Original Article

Dexmedetomidine and Fentanyl as an Adjuvant to Intrathecal Isobaric Ropivacaine for Surgery of Fracture Neck Femur; A Randomized, Double-Blind Comparison

Hemlata Hemlata[1*], Jyotsana Agarwal[1], Devendra Vikram Singh[1], Sateesh Verma[1]

Abstract

Background: Subarachnoid block (SAB) using isobaric ropivacaine provides rapid and reliable anesthesia with good muscle relaxation for lower limb surgeries. Fentanyl and dexmedetomidine are used as adjuvants to prolong intraoperative and postoperative analgesia. This study was done to compare their efficacy as an adjuvant to intrathecal ropivacaine for surgeries of fracture neck femur, as no such study has been done previously.

Materials and Methods: In this randomized, double-blind comparative study, 74 patients undergoing surgery for a fracture neck femur under SAB were randomly distributed into two groups. Group RD received 2.5 ml isobaric ropivacaine 0.75% (18.75 mg) with five µg of dexmedetomidine in 0.5 ml NS, and group RF received 2.5 ml isobaric ropivacaine 0.75% (18.75 mg) with 25µg Fentanyl (0.5ml) intrathecally. Block characteristics, hemodynamic changes, and other side effects were compared. Statistical analysis was done using SPSS Version 21.0 statistical analysis software.

Results: Time to onset of sensory block was earlier in group RD than in group RF (5.27±0.77 vs. 6.27±0.87 min). The total duration of sensory block, motor recovery by one level, complete motor recovery, and duration of motor block were significantly higher in the dexmedetomidine group. The mean rescue analgesic requirement was significantly higher in group RF than in group RD. In contrast, the time to first rescue analgesia was significantly later in group RD (292±16.75 vs. 190.41±12.93 min).

Conclusion: Dexmedetomidine produces earlier onset of sensory block, prolonged duration of sensory and motor blocks, and prolonged postoperative analgesia as compared to fentanyl when added as an adjuvant to ropivacaine for SAB.

Keywords: Spinal anesthesia, Analgesia, Postoperative pain, Fracture fixation, Pain

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Please cite this article as: Hemlata H, Agarwal J, Singh DV, Verma S. Dexmedetomidine and Fentanyl as an Adjuvant to Intrathecal Isobaric Ropivacaine for Surgery of Fracture Neck Femur; A Randomized, Double-Blind Comparison. J Cell Mol Anesth. 2023;8(1):22-30. DOI: https://doi.org/10.22037/jcma.v8i1.38244

Introduction

Fracture neck femur is common amongst elderly patients who are more likely to have associated cardiac, respiratory, and neurological complications

(1). A femur fracture is excruciatingly painful as the femoral nerve richly supplies periosteal tissue (2, 3). Subarachnoid block (SAB) provides rapid and reliable anesthesia with good muscle relaxation for patients undergoing surgery for lower limbs. Ropivacaine is an amide local anesthetic (LA) agent that, when administered via the intrathecal (IT) route, provides effective anesthesia with early motor recovery, thereby leading to early mobilization and decreased incidence of venous thromboembolism (4). Compared to bupivacaine, it is less cardiotoxic and neurotoxic (5).

Both opioid and non-opioid adjuvants can be added to the intrathecal LA agents to prolong the duration and quality of the block. Fentanyl is a centrally-acting synthetic opioid. Its use in SAB produces additional analgesia for both somatic and visceral pain without an increase in the level of the sympathetic block (6). Dexmedetomidine, an α_2 agonist, is a frequently used drug due to its hemodynamic, sedative, anxiolytic, analgesic, neuroprotective, and anesthetic-sparing effects. It is a highly selective α_2 agonist with an α_1 to α_2 ratio of 1:1600 (7). By its effect on spinal α_{2A} receptors (which mediate analgesia and sedation), dexmedetomidine prolongs analgesia when used as an adjuvant to LAs for the subarachnoid, epidural, caudal, scalp, and transversus abdominis plane blocks (8-10).

