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A Comparative Study of Analgesia with Ropivacaine and Dexmedetomidine vs Ropivacaine and Fentanyl in Epidural Anesthesia in Lower Limb Surgeries

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Abstract

Background: The popular techniques of regional anesthesia used for surgeries of lower limbs are Subarachnoid block is better term anesthesia and epidural anesthesia. Limitations of intrathecal anesthesia are short duration of analgesia, onset of sympathetic blockade rapidly and brief postoperative analgesia duration. *Aim:* To evaluate the synergistic effect of addition of dexmedetomidine to ropivacaine 0.75% and fentanyl to ropivacaine .75% in epidural anesthesia for surgeries of lower limbs. *Materials and Methods:* The study conducted in Gandhi hospital during period between December 2016 to November 2017. Institutional ethical committee clearance as well as informed consent from all patients was obtained from all patients. One hundred patients, who had various elective lower limb surgical procedures belonging to ASA class I and II were included in the study. Group RD (n = 50)–15 ml of 0.75% ropivacaine + 1.0 µg/kg of dexmedetomidine, Group RF (n=50) 15 ml of 0.75% ropivacaine and Fentanyl 1 µg/kg. *Results:* The mean time of onset of sensory blockade in group RD is 5.26 ± 1.49 mins and in RF 10.04 ± 2.5 mins. There is highly statistical significant difference between the groups (p = 0.000). The mean time taken for the onset of motor blockade is 11.22 ± 2.61 mins in group RD and 15.36 ± 3.28 mins in group RF There is statistical significant difference between the groups (p = 0.000). There is no statistically significant difference in the mean heart rate, mean systolic blood pressure, diastolic blood pressure and mean arterial pressure between groups at various intervals. Bradycardia and dry mouth seen only in the RD group none was in RF group. Hypotension, nausea and vomiting, tremors observed in both groups on comparision were stastically insignificant. *Conclusion:* Dexmedetomidine can be used as a more potent and safer alternative to Fentanyl in epidural anesthesia as a adjuvant to ropivacaine.

Keywords: Dexmedetomidine; Ropivacaine; Fentanyl; Epidural Anaesthesia

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Introduction

The most popular regional anesthesia techniques used for lower limb surgeries are intrathecal anesthesia and epidural anesthesia. Intrathecal anesthesia also called as sub arachnoid block has a fewer constraints like duration of anesthesia being shorter, extension of anesthesia cannot be made for prolonged surgeries, onset of sympathetic blockade being rapid, shorter post operative analgesia duration and troublesome complication of postdural puncture headache (PDPH). Hence the most preferred anaesthetic technique for lower

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limb surgeries these days is epidural anesthesia.[1] As it provides surgical anesthesia effectively and can meet the duration of surgical needs extensively, provides prolonged post operative analgesia, the incidence of hemodynamic changes is reduced as a result of sympathetic blockade as it produces segmental anesthesia unlike subarachnoid block anesthesia and there is no PDPH incidence as the dura is not pierced are the advantages of epidural anesthesia. For epidural anesthesia, different local anesthesia are used[1]. The disadvantage of lidocaine is its duration of action being intermediate and the disadvantage of bupivacaine though long acting, is increased fatal cardiac toxicity incidence after accidental intravascular injection, because of low dosage for cardiovascular collapse and central nervous system toxicity (cc/cns)[2]. Because of this reason, an increase in search for alternative drugs with desirable blocking properties of bupivacaine but with a greater margin of safety. The newer long acting amide local anaesthetics were Ropivacaine and levobupivacaine which have a wide margin of safety compared to bupivacaine, with all advantages.[2] Since, Ropivacaine has all the advantages of bupivacaine with lower cardiac toxicity,[3] it may be an ideal local anaesthetic for epidural anesthesia. Ropivacaine was found to be an effective local anaesthetic for epidural anesthesia in many studies.[4,5,6,7] Hence in our study ropivacaine was selected as the study drug. Fentanyl is a highly selective μ receptor agonist, which is mainly responsible for its analgesic properties. It acts by increasing intra-cellular calcium concentration which in turn increases K^+ conductance and hyperpolarization of cell membranes. This decreased membrane conductance decreases both pre and postsynaptic responses. Analgesia is produced principally through interaction with μ receptors at supra spinal sites. Fentanyl also binds to κ receptors causing spinal analgesia, sedation and anesthesia. Hence in this study, 0.75% ropivacaine with dexmedetomidine and 0.75% ropivacaine with fentanyl were compared as epidural anesthesia in lower limb surgeries.

