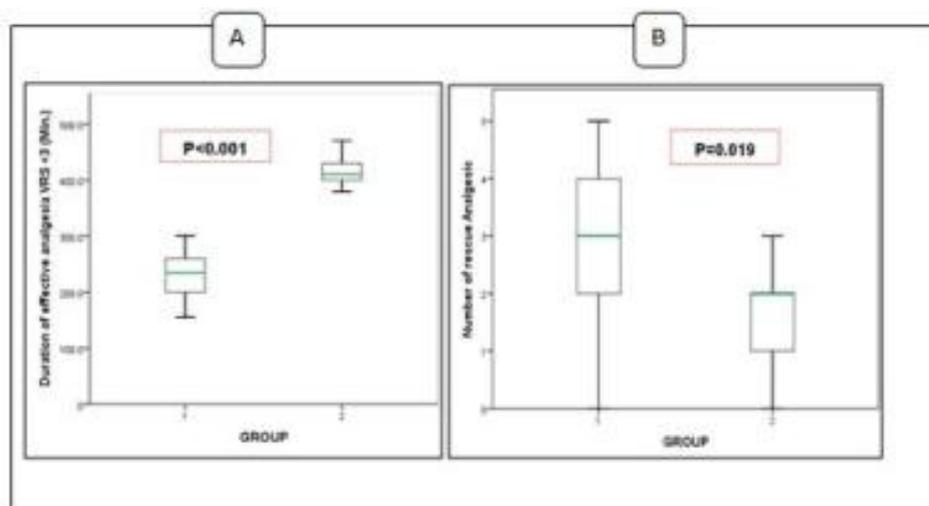**Figure 1:** Flow diagram of the study protocol

Figure 2: Box & Whisker Graph; (A) Duration of effective analgesia; (B) Number of rescue Analgesic
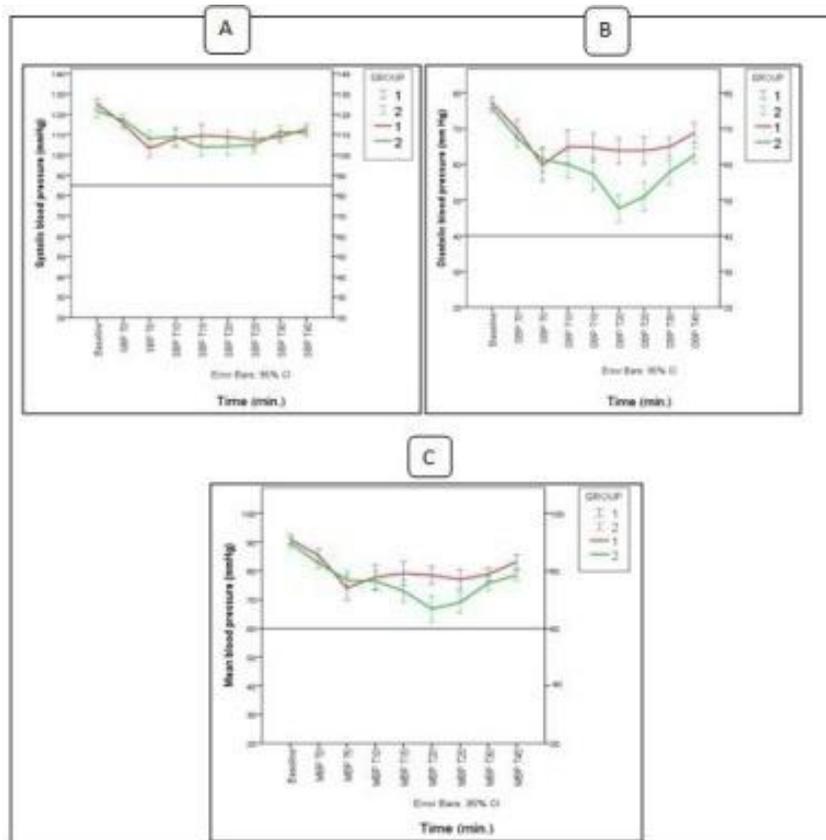
Figure 3: Error bar chart of intra-operative changes in systolic blood pressure (A) diastolic blood pressure (B) and mean blood pressure (C) between two groups (mean with 95% CI) till 45 min. (T45)
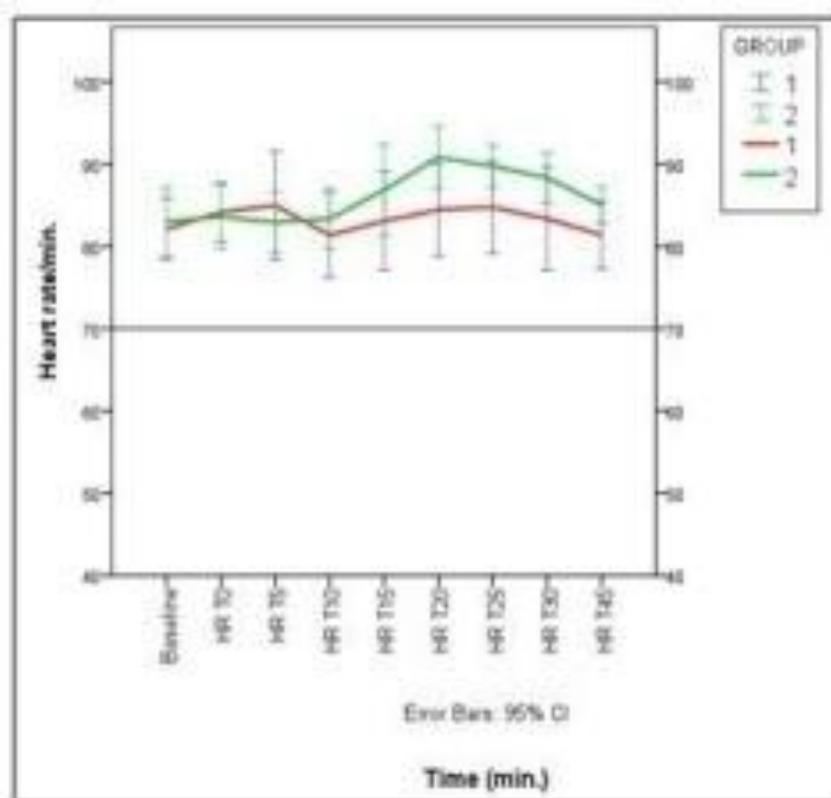

