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Comparison between Intrathecal Bupivacaine and Bupivacaine with Two Different Doses of Clonidine in Lower Limb and Lower Abdominal Surgeries

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Abstract: ***Clonidine, a centrally acting α2 adrenergic agonist has been under use as an adjuvant with hyperbaric bupivacaine for prolonging analgesia and maintaining hemodynamic stability during lower limb orthopedic and lower abdominal surgeries. This study is designed to compare the clinical effects of addition of two different doses of clonidine in the patients undergoing lower limb and lower abdominal surgeries. Materials and Methods: Our study consisted of 78 patients aged between 18-60 years of either sex, ASA physical status I and II undergoing elective lower limb surgeries were randomly selected for the study and were divided into three groups of 26 each. Group B-Received 0.5% hyperbaric Bupivacaine 15 mg intrathecally. Group C1-Received 0.5% intrathecal hyperbaric Bupivacaine 15 mg + Clonidine 15 mcg Group C2-Received 0.5% intrathecal hyperbaric Bupivacaine 15mg + Clonidine 30 mcg. Results: Administration of intrathecal clonidine to 0.5% hyperbaric Bupivacaine significantly prolonged duration of motor blockade. Total duration of analgesia was compared between three groups. Group C2 had longer duration of analgesia time with 285±17.40 minutes. Conclusion: Intrathecal addition of clonidine significantly prolongs the duration of motor block providing good postoperative analgesia as well as improved quality of block.***

Keywords: Intrathecal Bupivacaine, Clonidine, Sensory and Motor blockade

1. Introduction

Spinal anaesthesia is the most convenient anaesthetic technique that offers many advantages over general anesthesia like reduced stress response and improved postoperative pain relief. It is the most preferred technique for lower abdominal and lower limb surgeries. Even when a long acting local anaesthetic like bupivacaine is used, the duration of anaesthesia is short and higher doses of analgesics are required in post-operative period. Therefore achieving a subarachnoid block that provides high quality post-operative analgesia of consistently prolonged duration is an attractive goal.

Spinal adjuvant drugs have been used since the beginning of subarachnoid anaesthesia. Adrenaline, an alpha-2 agonist, was the first drug used to enhance duration of spinal anaesthesia, and morphine was the first opioid injected with eucaine in the lumbar spinal space to relieve vertebral pain. Opioids such as morphine, Fentanyl have been used as adjuvants to bupivacaine but they are associated with many side effects such as pruritis, nausea and vomiting, unpredictable respiratory distress etc[1]. So the use of newer adjuvants like Clonidine, Dexmeditomedine have been studied.

Clonidine is a selective alpha 2 adrenergic agonist and an imidazoline compound with alpha-2: alpha-1 selectivity ratio of approximately 220: 1.2 These properties were first described by Paalzow in 1974.3

Alpha-2 adrenergic agonists are the newer neuraxial adjuvants being studied to potentiate the intrathecal anaesthetics in terms of intraoperative analgesia and duration of sensory and motor block. The primary mechanism of action is believed to be at the level of spinal cord. This includes presynaptic and postsynaptic sites of action. Presynaptically alpha-2 receptor activation inhibits release of substance P from afferent C fibres within dorsal horn. Post synapticaly it inhibits development and subsequent transmission of integrated pain signs within second order neurons of substantia gelatinosa[4].

The antinociceptive properties of clonidine indicate that it might be useful as an alternative to intrathecal opioids for postoperative analgesia, thus avoiding the main adverse effects, such as respiratory depression, pruritus and urinary retention. The intrathecal application of clonidine increases the duration of both sensory and motor block, as well as postoperative analgesia. Studies conducted in past have used clonidine with different doses ranging from 15µg-150µg intrathecally as an adjuvant. Higher doses of clonidine have shown hemodynamic instability and systemic side effects at the cost of better analgesia[4, 5]. No ideal dose has yet been found that can result in optimum analgesia with minimal side-effects.

