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Research Article

Comparative Study of Dexmedetomidine versus Fentanyl as an Adjuvant to Ropivacaine (0.75%) in Epidural Anaesthesia in Lower Limb Orthopaedic Surgery

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ABSTRACT

Background: Dexmedetomidine and Fentanyl both possess hypnotic, sedative, analgesic properties and have been utilised as an additive in epidural anaesthesia. The purpose of this study is to compare the sedative and analgesic effects of Dexmedetomidine and Fentanyl when added epidurally with Ropivacaine (0.75%) during lower limb orthopaedic surgery.

Methods: The study comprised of 60 patients, both male and female, aged 18 to 60, who had ASA classification I or II for tibia fibula surgery. Two groups of patients were split up at random: Group RD contains– Ropivacaine (0.75%) 15ml + Dexmedetomidine (1microgm/kg) 0.5ml + 0.5ml sterile water (Total volume-16ml) and Group RF - Ropivacaine 15ml (0.75%) + 1ml Fentanyl (1microgm/kg) (Total volume-16 ml). The epidural space was maintained 4 cm within and situated between L3 and L4 space. Investigations were conducted on parameters such as sensory and motor block features, sedation score, hemodynamic factors and pain assessment. Using the student `t` test, statistical analysis was performed using STATAIC13 software.

Results: Onset of sensory analgesia at L1 and Complete sensory and motor blockage occurred much earlier in the RD group. Higher sedation scores and significantly prolonged postoperative analgesia was observed in RD group.

Conclusion: Dexmedetomidine is a safer and more effective epidural adjuvant than fentanyl because it provides stable hemodynamics, extended post-operative analgesia, early onset and development of sensory and motor effects and sedation.

Introduction

Epidural block is more useful and versatile procedure as it provides anesthesiologists the chance to provide both intraoperative and postoperative analgesia for lower limb orthopaedic procedures. When a local anaesthetic drug is coupled with an adjuvant, it provides better pain relief and prompt mobilisation [1]. However, epidural anaesthesia due to the use of significant amounts of local anaesthetics raises the risk of toxicity and harmful effects on hemodynamics, such as bradycardia and hypotension. Among all the local anaesthetic agents, Ropivacaine is a preferable substitute considering its lower toxicity to the heart and central nervous system [2-4]. Various adjuvants like Fentanyl [5], Buprenorphine [6], Ketamine [7], Midazolam [8], Clonidine [9] and Dexmedetomidine [10-11] are being used with local anesthetics. Dexmedetomidine and Fentanyl are very good hypnotic, sedative and analgesic

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drugs when added to epidural anesthesia as an adjuvant, but also as a part of opioid sparing strategy/opioid free analgesia (OSS/OFA) [12-14], we decided to compare Dexmedetomidine with Fentanyl. It was decided to add Fentanyl and Dexmedetomidine to Ropivacaine via an exclusive epidural route in order to prevent hemodynamic changes in high risk group of patients which might occur through intrathecal use of these drugs [15-16].

In light of all of these factors, we thus designed a prospective, randomised clinical trial to evaluate the sedative and analgesic effects of these two medications, when used epidurally as an adjuvant to Ropivacaine in individuals undergoing orthopaedic procedures on the lower limbs. Our investigation's aim was to assess characteristics of sensory, motor blockade, vital parameters, to evaluate level of sedation, duration of effective analgesia. Objectives were to study the haemodynamic variations and any untoward effects due to this addition.

Methods

The study was carried out following registration with the Clinical Trial Registry India (CTRI/2019/02/017400) and with approval from the Institutional Ethics Committee for Human Research (IECHR). It was a randomized, prospective and single blind study.

Sample Size Calculation

The mean value of the onset of analgesia at T10 for both Fentanyl and Dexmedetomedine was taken into consideration while calculating the sample size, with reference to the main study. Using the software program 'MedCalc', taking alpha error as 0.05, beta error as 0.20 and with a power of 80%, sample size comes out to be 29 in each group, so we decided to study 30 patients in each group [17].

Patients scheduled for elective lower limb orthopaedic surgery, patients of either gender and age range between 18 and 60 years old and American Society of Anaesthesiologists (ASA) Grade I and II were all included in the study. These patients underwent a comprehensive pre-operative evaluation. Exclusions from the study included patients who were morbidly obese, allergic to amide local anesthetics, had coagulopathy, were obstetric patients, or refused permission.

