ejpmr, 2020,7(1), 279-286

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

EFFICACY OF LOW DOSE INTRATHECAL CLONIDINE AS AN ADJUVANT TO 0.5% HYPERBARIC BUPIVACAINE FOR SPINAL ANAESTHESIA

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Article Received on 28/10/2019 **Article Revised on 17/11/2019** **Article Accepted on 07/12/2019**

ABSTRACT

Introduction: Spinal anaesthesia is a safe, reliable, inexpensive technique with the advantage of providing surgical anaesthesia and prolonged postoperative pain relief by using various adjuvant drugs along with local anaesthetic agents. The possibility that intracthecal administration of Clonidine may produce better analgesic effect compared to epidural administration, with fewer side effects and at lower doses, provides rational of evaluating intrathecal clonidine. Primary objective: To determine effectiveness of sensory and motor blockade with bupivacaine alone and Bupivacaine with low dose clonidine. Secondary objective: To study hemodynamic changes, side effects and postoperative analgesia between two groups. **Methods:** After institutional review, board approval and written informed consent, 100 patients with ASA physical status I-II, aged 20-50 years scheduled for elective lower abdominal and lower limb surgeries were included in this study. Patients with comorbidities like diabetes, hypertension and any absolute contraindication for spinal anaesthesia were excluded. Patients were randomly divided into 2 groups with 50 patients in each group. Group B received 0.5% hyperbaric Bupivacaine and Group BC received 0.5% hyperbaric Bupivacaine+ 1microgram/kg of inj.clonidine. Adequate block to initiate surgery was defined as a sensory block bilaterally. The onset, degree and duration of motor block were measured in both legs by using a modified Bromage scale. The sedation was judged by Ramsay sedation score and postoperative analgesia was judged by VAS score. **Observations and Results:** The differences in parameters were statistically significant. Onset was seen earlier in Group BC than in Group B. Sensory maximum Level T was seen at higher level in Group BC than in Group B.Lesser time was required in Group B to achieve two segment regression than group BC. Higher duration of sensory blockade was seen in Group BC than in group B. Higher duration of Motor blockade was seen in Group BC than in group B. There was no significant difference in basal and minimum pulse rate, basal systolic blood pressure and diastolic blood pressure, minimum systolic blood pressure and diastolic blood pressure, mean basal SPO2 between two groups. In the study there was no complications noted among all the subjects in both the groups. **Conclusion:** This study concludes that intrathecal clonidine in the dose of 1microgram/kg along with 12.5mg 0.5% hyperbaric bupivacaine leads to earlier onset and prolonged duration of sensory and motor blockade, excellent postoperative analgesia with minimal side effects with good hemodynamic stability.

INTRODUCTION

Spinal anesthesia is a safe, reliable and inexpensive technique with the advantage of providing surgical surgical anesthesia and prolonged post operative pain relief by using various adjuvant drugs along with local anesthetic agents. It blunts operative pain and autonomic, somatic and endocrine responses.[1,2] Hyperbaric bupivacaine(0.5%), an amide type of local anesthetic is commonly employed in intrathecal injections for lower abdominal and lower limb surgeries. However intrathecal bupivacaine alone may be insufficient to provide complete analgesia despite the high sensory block.[1,3] There have been reports that sensory block above T4 was obtained with 15-20mg but intraoperative analgesic supplementation was needed in almost all the patients. Therefore different drugs like opiods and non-opiods are used as an adjuvant drugs along with local anesthetic agents.[4] Recently alpha-2 adrenoreceptors agonists are being extensively evaluated as adjuvant to local anesthetic agents because of their sedative, analgesic and hemodynamic stabilizing effects in neuraxial anesthesia. Clonidine is known to prolong both sensory and motor block of local anesthetics. Intrathecal administration of clonidine acts on alpha-2 adrenoreceptors in spinal cord and blocks the conduction of C and A-delta fibers, increases potassium conductance and intensifies block of local anesthetics. It thus exerts its antinociceptive effect and provides dose-dependent analgesia. The possibility that intrathecal administration of clonidine may produce better analgesic effect compared to epidural administration, with fewer side effects and at lower doses, provides the rationale of evaluating intrathecal clonidine. Therefore it was proposed to conduct the study

of efficacy of low dose intrathecal clonidine along with 0.5% hyperbaric bupivacaine.