As per previous literature, dexmedetomidine and fentanyl potentiate the effects of LA in the subarachnoid block concerning different parameters like time of onset of sensory block, duration of sensory block, and motor block, and may have the same or different effect on blood pressure, heart rate. However, we did not find any study comparing these two drugs as an adjuvant to isobaric ropivacaine for surgery of neck femur fracture under SAB.

Hence, in this study, we compared the efficacy of dexmedetomidine and fentanyl added to intrathecal isobaric ropivacaine for surgeries of fracture neck femur under SAB. The primary objective was to compare the duration of the sensory block between the groups. The secondary objectives were to compare the groups' onset of sensory block, maximum block height, time to attain maximum sensory block, duration of motor block, and rescue analgesic requirement.

Methods

This randomized, double-blind prospective comparative study was conducted at our institute throughout the 1 year (November 2019 to October 2020) after approval from the institutional ethical committee (97th ECM II B-Thesis/P55). Eighty patients of either sex aged 18-75 years undergoing fracture neck femur surgeries and belonging to American Society of Anaesthesiologists (ASA) physical status I, II, and III were enrolled in this study. Written informed consent was obtained from all the patients. Patients with any contraindication to SAB, known hypersensitivity to any drugs used in the study, bilateral lower limb fractures, and spinal column deformities were excluded from the study. All enrolled patients were allocated randomly into two groups using a computer-generated random number table and sealed opaque envelope method. Group RD patients received 2.5 ml isobaric ropivacaine 0.75% (18.75 mg) with five µg of dexmedetomidine in 0.5 ml NS, and group RF patients received 2.5 ml isobaric ropivacaine 0.75% (18.75 mg) with 25µg Fentanyl (0.5ml). The patients and the anaesthesiologists involved in this study were blinded to group allocation. The study drugs were prepared by a separate anesthesiologist who was not involved in patient management or data collection. The data was recorded by another observer who was unaware of group allocation.

All the patients were premedicated with an alprazolam 0.5 mg tablet overnight. Patients were kept fasting for 8 hours before surgery. In the operating room, standard monitors were attached, including a pulse oximeter, non-invasive blood pressure, and electrocardiography. Baseline parameters like mean arterial pressure (MAP), heart rate (HR), and oxygen saturation(SpO2) were recorded. Co-loading was done intravenously with 10 ml/kg of lactated Ringer's solution. Under all aseptic precautions, SAB was performed at L3–L4 vertebral interspace with 25G Quincke's needle with the patient was sitting. After confirming the free flow of cerebrospinal fluid, the study drug was injected slowly intrathecally. After that, the patients were made supine.

Hemodynamic variables (HR, MAP, SpO2) were recorded at baseline (T0) and after that every 5 min to 30 min, then every 15 min for the next 30 min,