Materials and Methods

A prospective, randomized, double blind, case control, observational, interventional comparative study is designed during period between December 2016 to November 2017 in 50 patients. The study was undertaken after obtaining institutional ethical committee clearance as well as informed consent from all patients. Patients who met all inclusion criteria were randomly selected. No distinction is made between males and females. Informed written consent was obtained from all the patients. Using a computer generated random number table, randomization was done. One hundred patients, scheduled for various elective lower limb surgical procedures belonging to ASA class I and II were included in the study. Group RD (n = 50)- 15 ml of 0.75% ropivacaine + 1.0 μg/kg of dexmedetomidine (inj. Dextomid-1 ml = 100 mcg, 1 ml) Group RF (n = 50) 15 ml of 0.75% ropivacaine (Ropivacaine 0.75% preservative free – ROPIN 0.75% 20 ml ampoules, Neon laboratories, India) fentanyl 1 μg/kg inj Fentanyl -1 ml = 50 mcg, 2 ml.

Inclusion criteria: patients who were adult patients who were aged between 18 to 66 years of both sex, patients belonging to ASA class I and II, weight which is greater than 50 kgs and height should be between 150 to 180 cms.

Exclusion criteria: patients who refused regional anesthesia, who were pregnant, lactating, posted for emergency surgeries, obese patients with BMI greater than 30, patients having intracranial pressure raised, severe hypoyolemia, bleeding coagulopathy, local infection, uncontrolled hypertension, diabetes mellitus, neurological disorder, deformities of spine, cardiac and hepatic disease, allergy to local anaesthetics and dexmedetomidine.

A routine pre-anaesthetic examination was conducted on the evening before surgery assessing history and general condition of the patient, airway assessment by Mallampatti grading, nutritional status, height and weight of the patient, a detailed examination of the Cardiovascular system, Respiratory system and Central nervous system and examination of the spine. At bed time on the previous night, the patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally before surgery. On the previous night, they were kept nil orally 10 pm onwards. Patient's basal pulse rate and blood pressure were recorded on the day of surgery. In one of the upper limbs, a peripheral intravenous line with 18 gauge cannula after local anesthesia was secured. Recordings of heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), continuous electrocardiogram (ECG) monitoring and oxygen saturation (SpO_2) was done in all the patients who were preloaded with 500 ml of Ringer lactate 30 minutes prior to the epidural procedure. Multi parameter monitor was connected. Patients were in sitting position

for epidural anesthesia after that draped with the sterile clothes. Under aseptic precautions, after infiltrating skin with the 2% xylocaine waited for 2 minutes. By loss of resistance technique to air using 18G Tuohy needle via the midline approach at either L2-3 or L3-4 inter spinous space, next epidural space was identified. An epidural catheter was fixed and threaded at 3 cms inside the epidural space. After aspiration, a test dose of 3 ml of 2% lignocaine with 1:200000 adrenaline was injected through the catheter. Study drug prepared by another colleague anaesthetist who was unaware Of the study according to the randomized study numberd enerated against the patient. Drug 15 ml which was a mixture of the ropivacaine 0.75% and added study drugs. Dexmedetomidine or fentanyl. Dexmedetomidine which comes in ampoules 1 ml contains 100 µg/ml taken in the insulin syringe 0.1 ml contains 10 µg. According to the body weight dexmedetomidine solution added to the 0.75% ropivacaine solution. In our study we are taking as 1.0 µg/kg of dexmedetomidine. Fentanyl which comes in 2ml and 10 ml ampoules in which 1 ml contains 50 µg/ml. Drug was taken in 2 ml syringe in which 1ml contain 50 µg/ml. insulin syringe also used where drug requirement was more than one ml (for exact calculation of the drug according to body weight) added to the 0.75% ropivacaine according to the body weight. In our study we are taking 1 µg/kg of fentanyl. Using a short bevel 22 gauge needle, sensory blockade was assessed and on either side, it was tested in the mid clavicular line on the chest, trunk and lower limbs. Using modified Bromage scale, motor blockade in the lower limbs was assessed. Grade 0 means no motor block, grade 1 means inability to raise extended leg, able to move knees and feet, grade 2 means inability to raise extended leg and move knee, able to move feet and grade 3 means complete motor block of the lower limbs. Ramsay Sedation scale scoring was 1 if alert and wide awake (S1), 2 if arousable to verbal command (S2), 3 if arousable with gentle tactile stimulation (S3), 4 if arousable with vigorous shaking (S4) and 5 if unarousable (S5). Till the end of 1 hour, measurements of blood pressure, heart rate, and oxygen saturation was ecorded every 5 minutes and then every 15 minutes till the end of surgery. Using SPSS version 20.0, statistical analysis was done. By calculating mean, standard deviation, range, descriptive statistics was done. Using unpaired t- test two way repeated measure ANOVA and chisquare, the inferential statistics (test of significance) was done.