AIM: To study analgesic effect of low dose intrathecal clonidine as an adjuvant to 0.5% hyperbaric bupivacaine.

OBJECTIVES

1. To determine effectiveness of sensory and motor blockade with bupivacaine alone and bupivacaine with low dose clonidine.
2. To study hemodynamic changes in both groups.
3. To study side effects associated with administration of the study drug.
4. To compare the post-operative analgesia between two groups.

MATERIALS AND METHODS

After institutional review, board approval and written informed consent, 100 patients with ASA physical status I-II, aged 20-50 years scheduled for elective lower abdominal and lower limb surgeries were included in this study. Patients with comorbidities like diabetes, hypertension and any absolute contraindication for spinal anaesthesia were excluded. Patients having any absolute contraindications for spinal anesthesia were excluded. Patients were randomly divided into 2 groups with 50 patients in each group.

Group B: received 2.5ml(12.5mg) of 0.5% hyperbaric bupivacaine.

Group BC: received 2.5ml(12.5mg) of 0.5% hyperbaric bupivacaine+ 1microgram/kg of inj.clonidine.

Intravenous line was obtained with 18gauge cannula and preloading done with ringer lactate 7ml/kg. premedication is done with inj.ranitidine 50mg and inj.ondensatron 4mg IV. Monitoring was done using multiparameter monitor having pulse oximetry, ECG, NIBP, and SPO2. Under all aseptic precautions with patient in left lateral position, lumbar puncture performed at the level of L3-L4 interspace through a midline approach using 25G Quincke spinal needle and study drug injected after confirmation of needle tip in the subarachnoid space by free and clear flow of CSF.

The following parameters were noted

- Onset of sensory and motor blockade.
- Maximum dermatomal level of sensory blockade attained and the time taken for the same.
- Maximum level of motor blockade attained and the time taken for the same.
- Hemodynamic changes and side effects if any.
- Time for two segments sensory regression.
- Total duration of sensory and motor blockade, duration of surgery and duration of effective analgesia.

Sensory level was determined by pinprick tested every 1minute from time 0 that is injection of drug in subarachnoid space. Quality of motor blockade was assessed by modified Bromage scale. Intraoperative pulse rate, respiratory rate, blood pressure, oxygen saturation monitoring was done at 1,3,5,10 minutes and every 5minutes till end of the surgery. Quality of motor blockade is assessed according to modified Bromage scale.

Modified Bromage Scale

Grade 0- no motor block
Grade 1-inability to raise the extended leg
Grade 2-inability to flex the knee, able to flex the ankle
Grade 3-inability to flex the ankle complete motor block

Sedation was judged by Ramsay Sedation Score.

Postoperative analgesia was judged by VAS score and rescue analgesia was administered when VAS score >4 inj.diclo 75mg IM.

STATISTICAL ANALYSIS

Parametric data was expressed as mean+/- standard deviation. Analysis of data was done by using students unpaired t-test. P value less than 0.05 was considered to be significant.

RESULTS

1.Mean time for onset of sensory blockade in the control group was 4.336+/-1.555min and in the study group it was 2.220+/-0.528min and it statistically significant.

Table 1.

PARAMETER	GROUP B	GROUP BC	P VALUE
Onset of sensory Blockade	4.336+/-1.555	2.200+/-0.528	0.001

