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Original Research Article

A comparative study of dexmedetomidine versus clonidine in epidural anaesthesia to assess the level of sedation in patients undergoing lower abdominal and lower limb surgery

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ABSTRACT

Background: To compare study of dexmedetomidine versus clonidine in epidural anesthesia to assess the level of sedation in patients undergoing lower abdominal and lower limb surgery.
Methods: This was a comparative study conducted on admitted ASA grade I and II patients undergoing lower abdominal and lower limb surgeries. The patients were divided into three groups of 30 patients each, according to the epidural medication they received:-Group A-received 15ml of bupivacaine (0.5%) and dexmedetomidine (1.0µg/kg body weight) in 1ml of normal saline; Group B-received 15ml of bupivacaine (0.5%) and clonidine (2.0µg/kg body weight) in 1ml of normal saline; Group C-received 15ml of bupivacaine (0.5%) with 1ml of normal saline. The heart rate, blood pressure, sensory dermatome level, Motor blocked level, pain and VAS were recorded at different time intervals. The side effects were also noted.
Results: The baseline parameters were comparable among the groups. All the hemodynamic parameters and other study parameters were similar at Min. 0. All the hemodynamic parameters such as heart rate, blood pressure and SpO_2 were variable at different time intervals. Motor block level was significantly ($p<0.05$) lower in Group C than Group A and Group B from Min 50 to Min 90. The sedation score was observed to be nil in Group C. The post-op pain score became higher in Group C than Group A and Group B at subsequent time intervals. A 3 (10%) of the rescue agents was observed in Group C. Atropine (30%) and mephenteramine (10%) were common rescue agents in Group B. The bradycardia was observed in 30% patients of Group B and in 40% of Group A.
Conclusions: On addition of dexmedetomidine as adjuvant to bupivacaine in epidural anesthesia provides better anesthesia and sedation than clonidine as adjuvant to bupivacaine or bupivacaine alone with mild hemodynamic changes which are easily manageable.

Keywords: Clonidine, Dexmedetomidine, Epidural anesthesia, Lower abdominal, Lower limb

INTRODUCTION

Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-operative analgesia in lower abdominal and limb surgeries.[1] Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopedic surgery.[2,3] Many a time for achieving desired peri-operative anesthetic effect, invariably large volumes of local anesthetics are used, thereby increasing the possibilities of local anesthetic toxicity and deleterious hemodynamic consequences. Epidural bupivacaine is a commonly used technique for anesthesia and post-

operative analgesia.[4] It is widely used for caudal epidural analgesia in children because of its long duration of action and beneficial ratio of sensory to motor block. Bupivacaine 0.125-0.175% is the optimum concentration for this purpose, providing equivalent postoperative analgesia to bupivacaine 0.25% (4-8hrs), but with a shorter duration of motor block.[5]

The quality and duration of analgesia is improved when a local anesthetic is combined with alpha 2 adrenergic agonist. Both clonidine and dexmedetomidine are alpha 2 adrenergic agonists, which have analgesic properties and potentiate local anesthetic effects.[6,7] Neuraxial clonidine, enhances the action of local anesthetics, increases the intensity and duration of analgesia. It is known to have sedative properties and the side effects are hypotension and bradycardia.[8,9]

Dexmedetomidine is about 8 times more selective towards the alpha 2 adrenoreceptor than clonidine and hence allows the use of higher doses with less α_1 effect. It has been found to have hemodynamic stability, sedative, anxiolytic, analgesic, neuroprotective and anesthetic sparing effect. It causes more intense motor blockade and co-operative sedation without increasing the incidence of side effects.[10,11]

In the present work, we studied the comparison of sedation effect of epidural administered dexmedetomidine and clonidine.

METHODS

This was a comparative study conducted on admitted ASA grade I and II patients undergoing lower abdominal and lower limb surgeries in tertiary care hospital in north India. After getting permission from Ethical Committee of the Institute, patients posted for lower abdominal and lower limb surgery with no contraindications for regional anesthesia, were selected for study.