Results

Table 1: Demographics.

Age Distribution

Age in years	Group RD	Group RF
15–25	8	10
26–35	11	8
36–45	11	10
46–55	12	11
56–65	8	11
Total	50	50
Minimum age in years	18	20
Maximum age in years	56	60

Sex Distribution

Sex	Group RD Number (%)	Group RF Number (%)
Male	31 (62%)	36 (72%)
Female	19 (38%)	14 (28%)
Total	50 (100%)	50 (100%)
Weight (Kgs)	Group RD	Group RF
P Value-0.27	56.10 ± 6.11	58.64 ± 5.17
Height (cms)	Group RD	Group RF
Mean height in cms	169.03	170
Minimum height in cms	152	150
Maximum height in cms	180	180

Table 1 shows that the minimum age in groups RD and RF were 20 and 18 years respectively. The maximum age in both groups RD and RF was 65 years respectively. Between the Group RD and Group RF, there was no statistical significant difference in the age of patients. Both groups were similar with respect to age distribution (p>0.05). Between the groups, there is no statistical significant difference in the sex distribution of the patients. In both the groups there is a predominance of male patients. The mean body weight in group RD is 56.10 ± 6.11 kg and group RF is 58.64 ± 5.17 kg There is no statistical significant difference in the body weight of patients between the groups (p = 0.27). The mean height in group RD is 169.03 cm and RF is 170 cm. There is no statistical significant difference in the height between the groups.

Table 2: Type of surgical procedure, mean time for onset of sensory and motor block (mins), maximum level of sensory blockade attained, motor blockade grade.

Type of surgery	Group RD Number (%)	Group RF Number (%)
Both bones leg	12 (24%)	13 (26%)
Femur	23 (46%)	25 (46%)
Knee surgery	15 (30%)	12 (24%)

	Group RD	Group RF
Mean time for sensory onset (mins), SD	5.26 (1.49)	10.04 (2.55)
Mean time for motor onset (mins), SD	11.22 (2.61)	15.36 (3.28)

Maximum sensory level	Group RD	Group RF
T5	5	0
T6	38	31
T8	6	17
T10	1	2

Motor Blockade Grade	Group RD	Group RF
Bromage 1	0	15
Bromage 2	34	35
Bromage 3	16	0

Ramsay Sedation Score	Group RD	Group RF
S1	0	17
S2	15	33
S3	29	0
S4	6	0

Table 2 shows that there is no difference in type of surgical procedures in both the groups. The mean duration of surgery is 90.83 ± 23.12 mins in group RD and 96.83 ± 27.49 mins in group RF There is no statistically significant difference between the groups. The mean time of onset of sensory blockade in group RD is 5.26 ± 1.49 mins and in RF 10.04 ± 2.5 mins. There is highly statistical significant difference between the groups (p = 0.000). The mean time taken for the onset of motor blockade is 11.22 ± 2.61 mins in group RD and 15.36 ± 3.28 mins in group RF There is statistical significant difference between the groups (p = 0.000). Group RD had the highest level of T5 and highest level in RF group was T6. There is no significant difference between the two groups (p>0.05). Number of patients with Bromage 1 were 15 in group RF and 0 in group RD, whereas patients with Bromage 3 were 0 in group RF and 16 in group RD. More intense motor blockade of Bromage 3 was found in patients in group RD compared to patients in group RF, the p value being 0.001 is highly significant. Group RD had the highest score of 4 and highest score in group RF was 2. Dexmedetomidine had greater scores compared to fentanyl. There is statistically highly significant difference between the groups (p=0). The mean duration of sensory block is 359.30 ± 61.94 mins in group RD and 198.0 ± 24.05 mins in group RF There is statistically highly significant difference between the groups (p=0.001). The mean duration of motor blockade is 233.70 ± 15.26 mins in group RD 149.00 ± 14.21 mins in group RF. There is statistically highly significant difference between the group (p=0.001).

