Original Research Article

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A Comparative Study of Clonidine & Dexmedetomidine as an Adjuvant with Bupivacaine in Epidural Anaesthesia

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Abstract

Background: The introduction of adjuvants, have decreased the dose requirement of local anaesthetics, increased their onset of action, prolonged their action and improved the analgesia . *Aim:* To compare Clonidine and Dexmedetomidine as an adjuvant with Bupivacaine in epidural anaesthesia *Material and Methods*: 90 patients of either sex, between 18 to 65 years of age and belonging to ASA Grade I & II physical status were divided into 3 groups with 30 patients each. *Group 1:* 20ml 0.5% plain bupivacaine + 0.5ml saline (preservative free), *Group 2:* 20ml 0.5% plain bupivacaine + 2µg/kg clonidine, *Group 3:* 20ml 0.5%plain bupivacaine + 1 µg/kg dexmedetomidine. Statistical analysis was done using the statistical package(SPSS 15.0 evaluation version). Continuous co-varieties were compared using analysis of variance (ANOVA). The qualitative data comparison were studied using the Chi-squares test. *Result:* Time of sensory onset to T-10 in group 1 was 10.02±2.6 min, in group 2 was 9.82±3.10 min, and in group 3 was 7.10±2.10 min.The time of motor block onset to bromage 3 in group 1 was 20.36±34 min, in group 2 was 17.80±4.08 and in group 3 was 14.50±5.18 minutes. The time of motor block regression to bromage 0 in group 1 was 152 ± 12.2 minutes, in group 2 was 226.42±26.17 and in group 3 was 248.70±28.40 minutes. The incidence of side-effects was statistically non significant. *Conclusion:* Clonidine and dexmedetomidine are good alternatives to opioids as adjuvant to bupivacaine in epidural anaesthesia.

Keywords: Epidural; Dexmedetomidine; Clonidine; Bupivacaine; Adjuvant.

Introduction

Many techniques and drug regimens, with partial or greater success, have been tried from time to time by the mankind for the relief of pain [1].

But the introduction of regional anesthesia in the form of epidural anesthesia has markedly changed the method of pain relief both during surgical procedures and other pain symptoms.

Epidural anaesthesia is a central neuraxial block technique with many applications. The epidural space was first described by Corning in 1901, and Fidel Pages first used epidural anaesthesia in humans in 1921. In 1945 Tuohy introduced the needle which is still most commonly used for epidural anaesthesia. Improvements in equipment, drugs and technique have made it a popular and versatile anaesthetic technique, with applications in surgery, obstetrics and pain control. Both single injections and catheter techniques can be used. Its versatility means it can be used as an anaesthetic, as an analgesic adjuvant to general anaesthesia and for post-operative analgesia in procedures involving the lower limbs, perineum, pelvis, abdomen and thorax.

Local anaesthetics like bupivacaine for epidural anaesthesia through epidural cathether have been used with great success, but with the introduction of potent and short acting opioids like fentanyl and later other adjuvants, have decreased the dose

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requirement of local anaesthetics, increased their onset of action, prolonged their action and improved the analgesia with decreasing the side effects of local anaesthetics.

In this regard, the newer α-2 adrnergic agonists like dexmedetomidine and clonidine are now being used with greater success. They have both analgesic and sedative properties when used as adjuvants in regional anaesthesia [2].

Dexmedetomidine is an α2 adrenergic agonist, provides sedation, and anxiolysis. It is more selective α2 agonist. α2:α1 ratio is 1600:1, making it complete α2 agonist [3]. It was introduced in clinical practice in United States in 1999 and approved by FDA. The sedative and hypnotic effect is produced by action on α2 receptor in locus caeruleus. The analgesic effect is produced by action on α2receptor in locus caeruleus and within spinal cord [4]. Despite sound level of sedation with Dexmedetomidine there is limited respiratory depression providing wide safety margin. It has also been noted that α2 agonist have analgesic effect when injected via intrathecal or epidural route [5]. Dexmedetomidine is rapidly and extensively metabolized in liver and excreted in urine and feces.

Clonidine, an α2-agonist has been used with claims of many advantages. The mechanism of action of α2-agonist involves vasoconstriction and antinociception from α2 stimulation [6] of receptors in dorsal horn cells of spinal cord. Some side effects reported in literature are hypotension, bradycardia and sedation which are dose dependent.

The aim of the present study was to compare Clonidine and Dexmedetomidine as an adjuvant with Bupivacaine in epidural anaesthesia,with respect to

- Onset and duration of sensory and motor block,
- Duration of analgesia,
- Haemodyanamic changes,
- Adverse effect of drugs and
- Sedation

On the basis of the above parameters, overall assessment of efficacy of adding clonidine/ dexmedetomidine as adjuvant to Bupivacaine in epidural anaesthesia was done.

Material & Methods

After obtaining ethical committee approval and informed written consent from patient , the study was carried out on 90 patients of either sex , between 18 to 65 years of age and belonging to ASA Grade I & II physical status.

Exclusion Criteria

Patients with the history of uncontrolled labile hypertension, heart block, dysarrythmia, on cardiac medication (adrenergic receptor antagonist, calcium channel blocker or ACE inhibitor), addiction to narcotic, patient posted for LSCS and with any contraindication to epidural anaesthesia were not included in the study

- All the patients were thoroughly examined and investigated before the surgery. After pre-medication patient was randomly allocated into one of the three groups, each group consisting of 30 patients.*Group 1 (Control):* 20ml 0.5% plain bupivacaine + 0.5ml saline (preservative free) *Group 2 (Clonidine):* 20ml 0.5% plain bupivacaine + 2µg/ kg clonidine *Group 3 (Dexmedetomidine):* 20ml 0.5%plain bupivacaine+1µg/kg dexmedetomidine.
- Equal volume of drug was injected in each group and all patients were preloaded with 15ml/kg of Ringer Lactate .In the operation theatre pulse oximetry (Spo2), non- invasive blood /pressure (NIBP) and ECG were monitored and in sitting posture epidural cathether was placed into L2-L3 or L3-L4 epidural space under strict aseptic conditions, using Tuohy's needle with LOR technique.
- All the patients were observed for the - Onset, duration and quality of anaesthesia. Sensory block was assessed bilaterally by short hypodermic needle in mid clavicular line.Motor block was assessed by modified bromage scale. Sedation and pain was assessed by modified ramsay scale.Hemodynamic changes viz. Pulse rate & rhythm, B.P., ECG were recorded at regular intervals in peroperative & in post operative period.Any other untoward incidence such as nausea, vomiting, shivering, pruritis, respiratory depression and sedation was assessed.The changes in above parameters were clinically and statistically compared with the control group. Statistical analysis was done using the statistical package (SPSS 15.0 evaluation version). Data were expressed as either mean and standard deviation or numbers and percentages. Continuous co-varieties were compared using analysis of variance (ANOVA). The qualitative data comparison were studied using the Chi-squares test. The P value reported at the 95% confidence interval. $P<0.05$ was considered statistically significant .