Nishikawa and Dohi (1990) observed decreases in mean blood pressure (BP) 20 min after epidural injection in those given clonidine being 5%. We assumed decrease in mean BP being 10%. Assuming 80% power, 5% significance level with 95% confidence interval, a total of 26 patients were required in each group.

The patients were divided into three groups of 30 patients each; according to the epidural medication they received:

- **Group A**-received 15ml of bupivacaine (0.5%) and dexmedetomidine (1.0µg/kg body weight) in 1ml of normal saline.
- **Group B**-received 15ml of bupivacaine (0.5%) and clonidine (2.0µg/kg body weight) in 1ml of normal saline.
- **Group C**-received 15ml of bupivacaine (0.5%) with 1ml of normal saline.

The inclusion criteria were male and female patients aged 18 to 65 years, height between 140-180cms, weight between 35-5kgs and patients posted for lower abdominal and lower limb surgeries and belonging to ASA I and ASA II. Patients with known cardiac disease, contraindications for regional anesthesia, obese patients, known allergy to study drugs, refusal for regional anesthesia, hepatic disease and diabetes mellitus and pregnancy and lactation were excluded from the study.

Procedure

Patients were taken inside the OT; the monitors were attached including NIBP, ECG and pulse oximetry. Peripheral IV line was secured and IV fluid was started. Preloading was done with 10-15ml/kg Ringer lactate. The epidural catheter was placed under strict aseptic conditions with the help of loss of resistance method, using Touhy needle, at L2-L3 or L3-L4 inter-vertebral space, followed by 3ml test dose of xylocaine with adrenaline 1;200000. The hemodynamic changes, degree of analgesia, sedation level and postoperative analgesia, with any noted adverse effect, were compared in both groups. These values were recorded at 0, 5 10, 15, 20 and 30minutes and every 30 minutes subsequently.

Assessment of sedation was done with Four Point Sedation Scale.[12] Complication, if any, was noted and treated immediately. Bradycardia was considered as a decrease in heart rate below 50 beats per minute and was treated with i.v. Atropine, (0.5mg/kg BW). In case of hypotension, with a decrease in blood pressure less than 90/60mmHg of base line, i.v. mephenteramine bolus (6 mg) was given. Rescue analgesia with i.v. fentanyl at dose of 1µg/kg BW was used in case of inadequate analgesia.

Sensory dermatome level and two segment regression were checked with the help of spirit soaked in cotton in mid clavicular line bilaterally. Level of sedation was assessed by four point scale.[12,13] Motor blocked levels were checked with help of Modified Bromage Motor Scale, (with values of 0= no motor block, 1=inability to raise extended leg, 2=inability to flex knee, 3=inability to flex ankle joint). Pain was assessed with help of visual analogue scale (VAS).

Statistical analysis

The results are presented in mean ±SD and percentages. The Chi-square test was used to compare the categorical/dichotomous variables among the groups. The continuous variables were compared among the groups by one-way analysis of variance followed by Tukey's multiple comparison tests. The repeated measures of analysis of variance were used to find the effect time as well as time and group interaction in the continuous study parameters. The p-value <0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

There was no significant (p>0.05) difference in the mean age of Group A (32.93±13.30), Group B (34.50±14.75) and Group C (33.40±13.72) showing comparability of the groups in terms of age. Majority of the patients of Group A (73.3%), Group B (66.7%) and Group C (83.3%) were males with insignificant (p>0.05) difference. The anthropometric and vital events were also similar among the groups (Table 1). There was no significant (p>0.05) difference in heart rate among the groups at initial time interval (10min). However, a significant (p<0.01) difference was observed in the heart rate after 10 min among the groups with higher values in Group C than Group A and Group B. The repeated measures of analysis of variance indicated that there was no significant (p>0.05) effect of time interval with groups in the decrease in heart rate (Figure 1).