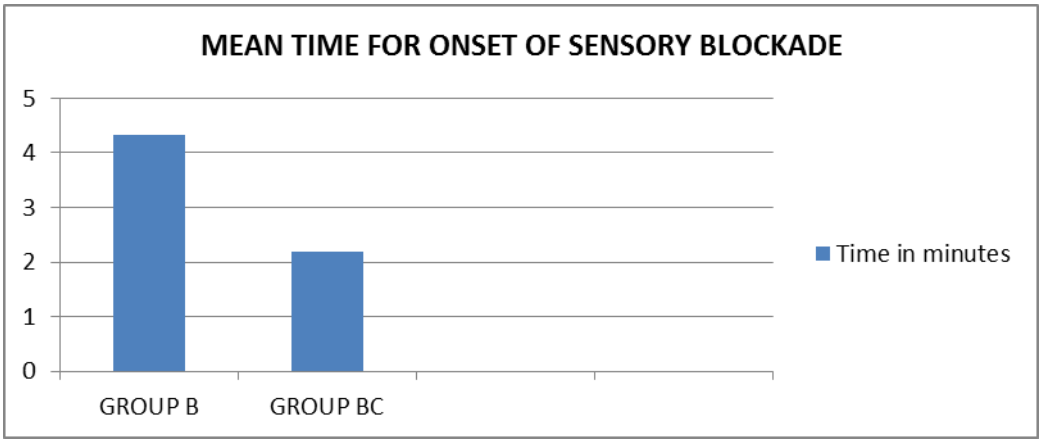
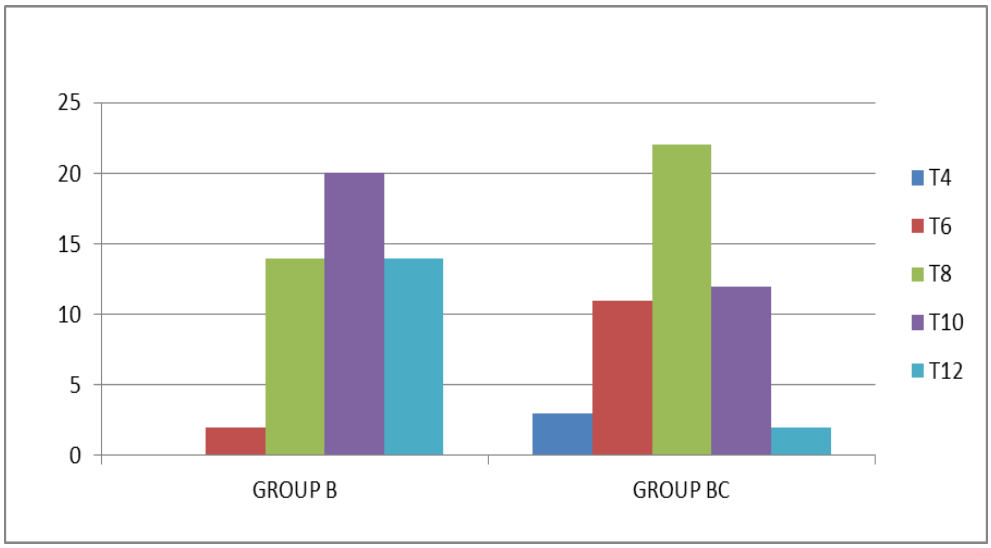


Figure 1.

2. Mean dermatomal level of sensory analgesia achieved in group was 9.840+1.707 and in group BC was 7.960+1.873 and it was statistically significant.

Table 2.

MAXIMUM LEVEL ACHIEVED(T)	GROUP B (NO. OF PATIENTS)	GROUP BC (NO.OF PATIENTS)	P VALUE
T4	0	3	P<0.05
T6	2	11	
T8	14	22	
T10	20	12	
T12	14	2	
MEAN	9.840+1.707	7.960+1.873	



MEAN DERMATOMAL SENSORY LEVEL ACHIEVED
Figure 2.

3. Mean time for onset of motor blockade in group B was 6.980+/-1.720min and in group BC was 2.408+/-0.612min. Thus it was earlier in group BC than group B and was statistically significant.

Table 3.

PARAMETER	GROUP B	GROUP BC	P VALUE
Mean time for onset of motor blockade(min)	6.980+/-1.720	2.408+/-0.612	0.001

