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A Comparative Study of Fentanyl and Dexmedetomidine with Ropivacaine for Epidural Anaesthesia in Major Abdominal Surgeries: Prospective, Randomised, Double Blind Study

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Abstract: ***Background: Ropivacaine is a pure S (-) Enantiomer of Bupivacaine. The advantage over bupivacaine is the lower degree of motor blockade, lesser cardio toxicity, thus making it a safer alternative. Fentanyl and dexmedetomidine have been added as adjuncts to Ropivacaine for further improvement in analgesia without intensifying adverse effects. This study was designed to compare the clinical efficacy and adverse effects of epidural Ropivacaine combined with Fentanyl and Dexmedetomidine as adjuncts for pain control following major abdominal surgery. Methodology: The study was conducted on 60 patients posted for elective major abdominal surgeries under general of ASA I, II and III physical status, between the ages 18-75 years. After appropriate premedication and insertion of epidural catheter, the surgery was done under general anaesthesia. They were randomly allocated into two groups to receive postoperative epidural infusion of either Ropivacaine 0.1% with fentanyl 1 mcg/ml for 48 hours or ropivacaine with dexmedetomidine 1mcg/ml. The efficacy was compared in terms of onset, quality of analgesia and residual motor blockade and any other adverse events. Results: The postoperative pain scores were similar among the two groups. There was no significant motor blockade with a mean VAS score which was consistently below 4 throughout the study period. The patients were hemodynamically stable and there were no significant adverse effects between the two groups. Conclusion: The study concludes that ropivacaine in combination with fentanyl and dexmedetomidine provided satisfactory analgesia with minimal adverse effects with a better hemodynamic profile and analgesia with dexmedetomidine when compared to fentanly.***

Keywords: Ropivacaine, Fentanyl, Dexmedetomidine, Epidural analgesia

1. Introduction

Postoperative pain relief after major abdominal surgery has become an indispensable component in anaesthesia. Epidural techniques are more promising in the management of postoperative pain as it improves the surgical outcome by reducing the central sensitization, pain-induced surgical stress response and subsequently organ dysfunction along with early postoperative recovery and rehabilitation. Low concentration of an epidural local anaesthetic agent alone or more commonly in combination with epidural opioids, provides adequate analgesia, also minimizes individual doses of each drug and their adverse effects than when used alone.

Bupivacaine is a racemic mixture of R(+) and S(+) enantiomer with increased affinity to sodium channels of neural and cardiac tissues which accounts for its greater toxicity.

Ropivacaine is an amino amide local anaesthetic introduced in 1957, a pure S(-) enantiomer, with additional properties such as long duration of action, less cardiotoxicity and greater sensory-motor separation when compared to racemic bupivacaine. Epidural Ropivacaine in concentrations less than 0.2% in combination with epidural opioids such as fentanyl have been studied and found to have better postoperative analgesia and reduced incidence of motor blockade.

Though these enhanced safety profile make these new local anaesthetics appealing for postoperative epidural analgesia, the doses of epidural Ropivacaine alone in concentration >0.1% produces significant amount of motor blockade in addition to adequate analgesia. By the addition of small dose of an epidural adjunct the concentration of ropivacaine used can be reduced. Thus, smaller concentrations of epidural Ropivacaine combined with opioids (morphine or fentanyl) or alpha 2 agonists like dexmedetomidine provides effective postoperative analgesia and reduces the incidence of undesired motor blockade.

Hence the present study was undertaken to compare the clinical efficacy of epidural with Ropivacaine 0.1% combined with fentanyl and dexmedetomidine in patient's undergoing elective intra-abdominal surgery.

2. Aims and Objectives of the Study

1) To determine the onset and quality of analgesia and residual motor blockade with epidural ropivacaine 0.1% with fentanyl 1mcg/ml.
2) To determine the onset and quality of analgesia and residual motor blockade with epidural ropivacaine 0.1% with dexmedetomidine 1mcg/ml.
3) To compare the clinical efficacy of the postoperative epidural analgesia between Ropivacaine 0.1% with fentanyl 2 mcg/ml and ropivacaine with dexmedetomidine 1mcg/ml
4) To study the adverse effects of epidural Ropivacaine 0.1% with fentanyl 1 mcg/ml and ropivacaine with dexmedetomidine 1mcg/ml

3. Methodology

After obtaining institutional ethics committee approval with written, informed consent from 60 patients admitted at Father Muller Medical College Hospital scheduled for major abdominal surgery under general anaesthesia with epidural for postoperative analgesia. They were belonging to ASA physical status I, II and III of either sex aged between 18 to 75 years.