Therefore this study was designed as an attempt to evaluate the effects of two different doses of clonidine in co-administration with bupivacaine during spinal anaesthesia, regarding the onset and regression of motor block, sensory block, postoperative analgesia and possible side effects.

2. Literature Survey

1) BS Sethi, Mary Samuel, Deepak Sreevastava conducted a study of 60 adult patients belonging to ASA I and II groups with low dose of clonidine (1 mcg/kg body weight) added to intrathecal bupivacaine 12.5 mg scheduled for gynecological surgeries under spinal

anaesthesia. They concluded that intrathecal clonidine significantly increases the duration of analgesia and provides quicker onset & prolonged duration of sensory and motor blocks as compared to bupivacaine alone. It also has an effect on sedation, heart rate; mean arterial pressure which does not however require any therapeutic intervention. Therefore clonidine can be used as a safe adjuvant to intrathecal bupivacaine.

2) H. Saxena, S. Singh, S. Ghildiyal, conducted a study in 2009 to compare the efficacy of three different doses of clonidine added to intrathecal hyperbaric bupivacaine in 80 adult patients undergoing below umbilical surgeries belonging to ASA I and II divided in 4 groups. Group 1 that is control group received 13.5 mg 0.5% hyperbaric bupivacaine only and group 2, 3, 4 received addition of clonidine to the hyperbaric bupivacaine in the doses of 15mcg, 30mcg, 37.5mcg respectively. They concluded that addition of clonidine to bupivacaine significantly reduces the onset time of sensory and motor blocks with increase in the duration of spinal block as compared to bupivacaine alone with 30 mcg as optimum dose.
3) Ranju Singh, Deepti Gupta, Aruna Jain, conducted a study to compare the efficacy of clonidine and fentanyl added to hyperbaric 0.5% bupivacaine in lower segment caesarean section with clonidine 50 mcg & 75 mcg and fentanyl 25mcg used. A total of 105 parturients scheduled for elective LSCS were studied. The primary outcomes studied were onset of block and duration of post operative analgesia and secondary outcomes were possible clonidine side effects like dryness of mouth, sedation and perioperative hemodynamic changes (hypotension and bradycardia) and side effects in newborn if any were studied. They concluded that addition of 75 mcg clonidine significantly prolongs duration of postoperative analgesia with no significant maternal side effects and no difference in neonatal outcome.
4) JahnabeeSarma, P. Shankara Narayana et al, conducted a study of150patients between 18 to 60 years of age undergoing lower limb surgeries, randomly dividing the patients into 3 groups. One receiving hyperbaric bupivacaine 0.5% alone, other two with 50mcg of clonidine and 5 mcg of dexmeditomedine added to intrathecal bupivacaine. They concluded that addition of low dose clonidine or dexmeditomedine produces significantly shorter onset of motor and sensory block &longer duration of block as compared to bupivacaine alone.
5) Amit Tyagi, ShivaniRastogi and Mahendra Singh et al, did comparative study on 60 patients divided in 2 groups with one group receiving 12.5 mg hyperbaric bupivacaine and other group receiving intrathecal hyperbaric bupivacaine 12.5 mg with 1mcg/kg clonidine posted for lower abdominal surgeries under spinal anaesthesia. They concluded that mean time of onset of sensory and motor block was faster in clonidine group compared to bupivacaine alone. The maximum upper level of sensory blockade attained was T6. Duration of postoperative analgesia prolonged without any side effects.

Objectives

The objectives of the study is to compare the effects in following 3 groups,

- Group B-Receiving 0.5% hyperbaric Bupivacaine 15 mg intrathecally.
- Group C1-Receiving 0.5% intrathecal hyperbaric Bupivacaine 15 mg with Clonidine 15µg added
- Group C2-Receiving 0.5% intrathecal hyperbaric Bupivacaine 15mg with Clonidine 30µg added.

To assess the effects with respect to the following parameters;

1) Duration of analgesia.
2) Onset and duration of sensory blockade.
3) Onset and duration of motor blockade.
4) Hemodynamic changes like heart rate and blood pressure.
5) Adverse effects of drug.

