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Comparative Study of Epidural Fentanyl versus Epidural Dexmedetomidine as Adjuvants to Ropivacaine for Post Operative Analgesia

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Abstract

Background: Epidural anaesthesia is a central neuraxial block technique which has the ability to prolong or extend the block via an indwelling catheter. Ropivacaine is a long-acting amino amide local anaesthetic. The onset of sensory and motor blockade may be delayed with ropivacaine. Fentanyl is a commonly used adjuvant for neuraxial block and dexmedetomidine has been used increasingly as adjuvant due to the added benefits and lower side effects. The present study is being undertaken to evaluate quality of epidural anaesthesia using fentanyl and dexmedetomidine as adjuvants to ropivacaine in infra umbilical surgeries for post operative analgesia.

Aims: The major aim of the study was to compare the quality of epidural anaesthesia for post-operative analgesia using fentanyl and dexmedetomidine as adjuvants to ropivacaine in infra umbilical surgeries.

Materials and Methods: 60 patients of both genders aged 18–60 years, ASA I/II physical status undergoing elective infra-umbilical surgeries were randomized into 2 groups. Group RD(n=30) patients received 17ml of 0.75% Ropivacaine + 1µg/kg Dexmedetomidine and group RF (n=30) patients received 17ml of 0.75% Ropivacaine + 1µg/kg Fentanyl. Epidural block characteristics observed included time to onset of analgesia at T10, maximum sensory analgesic level, time to complete motor blockade, time to first rescue analgesic and local anesthetic consumption. Data was compiled and analysed using ANOVA, Chi-square test and Fisher's exact test. Value of $P<0.05$ is considered significant.

Results: Demographic data was comparable between the 2 groups. Heart rate and mean arterial pressure values were lower in RD group compared to RF group. Time to onset of analgesia was 9.56 + 1.32 min in group RF and 7.28 + 1.27 min in group RD (p value < 0.001). Maximum sensory level achieved was T5 in group RF whereas in group RD it was T4 (p value < 0.001). Time taken to achieve maximum sensory level [12.82 + 2.74 min vs 17.54 + 2.88 min] (p value<0.001) and time for complete motor blockade [17.24 + 2.56 min vs 22.71 + 2.50 min] (p value<0.001) in minutes were earlier in group RD compared to group RF. Duration of analgesia was 367.80 + 12.59 min in group RD and 237.94 +14.08 min in group RF. There was significant difference in mean total dose consumption of local anaesthetic used over 24 hours post-operatively.

Conclusion: Dexmedetomidine is a better epidural adjuvant for post-operative analgesia compared to fentanyl as it provides prolonged post-operative analgesia and lower consumption of local anaesthetic.

Keywords: Ropivacaine; Dexmedetomidine; Fentanyl; Epidural anesthesia; Analgesia; Adjuvants; Infra-umbilical.

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Introduction

Pain in the postoperative period is one among the factors that delay recovery from anesthesia and surgery.[1] Inadequate pain relief can lead to delayed mobilization and increased morbidity and mortality. Epidural anesthesia is a central neuraxial block technique which has the ability to prolong or extend the block via an indwelling catheter in the post-operative period.[2]

Use of epidural analgesic technique for infra-umbilical surgery will provide effective pain relief with minimal side effects and high levels of patient satisfaction.[3] Among the local anesthetics used, Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres, resulting in a relatively reduced motor blockade with decreased potential for central nervous system toxicity and cardiotoxicity.[4] Hence in our study ropivacaine was selected as the study drug.

Opioids such as fentanyl provide a dose sparing effect of local anesthetic and superior analgesia but has possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression. Alpha (α)-2-Adrenergic receptor agonists like dexmedetomidine have sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing propertiesbut lacks respiratory depression, making it a useful and safe adjunct to epidural ropivacaine.[5]

Keeping this in mind, thisstudy was done to evaluate the efficacy and safety of dexmedetomidine and fentanyl as an adjuvant to epidural ropivacaine in patients undergoing infra-umbilical surgery.