Observations

Table 1: Distribution of patients according to their age

Mean age in years	Bupivacaine (Gp1)	Clonidine Gp (2)	Demedetomidine (Gp3)
<18	-	-	-
18-27	-	-	-
28-38	11	12	10
39-48	16	17	18
49-58	03	1	02
59-65	-	-	-
Total	30	30	30
Mean ± SD	41.36 ± 6.462	40.36 ±5.436	40.36 ±7.210

P value

Grp	1 and 2	1 and 3	2 and 3
P value	>0.05	>0.05	>0.05

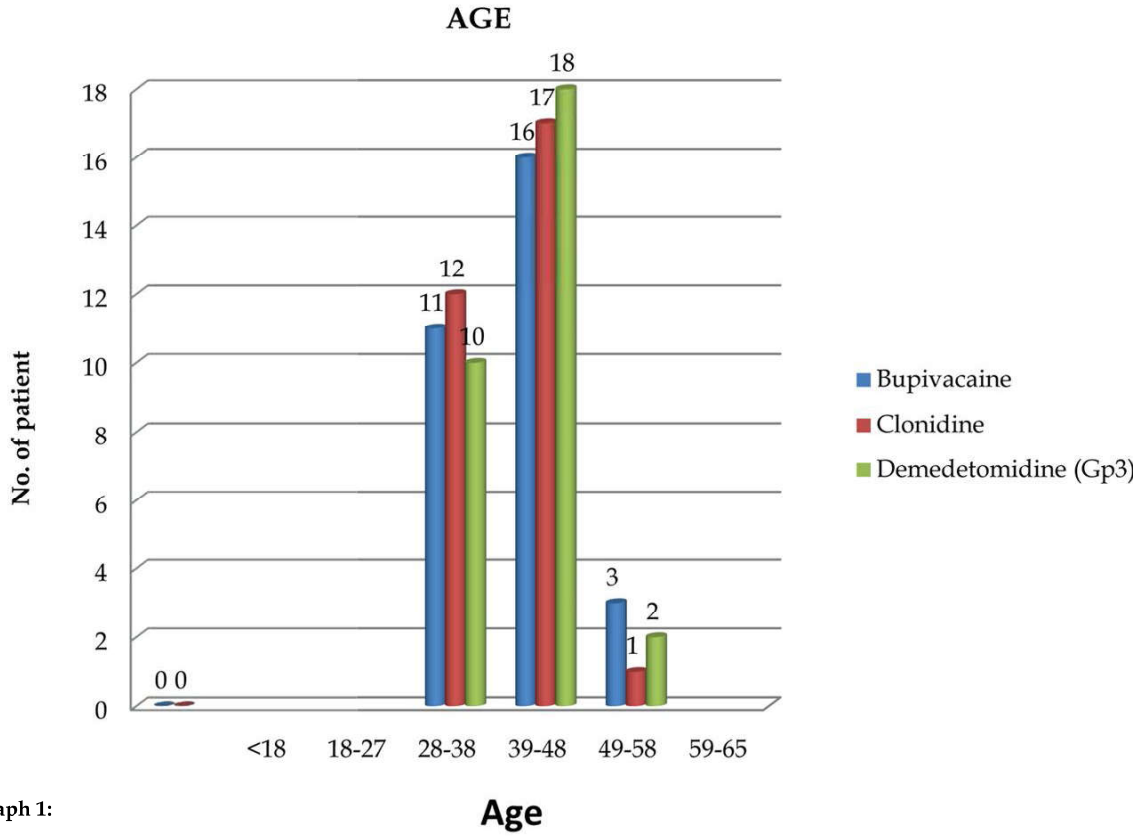
Result

The Mean Standard(MSD) Deviation of age in different Grps 1,2,3. The age distribution remain comparable and statistically insignificant in all age groups having P value> 0.05.

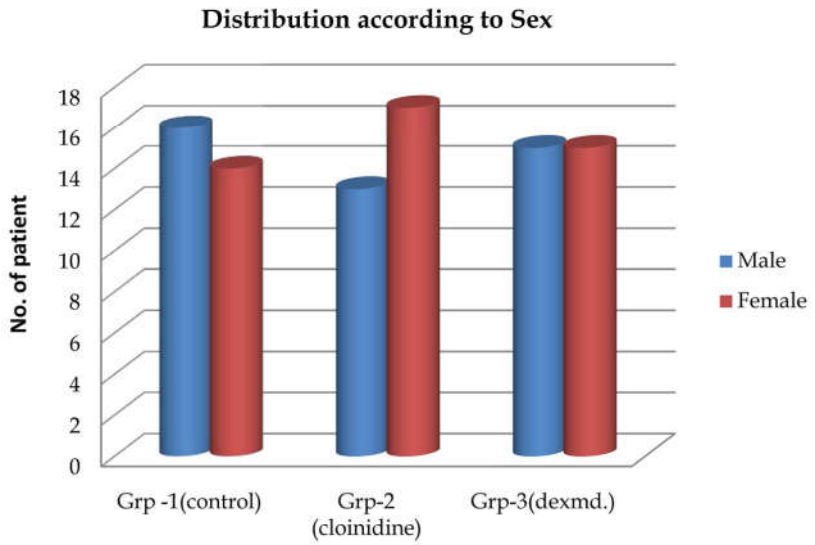
Table 2: Distribution of patient according to their sex

Group	Male	Female	Total	P value
Grp -1(control)	16	14	30	0.948>0.05
Grp-2 (cloinidine)	13	17	30	
Grp-3(dexmd.)	15	15	30	

Result: The sex distribution remains comparable in all the groups and statistically insignificant in all the groups having P value >0.05