Randomisation of patients to particular group was done by a white sealed Envelope method and they were randomly assigned into two groups:

Group RD: (n=30) Patients receiving Inj. Ropivacaine 0.75% 15 ml + Dexmedetomidine 1 mcg/kg (0.5ml) + Sterile Water (0.5ml) (Total volume 16ml)

Group RF: (n=30) Patients receiving Inj. Ropivacaine 0.75% 15ml + Fentanyl 1mcg/ kg (1ml) (Total volume 16ml)

(Total volume of Drug - 16 ml in each group)

Written informed consent was obtained from each of the chosen patients in both groups after they were fully briefed about the study. After being brought into the operating room, patients were given premedication in the form of injections of 0.2 mg of Glycopyrrolate and 4 mg of Ondansetron intravenously before the procedure. No sedative premedications were given. Ringer lactate (8–10 ml/kg) was used for preloading the patients. The baseline vital signs were recorded. The epidural space was identified at the L3–4 intervertebral space under all aseptic and antiseptic measures and the epidural catheter was fixed 4 cm inside the epidural space in the cephalad direction. The appropriate drug mixture was administered epidurally, vigilant and continuous monitoring was started immediately at a regular interval. The parameters listed below were noted:

- Time to onset of anaesthesia at L1 dermatomal level (min),
- Time to onset of anaesthesia at T10 dermatomal level (min),
- Peak sensory dermatomal level achieved,
- Time to achieve peak sensory level (min),
- Time to two segmental dermatomal regression (min),
- Time for regression to dermatomal level L1 (min).

Motor Block: (Assessed by Bromage scale)

- Time for onset of motor block (min),
- Maximum Bromage score achieved,
- Time for maximum Bromage score (min),
- Duration of motor block (min).

Vital Parameters: Pulse rate, blood pressure and Oxygen saturation were monitored. Pre-block recordings were made, followed by recordings at 1, 3, 5, 10, 15 and 30 minutes following the administration of epidural anesthesia and then every 15 minutes until the procedure was completed.

Pain Assessment- The Visual Analogue Scale (VAS) was used to assess pain. It was noted immediately following the procedure, 2 hours after procedure and then every four hours for the next twenty-four hours. When the VAS score was more than 4, rescue analgesia (RA) was administered intramuscularly as 1.5 mg/kg injection of Diclofenac sodium. In the first 24 hours following surgery, the total number of analgesics needed was recorded.

Sedation: was evaluated intraoperatively as well as postoperatively with the help of Ramsay Sedation Scale which is as follows (Table 1):

Table 1- Ramsay Sedation Scale

Sedation Score	Response
1	Anxious agitated or restless
2	Co-operative, oriented and tranquil
3	Responding to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus

5	Sluggish responses to light glabellar tap or loud auditory stimulus
6	No response to stimulus

Supplementary sedation if required was given in the form of Injection Midazolam 0.03mg/kg IV. Intraoperative and postoperative complications like bradycardia, hypotension, nausea, vomiting, respiratory depression, hypersensitivity to local anaesthetic, shivering, dryness of mouth, urinary retention were noted down if any.

Upon completion of the research, data was gathered and displayed as mean ± SD. STATAIC 13 software was utilized for analysis, along with paired unpaired Student `t` tests and Chi Square tests, to determine any differences in the outcomes between the two groups.

Results

The study involved 60 individuals who had lower limb surgery. Age, weight, sex, ASA grading and mean length of operation were similar in both group`s demographic characteristics(P>0.05) (Table 2). When Dexmedetomidine was added to Ropivacaine, the beginning of sensory block at the L1 level occurred earlier (4.15 ± 0.82 minutes) than when Fentanyl was added (4.80 ± 0.66 minutes) (P<0.05) (Table 3). Dexmedetomidine also provided higher sensory spread in shorter duration of time than in Fentanyl group (P<0.05). Group RD's two segmental dermatomal regression was seen to be slower than Group RF's (162.00 ± 11.27 minutes vs. 150.00 ± 10.17 minutes), with a statistically significant difference (P<0.001). Additionally, group RD experienced effective analgesia for a longer period of time (351.00+ 21.07 minutes vs. 279.00+ 33.56 minutes) than group RF (P<0.0001) (Table 4).

Moreover, it was observed that more patients in Group RD than in Group RF had dense motor block and that the onset of motor block occurred more quickly in Group RD (P<0.05). Group RD had a motor block that lasted much longer (232.00+21.40 minutes) than Group RF (213.33+14.93 minutes) (p<0.001) (Table 4). As opposed to group RF, group RD had greater average sedation scores (Table 5).