Table 1: Baseline characteristics of the patients.

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
Age in years, mean ±SD	32.93±13.30	34.50±14.75	33.40±13.72	0.90[a]
Male, no. (%)	22 (73.3)	20 (66.7)	25 (83.3)	0.33[b]
Female, no. (%)	8 (26.7)	10 (33.3)	5 (16.7)	
Weight in kgs	63.80±7.01	66.57±6.60	62.47±7.04	0.06 [a]
Height in cms	163.60±6.69	165.37±8.24	163.87±6.81	0.60 [a]
BMI	23.79±1.77	24.40±2.44	23.20±1.60	0.07 [a]
Heart rate	84.20±6.99	87.23±8.05	82.93±10.51	0.21
SBP	124.90±8.13	124.37±6.74	124.73±7.75	0.96
DBP	74.43±6.68	76.23±6.25	74.93±9.99	0.65
spO_2	99.33±0.80	99.23±0.72	99.13±3.46	0.94

[a]ANOVA test, [b]Chi-square test

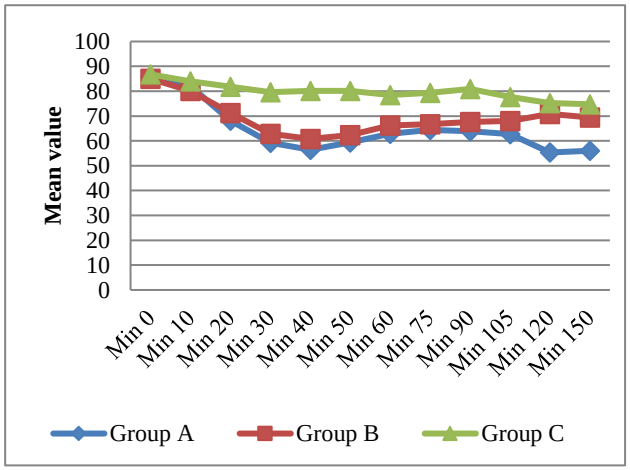

Figure 1: Comparison of heart rate across the time intervals among the groups.

There was no significant (p>0.05) difference in SBP and DBP among the groups at Min at initial time intervals (10min). However, a significant (p<0.05) difference was observed in the SBP and DBP after 10 min among the groups with higher values in Group C than Group A and Group B, suggesting that there was no significant (p>0.05) effect of time interval with groups in the change in SBP and DBP (Figure 2). There was no significant (p>0.05) difference in SpO_2 among the groups at Min 0 to Min 20. However, a significant (p=0.001) difference was observed in the SpO_2 after Min 30 and 90 among the groups. The repeated measures of analysis of variance indicated that there was significant (p=0.02) effect of time interval with groups in the change in SpO_2.

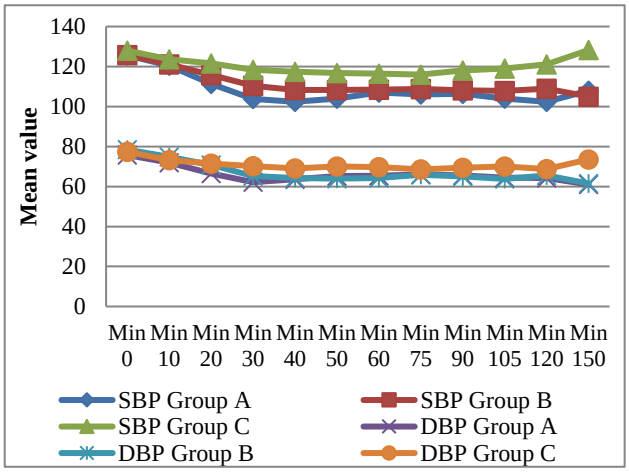

Figure 2: Comparison of SBP and DBP across the time intervals among the groups.

Height of sensory block T level was nil at Min 0 and 5 in all the groups. Sensory block T level was almost constant at the entire time interval among the groups.