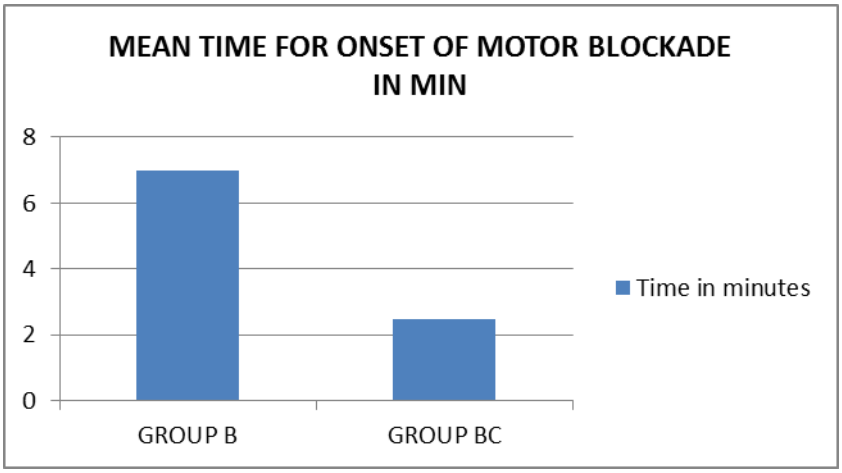


Figure 3.

4.Degree of motor blockade was assessed with modified Bromage scale. Complete motor blockade was 96% of patients in group BC while score was 80% in group B and was statistically significant.

Table 4

NO. OF PATIENTS			
DEGREE OF MOTOR BLOCKADE	**GROUP B**	**GROUP BC**	**P VALUE**
0	0	0	0.0277
I	0	0	
II	10	2	
III	40	48	
TOTAL	50	50	

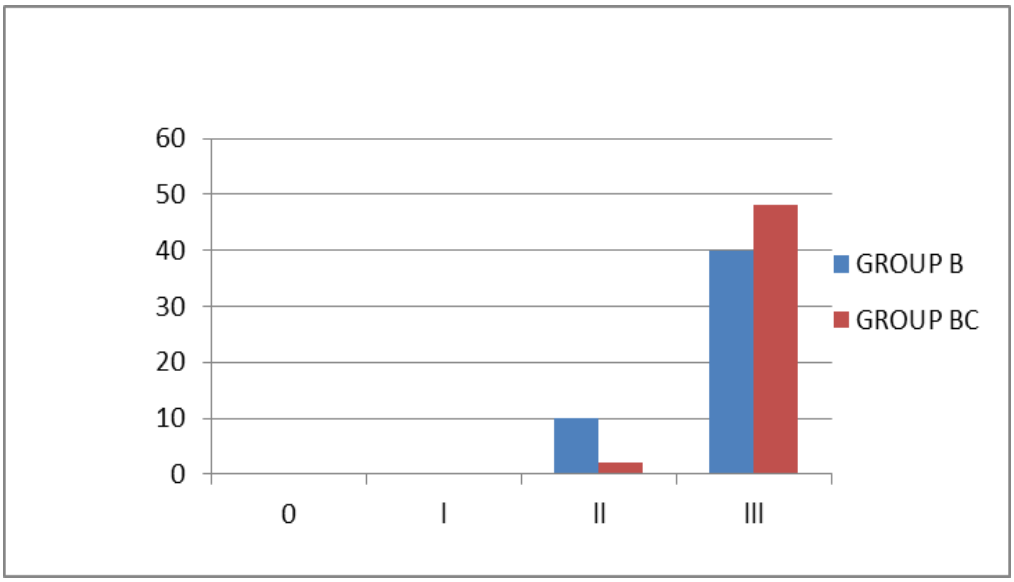


Figure 4.

5.Mean time of two segment regression of sensory analgesia in group B was 74.88+/-11.155min and in group BC it was 130.72+/-11.794min. This was statistically significant.

Table 5.

PARAMETER	GROUP B	GROUP BC	P VALUE
Mean time for 2 segment regression (min)	74.88+/-11.155	130.72+/-11.794	<0.001