Intraoperative VAS score was 0 in both the Groups. Mean VAS score was 0 for first 2 hours of postoperative period in Group RD, which increased slowly upto sixth hour, whereas VAS score was <2 during first two hours of post-operative period in group RF, which started increasing thereafter and analgesia was required during third to fourth hour. In the course of a 24-hour period rescue analgesics required were 1.83 + 0.65 in Group RD and 2.83 + 0.38 in Group RF respectively (Table 4). The statistical significance of this difference was P<0.0001, indicating that the Dexmedetomidine group required fewer analgesics during the postoperative period.

The table-6 shows the intraoperative and postoperative complications in both the Groups. It was observed that except for bradycardia (n=1) and mild hypotension (n=5) in RD group in contrast to RF group (bradycardia n=0 and hypotension n=3) rest of all side effects and complications were more in RF group. During the recovery phase, none of the patients experienced any problems such as bradycardia, hypotension, nausea, vomiting, respiratory depression, or urine retention.

Table 2- Demographic Data

	Group RD (Mean+S.D.)	**Group RF (Mean+S.D.)**	**P value**
Age in years (mean±SD)	30.57+5.49	32.10+5.99	>0.05
Weight in kg (mean±SD)	53.87+5.79	52.97+3.51	>0.05
Gender (Male: Female)	25:5	24:6	
ASA GRADING (I:II)	29:1	28:2	
Mean duration of surgery (minutes)	120.50+ 16.47	118.00+ 14.1	>0.05

Table 3- Assessment of Sensory and Motor Block

	Parameter	**Group RD (Mean +SD)**	**Group RF (Mean + SD)**	**P value**
1	Time to onset of sensory block at L1(min)	4.15± 0.82	4.80± 0.66	P< 0.05
2	Time to onset of sensory block at T10(min)	7.49 + 1.12	8.1 + 1.13	P<0.05
3	Peak sensory level achieved			
	T4	6 (20%)	0	
	T6	22 (73.33%)	11 (36.66%)	
4	Time to achieve peak sensory level (min)	14.12 +1.56	15.15 +1.91	P<0.05
5	Time to two segmental dermatomal regression (min)	162.0 +11.27	150.00+10.17	P< 0.001
6	Time for regression to L1(min)	224.0+12.49	213.0+14.18	P<0.05

Table 4- Assessment of motor blockade and effective analgesia

	Parameter	**Group RD Mean +SD**	**Group RF Mean + SD**	**P value**
1	Time for onset of motor block (min)	8.63 ± 0.95	9.45 ± 1.01	P<0.05
2	Maximum Bromage score achieved III	24 (80%)	16 (53.33%)	

3	Time to achieve maximum Bromage score (min)	16.10 ± 2.12	17.43 ± 2.64	P<0.05
4	Duration of motor block (min)	232.00 ± 21.40	213.33 ± 14.93	P<0.001
5	Duration of effective analgesia (minutes)	351.00 + 21.07	279.00 + 33.56	P<0.0001
6	Total no. of analgesia required in 24 hours duration	1.83 + 0.65	2.83 + 0.38	P<0.0001

Table 5- Sedation Score

Sedation score	Group RD	%	Group RF	%
Score -1	1	3.33	8	26.67
Score -2	0	-	10	33.33
Score -3	12	40	12	40
Score -4	17	56.67	0	-
Score -5	0	-	0	-
Score - 6	0	-	0	-

Table 6- Intraoperative Complications:

Parameter	Number of Patients (Group RD)	%	Number of Patients (Group RF)	%
Bradycardia	1	3.33	0	0
Hypotension	5	16.66	3	10
Nausea / Vomiting	0	0	2	6.66
Respiratory depression	0	0	0	0
Hypersensitivity to local anaesthetic	0	0	0	0
Shivering	1	3.33	4	13.33
Dryness of mouth	1	3.33	0	0
Urinary Retention	0	0	0	0

Discussion

There has long been knowledge of the interaction between opioids and local anesthetics [18-20]. Since the use of neuraxial opioids have been associated with a number of side effects, research has been done on alternative adjuvants; as a result, number of other adjuvants have been evaluated as opioid substitutes in an effort to prevent side effects like respiratory depression, nausea, vomiting, urinary retention, and pruritus [21]. Hence here we compared Fentanyl with Dexmedetomidine in order to get the better non-opioid alternative to Fentanyl under opioid free strategy [22].