Graph 1:

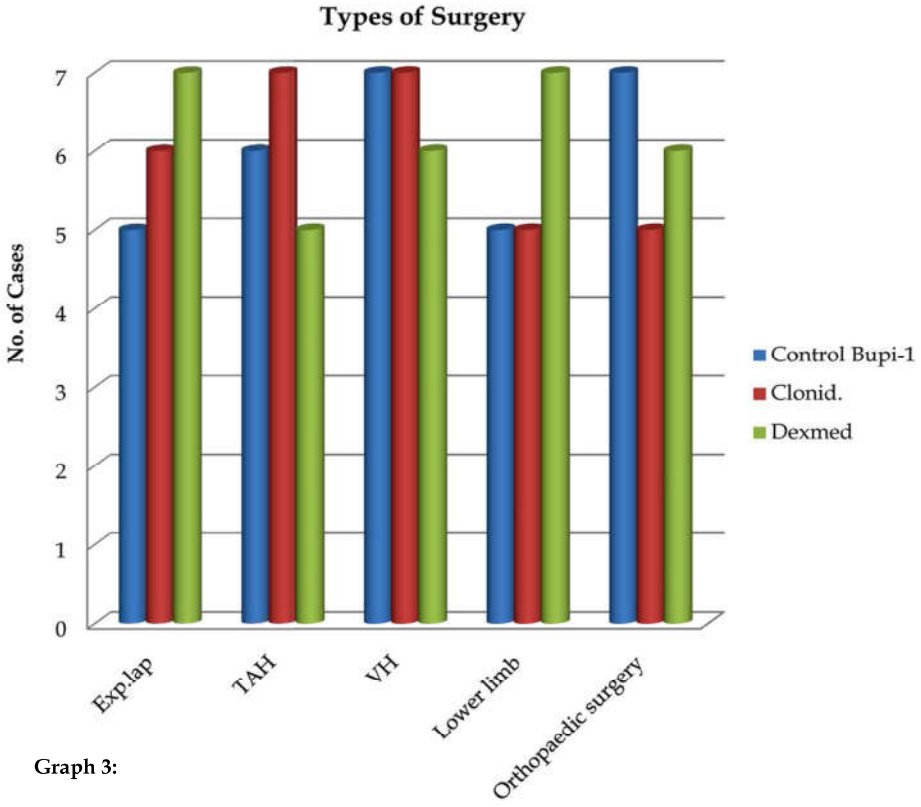


Graph 2:

Table 3: Distribution according to their type of surgery

Surgery	Control Bupi-1	Clonid. Grp 2	Dexmed Grp 3	Total	P –Value
Exp.lap	5	6	7	18	>0.05
TAH	6	7	5	18	
VH	7	7	6	19	
Lower limb	5	5	7	17	
Orthopaedic surgery	7	5	6	18	
Total	30	30	30	90	

Result: There was no significant differences between the groups according to the type of surgery and distribution remain comparable and statistically insignificant in all groups having **P value >0.05**



Graph 3:

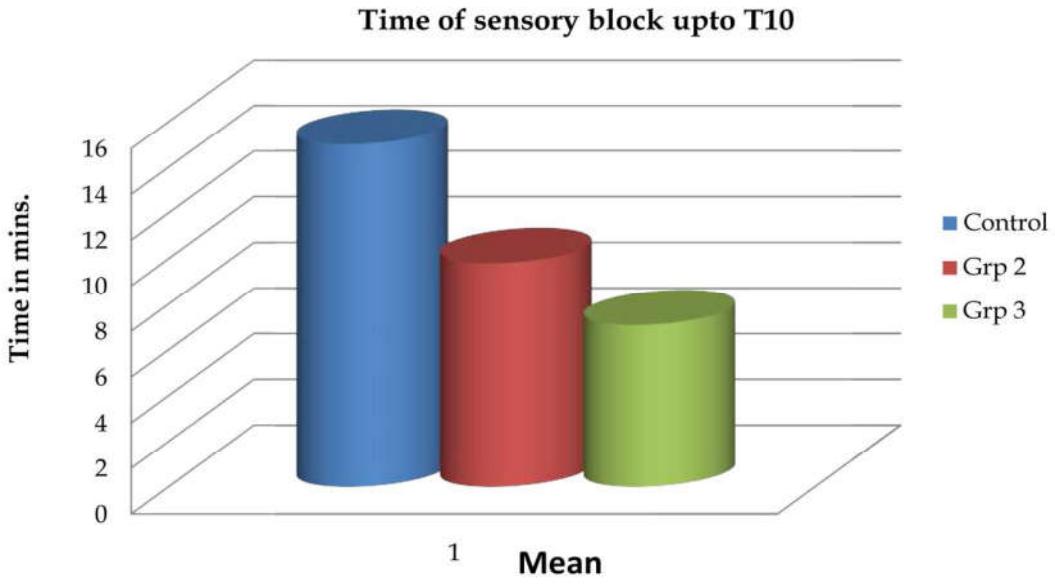
Table 4: Time of Sensory onset/block up to T-10 (in minutes)

Groups	Control (Bupiv.)	Grp 2 Clonidine	Grp 3 (Dexmed)	P value
Mean ±SD No. of cases	15.02 ± 2.6 30	9.82±3.10 30	7.10±2.10 30	<0.05

P value

Group	1 and 2	1and 3	2 and 3
P –value	<0.05	<0.05	<0.05

Result: It is evident from the table that the time of sensory onset was shortest in group 3 (dexmedetomidine) as compared to control and group2 (clonidine) The difference in time of sensory onset is statistically significant. (p<0.05)



