A COMPARATIVE STUDY OF EPIDURAL 0.5% LEVOBUPIVACAINE VERSUS EPIDURAL 0.5% LEVOBUPIVACAINE WITH DEXMEDETOMEDINE ON ANALGESIA AND HAEMODYNAMICS

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ABSTRACT: BACKGROUND: Levobupivacaine, the pure S enantiomer of bupivacaine has emerged as a safe local anaesthetic than its racemic counterpart. Dexmedetomidine the novel selective alpha 2 adrenargic agonist has several advantages when given through epidural route as an adjuvant. **AIM:** To compare plain 0.5% levobupivacaine with dexmedetomidine and 0.5% levobupivacaine epidurally for analgesia and haemodynamics. **METHODOLOGY:** 60 patients undergoing infraumbilical and lower limb surgeries were randomized to two groups. Group A (n=30) received only levobupivacaine 0.5% 20ml epidurally. Group B (n=30) received 50mcg of dexmedetomidine with levobupivacaine 0.5% 20ml epidurally. The time of onset of analgesia, duration of analgesia, the need for rescue analgesia and its effect on haemodynamic parameters and any adverse outcome were noted. Statistical work done by student t test and chi square test and $p < 0.05\%$ were taken to be significant. **RESULTS:** Dexmedetomidine fastens the onset of analgesia and prolongs the duration of analgesia without any disturbance in haemodynamic parameters and nil significant adverse effects. **CONCLUSION:** We conclude that dexmedetomidine can be used as an adjuvant to levobupivacaine which fastens the onset and prolong the duration of analgesia without any alteration in haemodynamics.

KEYWORDS: Levobupivacaine, Dexmedetomidine, Analgesia, Haemodynamics.

INTRODUCTION: Regional anaesthesia came popular from the time of Sir August Bier in 1898.¹ Intrathecal anaesthesia and epidural anaesthesia are the most popular regional anaesthesia techniques used for lower abdominal & lower limb surgeries. Epidural anaesthesia reduces the perioperative stress response to surgery and improves surgical outcome. Epidural anaesthesia and analgesia has become one among the best accepted techniques for lower abdominal & lower limb surgeries as it provides good sensory and motor blockade with contracted bowels retaining adequate spontaneous respiration, hemodynamic stability and also an indwelling epidural catheter facilitates further administration of analgesic doses for the postoperative period.²

Epidural anaesthesia reduces the incidence of hemodynamic changes due to sympathetic blockade as it produces segmental anaesthesia unlike subarachnoid block, provides effective surgical anaesthesia as compared to subarachnoid block even for prolonged procedures, incidence of postdural puncture headache is not encountered as dura is not pierced and provides prolonged postoperative analgesia.^{3,4} The S (-)-enantiomer of bupivacaine, levobupivacaine has advantages of decreased cardiovascular toxicity and there is also a relatively decreased motor nerve fiber penetration and block, thereby a decreased post-operative motor blockade and thus early ambulation of the patients can be achieved compared to the former bupivacaine.^{5,6,7} The addition of adjunctive agents (Opioids & alpha 2 agonists) to local anaesthetics via epidural and intrathecal routes may provide a dose sparing effect and increase the duration and quality of analgesia.

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Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with lower dose of local anaesthetic to achieve the desired anaesthetic effect.^{8,9} The addition of opioid does provide a dose sparing effect of local anaesthetic and superior analgesia but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression.⁹ Dexmedetomidine is a highly selective alpha 2 adrenergic agonist with greater receptor affinity than clonidine.¹⁰ In addition it also has hemodynamic stabilizing effects and reduction of anaesthetic drug requirements. Epidural dexmedetomidine does cause a manageable hypotension & bradycardia but the striking feature of this drug is its lack of opioid related side effects like respiratory depression, pruritis, nausea and vomiting.^{10,11,12}

Hence the present study is to evaluate the effects of addition of dexmedetomidine to epidural 0.5% levobupivacaine on analgesia and haemodynamic parameters in infraumbilical and lower limb surgeries.

AIM OF THE STUDY: To evaluate the effect of addition of Dexmedetomidine to epidural 0.5% Levobupivacaine solution on the duration of analgesia and haemodynamic changes in pulse rate and blood pressure compared to plain 0.5% epidural levobupivacaine.

METHODOLOGY: After getting approval from the institutional ethical committee 60 adult patients of either sex belonging to the age group 20-50 years weighing between 50-75kg with BMI ranging between 19-24, undergoing elective infraumbilical and lower limb surgeries with site of incision below T10 level were identified and randomly allocated to two groups through lots after getting written informed consent.