Aims and Objectives

1. To evaluate the effect of 1 µg/kg fentanyl versus 1 µg/kg Dexmedetomidine as adjuvant to 0.75% ropivacaine in terms of
   - Time to 2 segmental dermatomal regression
   - Regression to S1
   - First request for post-operative analgesia
   - Total dose consumption of local anaesthetic used over 24 hours
2. To study sedation and analgesia during and after surgery.

Materials and Methods

After obtaining written informed consent and approval from institutional ethical committee a prospective randomised double-blind comparative study was conducted on 60 patients aged 18 – 60 years of either sex, with height > 140cm and weight > 45kgs, belonging to American Society of Anesthesiologists grade I and grade II, undergoing elective infra-umbilical surgeries. Patients with contraindications for neuraxial blockade or allergy to the study drug or on alpha-2 antagonist treatment, patients posted for lower segment caesarean section, patients of American Society of Anesthesiologists grade 3 and above and aged< 18 and > 60 years, and patients who were morbidly obese and under nourished were excluded from our study.

After routine pre anaesthetic evaluation, patients were randomly allocated in to one of the two groups using numbers generated from www.random.org. The study drug was prepared by anesthesiologist not involved in the study.

- *Study group RD*-received 17ml of 0.75% Ropivacaine + 1µg/kg Dexmedetomidine.
- *Study group RF*-received 17ml of 0.75% Ropivacaine + 1µg/kg Fentanyl.

Result values were recorded using a pre-set Proforma.

Procedure: A routine pre-anaesthetic examination was conducted on the evening before the scheduled day of surgery, assessing:

1. History and general condition of the patient
2. Airway assessment by Mallampatti grading
3. A detailed examination of the systems like Cardiovascular system, Respiratory system and Central nervous system.
4. Examination of the Spine.

Basic lab investigations like Complete Blood Count, Fasting Blood Sugar or Random Blood Sugar, blood urea, serum creatinine, chest X-ray and Electrocardiograph were carried out. The entire procedure was explained to the patient.

All patients were kept fasting for 8 hours on the previous day of surgery. Patients were pre medicated with tab Alprazolam 0.5 mg and tab Ranitidine 150 mg on the night before the day of surgery.

In preoperative room, intravenous line was secured with 18 G IV cannula and were preloaded

with 10ml/kg of Ringer Lactate. Injection Ranitidine 50 mg was given intravenously half an hour preoperatively.

On the arrival to the operating room, Non-invasive blood pressure, pulse oximeter and three lead Electrocardiogram were connected. The baseline systolic, diastolic blood pressure (SBP, DBP), heart rate(HR) and oxygen saturation (SpO_2) were recorded. The patient was be placed in left lateral position and the back was prepared with betadine. With all aseptic measures the skin over L1–L2 interspace was anesthetized with 2 ml of 2% Lignocaine. A 18G Touhy needle was passed through this space and advanced slowly until it enters epidural space which was confirmed by loss of resistance to air technique. Then a 20 G epidural catheter was passed through the needle into epidural space and secured with minimum of 3–4 cm of catheter within the space.

The study drug was loaded in a 20 ml syringe by a senior anesthesiologist who was not involved in the study. After giving test dose with 2% Lignoadrenaline 3 ml, syringe was handed over to the anesthesiologist performing the epidural block, who was also the observer of the study. The patients were not aware of the drug being administered to them. Thus, both the observer and the patient were blinded.

17 ml of the solution containing 0.75% Ropivacaine plus study drug was injected through the epidural catheter intermittently over 3 min. The time at which injection was completed was considered as zero time of the study and all measurements were recorded from this point. All patients were given supplementary oxygen through a venturi mask at 6L/min.

The following parameters were monitored:

- Onset of sensory block assessed by bilateral pin prick method.
- Degree and level of motor blockade - using Modified Bromage scale.
- Level of sedation using Ramsay sedation scale before, during and after surgery.
- Hemodynamic changes – heart rate, blood pressure and respiratory rate.
- Time to two segmental dermatomal regression.
- Regression to S1.
- First request for post-operative analgesia.
- Total dose consumption of local anaesthetic used over 24 hours.
- Intra operative and post-operative complications if any was looked for, recorded and treated accordingly.