However, Motor block level was found to nil at initial time intervals (10min) in all the groups. Motor block level was significantly (p<0.05) lower in Group C than Group A and Group B from Min 50 to Min 90 and was insignificantly (p>0.05) lower at Min 105 and 120

(Figure 3). The sedation score was found to be nil at initial time interval (10 min) in all the groups.

However, it varied with the different time intervals in Group A and Group B and the sedation score was observed to be nil in Group C (Figure 4).

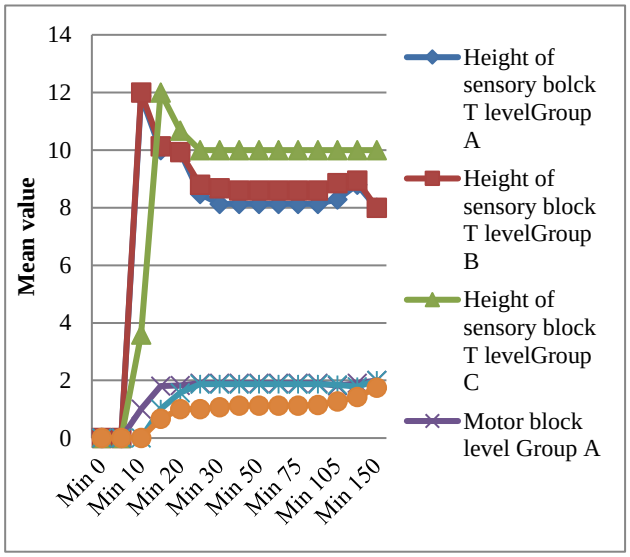

Figure 3: Comparison of height of sensory block T and motor block level across the time intervals among the groups.

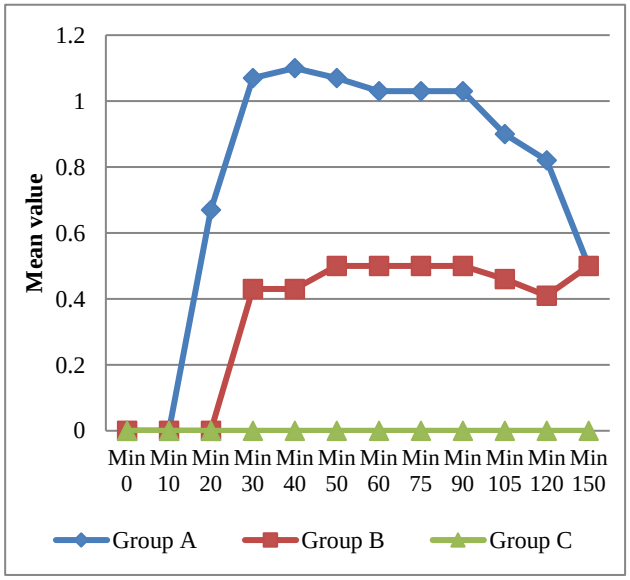

Figure 4: Comparison of sedation score across the time intervals among the groups.

The sedation level was observed to be nil in post-operation in Group C (Table 2). The intra-op pain score was found to be nil at initial 2 hrs in all the groups. The post-operative pain score was higher in Group C when compared to Group A and Group B at subsequent time intervals (Figure 5). The sensory level post-op was became nil at 5 hrs to 7 hrs in Group C and Group A. The motor blockade post-op was became nil at 5 hrs to 10 hrs in Group C and was insignificantly ($p>0.05$) different among the groups at 1 and 2 hrs. The motor blockade became nil in Group C after 4 hrs. 3 (10%) of the rescue agents was observed in Group C patients. However, atropine (30%) and mephenteramine (10%) were common rescue agents in Group B and in Group A atropine 12 (40%) and mephenteramine 7 (23.3%) rescue agent was used (Table 3).

We also checked the side effects of drugs in the different groups and observed that bradycardia was observed in 30% patients of Group B and in 40% of Group A. Hypotension was observed in 23.3% patients of Group A (Figure 6).