Inclusion criteria

1) Patients posted for elective upper and lower abdominal surgery under general anaesthesia.
2) Age between 18 to 75 years of either sex.
3) Written informed consent.
4) ASA physical status between I and III.

Exclusion criteria:

1) Emergency surgeries
2) Known hypersensitivity to local anaesthetics.
3) History of active neurological, cardiac, respiratory and renal diseases.
4) Blood dyscrasia, clotting disorders and platelet count <100000 mm3.
5) Patients with cutaneous infections or anatomical malformation of the spine.
6) 6. Weight > 100 kilograms, height <150cms or >185cms and age > 75 years.
7) Pregnant women

A detailed history and pre anaesthetic evaluation was done on the previous day and informed written consent was taken. Routine investigations like complete blood count, RBS, renal function test and coagulation profile was done. Electrocardiogram (ECG) and chest X ray whenever indicated was taken to rule out the presence of any active cardiac disease.
Patients were kept nil oral for at least 6 hours before the surgery. The patients were premedicated with Diazepam 0.1mg/kg on the night before surgery. After shifting to the operation theatre pulse oximeter, non-invasive blood pressure and electrocardiography monitors were connected and baseline vitals noted.

A peripheral intravenous line was secured IV fluids started. Under aseptic precaution in the lateral decubitus position, epidural catheter was inserted using 18-G Tuohy needle by loss of resistance technique. The epidural catheter was placed at levels according to the site of surgery: T7-T9 level for upper abdominal surgery and T9-T11 level for lower abdominal surgery. The epidural catheter was directed cephalad for a distance of 4 cm and fixed to the back of the patient. A test dose of 3 ml of 2% lignocaine with adrenaline 1:200000 was injected after negative aspiration to confirm proper placement of the catheter.

General anaesthesia was induced with Inj propofol 1-2mg/kg and tracheal intubation was facilitated with vecuronium 0.1 mg/kg. For intraoperative analgesia Inj Fentanyl 2mcglkg/hour was given. Anaesthesia was maintained with vecuronium. Mixture of Isoflurane with oxygen and nitrous oxide was used for maintenance of depth of anaesthesia. Lungs were ventilated with circle system. At the end of surgery, patients were reversed with neostigmine 0.05mg/kg i.v. glycopyrrolate 0.01mg/kg i.v. and then extubated when they met the clinical criteria.

After extubation, patients were randomly allocated in a double blinded manner into one of the two groups by means of sealed envelope to receive either:
1. Group 1- Ropivacaine 0.1%. with dexmedetomidine 1mcg/ml epidural
2. Group 2- Ropivacaine 0.1% with fentanyl 1mcg/ml epidural

An anaesthesiologist who took no part in the regional block prepared the study drug. Based on the height of the patient the initial bolus dose and the subsequent infusion doses were calculated as follows:

- Bolus dose:
- <160cm-8ml
- 160-170 cm-12ml
- >170cm-15ml

The pin prick method was used to test the level of the sensory blockade over the next 30 minutes before starting the infusion. If there was a failure to achieve adequate level of sensory blockade, the patients were excluded from the study.

Infusion dose:

- <160cm-4ml/hr
- 160-170cm-6ml/hr
- >170cm-8ml/hr

The time of initiating epidural drug administration at the end of surgery was noted and taken as time zero. No extra bolus injection or change of infusion rate was allowed. Tramadol 100mg i.v. was given as rescue analgesia if necessary and recorded. The total consumption of rescue analgesic drugs was recorded for 48 hours. The epidural catheter was removed on 2nd postoperative day and alternative analgesia was provided.

Pain intensity was recorded using VAS device every 30 minutes for first two hours and then every 4 hours till next 48 hours. Motor blockade was assessed according to a modified Bromage scale (0 = no motor blockade, 1 = inability to raise extended legs, 2 = inability to flex knees, 3 = inability to flex ankle joints).

The following parameters were noted:

1) Duration of analgesia: The time required for the first analgesic dose requirement was noted. Pain was scored on 10 cm Visual analogue scale at rest, during mobilization from supine to sitting position and when coughing every 4 hrs.
2) Residual motor blockade was evaluated by Modified Bromage scale. Motor block was evaluated every 4 hours after the end of surgery on first and second postoperative day. No testing for pain or motor blockade was done between 22:00 to 06:00 hrs. The ability to ambulate with assistance was tested once each on the 1st and 2nd postoperative day.

3) Adverse effects: Adverse events were recorded as either spontaneously reported by the patient or observed by the ward personnel or the investigator.

Any episodes of nausea, vomiting, pruritus was recorded and treated at patient request with 4mg ondansetron given slow intravenously.