In case of failure of epidural block and conversion to general anesthesia, those cases were excluded from the study. After the surgery, patients were shifted to the post anesthesia care and recovery unit where they remained until complete recovery of sensory and motor blockade was achieved.

Rescue analgesia: The onset of pain was managed by top up doses of 8 ml of 0.2% ropivacaine after operation.

Definitions of various parameters studied:

Degree and level of motor blockade: assessed by modified bromage scale.

Modified Bromage Scale (6)

0 – Able to perform a full straight leg raise over the bed for 5 sec.

1 – Unable to perform a leg raise but can flex the leg on knee.

2 – Unable to flex knee but can flex ankle.

3 – Unable to flex ankle.

4 – Unable to move toes.

Onset of sensory blockade: was defined as time taken from the completion of the injection of the study drug till the patient did not feel pin prick sensation at T10 dermatome.

Onset of motor blockade: was defined as the time taken from the completion of the injection of the study drug till the patient achieved motor blockade of Bromage score 1.

Time to 2 segmental dermatomal regression: was defined as the time taken from the completion of the injection of study drug to the sensory level to regress to 2 dermatomes lower from the highest dermatome achieved.

Regression of sensory block to S1: defined as the time taken from the completion of injection of study drug till regression of sensory level to S1 dermatome.

Regression of motor block: defined as time taken from the completion of injection of study drug till the patient attains modified Bromage 1.

Level of sedation: assessed by Ramsay Sedation Score.

Ramsay Sedation Score

1. Anxious and agitated.
2. Cooperative, oriented and tranquil.
3. Responds only to verbal commands.
4. Asleep with brisk response to light stimulation.
5. Asleep with sluggish response to light stimulation.
6. Asleep without response to stimulation.

First request for post-operative analgesia: was defined as the time for first complaint of pain from the time of completion of injection of study drug.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identifythe mean difference between two quantitative variables. p value (Probability that the result is true) of <0.05 was considered as statistically significantafter assuming all the rules of statistical tests.

Results

It is a prospective randomized double blind study with 60 patients randomly divided into two groups of 30 patients each, using www.random.org.

Group RD-received 17ml of 0.75% Ropivacaine + 1µg/kg Dexmedetomidine.

Group RF- received 17ml of 0.75% Ropivacaine + 1µg/kg Fentanyl.

In RF group mean age of participants was 40.03 ± 13.05 years and in RD group mean age was 41.20 ± 12.00 years. In Group RF, majority of subjects were in the age group ≤ 30 Years (30%) and in Group RD, majority of subjects were in the age group >50 years.In Group RF, 53.33% were females and 46.67% were males and in Group RD, 56.67% were females and 43.33% were males.In the study there was no significant difference in mean weight and height between two groups. There was no significant difference in demographic data between the groups in the study.

Mean Time to onset of analgesia at T10 in Group RF was 9.56 ± 1.32 min and in Group RD was 7.28 ± 1.27. Group RD achieved analgesia at T10 earlier than group RF.In group RF the maximum sensory level achieved was T5 dermatome level, whereas in group RD T4 dermatome was the maximum sensory level achieved.Mean Time to complete motor blockade in Group RF was 22.71 ± 2.50 min and in Group RD was 17.24 ± 2.56 min. Complete motor block was achieved earlier in RD group.

In the study there was statistically significant difference in sedation scores between two groups at all intervals of follow up except at baseline, 1min and 2 min. RD group had better sedation compared to RF group in our study. Group RF had achieved maximum sedation score of 2, and group RD had achieved maximum sedation score of 4. (Fig 1)

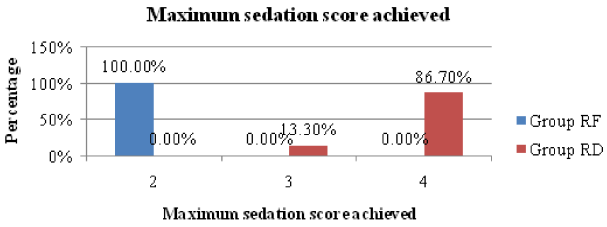

Fig. 1: Bar diagram showing comparison of maximum sedation score achieved between two groups.