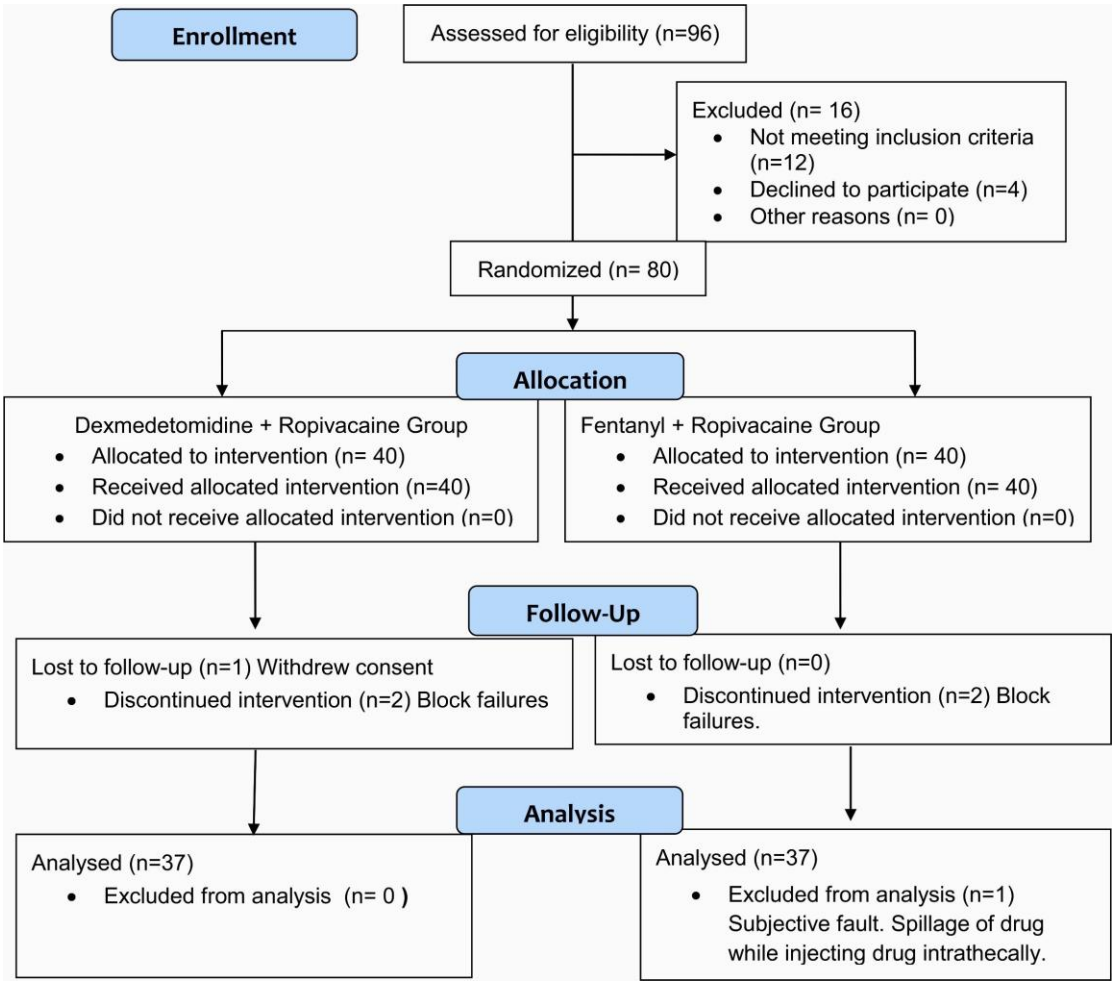

Figure 1. CONSORT Flow Diagram.

and after that every 30 min to 6 hours. Sterile pinprick was used to assess sensory dermatomal level every 2 min for the first 10 min and then every 5 min till three consecutive readings were the same (considered as Smax, the maximum height of sensory block achieved). After that, the sensory block was assessed every 30 min. The time taken from the administration of the intrathecal drug up to the time of the T10 sensory block was considered the Onset of sensory block. Duration of sensory block was defined as the time from the onset till the recession of sensory block to T12. If the level receded to T12 during the intraoperative period, GA was given for completion of the surgery, and the study was terminated. If T10 sensory level was not achieved within 20 min of administration of the drug, it was considered as block failure. Motor block was assessed every 2 minutes till complete motor block was achieved, then every 15 minutes till complete motor recovery as assessed using the Modified Bromage scale (Table 1).

In the postoperative period, patients were asked to score their pain severity on the standard 10-point visual analog scale (VAS Score 0=No pain to VAS Score 10=Worst possible pain). The VAS Score was assessed, and rescue analgesic was administered accordingly whenever the patient complained of pain and VAS≥3. The time to first rescue analgesia and the total number of rescue analgesia doses required in the first twenty-four hours post-operatively were recorded. Injection paracetamol (15mg/kg) intravenously (i.v.) was administered whenever pain did not subside (VAS≥3), even after administering an Injection of diclofenac (75mg) i.v.

Hypotension was defined as a 25% decrease in mean arterial pressure (MAP) from the baseline. Fluids and vasopressors (Inj. mephentermine 6mg i.v.) were

given to treat hypotension. Bradycardia was defined as HR<50/minute and was treated with an atropine injection of 0.6 mg i.v. any incidence of intraoperatively was recorded of nausea, vomiting, shivering, or pruritis. After the surgery, patients were shifted to the post-anesthesia care unit (PACU), where they were monitored until there was complete sensory and motor blockade recovery.