Figure 1 shows that there is no statistically significant difference in the mean heart rate between groups at various intervals. 4 patients in RD group developed bradycardia which was treated with inj.atropine 0.6 mg.

Figure 2 shows that there is no statistically significant difference in systolic blood pressure between both the groups. 7 patients in group RD and 4 patients in group RF developed hypotension which was treated with intravenous fluids and inj mephentermine.

Figure 3 shows that there is no statistically significant difference in diastolic blood pressure between both the groups.

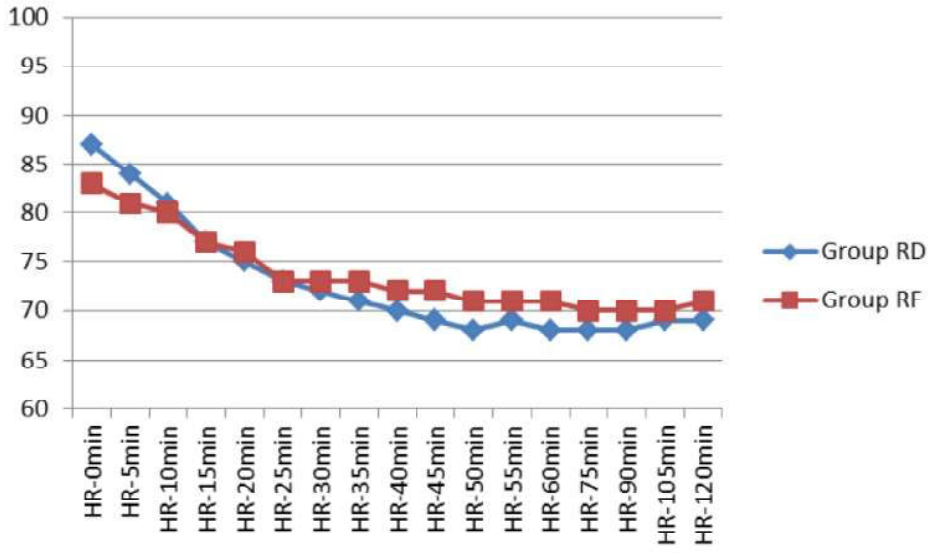

Fig. 1: Mean heart rate (bpm) at various time intervals.

Figure 4 shows that there is no statistically significant difference in mean arterial pressure between both the groups.

Table 3: Side effects

Side effect	Rd Group	Rf Group	p value
Bradycardia	4	0	0.02
Hypotension	7	4	0.16
Nausea & vomiting	4	8	0.109
Tremors	5	9	0.125
Dry mouth	4	0	0.02

Table 3 shows that bradycardia and dry mouth seen only in the RD group none was in RF group. Hypotension, nausea and vomiting, tremors observed in both groups which were stastically insignificant.

Initial four hours of the post operative period requirement of epidural top up was not required in the RD group, 50% of patients in RD group required epidural top ups in next 4–8 hrs, whereas after next 8 hrs all the patients in the two groups required epidural top ups. Another finding found that the intensity of the pain is less in the RD group compare to the RF group.