Figure 4: Error bar chart of intra-operative changes in heart rate between two groups (mean with 95% CI) till 45 min. (T45)

Table 1: Comparison of patient and surgery characteristics

Variable	Group 1 (n=30)	Group 2 (n=30)	P value
Age (year)	24.10±2.32	25.20±3.64	0.169
Weight (kg)	62.03±2.94	62.30±3.07	0.733
Height (cm)	159.73±2.76	159.30±3.63	0.605
ASA I/II	21:9	22:8	0.779
Baseline Heart rate, HR (beats/minute)	82.07±9.96	82.97±11.10	0.742
Baseline Systolic Blood Pressure, SBP (mmHg)	125.20±6.27	121.73±8.90	0.087
Baseline Diastolic Blood Pressure, DBP (mmHg)	77.33±4.08	75.97±3.76	0.183
Baseline Mean Arterial Pressure, MAP (mmHg)	90.90±4.24	89.67±4.49	0.279
Duration of surgery (minutes)	37.97±4.62	37.33±4.15	0.579

Results expressed as mean ± SD. P values highlighted in bold are significant. *n*: Number of patients, SD: Standard deviation

Table 2: Sensory, motor & analgesic characteristics

Variable	Group 1 (n=30)	Group 2 (n=30)	Odds ratio (95% confidence interval)	P value
Onset of sensory block (to reach T10) (min)	3.03±0.51	4.27±0.57	13.39 (1.28-139.51)	**<0.001**
Peak sensory block level	T5 (T5-T6)	T5 (T5-T6)	-	0.362
Time to reach maximum sensory block (min.)	5.47±1.66	7.97±0.69	1.79 (0.75-4.29)	**<0.001**
Two segment regression time (min.)	90.23±6.51	93.17±5.16	1.09 (0.91-1.32)	0.058
Regression to S1 level (min.)	129.00±13.67	128.50±10.26	1.01 (0.92-1.11)	0.873
Onset of motor blockade (Bromage 1) (min.)	3.25±0.64	4.84±0.54	12.08 (2.73-53.36)	**<0.001**
Onset of complete motor blockade (Bromage 3) (min.)	8.01±0.90	10.15±1.40	2.75 (1.01-7.52)	**<0.001**
Duration of motor blockade (min.)	111.00±10.53	108.83±8.57	1.01 (0.91-1.13)	0.386
Duration of effective analgesia VAS<3 (min.)	235.67±52.96	413.00±40.24	1.04 (1.02-1.07)	**<0.001**
Number of rescue analgesics	2.63±1.40	1.87±1.04	0.62 (0.39-0.97)	**0.019**