In the study there was statistically significant difference in mean heart rate between two groups at all the intervals of follow up intra-operatively except at baseline. Mean HR was significantly high in Group RF compared to Group RD. But this difference was not clinically significant and heart rate values remained within the normal physiological limits at all intervals. 3 patients in the dexmedetomidine group developed bradycardia and they were treated with Inj.Atropine 0.6mg. As tachycardia is not favorable during surgeries, RD group provides better hemodynamics. Post-operatively the difference in heart rate was not statistically significant.In the study there was statistically significant difference in mean MAP(mean arterial pressures) between two groups at all the intervals of follow up except at baseline, 1 min, 5 min, 1 hr 40 min and 1 hr 50 min. Mean mean arterial pressures was significantly high in Group RF compared to Group RD. But this was not clinically significant as MAP values were well within the normal limits at all intervals of follow up.3 patients in group RF and 6 patients in group RD developed hypotension which was managed with intravenous fluids and Inj.Ephedrine. As hypertension is not favorable in any surgeries, RD group provides better hemodynamics. Post-operatively there was no difference in mean arterial pressures between the groups.

Table 1: Comparison of parameters between two groups.

	Group				P Value
	Group RF		Group RD		
	Mean	SD	Mean	SD	
Time to 2 segmental dermatomal regression in minutes	111.00	5.05	142.12	5.57	< 0.001*
Regression to S1 in minutes	203.27	13.78	330.53	16.14	< 0.001*
Mean time for regression to Bromage 1 in minutes	177.63	11.60	262.08	10.45	< 0.001*
First request for post-operative analgesiain minutes	237.94	14.08	367.80	12.59	< 0.001*
Total dose consumption of local anesthetic used over 24 hrs (mg)	113.60	12.14	78.40	11.39	< 0.001*

Mean time to first request for post-operative analgesia in Group RF was 237.94 ± 14.08 min and in Group RD was 367.80 ± 12.59 min. Group RF required rescue analgesia earlier than group RD. (Table 1)

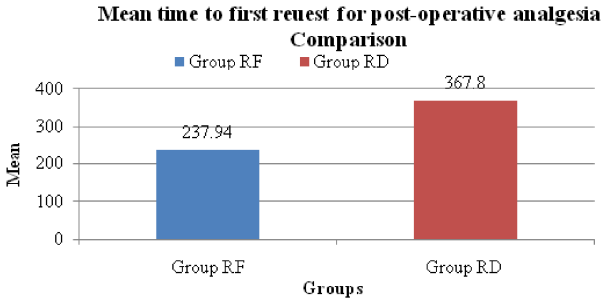

Fig. 2: Bar diagram showingcomparison of mean time to first request for post-operative analgesia between two groups.

Mean Total dose consumption of local anesthetic used over 24 in Group RF was 113.60 ± 12.14 mg and in Group RD was 78.40 ± 11.39. There was significant difference in mean Total dose consumption of local anesthetic used over 24 hrs between two groups. (Fig 2)

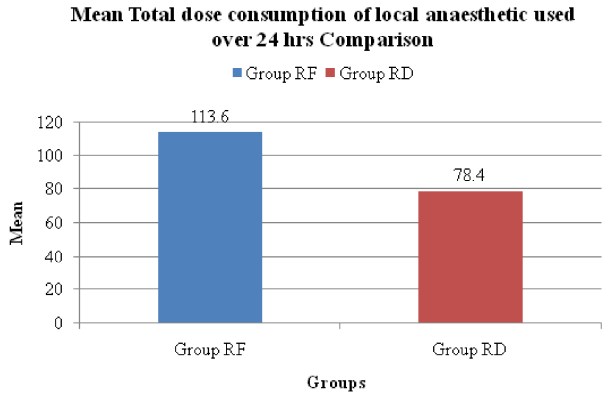

Fig 3: Bar Diagram Showing comparison of Mean Total dose consumption of local anaesthetic used over 24 hrs (mg) between two groups.