Any episode of hypotension (30% decrease of systolic blood pressure compared to baseline) noted from routine hemodynamic monitoring was recorded and treated with rapid infusion of 500 ml of normal saline solution or if resistant, with a vasopressor agent. Bradycardia was defined as heart rate less than50 beats per minute and was treated with Atropine 0.6mg i.v.

Respiratory depression was defined by a respiratory rate <10/min. If there was any fall in arterial oxygen saturation below 92% on routine monitoring, it was treated with oxygen supplementation.

The patients were evaluated for sedation scores (0=awake, 1=mild sedation, 2=moderate sedation, 3= severe sedation or unconscious) every 4 hours as per Ramsay sedation score.

4. Statistical Analysis

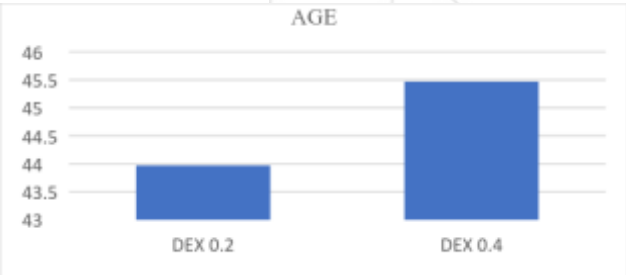
Results were expressed as mean and SD for quantitative variables. Qualitative data was presented as frequency. Chi square test and student t- test was used for the analysis. P value of <o.05 was considered significant. The statistical software SPSS version 18.0 was used for the analysis of data. Microsoft word and Excel were used to generate graphs and tables.

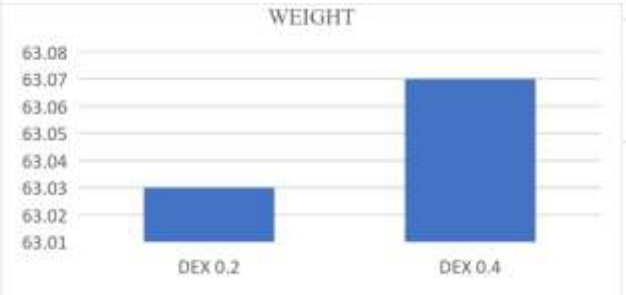
5. Results

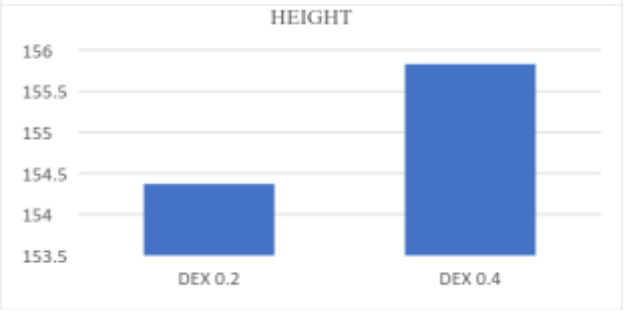
a) Demographic Data

	GROUP	N	Mean	Std. Deviation	T	Df	P VALUE
Age	DEX 0.2	30	43.97	12.552	-0.45	58	0.654
	DEX 0.4	30	45.47	13.263			
Weight	DEX 0.2	30	63.03	9.915	-0.013	58	0.989
	DEX 0.4	30	63.07	9.344			
Height	DEX 0.2	30	154.37	4.287	-1.316	58	0.193
	DEX 0.4	30	155.83	4.348			

The demographic data between the two groups was comparable with respect to age, weight, and height