In our analysis, the mean length of surgery performed, ASA grade and demographics were similar for both groups. The RD group experienced a shorter mean time (4.15±0.82) for the induction of anesthesia at the L1 dermatomal level compared to the RF group (4.80±0.66). (P<0.05) (Table 3) and the Dexmedetomidine group reached peak sensory level sooner than the Fentanyl group as well. Furthermore, a greater sensory level was attained with the addition of Dexmedetomidine (73% of patients exhibiting T6 level) in contrast to fentanyl (53% of patients exhibiting T8 level). Two segmental dermatomal regression discovered to be quite slower in Dexmedetomidine group in contrast to Fentanyl group which was very important statistically (P<0.001). Early onset and reduced time for the RD group to reach total sensory blockade can be accounted for by the fact that epidural Dexmedetomidine has more lipid solubility and greater selectivity for alpha 2 receptors, it was also seen that rapid onset and maximum motor blockade with Dexmedetomidine was due to Alpha 2 agonist`s ability to attach to motor neurons in the dorsal horn. Our results concur with those of a small number of other investigations that demonstrated that Dexmedetomidine causes sensory and motor block to occur quickly and to establish early [17, 23-25], However, onset and peak sensory level were identical in the Dexmedetomidine group compared to the Ropivacaine group, according to a study by Salgado et al [26].

Intraoperatively it was observed that most of the patients in group RD were calm and sedated with 56.67% patients showed Ramsay Sedation Score (RSS) 4, while only 1 (3.33%) patient remained anxious and agitated. (Table 5). In Fentanyl group 40% patients developed grade 3 sedation, while 8 (26.67%) patients remained anxious and agitated who required supplementary sedation [27-28]. Presynaptic alpha-2 adrenoreceptor activation in the locus coeruleus, which causes adenylate cyclase inhibition and possibly hypnotic response, is most likely the mechanism underlying Dexmedetomidine's sedative action, according to a 2015 study by Rastogi et al [25].

Hemodynamic stability was one of the noteworthy effects seen when Dexmedetomidine and Fentanyl were added to the epidural Ropivacaine as shown by some authors [27,30]. Both Groups saw an intraoperative drop in pulse rate, but these changes were within physiological limit (Figure 1). There was no discernible difference

between the groups during the intraoperative or postoperative periods (P>0.05). Only 1 individual in the group RD required treatment for bradycardia in the form of injection Atropine 0.6 mg IV. These negative chronotropic effect by Dexmedetomidine can be accounted for by the central action of these substances, which reduces sympathetic flow and norepinephrine release [29]. Opioids are also known to exhibit negative chronotropic effect. Rastogi et al (2015) [25] and Bajwa et al (2011) noted a drop in heart rate in the Dexmedetomidine group following a 35–60 minutes of epidural injection.

Both groups experienced a drop in blood pressure that was quickly managed with intravenous fluids and injections of Mephentermine 3-5 mg IV. This drop in blood pressure was within physiological bounds (Figure 2-3). The injection of a tiny amount of local anesthetic medication may account for the steady hemodynamics. through the epidural route and the appropriate adjuvant dose selection. Intrathecal block produces more haemodynamic instability as compared to epidural block. Nausea and vomiting were reported by two patients in the Fentanyl group, while no patients in Dexmedetomidine group had similar complaints. During and after surgery, none of the patients experienced a significant decrease in oxygen saturation or respiratory depression. Depression of the respiratory system is not characteristic of the alpha 2 adrenergic agonist group of drugs [27, 30-31]. Fentanyl as an opioid can cause respiratory depression but in this study its less likely to cause respiratory depression as it was given via epidurally and in much lower doses (1mcg/kg). Urinary retention was shown to occur more frequently in study by Bajwa et al but it was not finding in our study.

When compared to Group RF, Group RD's effective analgesic duration lasted considerably longer ($P < 0.0001$), it was also discovered in research conducted by Salgado et al, Kaur et al (2014) and Kiran et al [31]. As per Kaur et al. By hyperolarizing post synaptic dorsal horn neurons and inhibiting the release of C-fiber transmitters, Dexmedetomidine causes analgesia., while According to Rastogi et al. (2015), the addition of Dexmedetomidine has an analgesic effect by blocking substance P in the nociceptive pathway and by preventing the release of norepinephrine. Fentanyl primarily acts as an agonist at mu opioid receptors for increasing analgesia it also directly affects spinal nerve by piercing the dura mater, Gupta et al (2014). In line with previous research, the RD group required much less rescue analgesics overall ($P < 0.0001$) than the RF group.

