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Research Article

Effect of Clonidine as an Adjuvant to Bupivacaine in Epidural Anaesthesia

Geeta Karki[1*], Vishwadeep Singh[2], Priyank Srivastava[3], H.S. Nanda[4]
[1]Assisstant Professor, [2,3]Post Graduate student, [4]Professor and Head, Department of Anaesthesia, Sri Ram Murti Murti Smarak Institute of Medical Sciences, Bhojipura, Bareilly, U.P., PIN-243202, India

***Corresponding author**
Geeta Karki
Email: krkgits@gmail.com

Abstract: Epidural anaesthesia is the most preferred anaesthetic technique for lower abdominal and lower limb surgeries. The aim of the present study was to compare Clonidine as an adjuvant with Bupivacaine in epidural anaesthesia with respect to onset and duration of sensory and motor block, duration of analgesia hemodyanamic changes and adverse effects. The study was carried out on 60 patients of either sex ,aged 18 to 65 years of age and belonging to ASA Grade I & II physical status, scheduled for surgery under epidural anaesthesia. Patients were divided into two groups with 30 patients each. Group I was given 20ml 0.5% plain bupivacaine + 0.5ml saline and Group II was given 20ml0.5% plain bupivacaine + 2µg/kg clonidine.Sensory block was assessed by pin prick and motor block was assessed by modified bromage scale. Data were compared using paired t-test, analysis of variance (ANOVA) and chi-square test. The time of sensory onset upto T10 was shorter in group II (9.82±3.10 min) as compared to group I (15.02±2.6 min).The time of motor block onset to bromage 3 was shorter in group II (17.80±4.08 min) as compared to group I (20.36±3.4 min).The time of motor block regression to bromage 0 was longer in group II (226.42±26.17 min) as compared to group I (152±12.2 min).The time of sensory block regression and the duration of analgesia was also longer in group II. Thus clonidine seems to be a good choice as an adjuvant with bupivacaine in epidural anaesthesia.
Keywords: Epidural, Clonidine, Bupivacaine, Pin prick, Modified Bromage scale, Analgesia.

INTRODUCTION

"For all the happiness mankind can gain is not in pleasure, but in relief from pain". This was said by Dryden. The same feeling is being uttered by human beings since ages for pain is as old as mankind or even older. There are ample reasons to believe that it is inherent to life. And so is the looking for the methods of pain relief.

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].

Intrathecal and epidural anaesthesia are the most popular regional anaesthesia techniques used for lower abdominal and lower limb surgeries. Intrathecal anaesthesia has few limitations like short duration of anaesthesia, extension of anaesthesia cannot be prolonged, rapid and severe sympathetic blockade, shorter duration of postoperative analgesia and troublesome complication of postdural puncture headache (PDPH). Hence epidural anaesthesia is the most preferred anaesthetic technique for lower abdominal and lower limb surgeries The introduction of epidural anesthesia has markedly changed the method of pain relief both during surgical procedures and other pain symptoms. Epidural anaesthesia is unique in that it allows the titration of the dosage to attain the desired anaesthesia, analgesia and motor relaxation [2]. It is popular and offers several benefits to the patients, most importantly are staying awake, early family contact and early food intake [3]. It can provide desired analgesia even after the procedure has completed.

Epidural anaesthesia is a central neuraxial block technique with many applications. 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. For the anaesthetist, cardiovascular and respiratory stability, rapid postoperative recovery and the preservation of protective airway reflexes are the most important advantages of epidural anaesthesia [4].

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 requirement of local anaesthetics , hastened 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 [5]. Relief of pain during surgery is the primary aim and most important component of balanced anaesthesia. Adequate pain relief in post-operative period has always been a problem. Pain is severe on the first day after surgery and diminishes over the next 24 hours and is minimal afterwards. The main aim is to ensure that the patient gets relief at the appropriate time [6].

Thus it seems worthwhile to compare the efficacy of clonidine as an adjuvant to bupivacaine in epidural anaesthesia for intra-operative and post-operative pain relief.