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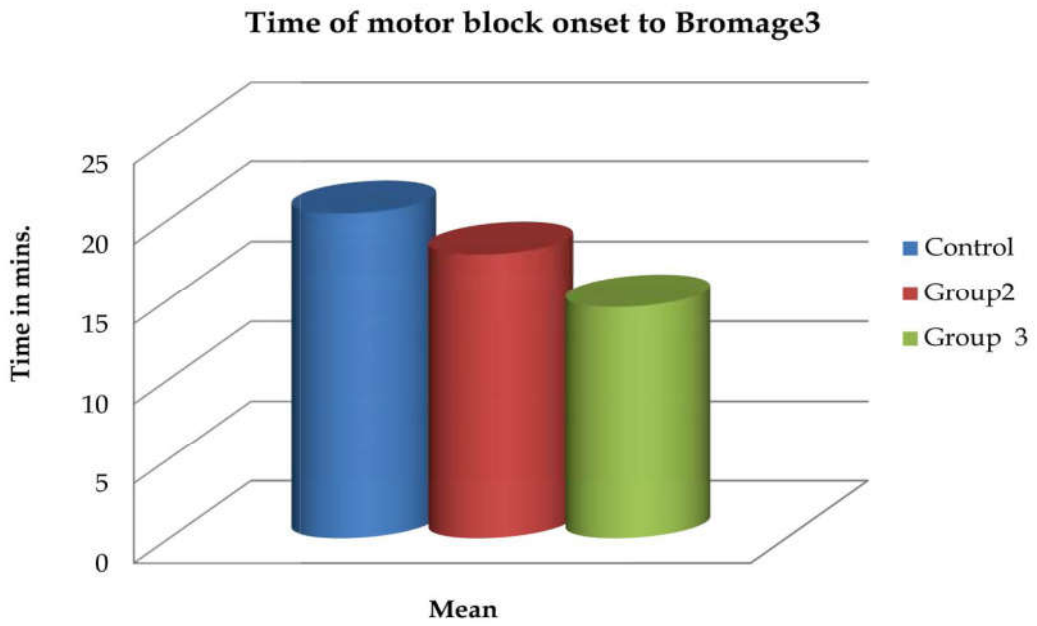


Graph 5:

Table 5: Time of motor onset to Bromage 3 (in minutes)

Groups	Control Bupiv.	Group2 Clonidine	Group 3 dexmed	P value
Mean ±SD	20.36±3.4	17.80±4.08	14.50±5.18	<0.05
No. of cases	30	30	30	

P value

Group	1 and 2	1 and 3	2 and 3
P value	<0.05	<0.05	<0.05

Result: It is evident from the table, motor block onset to Bromage 3 was shortest in Group III(dexmed) as compared to control and group2. The difference in time of motor block onset is statistically significant(P<0.05).

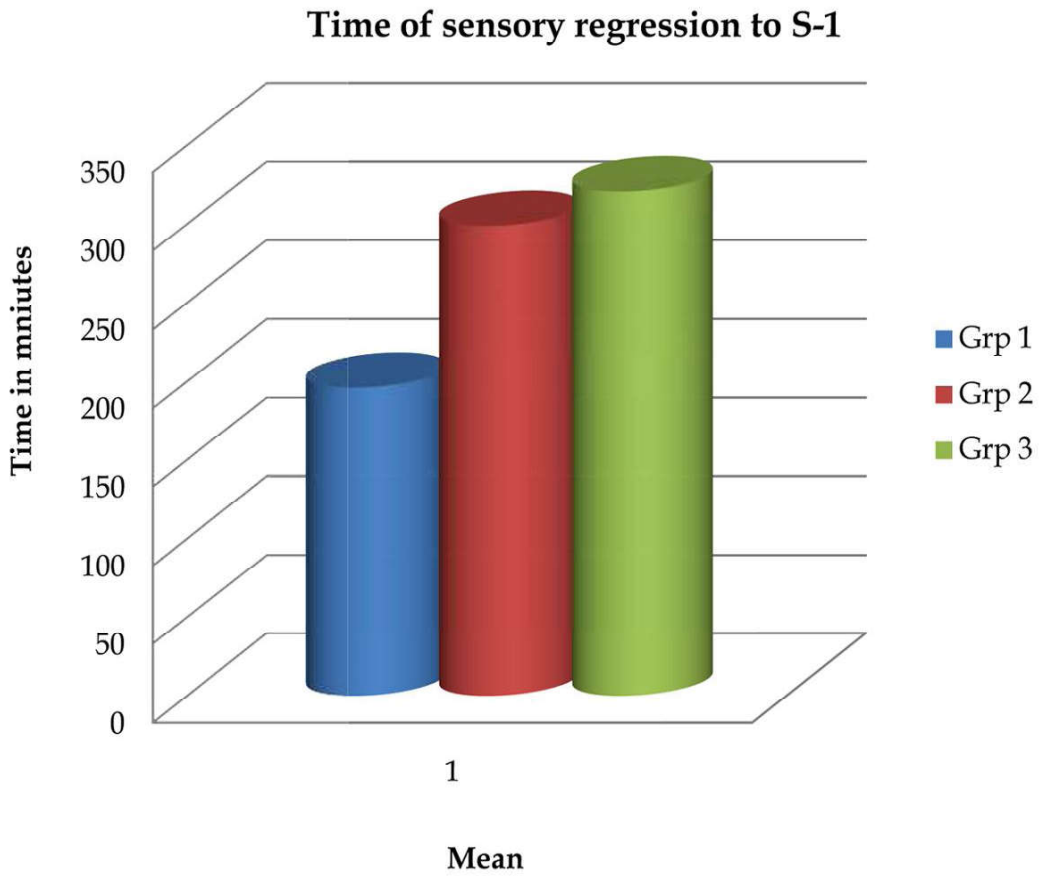
Table 6: Time of sensory regression to S-1(in minutes)

Groups	Grp 1 Bupiv.	Grp 2 Clonidine	Grp 3 Dexmed	P value
Mean ± SD	196±22	298.70±36.54	320.62±38.32	<0.05
No of cases	30	30	30	

P value

Group	1 and 2	1 and 3	2 and 3
P Value	<0.05	<0.05	<0.05

Result: it is evident from the table that time of sensory regression to S1 was longest in Group 3 (dexmedetomidine) as compared to control and group 2. The difference in time of sensory regression to S1 is statistically significant (P<0.05).