The statistical analysis was done using Statistical Package for Social Sciences Version 21.0 (SPSS Inc., Chicago, Illinois, USA) software. The values were represented as numbers (%) and Mean±SD. All the categorical data were compared using the Chi-square test. Continuous variables in two groups were compared by t-test and Mann-Whitney U test. A p-value <0.05 was considered significant.

The sample size was calculated based on variation in sensory block duration in the two groups according to the reference paper by Dolma et al. (11). A sample size of 37 patients in each group was found to be sufficient to detect a difference of 30 min in the duration of the sensory blockade at 80% power and 5% level of significance. A total of 40 patients were included in each group considering dropouts and block failures [Figure 1].

Results

Group RD and RF were comparable concerning demographic profile and baseline characteristics (Table 2). Most of the patients of group RD achieved T6 or higher T5 sensory level (67.6%), and the rest could achieve T8 sensory level (32.4%). In contrast, in group RF, only 35.1% of patients could achieve a T6 or higher T5 sensory level, and the majority could achieve a T8 sensory block level (64.9%) (Table 3). The mean time to achieve sensory block at T10 was significantly earlier in group RD compared to group RF (5.27±0.77 vs. 6.27±0.87 min). The mean time to attain maximum sensory block was earlier in group RD compared to group RF, but the difference was not statistically significant. The range of duration of sensory block in group RD was 180-232 min, while in group RF was 146-182 mins. The duration of the sensory block was also significantly longer in group RD than in group RF (Table 3).

Though patients of group RF achieved motor block at MB4 later than group RD, this difference was not statistically significant (Table 3). Time to motor recovery by one level (MB3) was significantly earlier in group RF than in group RD. The range of complete motor recovery time (MB0) in group RD was 291-334 min, while the same in-group RF was 230-274 min. The time to complete motor recovery and the total duration of the motor block was significantly earlier in group RF than in group RD (Table 3).

Two or more doses of rescue analgesia were required in a significantly higher proportion of group-RF cases than group-RD cases (86.4% vs. 43.2%; P < 0.001) (Table 4). The mean doses of rescue analgesia required were significantly higher, and the time to first rescue analgesia dose was significantly earlier in group RF than in group RD (Table 4).

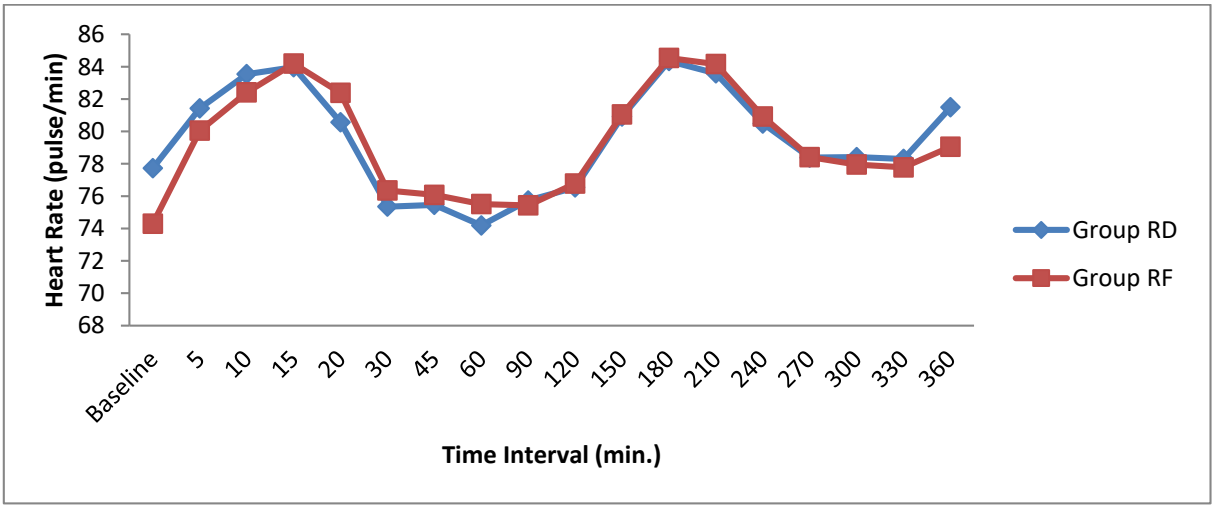

Figure 1. Mean Heart Rate (beats/min) in both groups at various time intervals.