Results expressed as mean ± SD. P values highlighted in bold are significant. *n*: Number of patients, SD: Standard deviation

Table 3a: Systolic and diastolic blood pressure monitoring (mmHg)

Time (min.)	Group 1 (n=30)	Group 2 (n=30)	Odds ratio (95% confidence interval)	P value
Baseline Systolic Blood Pressure, SBP (mmHg)	125.20±6.27	121.73±8.90	0.85 (0.75-0.98)	0.087
SBP-T0	115.40±6.68	117.07±8.21	1.17 (1.01-1.37)	0.392
SBP-T5	103.20±11.87	108.10±9.94	1.06 (0.98-1.15)	0.088
SBP-T10	108.17±11.47	109.10±12.13	1.10 (1.00-1.21)	0.761
SBP-T15	109.53±14.71	103.87±11.58	1.01 (0.92-1.09)	0.103
SBP-T20	109.00±7.38	104.20±11.18	0.83 (0.72-0.97)	0.056
SBP-T25	107.40±11.15	105.00±11.09	0.97 (0.88-1.07)	0.407
SBP-T30	108.97±7.44	111.17±8.53	1.19 (1.03-1.37)	0.292
SBP-T45	112.83±6.36	110.90±5.27	0.87 (0.75-1.02)	0.205
Baseline Diastolic Blood Pressure, DBP (mmHg)	77.33±4.08	75.97±3.76	0.97 (0.75-1.26)	0.183
DBP-T0	69.83±7.05	67.43±6.83	0.91 (0.75-1.10)	0.186
DBP-T5	59.80±12.30	61.43±9.28	1.14 (0.99-1.31)	0.564
DBP-T10	64.97±12.49	59.97±10.40	0.95 (0.82-1.10)	0.097
DBP-T15	64.73±10.65	57.23±11.89	1.35 (1.02-1.79)	**0.013**
DBP-T20	63.87±9.50	47.60±10.08	0.64 (0.47-0.87)	**<0.001**
DBP-T25	63.87±10.30	50.97±10.72	0.95 (0.83-1.08)	**<0.001**
DBP-T30	64.90±6.98	57.80±9.37	1.12 (0.91-1.36)	**0.002**
DBP-T45	68.80±7.59	62.63±6.00	0.64 (0.44-0.95)	**0.001**

Results expressed as mean ± SD. P values highlighted in bold are significant. *n*: Number of patients, SD: Standard deviation

Table 3b: Mean Arterial blood pressure monitoring (mmHg)

Time (min.)	Group 1 (n=30)	Group 2 (n=30)	Odds ratio (95% confidence interval)	P value
Baseline Mean Blood Pressure, MBP (mmHg)	90.90±4.24	89.67±4.49	1.06 (0.87-1.31)	0.279
MBP-T0	85.30±5.97	82.63±4.78	0.82 (0.67-1.00)	0.061
MBP-T5	74.10±11.53	76.80±7.99	1.14 (1.02-1.27)	0.296
MBP-T10	77.77±11.72	76.43±8.87	1.00 (0.92-1.09)	0.621
MBP-T15	79.13±11.12	73.00±10.45	1.13 (0.98-1.30)	**0.032**
MBP-T20	78.43±8.22	66.77±12.10	0.85 (0.74-0.97)	**<0.001**
MBP-T25	77.00±9.15	69.00±9.68	0.88 (0.77-1.02)	**0.002**
MBP-T30	78.77±5.84	73.77±5.75	1.22 (1.03-1.46)	**0.048**
MBP-T45	83.10±6.62	78.47±4.50	0.73 (0.57-0.92)	**0.002**

Results expressed as mean ± SD. P values highlighted in bold are significant. *n*: Number of patients, SD: Standard deviation

Table 4: Heart rate monitoring (beats/minute)