Table 2: Comparison of post-op sedation score across the time intervals among the groups.

Time interval	Group A (n=30)		Group B (n=30)		Group C (n=30)		p-value[1]
	Mean	SD	Mean	SD	Mean	SD	
Min 30	1.00	0.53	0.50	0.57	0.00	0.00	NA
Min 60	1.00	0.53	0.47	0.51	0.00	0.00	NA
Min 90	0.77	0.43	0.23	0.43	0.00	0.00	NA
Min 120	0.40	0.50	0.10	0.31	0.00	0.00	NA
Min 150	0.00	0.00	0.00	0.00	0.00	0.00	NA
Min 180	0.00	0.00	0.00	0.00	0.00	0.00	NA

[1]ANOVA test, *Significant, NA-Not applicable

Table 3: Comparison of rescue agents among the groups.

Rescue agents	Group A (n=30)		Group B (n=30)		Group C (n=30)	
	No.	%	No.	%	No.	%
Atropine	12	40	9	30.0	0	0.0
Mephenteramine	7	23.3	3	10.0	3	10.0

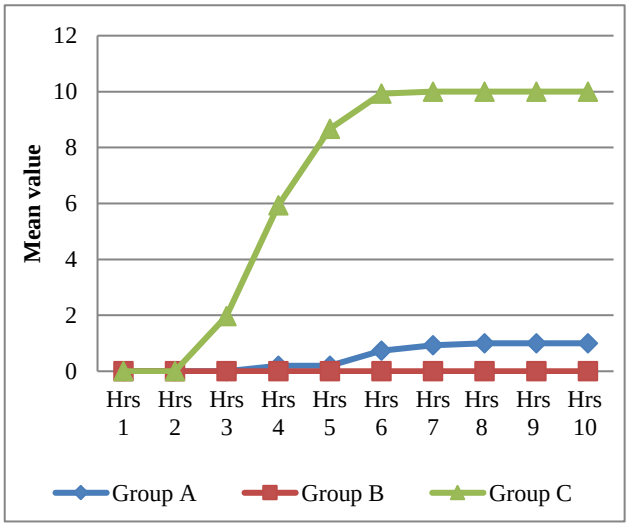

Figure 5: Comparison of pain post-op across the time intervals among the groups.

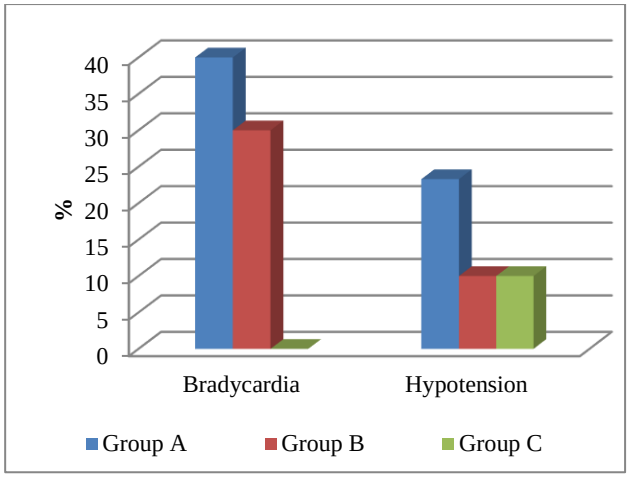

Figure 6: Comparison of side effects among the groups.

DISCUSSION

The present study was under taken in a tertiary care hospital involving patients of ASA I or II and between 18 to 65 years of age, undergoing lower abdominal and limb surgeries under epidural anesthesia. We formulated a hypothesis based on previous studies and available literature that dexmedetomedine and clonidine may produce sedation, in addition to improvement in the quality of block when used as adjuvant in epidural anesthesia. To maintain uniformity all the patients were administered same volume of epidural catheter test dose (3ml of xylocaine with adrenaline) and epidural medication volume (16ml). The demographic variables were comparable in all the three groups which did not have any confounding effect on the results in this study.