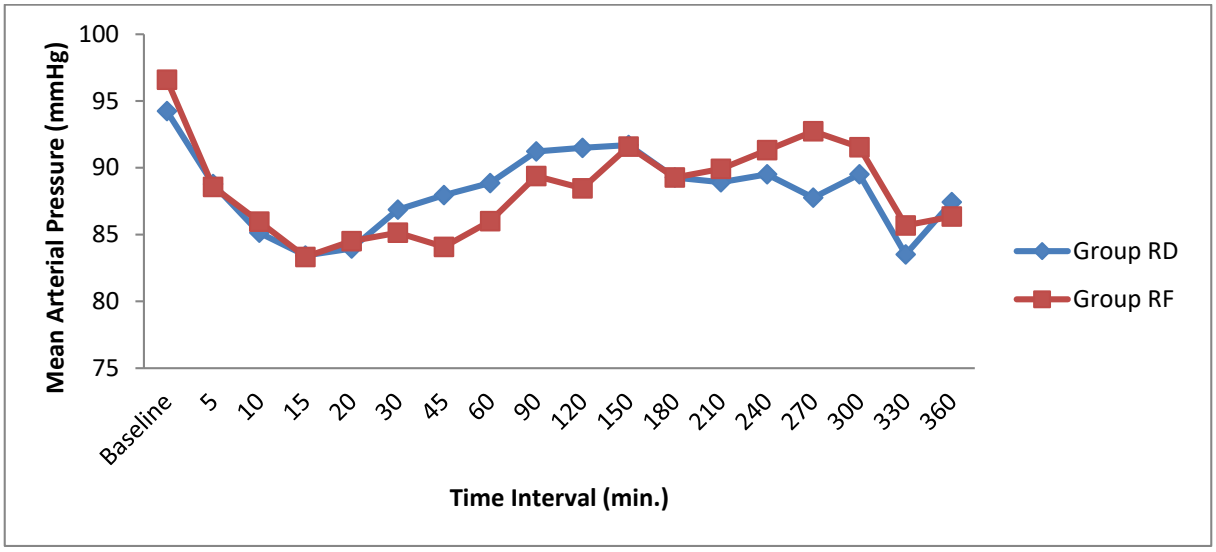

Figure 2. Mean Arterial Pressure (mmHg) in both groups at various time intervals.

Table 1: Modified Bromage Scale.

Score	Description
0 (MB0)	Able to move hip, knee, ankle, and toes
1 (MB1)	Unable to move hip, able to move knee, ankle, and toes
2 (MB2)	Unable to move hip and knee, able to move ankle and toes
3 (MB3)	Unable to move hip, knee, and ankle, able to move toes
4 (MB4)	Unable to move hip, knee, ankle, and toes

Table 2: Comparisons of baseline characteristics between group RD and group RF patients.

Demographic factors	Group-RD (n=37)	Group-RF (n=37)	p-Value
	Mean±SD	Mean±SD	
Age (years)	60.57±8.20	60.73±9.90	0.939
Weight (kg)	65.97±7.22	66.62±6.64	0.689
Height (cm)	166.59±3.14	166.16±2.92	0.542
BMI (kg/m²)	23.72±2.00	24.08±1.71	0.409
Duration of surgery	99.95±12.41	99.08±11.21	0.754
	No. (%)	No. (%)	
Gender (Female/Male)	18(48.6)/19(51.4)	19(51.4)/18(48.6)	0.816
Socio-economic status (Low/Middle)	21(56.8)/16(43.2)	22(59.5)/15(40.5)	0.814
ASA Grade I/II/III	6(16.2)/28(75.7)/3(8.1)	7(18.9)/26(70.3)/4(10.8)	0.863
BMI kg/m²			
Normal(18.5-24.9)	29(78.4)	26(70.3)	0.425
Overweight(25-29.9)	8(21.6)	11(29.7)	

At baseline and 5m, 10m, 90m, 300m, 330m, and 360m, the mean HR of group RD was higher than group RD, while at the rest of the periods, the mean HR was higher in group RF. The difference in mean HR between the groups was insignificant at any point of observation (Figure 2).