Time (min.)	Group 1 (n=30)	Group 2 (n=30)	Odds ratio (95% confidence interval)	P value
Baseline Heart Rate, HR (beats/minute)	82.07±9.96	82.97±11.10	**1.02 (0.95-1.09)**	0.742
HR-T0	84.13±9.58	83.57±10.49	**0.97 (0.89-1.04)**	0.828
HR-T5	84.93±17.68	82.90±9.84	**0.95 (0.89-1.00)**	0.584
HR-T10	81.37±13.84	83.33±9.76	**1.05 (0.98-1.13)**	0.527
HR-T15	83.07±16.17	86.83±14.92	**0.94 (0.87-1.01)**	0.352
HR-T20	84.43±15.06	90.80±10.25	**1.09 (0.97-1.21)**	0.061
HR-T25	84.73±14.91	89.73±6.89	**1.02 (0.92-1.12)**	0.101
HR-T30	83.33±16.89	88.33±8.16	**1.00 (0.92-1.09)**	0.150
HR-T45	81.37±10.99	85.00±5.81	**1.05 (0.94-1.17)**	0.115

Results expressed as mean ± SD. P values highlighted in bold are significant. *n*: Number of patients, SD: Standard deviation

Discussion

We used isobaric 0.5% ropivacaine with intrathecal fentanyl and nalbuphine as adjuvants in our study. Ropivacaine is now gaining popularity due to its reduced cardiac toxicity.[9] Various studies revealed that intrathecal administration of 0.5% ropivacaine or 0.5% bupivacaine resulted in a similar effective spinal anesthesia with less hypotension than bupivacaine. [10, 11]

The literature on the comparison of 20 μg intrathecal fentanyl and 0.8 mg nalbuphine as adjuvants to 0.5% isobaric ropivacaine in patients undergoing lower segment cesarean section is scarce. Apart from the study by babu et al.[16], no other comparative study fully explored this novel issue.

As previous studies clearly demonstrated that 0.8 mg nalbuphine dose provides adequate analgesic effect without side effects, beyond that dose (1.6 mg or 2.4 mg) it showed ceiling effect to analgesia and increase in side effects.[12,13,14,15] Hence they recommended the dose of 0.8 mg for intrathecal injection for nalbuphine.

In our study, both the groups were comparable with respect to age, height, weight, ASA grade, duration and type of surgery.

In the present study, sensory and motor block characteristics, analgesia efficacy, sedation and hemodyanamic changes were analyzed in detail between two groups.

Sensory Block Characteristics: In our study, we observed that the time required for onset of sensory block and time to reach maximum sensory block was significantly faster in group 1 than group 2, which corroborate with the study of Babu *et al*.[16], similar results were also observed by Venkata *et al*.[17], and Kaur et al.[18] However Gomaa *et al*.[19], Gupta *et al*.[20], Ahmed *et al*.[21],

and Naaz et al.[14] observed no difference in onset of sensory block.

In our study, there was no statistically significant difference in the duration of sensory block between the groups. This finding is similar to Prabhakaraiah UN et al.[22], Naaz et al.[14], and Gomaa et al.[19] Prolonged duration of sensory block has also been observed with fentanyl in some of the studies. [23, 24]

Motor Block Characteristics: The onset of motor blockade (Bromage 1 & 3) was significantly more rapid with group 1 than group 2 in our study and this can be due to high lipid solubility and rapid tissue uptake of fentanyl than nalbuphine. Gomaa et al.[19] also found similar results. However Tiwari et al.[25], and Bindra et al.[26] Contradict to our study and found no statistically significant difference in the onset of motor block.

The duration of motor block was comparable in both groups and this finding coincides with results of other studies. [19, 26, 27]

Sedation: Both groups were comparable with regard to sedation at 30, 60, 90 and 120 min in our study. Gupta et al.[20] showed comparable sedation scores with intrathecal fentanyl and nalbuphine. Whereas Bindra et al.[26] and Cowan et al.[28] observed increased sedation with intrathecal fentanyl.

Perioperative Analgesia: The duration of post-operative analgesia was significantly more in the nalbuphine group (group 2) than fentanyl group (group 1). If we consider the 24 hour analgesic consumption, Patients who received intrathecal nalbuphine required significantly lesser number of rescue analgesics than fentanyl group.

Yaksh and Bisnbaeh in their study titled as "intrathecal nalbuphine for cesarean delivery: Are we ready?" mentioned that the general trend of human studies on neuraxial nalbuphine is that epidural or intrathecal delivery of nalbuphine produces a significant analgesia accompanied by minimal side effects. [29]

There are very few studies with ropivicaine and nalbuphine, especially in obstetrics. The difference is that they did a controlled study and ours is a comparative study with fentanyl.[15,30] This study is first of its kind randomized study in obstretic patients in which we have done detailed analysis of isobaric ropivacaine (0.5%) with fentanyl and nalbuphine as adjuvants for spinal anesthesia.