The aim of the present study was to evaluate the efficacy of Clonidine as an adjuvant with Bupivacaine in epidural anaesthesia on the basis of onset and duration of sensory and motor block,duration of analgesia, haemodyanamic changes, adverse effect of drugs and sedation .

MATERIAL AND METHODS

After obtaining ethical committee approval and informed written consent from patients, the study was carried out on 60 patients of either sex, between 18 to 65 years of age and belonging to ASA Grade I & II physical status.

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.

The patients were randomly divided into two groups with 30 patients each.

Group 1 (Control): 20ml 0.5% plain bupivacaine + 0.5ml saline (preservative free)

Group 2 (Clonidine): 20ml 0.5% plain bupivacaine + 2µg/kg clonidine.

In each group equal volume was injected. All patients were preloaded with 15ml/kg of Ringer Lactate .In the operation theatre pulse oximetry (Spo_2), 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.

Onset, duration and quality of anaesthesia were assessed. Sensory block was assessed bilaterally by short hypodermic needle in mid clavicular line. Motor block was assessed by modified bromage scale. Sedation 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 are 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 was done using the Chi-square test. The p value reported at the 95% confidence interval. $p<0.05$ was considered statistically significant. $p>0.05$ was considered statistically non significant.

RESULTS

The objective of the present study was to evaluate the efficacy of Clonidine as an adjuvant with Bupivacaine in epidural anaesthesia on the basis of onset and duration of sensory and motor block, duration of analgesia, haemodyanamic changes and adverse effects. The patients undergoing lower abdominal or lower limb surgery under epidural anaesthesia were randomly divided into two groups with 30 patients each.

The age distribution was comparable and statistically insignificant in both groups having p value> 0.05. The sex distribution was also comparable in the two groups and statistically insignificant having p value >0.05 (Table 1). The types of surgeries in the two groups were also comparable (Fig. 1).

Table 1: Demographic distribution of patients

Groups	Group I (control) Mean ± SD	Group II (clonidine) Mean ± SD	p value
Total no. of patients	30	30	
Age (years)	41.36 ± 6.46	40.36 ± 5.44	> 0.05
Sex (M:F)	16: 14	13:17	> 0.05