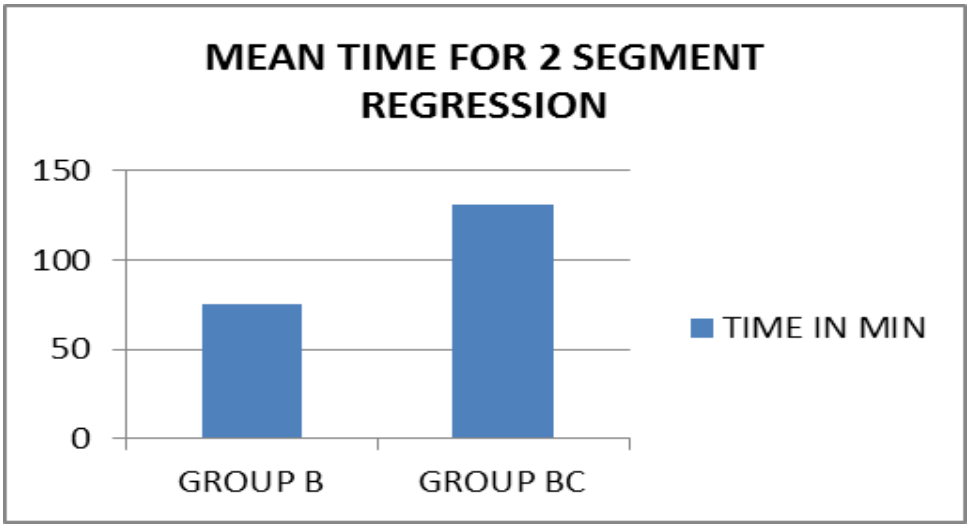


Figure 5

6.The duration of rescue analgesia in group B was 152.28+16.267min while it was 343.04+29.178 in group BC. This difference was statistically significant.

Table 6

GROUP	NO. OF PATIENTS	MEAN DURATION OF ANALGESIA IN MIN	S.D.	t-Value	P
GROUP B	50	152.28	16.267	40.378	0.001
GROUP BC	50	343.04	29.178		

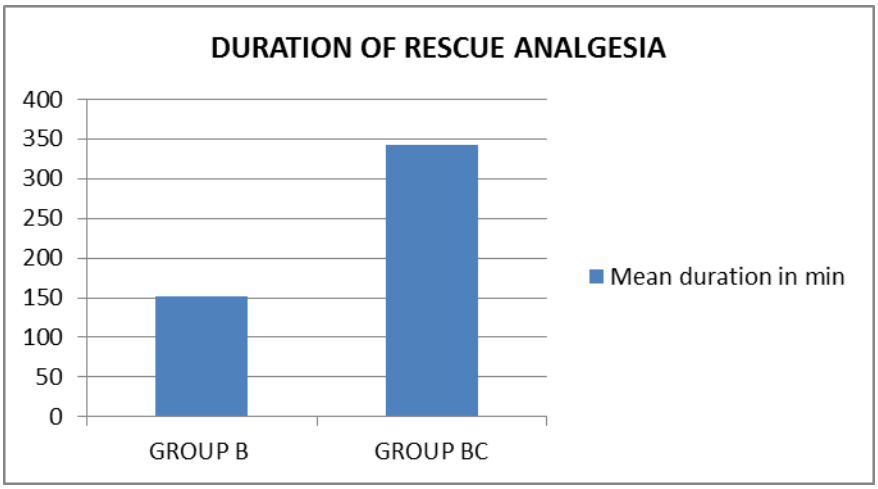


Figure 6.

7.Mean basal pulse rate in Group B was 89.44+/-9.664 per min and in Group BC was 91.56+/-4.477 per min. This was statistically significant.

Table 7.

PARAMETER	GROUP B	GROUP BC	P VALUE
Basal PR	89.44+/-9.664	91.56+/-4.477	>0.05
Minimal PR	73.76+/-5.850	76.240+/-7.224	>0.05
Maximum PR	100.58+/-4.891	101.920+/-4.628	>0.05