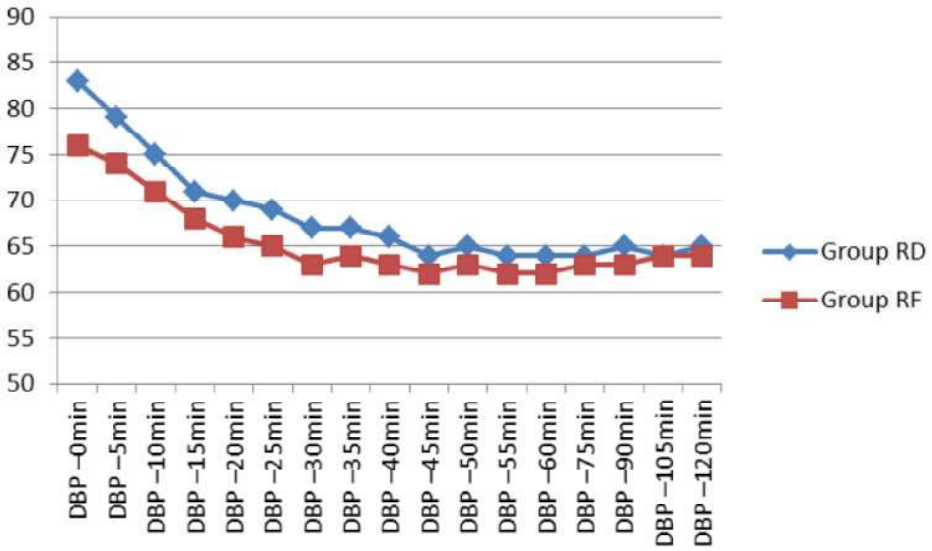

Fig. 2: Mean systolic blood pressure (mmHg) at various intervals.

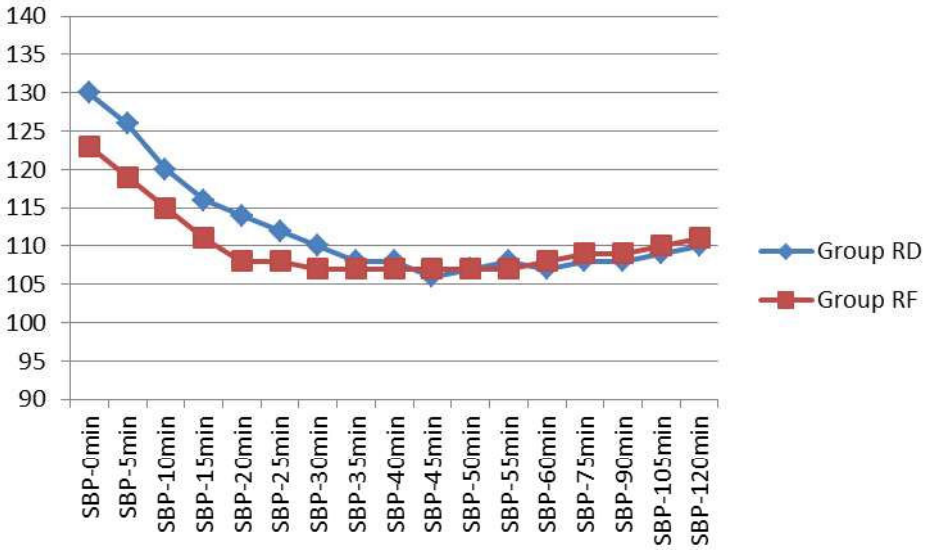

Fig. 3: Mean diastolic blood pressure (mmHg) at various time intervals.

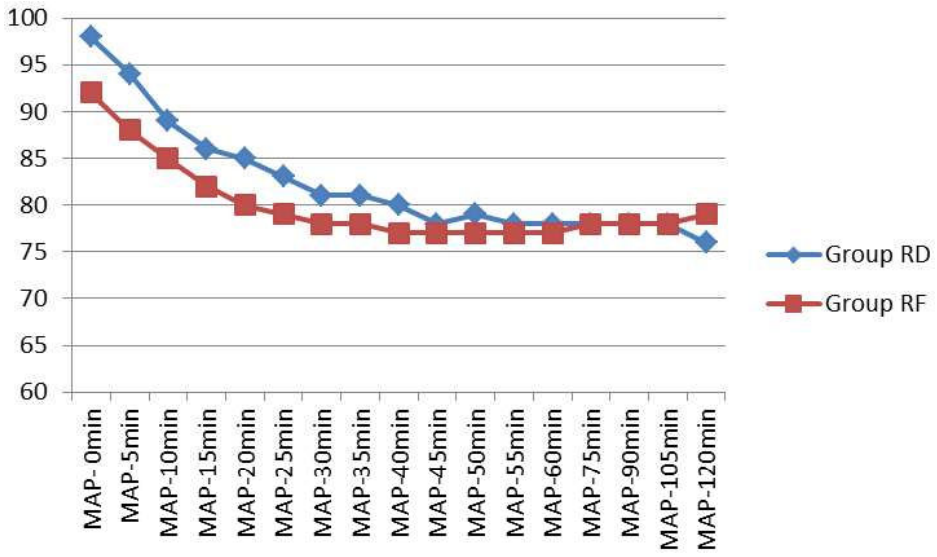

Fig. 4: Mean arterial pressure (mmHg) at various time intervals.