Though Bradycardia and Hypotension were observed in more patients of Group RD than in Group

Table 3: Intergroup comparison of sensory and motor block properties.

	Group-RD (n=37)	Group-RF (n=37)	p-Value
	No. (%)	No. (%)	
Maximum block height achieved (Smax)			
T8	12(32.4)	24(64.9)	
T6	23(62.2)	11(29.7)	0.011*
T5	2(5.4)	2(5.4)	
	Mean±SD	Mean±SD	
Time to achieve sensory block at T10	5.27±0.77	6.27±0.87	<0.001*
Time to attain maximum sensory block	8.95±1.39	9.46±1.17	0.090
Duration of sensory block (recession to T12)	207.89±13.60	166.30±10.18	<0.001*
Time to achieve motor block at MB4	10.30±1.20	10.89±1.37	0.051
Time to recovery to motor block level MB3	287.73±11.46	220.68±11.05	<0.001*
Time to complete motor recovery MB0	315.70±11.60	250.49±10.85	<0.001*
Duration of motor block (from MB4 to MB0)	305.4±11.51	239.00±11.34	<0.001*

***:** Significant result ($p<0.05$).

Table 4: Intergroup comparison of rescue dose requirement.

	Group-RD (n=37)	Group-RF (n=37)	p-value
	No. (%)	No. (%)	
Number of patients requiring			
Single dose	21(56.8)	5(13.5)	
Two doses	13(35.1)	14(37.8)	<0.001
Three doses	3(8.1)	18(48.6)	
	Mean±SD	Mean±SD	
Number of doses of rescue analgesia	1.51±0.65	2.35±0.72	<0.001
Time to first rescue analgesic dose (minutes)	292.00±16.75	190.41±12.93	<0.001

RF, the differences were insignificant (Figure 2). No patient had HR<45/min at any observation point; it resolved spontaneously except for one patient in group RD who required an atropine injection of 0.6 mg i.v. once. The incidence of side effects like nausea, pruritis, shivering, and vomiting was more in group RF than in group RD. However, the differences were not significant (Figure 3).

Discussion

In the current study, we tried to compare the effect of dexmedetomidine and midazolam when used as adjuvants with SAB is a commonly used technique for patients undergoing lower limb surgeries. It offers advantages over GA by providing better intraoperative and postoperative analgesia and reduced risk of postoperative deep vein thrombosis and confusion.

Table 5: Comparison of other side effects among the Study Population.

Side Effects	Group-RD (n=37)	Group-RF (n=37)	Significance of differences	
	No. (%)	No. (%)	χ^2	'p'
Bradycardia	5(13.5)	2(5.4)	1.420	0.233
Hypotension	4(10.8)	3(8.1)	0.158	0.691
Any other side effect	5(13.5)	12(32.4)	3.742	0.053
Nausea	1(2.7)	3(8.1)	1.057	0.304
Pruritis	1(2.7)	3(8.1)	1.057	0.304
Shivering	2(5.4)	4(10.8)	0.725	0.394
Vomiting	1(2.7)	2(5.4)	0.347	0.556

Both dexmedetomidine and fentanyl potentiate the effects of LAs in SAB concerning different parameters. This study was done to compare the efficacy of dexmedetomidine five µg and fentanyl 25µg added to 18.75 mg of intrathecal isobaric ropivacaine for surgeries of fracture neck femur. Doses of dexmedetomidine and fentanyl used in our study were based on a previous study by Rahimzadeh et al. in which they had compared dexmedetomidine five µg and fentanyl 25 µg as an adjuvant to bupivacaine for intrathecal analgesia in lower limb surgeries (12).

In our study, adding dexmedetomidine produced earlier onset of sensory blockade, prolonged duration of sensory and motor block, prolonged analgesia, and decreased rescue analgesia requirement compared to fentanyl with adequate hemodynamic stability and minimal hemodynamic stability side effects.