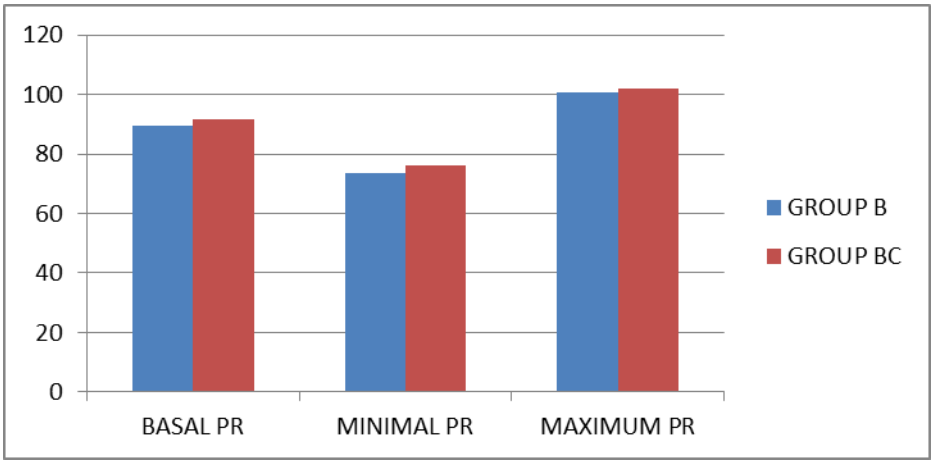


Figure 7.

8.Mean basal systolic arterial pressure was 126+/-5.212mmhg in group B and 126+/-4.736mmhg in group BC but this difference was statistically insignificant. Mean diastolic blood pressure was 82.820+/-3.121mmhg in group B and 83.820+/-3.078mmhg in group BC but this difference was statistically insignificant. The changes in SPO2 in both groups was also statistically insignificant.

9.The complications like nausea, vomiting, hypotension, bradycardia, shivering and headache in both groups was also statistically insignificant.

10.Sedation score in group B was 1.34+0.479 and in group BC it was 2.22+0.418. The difference among two groups was statistically significant.

Table 8

GROUP	NO.OF PATIENTS	MEAN SEDATION SCORE	S.D.	t-value	P
GROUP B	50	1.34	0.479	9.789	0.001
GROUP BC	50	2.22	0.418		

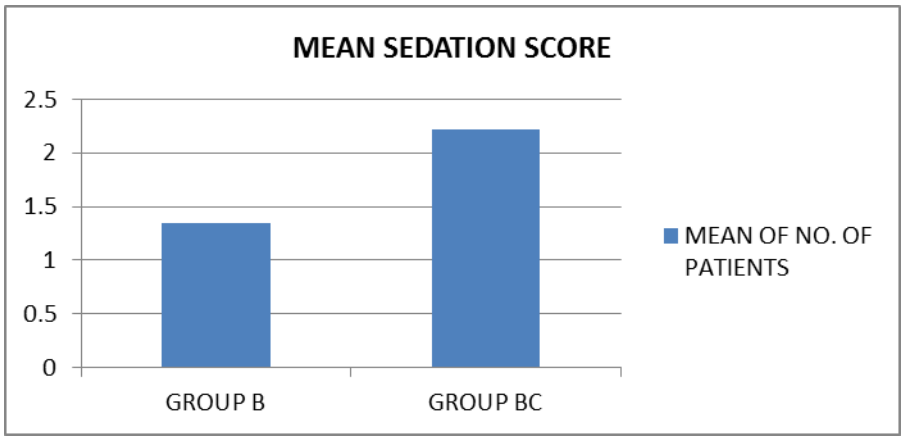


Figure 8.

DISCUSSION

The subarachnoid block had occupied an important place in the practice of anesthesia since the time it is known. After the discovery of opiate receptors in the substantia gelatinosa of spinal cord intraspinal narcotic analgesia came into existence as a new method of analgesia. However a wide variety of clinical relevant non nociceptive side effects may occur. Clonidine is a selective partial alpha-2 adrenergic agonist with selectivity ratio of about 200:1 in favor of alpha-2 receptors. It stimulates inhibitory alpha-2 adrenergic receptors to reduce central neural transmission in the spinal neurons. The alpha-2 adrenoreceptors are located on the afferent terminals of both peripheral and spinal neurons, on neurons in the superficial laminae of the spinal cord and within several brainstem nuclei implicated in analgesia(32). In this study 100 patients were divided in two groups of 50 each. Group B received 0.5% hyperbaric bupivacaine 2.5 ml(12.5mg) intrathecally. Group BC received 0.5% hyperbaric bupivacaine 2.5ml(12.5mg) and 1microgram/kg clonidine intrathecally. The control group B and the study group BC were comparable with respect to their demographic parameters like age, height, weight and sex