Discussion

Ropivacaine and dexmedetomidine and fentanyl were the drugs selected for epidural anesthesia in our study. For epidural anesthesia for lower limb orthopaedic surgeries, Ropivacaine is being regularly used. Ropivacaine, has structural similarity to bupivacaine. Dexmedetomidine has been studied by various authors as an adjuvant to epidural local anaesthetic[8,9] Fentanyl is frequently used iv opioid and intrathecal and epidural opioid for post operative pain and cancer pain also as known for its cardiac stability.[10] So in our study taken as adjuvant with ropivacaine in epidural anesthesia. For epidural anesthesia, few studies have compared ropivacaine and dexmedetomidine and with fentanyl also. In our study the mean time for onset of sensory analgesia at T10 is 5.26 ± 1.49 mins in group RD and 10.04 ± 2.55 mins in group RD. This is statistically highly significant (p<0.001), whereas Bajwa SJ *et al.*[11] showed onset of sensory analgesia at T10 in ropivacaine + dexmedetomidine group was 7.12 ± 2.44 mins VS 9.14 ± 2.94 mins in ropivacaine + fentanyl group and this is also statistically significant similar to our study. Though Saravia P.S.F *et al.*[12] found no significant change in the onset time for sensory block between ropivacaine and ropivacaine dexmedetomidine groups. The studies conducted by Bajwa SJ[13] showed onset of sensory analgesia at T10 in ropivacaine + dexmedetomidine group was 8.52 ± 2.36 min vs 9.72 ± 3.44 min in ropivacaine + clonidine group and this is statistically significant similar to our study. And supports our study. In our study the maximum level of sensory block in group RD was T4 (n = 5) and in group RF was T8. The range of block was very wide in both the groups (T12–T4). Bajwa SJ, Arora V, Kaur J *et al.*[11] showed maximum level of sensory block at T4–6 level in group RD compared to T5–T7 in group RF which was similar with our study, supports our results also. Saravia PSF *et al.*[12] found maximum level of sensory block at T6 between only ropivacaine and ropivacaine with dexmedetomidine groups. The study conducted by Bajwa SJ *et al.*[13] showed maximum level of sensory block at T5–6 level in group RD compared to T6–T7 in group RC which compares with our study, supports our study. In our study the duration of sensory block is longer with RD group than the RF group. This is statistically highly significant (p<0.001). Similar to our study conducted by Bajwa SJ *et al.*[11] who observed the mean duration of analgesia to be 366.62 ± 24.42 mins in group RD compared to 242.16 ± 23.86 mins within group RF which was highly significant. Supports our study even though in our study duration of sensory block of RF group less than the study conducted by the Bajwa SJ *et al.*[11] but duration of sensory block by RD similar to this study supports our result. Onset of motor blockade the onset of motor blockade was 11.22 ± 2.61 min in group RD and 15.36 ± 3.28 mins in group RF. This is statistically significant. The study conducted by Bajwa SJ *et al.*[11] showed that there is significantly earlier motor block onset in the (18.16 ± 4.52) patients who were administered RD as compared to RF group (22.98 ± 4.78). In our study motor blockade is