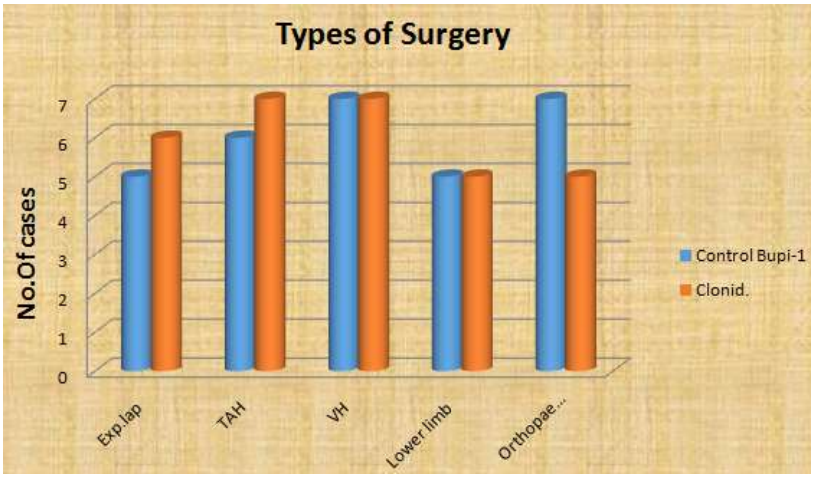

Fig. 1: Distribution of types of surgery in the two groups

The time of sensory onset upto T10 was 9.82±3.10 minutes in group II (Clonidine) and 15.02±2.6 minutes in group I (Control). The difference in the two groups was statistically significant (Table 2). So it indicates that clonidine as an adjuvant shortens the time of sensory onset. The time of motor block onset to bromage 3 was 17.80±4.08 minutes in group II (clonidine) and 20.36±3.4 minutes in group I (control) (Table 3). So it indicates that addition of clonidine as an adjuvant shortens the time of motor block onset. The time of sensory block regression was 298.70±36.54 mins in group II (clonidine) and 196±22 min in group I (control) (Table 4). So it indicates that addition of clonidine as an adjuvant to bupivacaine prolongs the time of sensory regression. The time of motor block regression to bromage 0 was 226.42±26.17 minutes in group II (clonidine) and 152±12.2 minutes in group I (control) (Table 5). So it indicates that addition of clonidine as an adjuvant with bupivacaine prolongs the time of motor block regression. As shown in Table 6 the duration of analgesia was prolonged by adding clonidine to bupivacaine. The duration of analgesia was 180±50mins in group I (control) and 302.70±20.76 mins in group II (clonidine).The Ramsay sedation score was more with clonidine than in the control group as shown in Fig. 6. As shown in Table 7 and 8, the haemodynamic changes were comparable at base line. Blood pressure started falling after 5min of epidural anaesthesia. But after 45min it started returning to base line values. There was no statistically significant difference ($p \geq 0.05$) in heart rate between two groups (Table 9).

Among the side effects, dry mouth and nausea were the most common side effects in both groups but the incidence was more in group II than in group I. Vomiting was similar in both the groups (Fig. 5).

Table 2: Time of Sensory block upto T-10 (in minutes)

Groups	Group 1	Group 2	p value
Mean ±SD (Minutes)	15.02 ± 2.6	9.82±3.10	<0.05
No. of cases	30	30	

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

Groups	Group 1 (Control)	Group2 (Clonidine)	p value
Mean ±SD (Minutes)	20.36±3.4	17.80±4.08	<0.05
No. of cases	30	30	

Table 4: Time of sensory regression to S-1(in minutes)

Groups	Group 1 (Control)	Group 2 (Clonidine)	p value
Mean ±SD (Minutes)	196±22	298.70±36.54	<0.05
No. of cases	30	30	

Table 5: Time of Motor block regression to Bromage 0 (in minutes)

Groups	Group 1 (Control)	Group 2 (Clonidine)	p value
Mean ± SD (Minutes)	152±12.2	226.42±26.17	<0.05
No.of cases 30	30	30	

Table 6: Comparison of duration of analgesia

Groups	Group I	Group II	p value
Mean± SD (Minutes)	180±50	302.70±20.76	<0.05

Table 7: Variation in systolic Blood pressure (in minutes)

Time (minutes)	Group I (mmHg) Mean ± SD	Group II (mmHg) Mean ± SD	p value (mmHg) Mean ± SD
0	128±6.02	129.5±5.04	>0.05
5	127.2±5.03	127.4±2.04	>0.05
10	125.6±3.04	121.2±4.06	<0.05
15	118.57±5.41	110.23±6.24	<0.05
30	116.97±7.22	109.06±5.36	>0.05
45	114.23±6.12	107.78±8.40	>0.05
60	113.74±5.32	107.03±5.30	>0.05
75	112.66±5.41	106.23±6.12	>0.05
90	110.78±6.24	105.20±5.68	>0.05
105	111.28±3.04	107.70±4.28	>0.05
120	114±5.78	109.38±7.73	>0.05

As indicated by Mean and P values in above tables, the systolic BP was comparable at base line (p>0.05). After 5 minutes, the systolic BP started falling in each group, but fall in SBP was statistically significant (p <0.05) in group 2 as compared to control (Bupivacaine). SBP started returning to base line after 45mins.

Table 8: Variation in Diastolic Blood Pressure (in minutes)

Time (Minutes)	Group I	Group II	p value
0	79.60 ± 5.30	80.20±4.08	> 0.05
5	78.10±4.78	79.14±4.34	> 0.05
10	76.36±4.12	74.42±4.18	< 0.05
15	72.76±2.24	63.66±2.18	<0.05
30	70.18±1.24	62.62±2.18	>0.05
45	69.34±2.36	62.10±1.96	>0.05
60	69.66±3.46	62.56±3.58	>0.05
75	70.76±3.38	62.60±3.08	>0.05
90	72.74±5.64	64.66±5.76	>0.05
105	74.76±4.48	66.38±4.42	>0.05
120	76.10±4.96	68.33±4.90	>0.05

As indicated by Mean and P value in table DBP was comaparable at base line (p>0.05)After 5mins DBP fell in each group. But fall in DBP was statistically significant (p<0.05) in group2 as compared to control group. After 45 mins there was no statistically significant change in (p>0.05) in DBP in different groups.