Graph 6:

Table 7: Time of Motor block regression to Bromage 0 (in minutes)

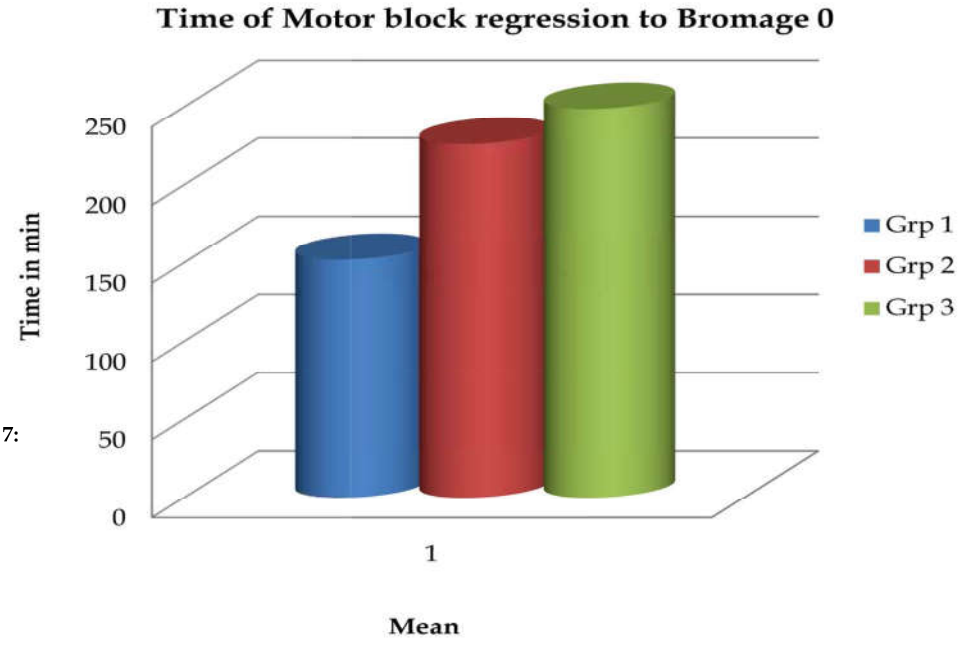
Groups	Grp 1 Bupi.	Grp 2 Clonidine	Grp 3 Dexmed	P value
Mean ± SD	152±12.2	226.42±26.17	248.70±28.40	<0.05
No.of cases 30	30	30	30	

P value

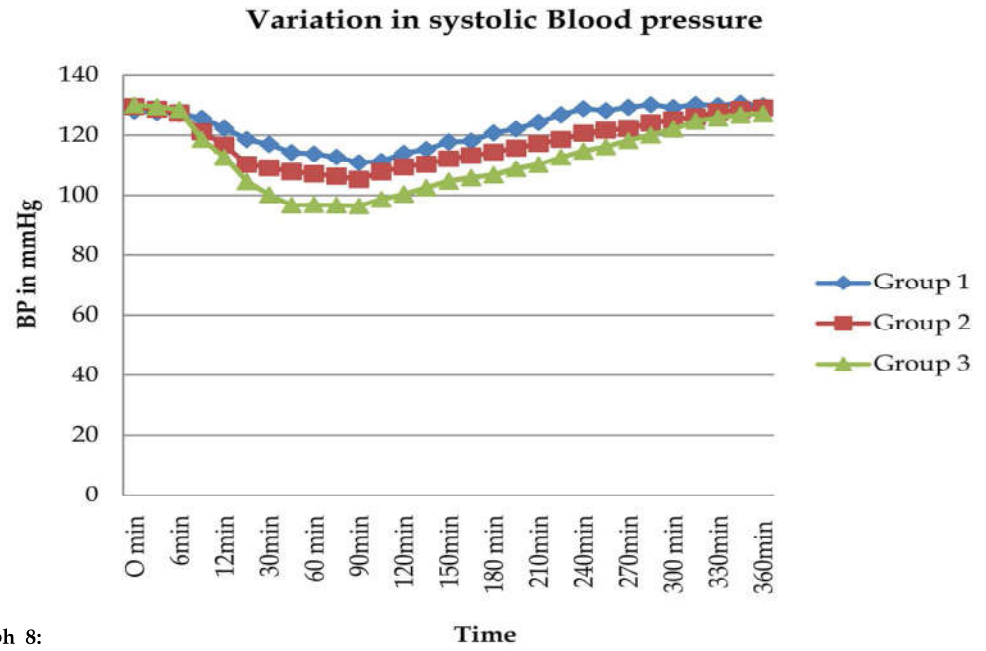
Group	1 and 2	1 and 3	2 and 3
P value	<0.05	<0.05	<0.05

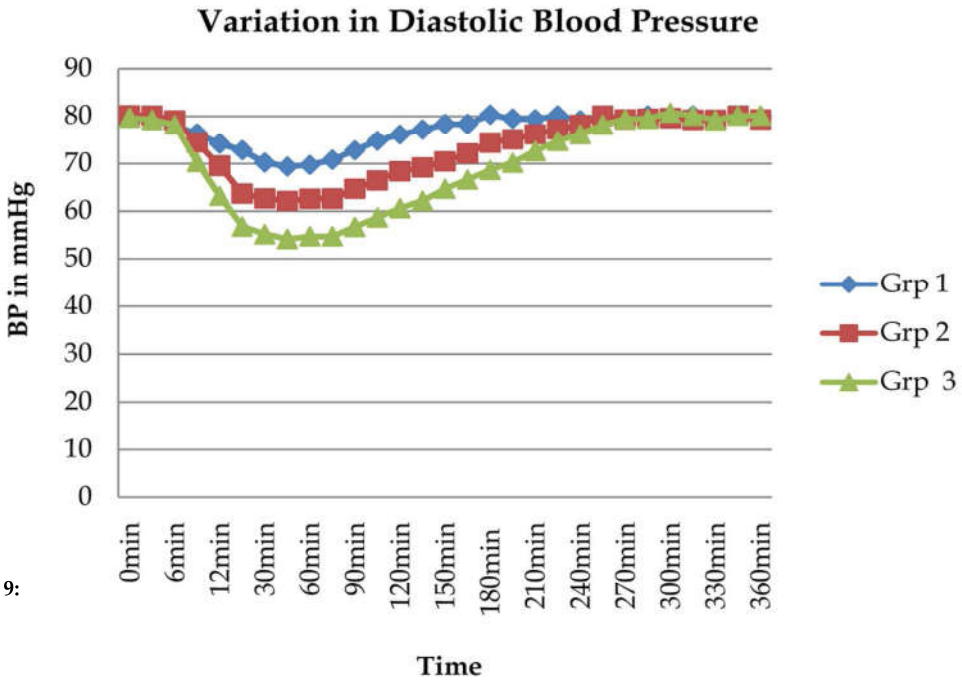
Result: It is evident from the table that the time of motor block regression to Bromage 0 was longest in Group3 (dexmedetomidine) as compared to control and group2 (clonidine). The difference in time of motor block is statistically significant P<0.05.