assessed using modified Bromage scale and onset was taken as soon as the patient developed grade I motor blockade. In our study it was found that group RD produced more intense motor block than group RF. 16 patients in RD group had grade 3 motor block compared with 0 patients in group R. Also 15 patients in RF group had grade 1 motor block compared with 0 patients in group RD group. This is statistically highly significant (p<0.001). In a study conducted by Bajwa SJ *et al.*[11] Motor block was assessed using modified Bromage scale and complete motor block was achieved significantly earlier in RD group than the RF group so it supports our study. Saravia PSF *et al.*[15] found maximum motor block at level 3 in 68% and 32% had grade 1 and 2 block with no patient remained in grade 0 motor block in ropivacaine and dexmedetomidine group patients. Whereas in plain ropivacaine group, 29% of patients remained with grade 0 motor block, 47% and 24% grade 1 and 2. Our study compares with this study as more number of patients had grade 3 motor blockade in both the studies. The duration of motor block with RD group is more prolonged than with group RF, which is statistically highly significant (p<0.001). A study similar to our study conducted by Bajwa SJ *et al.*[11] earlier return of motor power to Bromage 0 in the RF group (178.52 ± 23.29) as compared to RD group patients (259.62 ± 21.38) (p = 0.009) Supports our study In a study conducted by Saravia PSF *et al.*[15] found the duration of motor blockade was significantly higher in the ropivacaine with dexmedetomidine group, averaging 30% higher than that observed in the ropivacaine plain group similar to our study. The studies conducted by Bajwa SJ *et al.*[16] showed the mean duration of motor blockade was 246.72 ± 30.46 mins in ropivacaine + dexmedetomidine group and 228.44 ± 27.18 mins in ropivacaine + clonidine group. This was not statistically significant. There is no statistically significant difference in the heart rate between the two groups at various time intervals. 4 patients in RD group developed bradycardia which was treated with inj.atropine 0.6 mg. No patients in group RF developed significant bradycardia. The above result is consistent with the study conducted by Bajwa SJ *et al.*[11] wherein there was no statistically significant difference in the heart rate intra and postoperatively. There was no statistically significant difference in SBP, DBP, MAP monitored at various intervals between the two groups. In the studies conducted by Bajwa SJ *et al.*[11], no statistical significant difference was found in SBP, DBP, MAP in both the groups which compares with our study. Group RD had sedation score of 4 and in group RD was 2 which is high when compared. Dxmedetomidine had greater scores compared to Fentanyl. This is statistically highly significant (p=0.001). Similar results were observed by Bajwa SJ *et al.*[11] Dexmedetomidine has gained a lot of popularity as a sedative agent and similar findings were observed in our study as 38% and 42% of patients exhibited grade II and grade III sedation as compared to 16% and 2% of patients in the RF group, respectively. These sedation scores were highly significant on statistical comparison (p<0.001). Only 12% of the patients in the RD group had sedation scores of 1 as compared to 82% wide and awake patients in RF group which was a highly significant statistical entity (p<0.001). Similar results were also observed by Bajwa SJ *et al.*[11] Mean sedation scores were significantly higher in dexmedetomidine group compared to clonidine group (p<0.0001). In RD group, 4 patients developed bradycardia which was treated with inj.atropine 0.6 mg and hypotension seen in 7 patients in group RD and 4 patients in group RF which was treated with intravenous fluids and inj mephentermine 6 μg. Nausea and vomiting was noticed 4 patients in RD group where as 8 patients in RF group which was treated with inj iv ondansetron 4 mg. Dry mouth was noticed 4 patients in RD group and none in the RF group. Patients were reassured above it. Tremors was noticed 5 patients in RD group where as 9 patients in RF group treated with injection iv pethidine 25 mg. All above side effects also noticed in the study conducted by the Bajwa SJ *et al.*[11] and supports our study. Dry mouth incidence in RD group less compared to the study conducted by Bajwa SJ *et al.*[11] in our study we have used 0.6 μg/kg where as they used 1 μg/kg. On other side effects except the dry mouth are not stastically significant. After completion of the surgery if the patient complains of the pain epidural top up given with the 0.2% ropivacaine 8 ml only. The postoperative analgesia requirement as epidural topups was less in the RD group than the RF group. This was supported by the study conducted by the Bajwa SJ *et al.*[11] studied synergistic properties of LA and dexmedetomidine. They showed the ability to reduce the dose of local anesthetic in both the groups but also the postoperative analgesia duration was significantly prolonged in patients in whom dexmedetomidine was administered as adjuvant with LA.

Conclusion

Dexmedetomidine given epidurally with ropivacaine produces synergistic effect of profound

and motor blockade and sensory blockade duration being prolonged. There is relatively less incidence of complications and side effects when dexmedetomidine used as adjunct in the epidural anesthesia. Hence its concluded that dexmedetomidine can be used as a more potent and safer alternative to Fentanyl in epidural anesthesia as a adjuvant to ropivacaine.

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