In patients who received epidural clonidine the values of heart rate were intermediate in between the other two groups in this study. This variation among the groups regarding heart rate might be because of drug might causing sedation or may have direct sympatholytic property in the present study. Our findings are supported by previous studies.[14,15] We found the mean SBP being highest in the group C which used plain bupivacaine without any adjuvant as compared to two other groups while SBP was lowest in group A which used dexmedetomidine at most of time during study period except at time of shifting when SBP were similar in all three groups with no statistically significant difference. We observed no significant differences during first 10 minutes after epidural medication, significant difference was observed after10 minute with higher value in group C. The results of Schnaider et al, showed that epidural dexmedetomidine and clonidine decreased in BP.[14] Yallapragada et al, also observed that epidural dexmedetomidine caused hypotension.[16] As in the other studies we also observed no difference among the groups regarding SpO_2.[17-19]

The rapid achievement of T-10 level block in group A and B is probably due to clonidine/dexmedetomidine used as adjutants in the present study. Thus, the addition of epidural clonidine or dexmedetomidine as epidural adjuvant, ensure a rapid spread of block (onset). The observed mean time between epidural medications to surgical incision in our study was 15 minutes in group A and group B and 20 minutes in group C in this study. Hence, addition of clonidine or dexmedetomidine, as an epidural medication reduce, time from epidural medication to surgical incision.

In our study, comparison of maximal dermatomal height achieved in three groups revealed no statistically significant difference among the groups. The faster onset of motor block is probably due to potentiation of effect by dexmedetomidine and clonidine in this study. The findings of the present study are similar to other studies.[16,20,21] Attri et al, suggested that Epidural dexmedetomidine as an adjuvant to ropivacaine is associated with prolonged sensory and motor block, when compared to plain ropivacaine.[22]

Post operative sedation scores upto 120 min in the all time intervals was higher in group A than group B in this study. At 150 min, sedation score was 0 in both Group A and B. Group C had sedation score 0 in entire post operative period. Thus, dexmedetomidine had more sedative effect than clonidine as epidural adjuvant. These findings was similar to studies by Abd Elsayed et al, Deepak et al, Bajwa et al and inconsistence with previous studies.[15,19,21,23] The duration of analgesia in Group C was 4 hours where as in Group A and B was more than 10 hours. Rescue analgesia was given at VAS score of 4 in this study. However, the time for rescue analgesia was shorter for group C than group A and B, it prolonged in Group B than Group A in the present study. These findings are consistent with other studies.[24,25] Bradycardia (HR <50/minutes) was observed in 9 (30 %) of patients in group B and 12 (40 %) of group A, hypotension was observed in 7 (23.3%) patient in Group A, 3 (10%) in Group B and 3 (10%) in Group C in the present study. The similar results were also noted in the other studies.[15,16,23,24]

In the present study, three (10%) patients require mephenteramine to treat hypotension in Group C. However, atropine was given to 9 (30%) patients for bradycardia and mephenteramine was given to treat hypotension in three (10%) patients in group B and atropine was used in 12 (40%) patients to treat bradycardia and mephenteramine to treat hypotension in 7 (23.3%) patients in group A as rescue agent. These adverse effects were occur with dexmedetomidine, an imidazole compound, is the pharmacologically active dextro isomer of medetomidine that displays specific and selective α_2-adrenoceptor agonist. The mechanism of action is unique and differs from those of currently used sedative agents, including clonidine. Activation of the

receptors in the brain and spinal cord inhibits neuronal firing, causing hypotension, bradycardia.[17]

CONCLUSION

On addition of dexmedetomidine as adjuvant to bupivacaine in epidural anesthesia provides better anesthesia and sedation than clonidine as adjuvant to bupivacaine or bupivacaine alone with mild hemodynamic changes which are easily manageable.

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