Our study's onset of sensory blockade was significantly faster in group RD than in group RF. Our results were similar to an El Attar et al. (13) study, which found that dexmedetomidine has faster sensory onset compared with fentanyl as an adjuvant to bupivacaine when injected intrathecally. Ravipati et al. and Saadalla and Khalifa also observed faster onset of the sensory block with dexmedetomidine than with fentanyl (14, 6). In a study by Saadalla and Khalifa, the onset was much faster in the dexmedetomidine group than in our study (2.23±1.05 min vs. 5.27±0.77 min). It could be due to their study's higher dose of dexmedetomidine (10µg) and the use of hyperbaric bupivacaine instead of isobaric ropivacaine.

In our study, the range of height of maximum sensory block achieved (Smax) was T5- T8 in both the groups but T6 or higher level was achieved more frequently with dexmedetomidine than fentanyl. Similarly, Nayagam et al. (15) observed that intrathecal dexmedetomidine was associated with a higher peak sensory block level than fentanyl. In our study, the mean time to attain maximum sensory block level (TSmax) was comparable in both groups. This finding is consistent with a study by Rahimzadeh et al. (12).

Our study's total duration of sensory block was significantly more in Group RD than in Group RF. Similarly, El Attar et al., Mahendru et al., and Safari et al. also found a prolonged sensory block with dexmedetomidine compared to fentanyl and other adjuvants added to intrathecal LA (13, 16-20).

In the present study, the mean time of motor block onset was comparable in both groups. Similar findings were reported by Ravipati et al. and Mahendru et al. (14, 16). However, El Attar et al. observed that intrathecal dexmedetomidine has a faster motor block onset than fentanyl (13). This inconsistency may be due to the use of hyperbaric bupivacaine instead of isobaric ropivacaine in their study and the higher total volume of the injected drug (3.5 ml) compared to 3.0 ml in ours.

In our study, the time taken for motor recovery by one level, to MB3, time to complete motor recovery (MB0), and duration of motor block (MB4-MB0) were significantly greater in group RD than group RF. Similarly, El Attar et al., Mahendru et al., and Safari et al. concluded that dexmedetomidine is associated with increased duration of the motor block compared to various other adjuvants when added to intrathecal LA (13, 16, 17).

Our study's mean doses of rescue analgesia were significantly higher in Group RF than in Group RD. The time to first rescue dose was significantly later in Group-RD as compared to the fentanyl group. Previous studies by Dolma et al. (11) and Kumar et al. (21) found that the onset of analgesia was significantly earlier in group ropivacaine plus dexmedetomidine (DR) as compared to group ropivacaine (R). The duration of analgesia was significantly longer in group DR than that in group R. Moreover, the requirement of mean dose of rescue analgesic was significantly lower in group DR as compared to group R. Similarly, Rahimzadeh et al. (10) also found that time to first rescue analgesia request was later in dexmedetomidine group as compared to fentanyl group.

In our study incidence of bradycardia was more in group RD as compared to group RF, but the difference was not statistically significant. Ravipati et al. also found a higher incidence of bradycardia in the dexmedetomidine group (14). Moreover, the difference was statistically significant (P = 0.037) in the study by Ravipati et al. in contrast to ours. It may be explained by using a lesser dose of fentanyl (20 µg) in their study than ours (25 µg).

In our study, the incidence of other side effects like nausea, vomiting, pruritis, and shivering was

higher in the fentanyl group, but the difference was insignificant. Rahimzadeh et al. reported that the incidences of nausea and vomiting were more in the fentanyl group, but the difference was insignificant (12).

The present study was single-centric and not large enough to reveal significant differences in clinical efficacy data between the groups and to detect uncommon adverse events. A large multi-centric study should be conducted in the future. Another limitation was using the VAS score for assessing pain which is a subjective test for evaluating outcomes and is subject to bias. The lack of a control group was another limiting factor.

Conclusion

To conclude, dexmedetomidine five µg provides earlier sensory blockade, prolonged sensory and motor block duration, increases the level of maximum sensory block achieved, and prolongs the duration of analgesia compared to fentanyl 25 µg when used as an adjuvant to 2.5ml of isobaric ropivacaine for SAB. Both provide adequate hemodynamic stability and minimal side effects.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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