Graph 7:



Graph 8:





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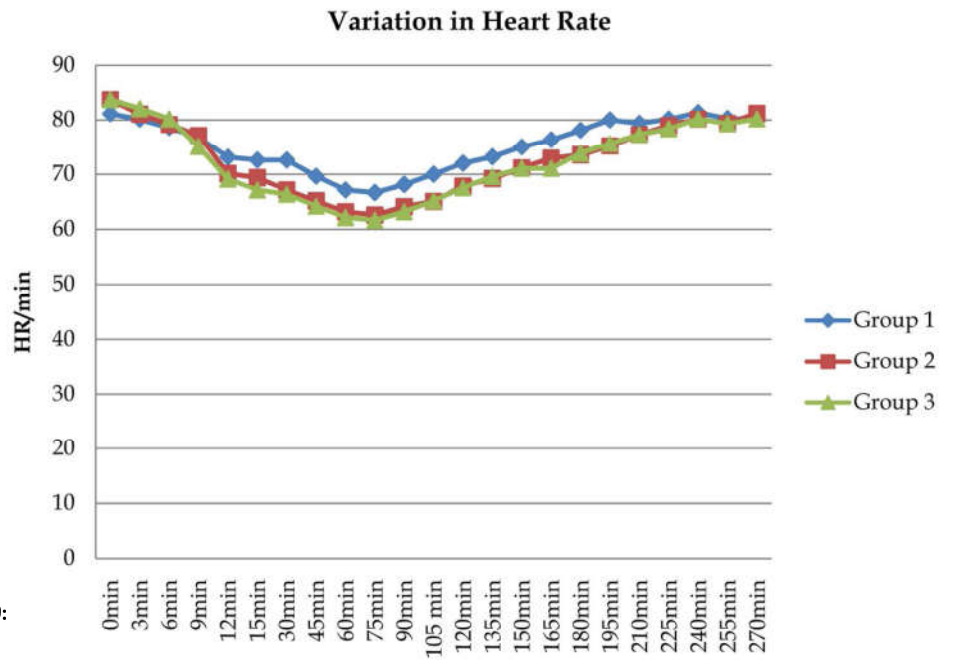


Graph 10:

Table 8: Distribution of patients according to Score RSS

Sedation score	Group I Control	Group 2 Clonidine	Group 3 Dexmed	P value
S1	10	10	5	
S2	20	15	14	<0.05
S3	-	5	11	
S4	-	-	-	

P value	1 and 2 <0.05	1 and 3 <0.05	2 and 3 <0.05

Graph 11:

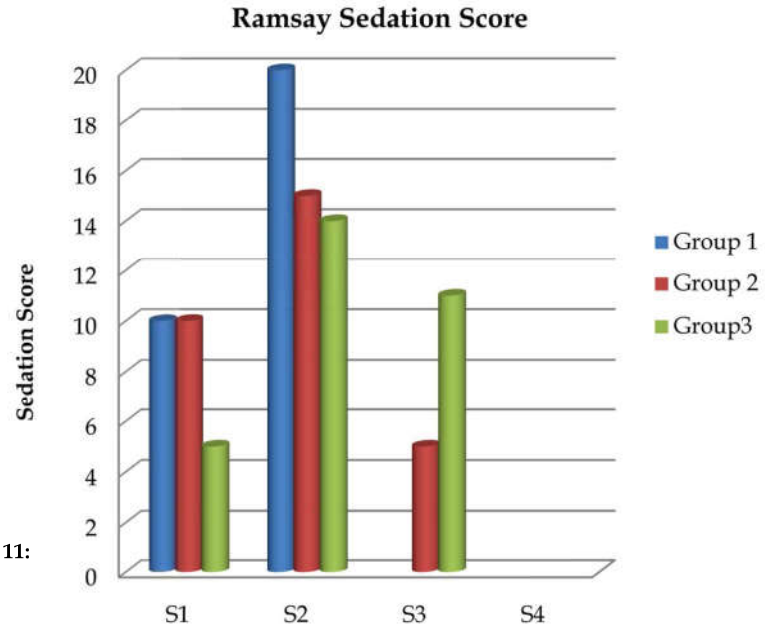


Table 9: Duration of Analgesia (in minutes)

Groups	Group 1 Control	Group 2 Clonidine	Group 3 Dexmed
Mean± SD	180±5	302.70±20.76	338±30.15
P value	**1 and 2**	**1 and 3**	**2 and 3**
	<0.05	**<0.05**	**<0.05**

Result: It is evident from the table that maximum duration of analgesia(338±30.15min) was in Group 3 (Dexmedetomidine) followed by Group 2 (clonidine) (302.70±20.76min) and then in Group 1(Bup) (180±50min). The difference in analgesia duration was statistically significant. (P<0.05)

Graph 12:

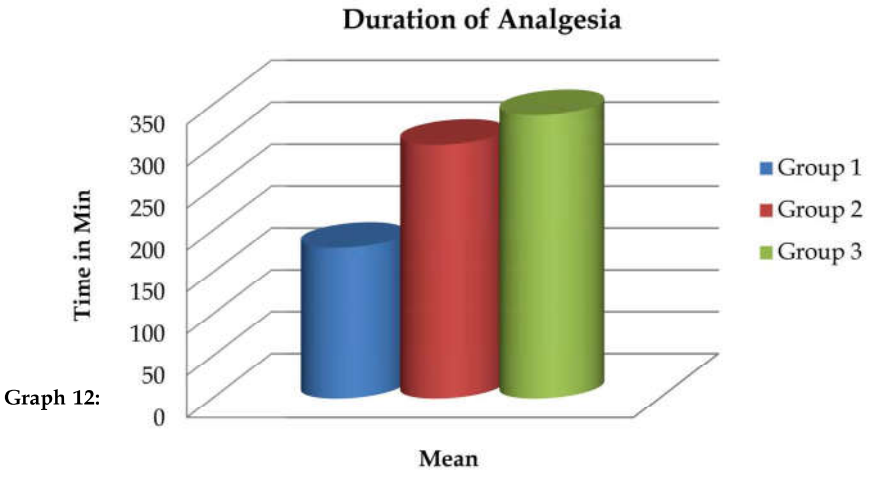
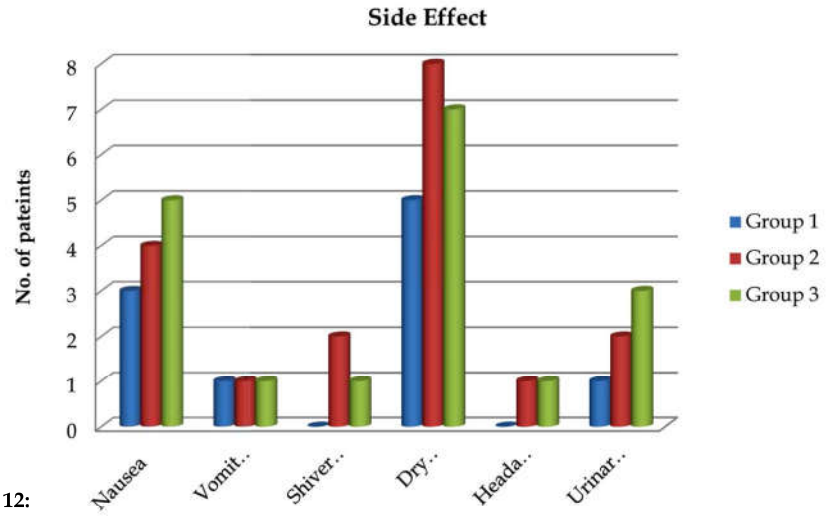


Table 10: Side effects

Side effects	Group 1	Group 2	Group 3	P value>0.05
Nausea	3	4	5	
Vomiting	1	1	1	
Shivering	0	2	1	
Dry mouth	5	8	7	
Headache	0	1	1	
Urinary retention	1	2	3	



Graph 12:

Result

In present study the age (Mean±SD) in group 1 was 41.36±6.46 years, in group 2I was 40.36±5.43 years and in group 3 was 40.36±7.21years. The age is comparable in all age groups as evident from Table 1.

Distribution according to sex was also comparable among the three groups. This is shown in Table 2. There was no significant difference between the groups according to the type of surgery and distribution remain comparable and statistically insignificant in all groups having (P value >0.05).

The time of sensory onset to T-10 in group 1 was 10.02±2.6min, in group 2 was 9.82±3.10 min, and in group 3 was 7.10±2.10min. The onset of sensory block was shortest in group 3 as compared to control and group 2. The difference in time of sensory onset is statistically significant (P<0.05).

The time of motor block onset to bromage 3 in group 1 was 20.36±34 minutes, in group 2 17.80± 4.08 and in group 3 was 14.50±5.18 minutes. It is evident from Table 5, motor block onset to Bromage 3 was shortest in group 3 (dexmedetomidine) as compared to control and group 2. The difference in time of motor block onset is statistically significant (P<0.05).

The time of sensory regression to S1 was longest in group 3 (dexmedetomidine) as compared to control and group 2. The difference in time of sensory regression to S1 is statistically significant (P<0.05) as evident from Table 6.

The time of motor block regression to bromage 0 in group 1 was 152±12.2 minutes , in group 2 was 226.42±26.17 and in group 3 was 248.70±28.40 minutes. The time of motor block regression was longest in group 3 followed by group 2 as compared to group 1. The difference in time of motor block regression is statistically significant (P<0.05).

The maximum duration of analgesia (338±30.15min) was in group 3 (dexmeditomidine) which was followed by group 2 (clonidne) 302.70±20.76 min and minimum in group 1 (Bupivacaine) 180±50 min. The difference was statistically significant (P<0.05).

The incidence of side-effects like vomiting, headache, shivering urinary retention and dizziness were comparable in all the groups and statistically non significant. The incidence of dry mouth (8 patients in group 2, 7 patients in group 3 and 5 patients in group 1) was the most common side effect but was statistically non-significant (P >0.05).

Discussion

The present study entitled "A comparative study of clonidine and dexmedetomidine as an adjuvant to bupivacaine in epidural anaesthesia" was designed to compare the efficacy of epidural dexmed 1mcg/kg and clonidine 1.5mcg/kg as an adjuvant to 0.5% bupivacaine in epidural anaesthesia with respect to onset and duration of sensory and motor block, duration of analgesia, heamodynamic changes, adverse effect of drugs and sedation.

The study was carried out on 90 patients of ASA Grade I and II of both the sexes between 18 to 65 years of age, scheduled for lower abdomen and lower limb surgeries.

Base Line Comparison of Groups

The study included the patients of age group between 18 to 65 years of age. In present study the age (Mean± SD) in group 1 was 41.36±6.46 years, in group 2 40.36±5.43 years and in group 3 was 40.36 ± 7.21years. The age is comparable in all age groups. This is shown in Table 1. Distribution according to sex was also comparable among the three groups. This is shown in Table 2.

Time of sensory onset up to T-10 (in Minutes)

In our study time of sensory onset to T-10 in group 1 was 10.02 2.6min, in group 2 was 9.82± 3.10 min, and in group 3 was 7.10±2.10min. The onset of sensory block was shortest in group 3 as compared to control and group 2. Thus clonidine and dexmedetomidine as an adjuvant to bupivacaine in epidural anaesthesia hasten the onset of sensory block.

Shobhana Gupta et al [7] in 2010 studied the effect of clonidine as an adjuvant with bupivacaine in epidural anaesthesia.They used 1mcg/kg of clonidine with bupivacaine 1.5mg/kg. Their time of sensory onset was 493.8±1.66seconds.This is comparable with our time of onset.

K Syal et al [8] in 2011 used bupivacaine 0.125% along with clonidine 60mcg. The time of sensory onset was 8.64±1.77 minutes. This time is comparable with our time of onset. They concluded that Clonidine is a useful adjuvant to bupivacaine for epidural labour analgesia and can be considered as alternative to opiods.

Chand T et al [9] in 2012 used bupivacaine 0.125% and clonidine 50mcg for post operative lumbar epidural analgesia. The time of sensory onset was 8.64±1.542 minutes. This time is comparable with our study.

Sukhminder Jit Singh Bajwa et al [10] in 2010 used 20 ml of ropivacaine and 75mcg of clonidine. The time of sensory onset was 8.64±2.56 mins, this time is comparable with that of our study.