GROUP A: 30 patients who received 20ml of epidural 0.5% Levobupivacaine with 0.5ml distilled water.

GROUP B: 30 patients who received 20ml of epidural 0.5% Levobupivacaine with 0.5ml of Dexmedetomidine containing 50µg.

Patients not willing for the study, pregnant women, ASA III & ASA IV patients, patients who are known allergic to study drugs, patients in sepsis, patients undergoing emergency surgeries, patients having infection at the site of injection, coagulopathy or other bleeding diathesis were excluded from the study.

After included in the study, the patients were explained about the procedure and shifted to the operation theatre where a good peripheral intravenous access was secured using 18 gauge cannula and baseline non-invasive blood pressure, ECG, pulse rate and SpO₂ were recorded. Injection Midazolam 0.03mg/kg IV was given as standard premedication. All patients received Ringer lactate solution 20ml/kg as preloading solution before the block. Intravenous fluids were given as per body weight and operative loss requirement. Patients were put in right lateral position and skin over the desired site was infiltrated with 1% lignocaine 2ml. L2-L3/L3-L4 interspaces were selected and epidural space identified using 18G Tuohy needles, midline approach, using loss of resistance technique with air. After exclusion of blood in the needle with negative aspiration, 2ml of 0.5% levobupivacaine was injected to exclude intrathecal placement of the needle. After which epidural catheter was inserted and fixed 5cm inside. Now patients in group A received 18ml of 0.5% Levobupivacaine with 0.5ml distilled water and group B received 18ml of 0.5% Levobupivacaine plus

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0.5ml of Dexmedetomidine containing 50µg epidurally. Baseline pulse rate, SpO₂ at room air, noninvasive blood pressure was recorded. Cardio respiratory parameters were monitored continuously and recordings were made every 5 minutes until 30 minutes and at 10 minute interval for the first 2 hours and thereafter for every hour till 6 hours. Intraoperatively, incidence of bradycardia (Heart rate<50beats per minute) will be treated with 0.6mg of injection atropine i.v and hypotension (Systolic blood pressure falling more than 20% from the baseline value) will be treated with injection ephedrine 6 mg IV. Duration of analgesia was recorded as time interval from the completion of administration of anaesthetic agent to the time when the patient complains of pain at the surgical incision site with VAS score >3. Procedure was explained and the patients were taught to assess the onset of pain using the visual analogue scale (VAS). In the visual analogue scale the patients were shown a scale of 10 cm length. Zero end of the scale was taken as 'No pain' and 10 cm mark as 'Maximum pain'. Intensity of pain increases gradually from '0' to '10'. VAS score was assessed hourly from the time of completion of surgery. Patients were instructed to point the onset of pain on the scale when VAS score>3. During surgical procedure adverse effects like nausea, vomiting, dry mouth, dizziness, headache, respiratory depression, pruritis and shivering were recorded.

Any postoperative untoward side effects were noted for 48 hours.

STATISTICAL ANALYSIS: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD and results on categorical measurements are presented in percentage (%). Chi-square test has been used to find the significance of study parameters on categorical scale between two groups. Student't' test has been used to determine the significance between two group means. All analyses were two tailed and p <0.05 was considered significant. SPSS version 16.0 was used for data analysis.

RESULTS: All the 60 patients completed the study protocol. There were no significant differences in the age, sex, ASA physical status, height and weight as mentioned in Table 1.

VARIABLE	GROUP A	GROUP B
AGE (YRS)	35.17± 4.969	34.63±5.147
GENDER(N)		
MALE	22	22
FEMALE	8	8
ASA		
1	25	25
2	5	5
WEIGHT(KGS)	61.77±5.250	61.20±4.290

Table 1: Demographic Characteristics

There was no statistically significant difference between the two groups in the duration of surgery with P value being 0.856.

DURATION OF SURGERY (IN MINUTES)			
GROUP	MEAN	STANDARD DEVIATION	p-VALUE
A	85.67	15.241	0.856
B	86.60	19.963	

Table 2: Duration of surgery by group

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Fig. 1: Duration of surgery

The duration of analgesia is prolonged with group B (477.83 minutes) when compared to group A (351.67 minutes) which shows statistical significance with p value of 0.000.