Table 9: Variation in Heart Rate (in minutes)

Time (Minutes)	Group I	Group II	p value
0	81.14±10.48	83.70±5.90	>0.05
5	78.60±8.28	79.16±8.10	>0.05
10	76.76±7.45	77.14±8.23	>0.05
15	72.60±3.40	69.38±5.24	>0.05
30	72.60±6.20	67.16±3.24	>0.05
45	69.64±4.48	65.16±4.37	>0.05
60	67.14±3.28	63.17±3.19	>0.05
75	66.66±2.28	62.60±2.27	>0.05
90	68.15±3.74	64.12±3.82	>0.05
105	70.0±3.15	65.04±3.0	>0.05
120	72.0±1.08	67.83±1.09	>0.05

As indicated by Mean and P-value, the Heart Rate was comparable at base line (p>0.05) though there was fall in heart rate, but there was no significant difference (p>0.05) of heart rate in between different groups.

Table 10: Side Effects

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

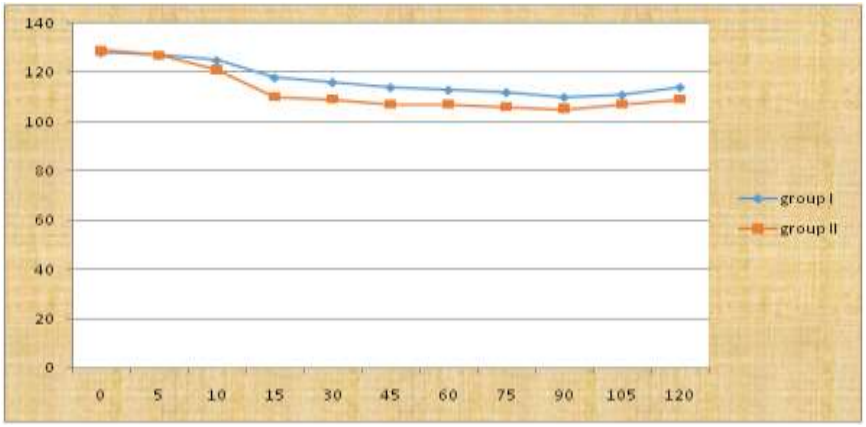

Fig. 2: Changes in Systolic blood pressure

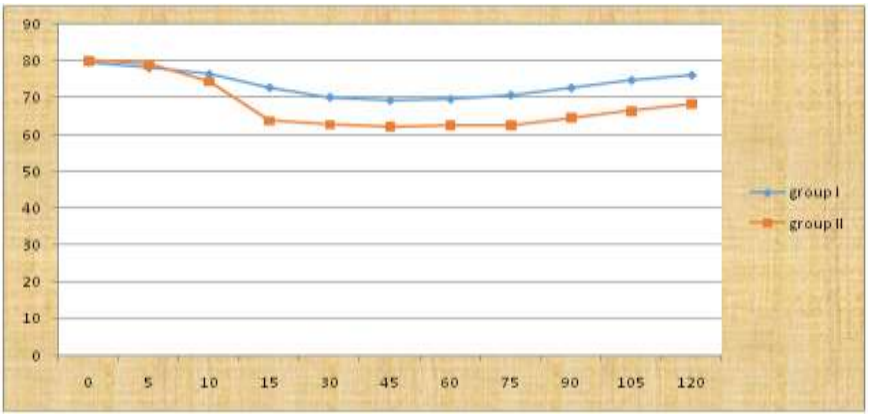

Fig. 3: Changes in Diastolic blood pressure

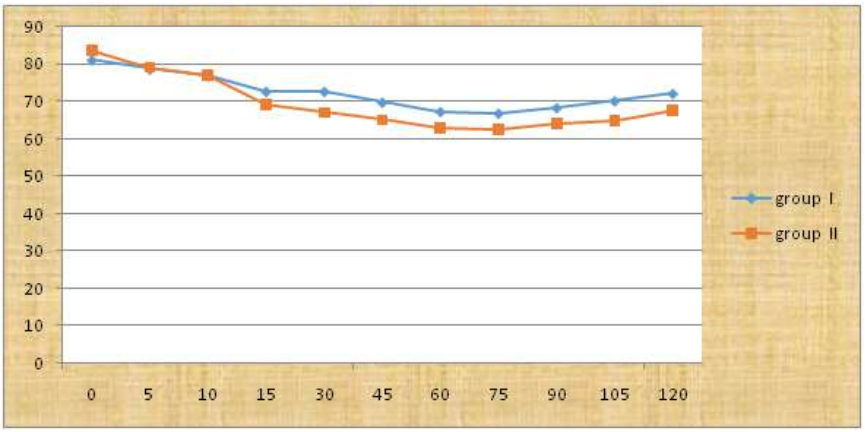

Fig. 4: Changes in Heart rate

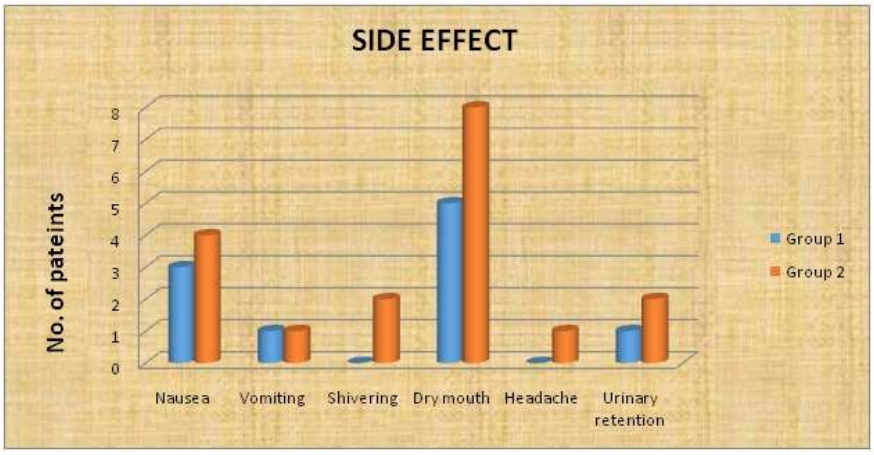

Fig. 5: Incidence of side effects

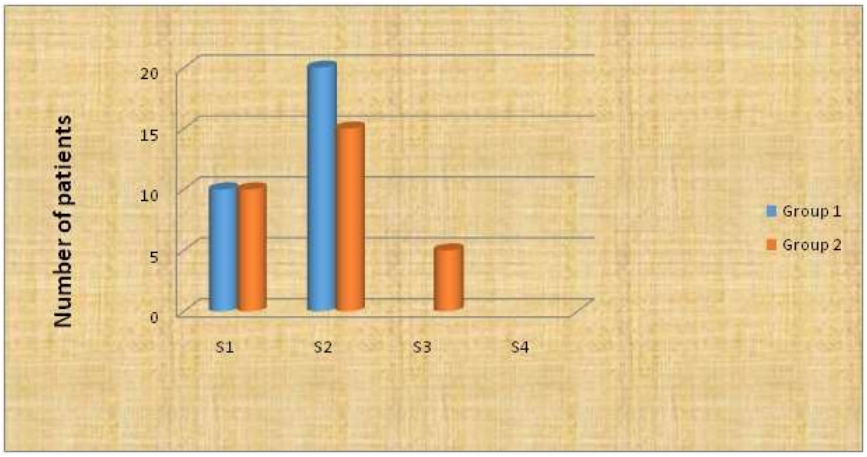

Fig. 6: Distribution of patients according to sedation

DISCUSSION

The present study was designed to compare the efficacy of epidural clonidine 2mcg/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 60 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 I was 41.36 ± 6.46years and in group II was 40.36 ± 5.43years. The age was comparable in both groups. This is shown in Table 1.