While considering side effects/complications, they were minimal as shown in table 6. None of the patients had any life threatening complications nor any requiring major intervention or treatment. This may be explained by the controlled action of drug administered via epidural route.

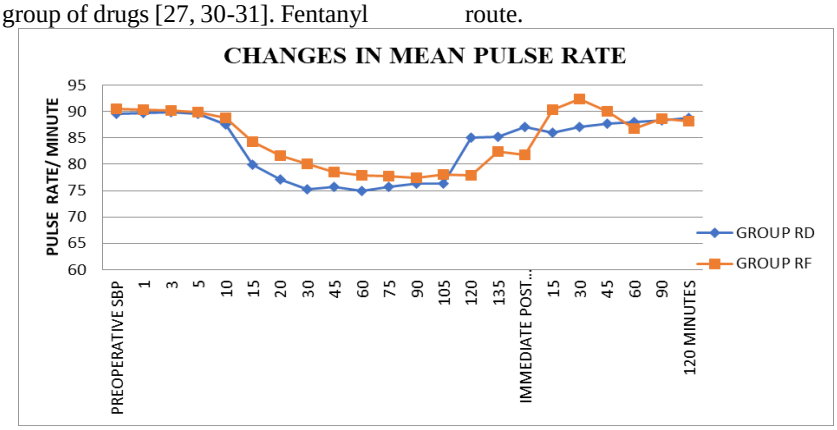

Figure 1- Changes in mean pulse rate

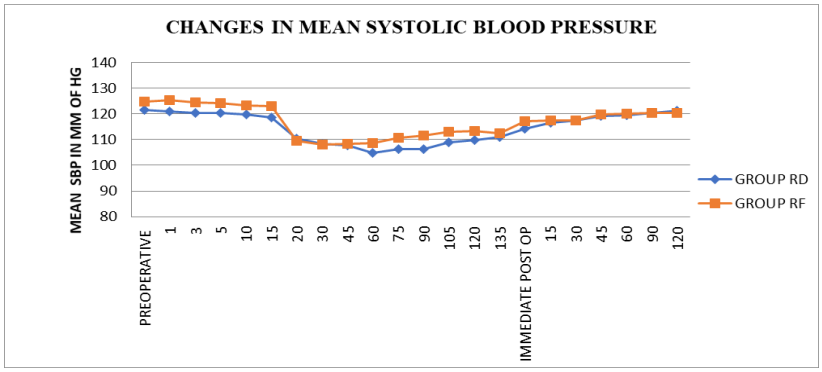

Figure 2- Changes in mean Systolic Blood Pressure

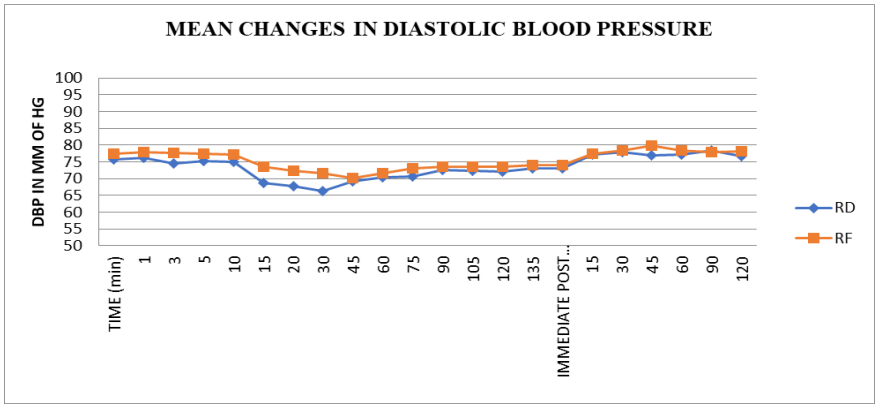

Figure 3- Mean changes in Diastolic Blood Pressure

Limitations

Although statistically significant results were obtained, a large size sample or multicentric study might be more conclusive especially with regards to side effects and complications.

Conclusion

From our study results, following conclusion can be drawn that Dexmedetomidine (1mcg/kg) can be a safer and more effective substitute for Fentanyl (1mcg/kg) in conjunction with Ropivacaine (0.75%) as it offered persistent sensory and motor blockage with a quick onset, better sedation and prolonged post-op analgesia when administered epidurally. Addition of Dexmedetomidine does not cause haemodynamic instability as compared to Fentanyl, also Dexmedetomidine can be a suitable alternative to opioids under opioid free analgesia/strategy with lesser side effects profile.

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