DURATION OF ANALGESIA (IN MINUTES)			
GROUP	MEAN	STANDARD DEVIATION	p-VALUE
A	351.67	54.730	0.000
B	477.83	44.580	

Table 3: Duration of analgesia

Fig. 2: Duration of analgesia

The heart rate recorded between 30 to 100 minutes was found to be statistically significant between the 2 groups.

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TIME INTERVAL (MINUTES)	GROUP	MEAN HEART RATE (BEATS/MINUTE)	STANDARD DEVIATION	p-VALUE
Basal	A	83.73	6.384	0.061
	B	87.20	7.622	
1	A	86.60	6.871	0.056
	B	89.93	6.357	
5	A	83.10	7.355	0.068
	B	86.73	7.763	
10	A	81.40	6.371	0.600
	B	82.27	6.362	
15	A	79.13	6.678	0.439
	B	77.67	7.845	
25	A	76.20	5.616	0.029
	B	72.20	8.006	
30	A	74.87	5.625	0.000
	B	68.60	7.185	
40	A	73.53	6.616	0.000
	B	65.13	7.514	
50	A	72.93	6.074	0.000
	B	62.33	7.685	
60	A	71.47	5.823	0.000
	B	62.07	6.918	
70	A	72.00	4.751	0.000
	B	62.64	5.813	
80	A	71.50	4.628	0.000
	B	62.59	6.073	
90	A	71.41	3.519	0.000
	B	61.00	3.658	
100	A	70.25	5.175	0.000
	B	62.00	3.225	
110	A	68.50	4.726	0.156
	B	63.20	5.215	
120	A	70.00	2.000	0.025
	B	62.67	3.055	

Table 4: Haemodynamic changes- Heart Rate

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Fig. 3: Haemodynamic changes- Heart

Mean arterial blood pressure recorded at 5, 10, 15, 20, 25, 30, 40, 50, 60 minutes were found to be statistically significant.

TIME INTERVAL (MINUTES)	GROUP	MEAN OF MEAN ARTERIAL BLOOD PRESSURE (MM HG)	STANDARD DEVIATION	p-VALUE
Basal	A	90.97	5.327	0.787
	B	90.60	5.143	
1	A	90.73	5.105	0.316
	B	89.27	6.085	
5	A	87.83	5.497	0.008
	B	83.47	6.816	
10	A	85.33	4.751	0.002
	B	79.60	8.067	
15	A	83.03	4.664	0.000
	B	77.10	6.989	
20	A	81.73	5.977	0.002
	B	75.67	8.049	
25	A	81.20	6.718	0.000
	B	74.40	7.403	
30	A	79.50	7.385	0.019
	B	74.70	8.014	
40	A	79.57	6.831	0.005
	B	73.27	9.791	

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50	A	79.17	7.525	0.005
	B	73.13	8.402	
60	A	78.63	7.872	0.034
	B	74.30	7.603	
70	A	78.76	6.162	0.128
	B	76.14	6.604	
80	A	79.65	7.307	0.392
	B	77.27	7.985	
90	A	80.47	7.383	0.216
	B	76.93	8.204	
100	A	81.62	5.829	0.400
	B	78.55	8.745	
110	A	80.50	6.856	0.934
	B	80.00	9.798	
120	A	77.67	3.055	0.672
	B	76.33	4.041	

Table 5: Haemodynamic changes- Mean Arterial Pressure

Fig. 4: Haemodynamic changes- Mean Arterial

There was no significant difference between the two groups with regards to oxygen saturation.

TIME INTERVAL (MINUTES)	GROUP	MEAN OF SpO ₂ (%)	STANDARD DEVIATION	p-VALUE
Basal	A	98.67	0.661	0.676
	B	98.60	0.563	
1	A	90.00	0.651	0.831
	B	98.67	0.547	
5	A	98.70	0.535	0.221
	B	98.53	0.507	

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10	A	98.63	0.556	0.054
	B	98.37	0.490	
15	A	98.60	0.675	0.829
	B	98.57	0.504	
20	A	98.60	0.563	0.339
	B	98.47	0.507	
25	A	98.70	0.596	0.108
	B	98.47	0.507	
30	A	98.70	0.651	0.190
	B	98.50	0.509	
40	A	98.53	0.571	0.001
	B	98.53	0.571	
50	A	98.43	0.504	0.634
	B	98.50	0.572	
60	A	98.57	0.626	0.652
	B	98.50	0.509	
70	A	98.53	0.507	0.122
	B	98.33	0.479	
80	A	98.83	0.648	0.062
	B	98.53	0.571	
90	A	98.50	0.572	0.812
	B	98.47	0.507	
100	A	98.60	0.621	0.174
	B	98.40	0.498	
110	A	98.50	0.572	0.473
	B	98.40	0.498	
120	A	98.67	0.606	0.111
	B	98.43	0.504	

Table 6: Oxygen saturation

Figure 5: Oxygen saturation

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Adverse effects were reported in 16.7% of patients in group A and 30% of patients in group B. But hypotension/bradycardia (fall of >20% from the baseline) requiring treatment with Inj. Ephedrine/Inj. Atropine were found to be statistically insignificant while comparing the two groups.