Most of the studies on intrathecal fentanyl and nalbuphine as adjuvant to hyperbaric bupivacaine revealed the duration of post-operative analgesia was prolonged in nalbuphine group than fentanyl group.[14,26,30] However, Gomaa et al. did not find any significant difference in the duration of analgesia between the two.[19]

Hemodynamics Changes

The hemodynamic characteristics of mean HR and SBP at baseline and intraoperatively were comparable and there was no statistically significant difference in HR, SBP, and SpO2 during intra-operative periods between both the groups ($P > 0.05$). Most of the other studies also had similar results. [16,19,20]

However, in our study we found a new observation that diastolic & mean blood pressure fall is more in nalbuphine group, but systolic blood pressure remains preserved and also mean blood pressure is maintained above the desired level (>60 mm Hg) throughout the surgery. Nalbuphine group of patients did not require any additional medical intervention in comparison to fentanyl group for intra-operative management of hemodynamics. This is a new finding of our study, which need to validate on future studies.

Most of the studies in the literature were on intrathecal fentanyl and nalbuphine as adjuvant to hyperbaric bupivacaine versus our literature first comparative study that fully explored the intrathecal fentanyl and nalbuphine as adjuvant to 0.5% isobaric ropivacaine.

We have compared our results above with bupivacaine studies (as no comparative studies except babu et al, only controlled studies on

isobaric ropivacaine) and found results similar or even better in terms of hemodynamics.

The issue with intrathecal nalbuphine is regarding its neurotoxicity. None of the studies in humans done till date reported any signs of neurotoxicity in the perioperative period.

Conclusion

We conclude that both fentanyl 20 μg and nalbuphine 0.8 mg are effective adjuvants to 0.5% ropivacaine in LSCS. However, Intrathecal fentanyl is associated with significantly earlier onset of sensory and motor blockade with comparable duration of block. Whereas, intrathecal nalbuphine 0.8 mg has significantly prolonged duration of postoperative analgesia when compared to intrathecal fentanyl 20 μg with minimal side effects and also reduces total analgesic requirement.

Systolic BP, HR, RR and oxygen saturation are preserved in both groups. In terms of hemodynamic stability, both groups are comparable.

References

1. Rosenquist RW, Vrooman BW. Chronic pain management. In: Morgan GE, Mikhail MS, Murray MJ, editors. Clinical Anesthesiology. 5th ed. New York: Tata McGraw Hill; 2013. 1025.
2. Tejwani GA, Rattan AK, McDonald JS. Role of spinal opioid receptor in the antinociceptive interaction between intrathecal morphine and bupivacaine. Anesth Analg 1992; 74:726-34.
3. Gunion MW, Marchionne AM, Anderson TM. Use of the mixed agonist antagonist nalbuphine in opioid based analgesia. Acute Pain 2004; 6:29-39.
4. Covina BG. Pharmacology of local anaesthetic agents. Br J Anaesth. 1986; 58:701-16.
5. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. Drugs. 2000; 60:1065-93.
6. Akerman B, Hellberg IB, Trossvik C. Primary evaluation of the local anaesthetic properties of the amino amide agent ropivacaine (LEA 103). Acta anaesthesiologica Scandinavica. 1988; 32:571-78.
7. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965; 16:55–69.
8. Ramasay MA, Savege TM, Simpson BR. Controlled sedation with alphaxalone. Br Med J. 1974; 2:656–59.
9. Malinovsky JM, Charles F, Kick O, Lepage JY, Malinge M, Cozian A, *et al.* Intrathecal anesthesia: Ropivacaine versus bupivacaine. Anesth Anal 2000; 91:1457- 60.
10. McNamee DA, McClelland AM, Scott S, Milligan KR, Westman L, Gustafsson U. Spinal anaesthetic: Comparison of plain ropivacaine 5mg/ml with bupivacaine 5mg/ml for major orthopedic surgery. Br J Anaesth 2002; 89:702- 06.
11. Whiteside JB, Burke, Wildsmith JA. Comparison of ropivacine 0.5% (in glucose) with bupivacine 0.5% (in glucose 8%) for spinal anaesthesia for elective surgery. Br J Anaesth 2003; 18:521- 25.
12. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti R. Advantages of intrathecal nalbuphine, compared with intrathecal

morphine, after caesarean delivery: an evaluation of prospective analgesia and adverse effects. Anesth Analg. 2000; 91:601-05.