with no statistical difference. Duration of surgeries and types of surgeries in two groups was also comparable and statistically found insignificant. In our study the mean time taken for onset of sensory blockade is 4.336+1.555min in control group and 2.200+0.527 min in clonidine group. Saxena H et al(23) in 2010 did the study in dose dependent manner and in this study there was significant reduction in onset time. Similar significant reduction in mean onset of sensory blockade was found in study done by Grandhe R P et al(34) and Kanazi G E et al(24). In the present study maximum level of sensory blockade was T6 in control group and T4 in study group. In group B mean level of analgesia was 9.840+1.707 while in group BC was 7.960+1.873. In group BC more number of patients had higher level than in group B. This difference was found to be statistically significant. This result concurs to study done by De Kock (39) Dobridenjov(17) and Strebel S et al. In their study also maximum sensory level attained in clonidine group was T8 and T6. In our study in group B mean time to achieve maximum sensory level was 6.444+0.504min and in group BC was 3.721+0.697min. There was statistically significant decrease in mean time taken for maximum sensory blockade in clonidine group. In a study conducted by Saxena H et al (23) mean time taken for maximum sensory level was 7.3+1.25 in control, 6.8+1.2min in group BC 15microgram, 7.4+1.31min in group BC 30microgram and 6.7+1.12min in group BC37.5microgram which was more than the value in our study. This could be due to more dose of clonidine used in our study. Mean duration for two segment regression in control group in our study was 74.88+11.155min while it was 130.72+11.794 min with study group(group BC). There was statistically significant increase in mean time for 2 segment regression in clonidine group as compared to control group. This compares with the study conducted by Kanazi G E et al(24). Our study was also consistent with studies done by Dobrydnjov I et al(17), Saxena H et al(23), Sethi B S et al(4). In the present study mean total duration of sensory blockade in group B was 130.4+13.242min while in group BC was 307.4+41.933min. In a study conducted by Kanazi et al in 2006 total duration of sensory blockade in group B was 190+48 min while it was 272+38min in group BC. In our study onset of motor blockade in group B was 6.980+1.720min and in group BC 2.408+0.612min. There was statistically highly significant decrease in mean time for onset of motor blockade in clonidine group. In a study conducted by Saxena H et al(23) onset of motor blockade was 7.41+0.55 min in control group and 2.20+0.50min in group BC 37.5 microgram clonidine used. This result concurs with our result. In a study conducted by Kanazi GE et al(24), Saxena et al(23), De Kock M et al(39) where authors observed a significant decrease in mean time for onset of motor blockade which conquers with our study. In our study time required for maximum motor blockade in group B was 8.920+0.944min and in group BC was 6.772+0.894min. There was statistically significant decrease in the time required to achieve maximum motor blockade in clonidine group. In a study conducted by Agreta et al(26) in 2012, the mean time of achievement of motor block (Bromage 3) was significantly shorter in the group BC compared with group B which conquers with our study. The duration of motor blockade was 147.80+13.893min in control group and 307.34+46.029min in clonidine group. There was statistically significant difference in two groups. It is comparable with study done by Kaabachi O et al (60) who observed mean duration of motor blockade to be 252+79 min when using clonidine of 1microgram/kg. In our study mean duration of rescue analgesia was 152.28min with group B while it was 343.04min with group BC, this data was statistically significant. Similar to our study Sethi B S et al (4) found that there is prolongation of duration of analgesia in clonidine group. Mean Basal, Minimal and Maximum pulse rate were comparable in both the groups($P > 0.05$).There was no significant difference in Basal and Minimum SBP as well as Basal DBP and Minimum DBP between two groups. Patients were hemodynamically stable in both groups. Sedation was assessed by Ramsay sedation score. None of the patients in whom clonidine was used had a sedation score of more than 3.

CONCLUSION

From the present study it can be concluded that intrathecal clonidine in the dose of 1microgram/kg along with 12.5mg 0.5% hyperbaric bupivacaine lead to earlier onset and prolonged duration of sensory and motor blockade, excellent postoperative analgesia, with minimal side effects, with good hemodynamic stability. In conclusion intrathecal low dose clonidine in a dose (1microgram/kg body weight) along with 0.5% hyperbaric bupivacaine is an addition into anesthesiologist's armamentarium for spinal anesthesia in patients undergoing elective lower abdominal and elective lower limb surgeries.

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