ADVERSE EFFECTS		GROUP	
		Group A	Group B
Dry Mouth	Count % within Group	-	1 3.33%
Nausea Vomiting	Count % within Group	1 3.33%	1 3.33%
Shivering	Count % within Group	-	2 6.67%
Urinary Retention	Count % within Group	2 6.67%	-
Hypotension	Count % within Group	2 6.67%	3 10%
Bradycardia	Count % within Group	-	2 6.67%

Table 7: Distribution of adverse effects

Group	Yes	%	No	%
A	5	16.67	25	83.3
B	9	30	21	70.0
Total	14	23.33	46	75.40

Table 8: Overall distribution of adverse effects

p-value- 0.3598

Figure 6: Distribution of adverse

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DISCUSSION: This study compared the effects of addition of epidural dexmedetomidine (50 micrograms) to epidural 0.5% levobupivacaine 20ml. Demographic parameters such as age, sex, height & weight have no statistical difference between the two groups. Distribution of ASA status was also similar in both groups.

The results of our study demonstrates that adding dexmedetomidine to 0.5% Levobupivacaine increases the duration of analgesia compared to plain Levobupivacaine. Timing of rescue analgesia was noted in both the groups and the mean duration of analgesia was found to be highly significant in group B (Mean time- 477.83 mins) with p value of 0.000 in comparison with group A (Mean time-351.67 mins) which was comparable to study conducted by Manal,¹³ Kopacz¹⁴ and Saurav¹⁵ et al.

The fall in heart rate in group B was maximum between 30 mins to 100 mins which showed statistical significance compared to group A which were comparable to Carpenter and Hell et al^{16,17} But decrease in heart rate more than 20% from the baseline or less than 50 beats/min which needed treatment with atropine was found in 2 out of 30 patients in group B and was not found in any of the group A patients which is statistically insignificant which were comparable to studies by Wang,¹⁸ Elhakim¹⁹ and Oriol^{20,21} et al. Similarly fall in systolic, diastolic & mean arterial blood pressure in group B was maximum from 5 to 70 mins with statistical significance compared to group A. But the fall in systolic blood pressure >20% from baseline or less than 90 mm Hg which necessitated treatment with ephedrine was found in 7 patients in group B patients as compared to 1 patient in group A which is also statistically non-significant. Though there was fall in systolic blood pressure <90mm Hg in 7 out of 30 patients in group B patients, their MAP never went below 60mm Hg which correlates with the study conducted by Bajwa et al.^{22,23} and Ralli et al²⁴ with the use of epidural Dexmedetomidine. Also postoperatively, heart rate & blood pressure remained stable in both the groups. The stable hemodynamics can be explained on the basis of the concentration of Levobupivacaine used and the selection of suitable dose of Dexmedetomidine.

Adverse effects were noted only in 5 out of 30 patients in group A and in 9 patients in group B which is statistically non-significant. Among group B patients, dry mouth was reported in 2 patients. Shivering in 2 patients, urinary retention, nausea & vomiting were observed one in each of the patients. Only 13% of the patients in group B experienced adverse effects which are statistically non-significant compared to group A patients. These findings correlate well with the study conducted by Neal et al¹⁴ and Ralli et al,²⁴ where similar adverse effects experienced were reported to be only mildly discomforting to the patients. None of the patients in group B had profound deep sedation or respiratory depression.

CONCLUSION: This study concludes that combining Dexmedetomidine 50 micrograms with 0.5% Levobupivacaine epidurally helps in prolonging the duration of analgesia and decreases the need for rescue analgesia. Changes in hemodynamic parameters (Blood pressure & Heart rate) were very minimal in the Dexmedetomidine group. Adverse effects encountered with Dexmedetomidine were also acceptable with only mild discomfort to the patients. Absence of respiratory depression is a remarkable feature of Dexmedetomidine when given epidurally.