13. Jyothi B, Shruthi Gowda, Safiya I Shaikh. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopaedic surgeries. Indian Journal of Pain. 2014; 28:18-21.

14. Naaz S, Shukla U, Shrivastav S, et al. A Comparative Study of Analgesic Effect of Intrathecal hyperbaric bupivacaine with Nalbuphine and Fentanyl as Adjuvant in Lower Limb Orthopaedic Surgery. J Clin Diagn Res. 2017;11:UC25-28

15. Borah TJ, Dey S, Yunus M, et al. Effect of different doses of intrathecal nalbuphine as adjuvant to ropivacaine in elective lower limb surgeries: A dose finding study. Indian J Anaesth. 2018; 62:865-70.

16. Babu KV, Kumar GP, Harinath G. Evaluation of the Efficacy of Intrathecal Fentanyl Versus Intrathecal Nalbuphine as Adjuvants to 0.75% Ropivacaine for Post-operative Pain Relief in Cesarean Section: A Double-blind Randomized Comparative Study. IJSS 2017; 5: 5-10.

17. Venkata HG, Pasupuleti S, Pabba UG, Porika S, Talari G. A randomized controlled prospective study comparing a low dose bupivacaine and fentanyl mixture to a conventional dose of hyperbaric bupivacaine for cesarean section. Saudi J Anaesth 2015; 9:122- 27.

18. Kaur M, Katyal S, Kathuria S, Singh P. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery. Saudi J Anaesth 2011; 5:202-07.

19. Gomaa HM, Mohamed NN, Zoheir HA, Ali MS. A comparison between post- operative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after caesarean section. Egypt J Anaesth 2014; 30:405- 10.

20. Gupta K, Rastogi B, Gupta PK, Singh I, Bansal M, Tyagi V. Intrathecal nalbuphine versus intrathecal fentanyl as adjuvant to 0.5% hyperbaric bupivacaine for orthopedic surgery of lower limbs under subarachnoid block: A comparative evaluation. Indian J Pain 2016; 30:90- 95.

21. Ahmed F, Narula H, Khandelwal M, Dutta D. A comparative study of three different doses of nalbuphine as an adjuvant to intrathecal bupivacaine for postoperative analgesia in abdominal hysterectomy. Indian J Pain 2016; 30:23- 28.

22. Prabhakaraiah UN, Narayanappa AB, Gurulingaswamy S et al. "Comparison of Nalbuphine Hydrochloride and Fentanyl as an Adjuvant to Bupivacaine for Spinal Anesthesia in Lower Abdominal Surgeries:" A Randomized, Double-blind Study. Anesth Essays Res. 2017; 11:859-63.

23. Singh H, Yang J, Thornton K, Giesecke AH. Intrathecal fentanyl prolongs sensory bupivacaine spinal block. Can J Anaesth 1995; 42:987- 91.

24. Bidikar M, Mudakanagoudar MS, Santhosh MC. Comparison of intrathecal levobupivacaine and levobupivacaine plus fentanyl for cesarean section. Anesth Essays Res 2017; 11:495- 98.

25. Tiwari AK, Tomar GS, Agrawal J. Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: A randomized prospective double- blind clinical study. Am J Ther 2013; 20:592- 95.

26. Bindra TK, Kumar P, Jindal G. Postoperative Analgesia with Intrathecal Nalbuphine versus Intrathecal Fentanyl in

Cesarean Section: A Double-Blind Randomized Comparative Study. Anesth Essays Res. 2018; 12:561-65.

27. Bisht S, Rashmi D. Comparison of intrathecal fentanyl and nalbuphine: A prospective randomized controlled study in patients undergoing total abdominal hysterectomy. Anaesth Pain Intensive Care 2017; 21:194- 98.

28. Cowan CM, Kendall JB, Barclay PM, Wilkes RG. Comparison of intrathecal fentanyl and diamorphine in addition to bupivacaine for caesarean section under spinal anaesthesia. Br J Anaesth 2002; 89:452- 58.

29. Yaksh T, Birnbach DJ. Intrathecal nalbuphine after cesarean delivery: are we ready? Anesth Analg 2000; 91:505-08.

30. Seetharam KR, Bhat G. Effects of isobaric ropivacaine with or without fentanyl in subarachnoid blockade: A prospective double-blind, randomized study. Anesth Essays Res. 2015; 9:173-77.