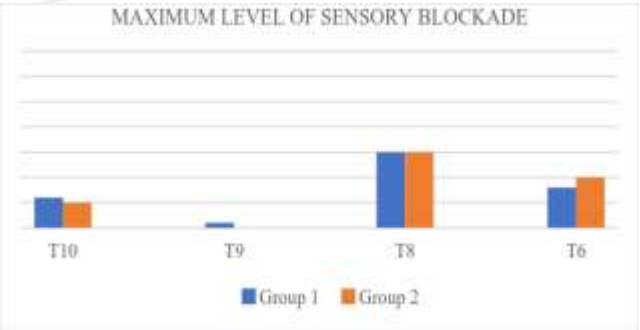




A. Maximum Level Of Sensory Blockade Attained

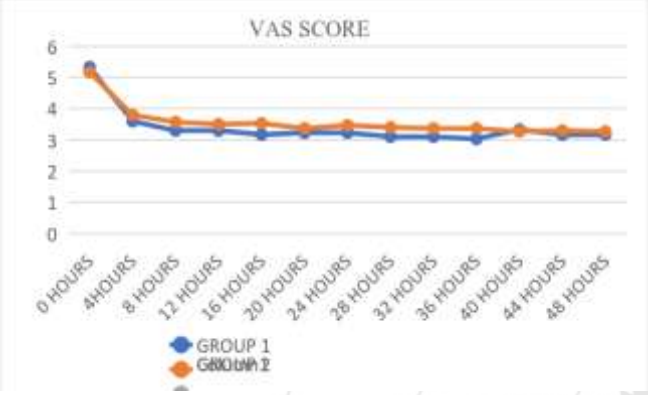
Among 60 patients, 11 patients had sensory block till T10, one patient had sensory block till T9, 30 patients (50%) had sensory block at T8 and 18 patients had sensory block at T6

		Group 1	Group 2	Total
Maximum sensory level	T10	6 20.0%	5 16.7%	11 18.3%
	T9	1 3.3%	0 0%	1 1.7%
	T8	15 50%	15 50%	30 50.0%
	T6	8 26.7%	10 33.3%	18 30.0%
Total		30 100.0%	30 100.0%	60 100.0%



B. Visual Analogue Score:

Time Interval	Group 1	Group 2	P Value
0 HOURS	5.33±1.918	5.17±1.510	0.710
4HOURS	3.60±1.192	3.80±0.551	0.408
8 HOURS	3.30±1.022	3.57±0.626	0.228
12 HOURS	3.30±0.915	3.50±0.572	0.314
16 HOURS	3.17±0.834	3.53±0.730	0.075
20 HOURS	3.23±0.971	3.37±0.556	0.517
24 HOURS	3.23±1.006	3.47±0.730	0.308
28 HOURS	3.10±0.845	3.40±0.770	0.156
32 HOURS	3.10±0.845	3.37±0.765	0.205
36 HOURS	3.03±0.805	3.37±0.765	0.116
40 HOURS	3.33±1.398	3.27±0.583	0.810
44 HOURS	3.17±0.913	3.30±0.596	0.506
48 HOURS	3.17±0.913	3.27±0.583	0.615

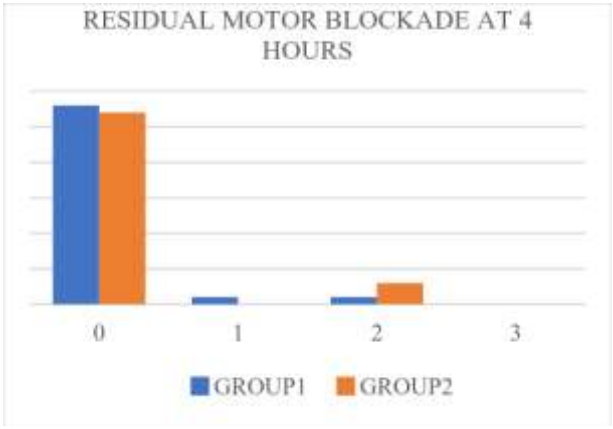


VAS scores were higher among Group 2 compared to Group 1 at different time intervals but was statistically insignificant. Mean VAS scores were consistently below 4 throughout the study period in both the Groups. However, in the immediate postoperative period at 0 Hours, Mean VAS score was above 4, but statistically insignificant.

C. Residual Motor Blockade

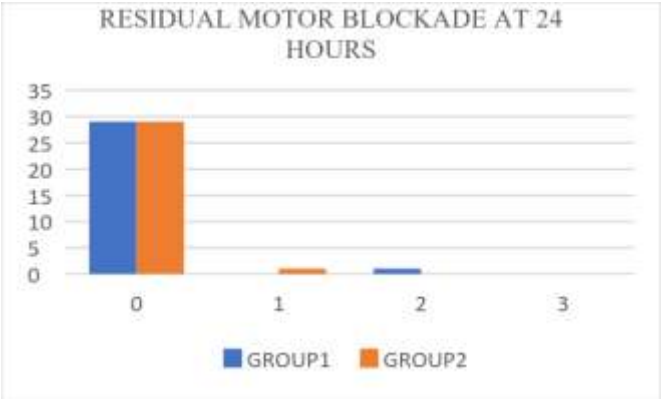
a. 4 Hours:

Residual Motor Blockade	Group1	Group2	P Value
0	28(93.30%)	27(90%)	
1	1(3.30%)	0(0%)	
2	1(3.30%)	3(10.0%)	
3	0(0%)	0.(0%)	0.365