SamyElsayed et al [11] in 2013 used 1 mcg of dexmedetomidine with bupivacaine, the time of sensory onset was 7.2±1.8mins. This time is comparable with time of onset in our study .They compared Intra operative conditions and quality of postoperative analgesia after adding dexmedetomidine to epidural bupivacaine and fentanyl in elective caesarean section using combined spinal-epidural anaesthesia.

Manal M et al [12] in 2014 used 20ml 0.5% levobupivacaine and 1.5mcg/kg dexmedetomidine in epidural anaesthesia. The time of sensory onset was 12.60±5.90 minutes.They concluded that Dexmedetomidine is a good alternative to morphine as an adjuvant to levobupivacaine in epidural anaesthesia in mojar abdominal surgeries.

Sukhminder Jit Singh Bajwa et al [13] in 2011, used 17ml of 0.75% ropivacaine and 1.5mcg/kg of dexmedetomidine. The time of onset of sensory block to T-10 was 8.52±2.36 minutes. This time is comparable with our study.

BajwaSJ et al [14] in 2011 used ropivacaine + dexmedetomidine and ropivacaine + fentanyl with 50 patients in each group. Inj Ropivacaine ,15 ml 0.75% was administered epidurally in both the groups with addition of 1ug/kg of dexmedetomidine and 1 ug/kg of fentanyl in second group. The onset of sensory analgesia to T-10 in ropivacaine and dexmedetomidine was 7.12±2.44 minutes.This time is comparable with our study.

S Shaikh et al [15] used 15ml of bupivacaine 0.5%, the time of onset was15.76± 2.95 minutes. This time is comparable with our study.

Park et al [16] used 20ml of 0.5% bupivacaine and observed that the time of onset upto T-6 was 17.6± 7.7minutes. This time of sensory onset is comparable with our time.

Time of Motor Block Onset to Bromage 3(IN MINUTES)

In our study time of motor block onset to bromage 3 in group 1 was 20.36±34minutes, in group 2 was 17.80±4.08 and in group 3 was 14.50±5.18 minutes. The onset was earliest in group 3I as compared to group 1 and group 2. That is clonidine and dexmeditomidine as adjuvant shorten the time of motor block onset.

Shobhana Gupta et al [7] in 2010 studied the effect of clonidine as an adjuvant with bupivacaine in epidural anaesthesia. They used 1mcg/kg of clonidine with bupivacaine 1.5mcg/kg. Their time of motor onset was 15.60±3.09 minutes. This time is comparable with our time of onset.

K Syal et al [8] in 2011 used bupivacaine 0.125% along with clonidine 60mcg . The time of motor onset was 15.20±4.08 minutes. This time is comparable with our study.

Sukhminder Jit Singh Bajwa et al [10] in 2010 used 20ml of ropivacaine and 75mcg of clonidine. The time of onset was 17.34±4.48minutes. This time is comparable with our study.

SamyElsayed Hanoura et al [11] used 1mcg/kg of dexmeditomidine with bupivacaine, the time of

motor onset was 11.50±4.18 minutes. This time is comparable with our study.

Manal M et al [12] in 2014 used 20ml of 0.5% levobupivacaine and 1.5mcg/kg dexmedetomidine in epidural anaesthesia. The time of motor onset was 18.16±4.48 minutes. This time of onset is comparable with our study.

Sukhminder Jit Singh Bajwa et al [13] in 2011 used 17ml of 0.75% ropivacaine and 1.5mcg/kg of dexmedetomidine. The time of motor onset was 17.24±5.16 minutes. This time is comparable with our study.

Saravia P.S.F. Sabbag et al [17] in 2008 evaluated clinical characteristics of epidural anaesthesia performed with 0.75% ropivacaine associated with dexmedetomidine .The study included two groups :Control group and Dexmedetomidine group of 20 patients each.The onset of motor blockade in Dexmedetomidine group was 15.36±3.28 minutes. This time of onset is comparable with our study.

Time of Motor Block Regression to Bromage 0 (IN MINUTES)

In our study time of motor block regression to bromage 0 in group 1 was 152±12.2 minutes , in group 2 was 226.42±26.17 and in group 3 was 248.70±28.40 minutes .The time of motor was longest in group 3 followed by group 2 as compared to group 1 .That is both the adjuvants prolonged the time of motor block regression .

Hemodynamic Changes

Baseline systolic BP, diastolic BP, heart rate were comparable. After epidural anaesthesia, there was fall in systolic, diastolic BP and HR in each group, but fall in group 2 and group 3 was more as compared to control group. But after 45 minutes they returned to baseline values. Though fall in BP was more in group 3, but not significant. There was no stastical significant difference (P>0.05) of heart rate in between different groups. There was no statistically significant difference. Similar results were also found by Sukhminder Jit Singh et al,Vikram Arora et al, Shobhna Gupta et al, K Sayal et al. Sukhminder Kaur Bajwa et al 2010, Gurpreet Singh. They all had observations similar to our study.

Sedation (Ramsay Sedation Score)

Sedation score was more in group 3(dexmeditomidine) between 60-120 minutes after epidural anaesthesia, followed by group 2 (Clonidine) between 60-120 minutes and then in Group 2(Bupivacaine).Table II shows our results that are comparable with Bajwa SJ et al [14], They found the sedation score was more in Dexmedetomidine group than in clonidine group. Rajini Gupta et al [18] in 2011, found that sedation score was more in dexmeditomidine than other group.C

Duration of Analgesia:

The maximum duration of analgesia (338±30.15min) was in group 3 (dexmeditomidine) which was followed by group 2 (clonidne) of 302.70±20.76 min and minimum by group 1 (Bupivacaine) of 180±50 min. The difference was stasitically significant ($p<0.05$)

Side Effets

The incidence of side-effects like vomiting, headache, shivering urinary retention and dizziness were comparable in all the groups and statistically non significant. The incidence of dry mouth (8 patients in group 2, 7 patients in group 3 and 5 patients in group1) was the most common side effect but was statistically non-significant ($p >0.05$).

Conclusion

Epidural anaesthesia is a popular technique because of its numerous advantages. It is a common practice to add adjuvants to local anaesthetics in epidural anaesthesia to improve the quality of anaesthesia and analgesia. It can be concluded from our study that clonidine and dexmedetomidine are good alternatives to opioids as adjuvant to bupivacaine in epidural anaesthesia.

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