REFERENCES:

1. Michael J cousins, Bernadette T. Veering. Epidural neural blockade, Chapter 8. Neural blockade in Clinical Anaesthesia and management of pain, Third edition; 1998: 243-312.
2. Simpson BP, Park House J. The problems of postoperative pain. *Br J Anaesthesia* 1961; 33: 36.
3. Lofgren N: Studies on local anaesthetics-xylocaine Stockholm, Ivan Haeggstone, 1948.
4. Gordh T Lidocaine: the origin of modern local anaesthetics-1949. *Anaesthesiology*, 2010 Dec; 113(6): 1433-7.
5. Tolivo L Ann. *Chir Gynaecol Fenn*: Study on bupivacaine comparing with lidocaine. *Br J Anaesthesia* 1963; 52: 513.
6. Hinn F, Brattsand R: Some pharmacological and toxicological properties of a new long acting local anaesthetic. *Acta Anaesth Scand*; 1966; 2145.
7. Huang YF, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous levobupivacaine and bupivacaine in sheep. *Anesth analg* 1998; 86: 797-804.
8. A Comparison of the electrocardiographic cardiotoxic effects of racemic bupivacaine, levobupivacaine and ropivacaine in anesthetized swine. *Anesth analg* 2000; 90: 1308-14.
9. Crina L Burlacu, Donal J Buggy. Update on local anaesthetics: focus on levobupivacaine. *Therapeutics and clinical risk management* 2008; 4(2)381-392. *ollin V J. Principles of anaesthesiology*. Third edition. Philadelphia: Lea and Febiger; 1993.
10. Mcleod GA, Burke D. Levobupivacaine. *Anaesthesia* 2001; 56: 331-41.
11. Casati A, Baciarello M. Enantiomeric local anesthetics: can ropivacaine and levobupivacaine improve our practice? *Curr Drug Ther* 2006; 1: 85-9.
12. Sukhminder Jit Singh Bajwa, Jasleen Kaur. Clinical profile of Levobupivacaine in regional anaesthesia: A systemic review. *Journal of Anaesthesiology clinical pharmacology*; 29(4): 532.
13. Manal M Kamal, Sahar M Talaat. Comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levobupivacaine in major abdominal surgery. *Egyptian J Anaesth* 2014, 30: 137-141.
14. Kopacz DJ, Helman JD, Nussbaum CE. 2001. A comparison of epidural levobupivacaine 0.5% with or without epinephrine for lumbar spine surgery. *Anesth Analg*; 93: 755-60.
15. Dilek B Saurav, Ayre Hanci, Ulufer Sivrikaya, Metin Bektas, Leyla T Kilinc. The effects of different concentrations and equivalent volumes of levobupivacaine in epidural anaesthesia. *Current therapeutic research* April 2011; volume 72: 52.
16. Liu S Carpenter RL, Neal JM. Epidural anaesthesia and analgesia: Their role in postoperative outcome. *Anaesthesiology* 1995; 82: 1474-506.
17. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. *Crit care* 2000; 4: 302-8.
18. Wang LZ, Chang XY, Liu X, Hu XX, Tang BL. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient controlled epidural analgesia during labour: A randomized clinical trial. *Chin med J (Engl)* 2010; 123: 178-83.
19. Elhakim M, Abdelhamid D, Abdel Fattach H, Magdy H. Effect of epidural dexmedetomidine on intraoperative awareness and postoperative pain after one lung ventilation. *Acta Anaesthesiol Scand*. 2010 Jul; 54: 703-9.

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20. Oriol-Lopez SA, Maldonado-Sanchez KA, Hernandez-Bernal CE, Castelazo-Arredondo JA, Moctezuma R. Epidural dexmedetomidine in regional anaesthesia to reduce anxiety. *Revista Mexicana de Anaesthesiologia* 2008; 31(4): 271-77.
21. Kanazi GE, Aouad MT, Jabbour-Khoury SL, et al. Effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *Acta Anaesthesiol Scand* 2006; 50: 222-7.
22. Bajwa S, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopaedic surgeries. *Saudi J Anaesth* 2011; 5: 365-70.
23. Bajwa SJS, Bajwa SK, Kaur J. Dexmedetomidine and clonidine in epidural anaesthesia: A Comparative evaluation. *Indian J Anaesth* 2011; 55(2): 116-121.
24. Mantouvalou M, Ralli S, Arnaoutoglou H, Tziris G, Papadopoulos G: Comparison of epidural plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgeries. *Acta Anaesthesiol Belg* 2008; 59: 65-71.

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