Distribution according to sex was also comparable among the three groups. This is shown in Table 1.

Time of sensory onset

In our study time of sensory onset in group I was 10.02 ±2.6mins and in group II 9.82± 3.10mins. The onset of sensory block was shorter in group II as compared to control, thus clonidine as an adjuvant shortens the time of sensory onset as compared to bupivacaine alone.

Gupta S *et al*. [7] 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. Syal K *et al*. [8] 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 opioids. Chand T *et al*. [9] studied comparison of bupivacaine–clonidine and bupivacaine-fentanyl for post operative lumbar epidural analgesia. They used bupivacaine 0.125% and clonidine 50mcg. The time of sensory onset was 8.64 ± 1.542 minutes. This time is comparable with our study. Bajwa S *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 our time of onset. Bajwa S *et al*. [11] used 17ml of 0.75% of ropivacaine and 2mcg/kg of clonidine. The onset time of sensory block at T-10 was

9.72 ± 3.44mins. This time is comparable with our time of onset.

Time of Motor Block Onset to Bromage 3 (In Minutes)

In our study time of motor block onset to bromage 3 in group I was 20.36 ± 34minutes and in group II 17.80 ± 4.08 minutes. The onset was earlier in group II as compared to group I. That is clonidine as adjuvant shortens the time of motor block onset which is evident in various other studies conducted in the past. Gupta S *et al*. [7] studied the effect of clonidine as an adjuvant with bupivacaine in epidural anaesthesia. Their time of motor onset was 15.60 ±3.09 minutes. This time is comparable with our time of onset. Syal K *et al*. [8] 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. Bajwa SJ *et al*. [10] in their study found the time of onset was 17.34 ± 4.48minutes. This time is comparable with our study. Bajwa SJ *et al*. [11] in 2011 found the time of motor onset was 19.52 ± 4.06minutes. This time is comparable to that in 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 I was 152 ± 12.2 minutes and in group II 226.42 ± 26.17 minutes .The time of motor block regression was longer in group II as compared to group I .That is clonidine prolonged the time of motor block regression .

Hemodynamic Changes

Baseline systolic BP, diastolic BP and heart rate, oxygen saturation were comparable. After epidural anaesthesia, there was fall in systolic, diastolic BP and HR in each group,but fall in group II was more as compared to control group. But after 45 minutes they returned to baseline values. Though fall in BP was more in group II,but not statistically significant (Table 7, 8). There was no statistically significant difference ($p>0.05$) in heart rate in between the groups. Similar results were also found by Bajwa SJ *et al*. [10, 12], Gupta S *et al*. [7], Sayal K *et al*. [8]. They all had observations similar to our study.

Sedation (Ramsay Sedation Score)

Sedation score was more in group II (Clonidine) between 60-120 minutes than in Group I (Bupivacaine). The results are comparable to the results of the studies conducted in the past. Jyoti *et al*. [13] conducted a study of combination of epidural bupivacaine with clonidine and bupivacaine for post operative analgesia. They found that in the bupivacaine group, most of the patients were awake, alert (sedation score 1) and only 16-17% of patients were drowsy(sedation score2) in between 45-90 mins after epidural dose no patient was found asleep(sedation score 3). In bupivacaine + clonidine group after 15mins of drug administration 29 patients were asleep (sedation score 3) and from 30mins until 2 hours 100% patient were asleep (sedation score 3) and upto 70% patients were asleep at 3 hrs, by 4 hours all the patients were awake and alert (sedation score 1). This is similar to that in our study. Similar results were also found in the studies conducted by Boica B *et al*. [14], Eisenach JC *et al*. [15], and Mendez R *et al*. [16].

CONCLUSION

It can be concluded from this study that clonidine when given epidurally with bupivacaine produces synergistic effect of profound and prolonged motor block, prolonged sensory block and analgesia prolonged to the postoperative period with minimal side effects. Thus clonidine can be a good alternative choice to opioids as an adjuvant to bupivacaine for epidural blockade in lower abdominal and lower limb surgeries.

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