In the study, clinically significant extent of hypotension was observed in RD group compared to RF group. Nausea and vomiting were more common in the Ropivacaine + Fentanyl group in the study. Pruritis was seen to a statistically significant extent in RF group compared to group RD. Dry mouth was more common in RD group. (Fig 3) Other side effects were comparable between the two groups and were statistically and clinically insignificant. No respiratory depression was seen in any of the patients in the study groups. (Fig 4)

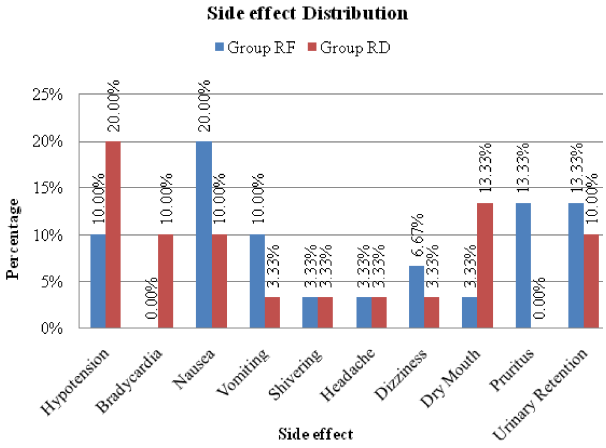

Fig. 4: Bar diagram showing Side effect distribution between two groups.

Discussion

Postoperative pain is a major obstacle for early postoperative ambulation. It increases the risk of venous thromboembolism and respiratory complications and prolongs hospital stay.[7] Epidural analgesia offers superior pain relief and early mobilization especially when local anesthetic dose is combined with an adjuvant as compared to local anesthetic used alone.[6] In the present study, we used fixed dose and concentration of ropivacaine i.e. 17 ml of 0.75% ropivacaine in both the groups as the volume of the study drug because the influence of height and weight on the spread of epidural block is little, and usually not clinically significant unless considering the extremes of the spectrum.[8]

In our study the results show that addition of epidural Ropivacaine with Dexmedetomidine significantly prolongs the duration of sensory and motor block with improved quality of

postoperative analgesia and lesser requirement of local anesthetic for post-operative analgesia as compared to Ropivacaine combined with fentanyl. These observationsare in agreement with the similarstudies.[1,3,6,8,9,10]

Dexmedetomidine acts by binding to the presynaptic C-fibers and post synaptic dorsal horn neurons. They produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarisation of post synaptic dorsal horn neurons.[9] Fentanyl acts primarily as an agonist at μ-opioid receptors to enhance the analgesia. The dorsal roots (primary afferent tissues) contain opioid-binding sites and fentanyl either acts directly on the spinal nerve or by penetrating the duramater to act at the spinal roots.[10]

Time to 2 segmental dermatomal regression,Regression to S1, Mean time for regression to Bromage 1 was earlier in group RF compared to group RD. Bajwa SJ et al also found similar results in their study.

First request for post-operative analgesia is earlier in RF group and, Total dose consumption of local anesthetic used over 24 hrs was higher in RF group.

Dexmedetomidine is a better adjuvant to epidural ropivacaine when compared to fentanyl, with early onset and prolonged duration of sensory and motor blockade with better hemodynamic stability and intraoperative sedation and also analgesic sparing effect in the postoperative period.

The decrease in HR caused by α-2 agonist can again be explained on the basis of their central action whereby they decrease sympathetic outflow and nor-epinephrine release. Dexmedetomidine does not decrease gut motility, hence it prevents intraoperative and postoperative nausea and vomiting.[8]

Limitation

- Serum levels of local anesthetic was not measured
- Motor block was not assessed after the top up dose.

Conclusion

Dexmedetomidine gave longer post-operative analgesia with sedation than fentanyl and also resulted in lower consumption of post-operative local anesthetic.

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