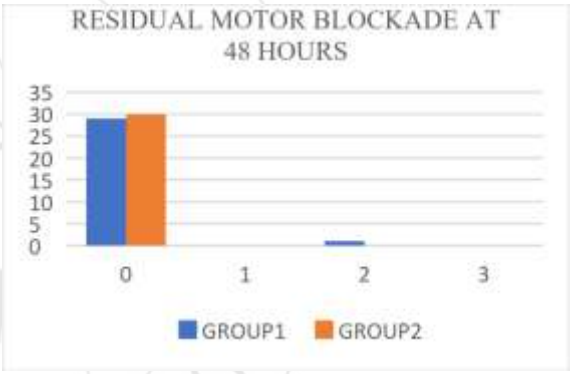
b. 24 HOURS:

Residual Motor Blockade	Group1	Group2	P Value
0	29(96.7%)	29(96.7%)	
1	0(0%)	1 (3.30%)	
2	1 (3.30%)	0(0%)	0.368
3	0(0%)	0(0%)	



c. 48 HOURS:

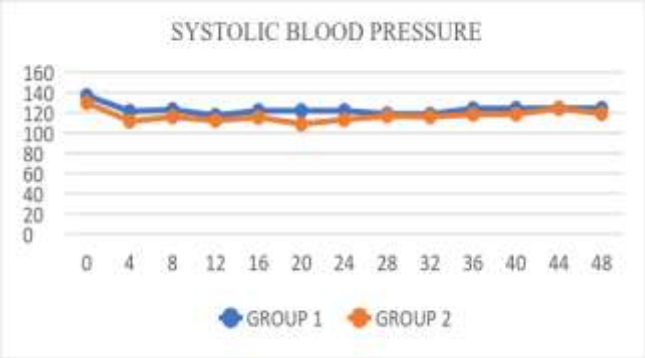
Residual Motor Blockade	Group1	Group2	P Value
0	29(96.7%)	30(100%)	
1	0(0%)	0(0%)	
2	1 (3.30%)	0(0%)	
3	0(0%)	0(0%)	0.313



Two patient had residual motor blockade in Group 1 at 4 hours compared to 3 patients in group 2. However, no patients had residual motor blockade at 24 and 48 hours in Group 2 where as one patient had residual motor blockade at similar time interval in Group 1. But, there is no statistically significant difference in the residual motor blockade at various time interval between the two groups.

D. Systolic Blood Pressure

Time Interval	Group 1	Group 2	P Value
0	137±22.96	130±18.92	0.182
4	121.33±24.179	111.67±24.927	0.133
8	123±20.123	115.80±18.891	0.111
12	117.33±24.464	112.37±26.534	0.454
16	122.07±20.185	115.37±18.440	0.185
20	121.97±19.168	108.77±33.256	0.060
24	122±15.803	113.07±27.428	0.128
28	118.70±23.486	116.67±17.450	0.705
32	118.47±26.452	115.93±17.422	0.663
36	124.13±17.815	118.33±17.167	0.204
40	124.27±17.512	118.37±18.068	0.204
44	124.57±16.952	148.23±16.418	0.428
48	124.37±16.134	119.43±16.821	0.251



Overall, the mean systolic blood pressure was on the lower side in Group 2 in comparison with Group 1 at different time intervals, but was statistically insignificant.

E. Heart Rate

Time Interval	Group1	Group2	P Value
0	91.83±15.37	84.10±11.917	0.033
4	89.23±15.099	107.13±12.63	0.446
8	86.03±12.634	76.47±21.471	0.040
12	84.27±11.154	75.47±21.855	0.054
16	84.50±11.599	80.90±8.946	0.183
20	83.70±10.551	80.13±9.902	0.182
24	82.33±11.321	79.93±8.956	0.366
28	82.70±11.689	78.9±15.302	0.284
32	83.17±10.554	77.83±16.989	0.149
36	83.17±11.706	80±8.404	0.234
40	83.70±10.790	80±7.978	0.143
44	82.50±10.075	80.80±9.076	0.495
48	80.90±7.928	80.90±7.928	0.226

The mean heart rate was significantly ($p<0.005$) lower in Group 2 than group 1 at 0, 8 and 12 hours interval. There is no statistically significant difference in mean heart rate between the two groups other time intervals. None of the patients required Atropine for bradycardia.

6. Conclusion

In conclusion, continuous epidural infusion of Ropivacaine 0.1% with Fentany 1mcg/ml and Ropivacaine 0.1% with Dexmedetomidine 1mcg/ml in major abdominal surgery provides satisfactory postoperative analgesia in the concentrations used along with minimal or no adverse effects. Dexmedetomidine provids a better hemodynamic profile and better sensory blockade when compared to fentanly. We conclude that, these drugs can be used as a safer alternative to Bupivacaine for postoperative epidural analgesia in major abdominal surgery.

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