3. Methodology

Source of Data: This clinical study was conducted on 78 adult patients of ASA physical status I & II in the age group of 18 to 60 years, of either sex, posted for elective lower limb & lower abdominal surgeries under spinal anaesthesia at Chigateri General Hospital, Women and Children Hospital and Bapuji Hospital attached to J. J. M. Medical College, Davangere, over a period of 24 months fulfilling the inclusion criteria and exclusion criteria.

Study type: Prospective Randomised

Duration of study: Two years.

Sample size: 78

Method of data collection:

Sampling: We used systematic random sampling technique to select 78 patients out of all patients meeting the inclusion criteria.

Inclusion Criteria:

1) Elective surgeries.
2) Adults between 18 to 60 years
3) ASA grade I & II.
4) Patients should remain in hospital for 24 hrs after surgery.
5) Either sex.

Exclusion Criteria:

Patients with:
1) Emergency cases.
2) Patients who refused to participate in this study.
3) ASA grade III/IV.
4) Patients with allergy to bupivacaine or clonidine.
5) Bleeding disorders.
6) Anatomical abnormalities of spine.

7) Morbidly obese patients.
8) Patients with significant cardiovascular, renal and hepatic dysfunction.
9) Having contraindication to subarachnoid block.
10) Uncontrolled Diabetes mellitus.
11) Hypertension.
12) Patients with increased intracranial pressure.

4. Observation and Results

There were no intergroup difference as regards to the demographic profile and ASA physical status of patients enrolled in our study.

The mean age in group B is 43.50±9.70 years, mean age in group C1 is 40.77±9.70 years and mean age in group C2 is 39.73±10.62 years with p value of 0.326 is comparable among three groups. The mean weight in group B is 62.35±3.48 kg, 64.65±2.69 kg in group C1 and 64.10±2.3 kg in group C2 with p value of 0.071. The mean height in group B is 167.19±3.72 cms, group C1 has 162.26±5.46 cm and 162.03±5.59 cm in group C2 with p value of 0.365. The samples are height and weight matched (Graph 1).

Samples are gender matched with p value = 0.948. In group B, there were 16 males and 10 females and in group C1 there were 15 males and 11 females and group C2 16 males and 10 females. The samples are comparable among the three groups.
There were 20 participants belonging to ASA I in group B, 22 in group C1 and 21 in group C2. ASA II patients were 6 in number in group B, 4 in group C1 and 5 in group C2. This was statistically not significant with p value of 0.431. ASA III and IV were not taken as per exclusion criteria.

The mean time of onset of sensory blockade was 2.29±0.39 min in group B, 2.15±0.32 min in group C1 and 1.5±0.44 min in group C2 which is statistically comparable with a significant p value of 0.001, suggest that group C2 has a faster onset compared to group B and group C1. The onset of motor blockade was also faster in group C2 with p value of 0.001 which is statistically significant (Table 1).

Highest level of sensory block achieved in group B was T6 with 18 (69.2%) of patients achieving it. Highest level of block in group C1 and group C2 was T4 with 2 (7.7%) and 1 (3.8%) of patients respectively. These findings were statistically significant with p value of 0.003 suggesting clonidine group had highest level of sensory blockade achieved. In group B, 96.2% of patients had complete motor blockade while 100% of patients had complete motor blockade in group C1 and group C2. P value was 0.363 which is statistically not significant.

The mean duration of sensory blockade in group B was 182.89±12.02 min, 223.88±24.79 min in group C1 and 261.03±18.78 min in group C2 with p value of 0.001 which is statistically highly significant. The mean duration of motor block in group B was 186.03±18.45 min, group C1 was 215.69±21.50 min and 243.50±18.73 min in group C2. P value is 0.001 which is significant. Total duration of analgesia was compared between three groups. Group C2 had longer duration of analgesia time with 285.00±17.40 minutes (Table 2, Graph 2)

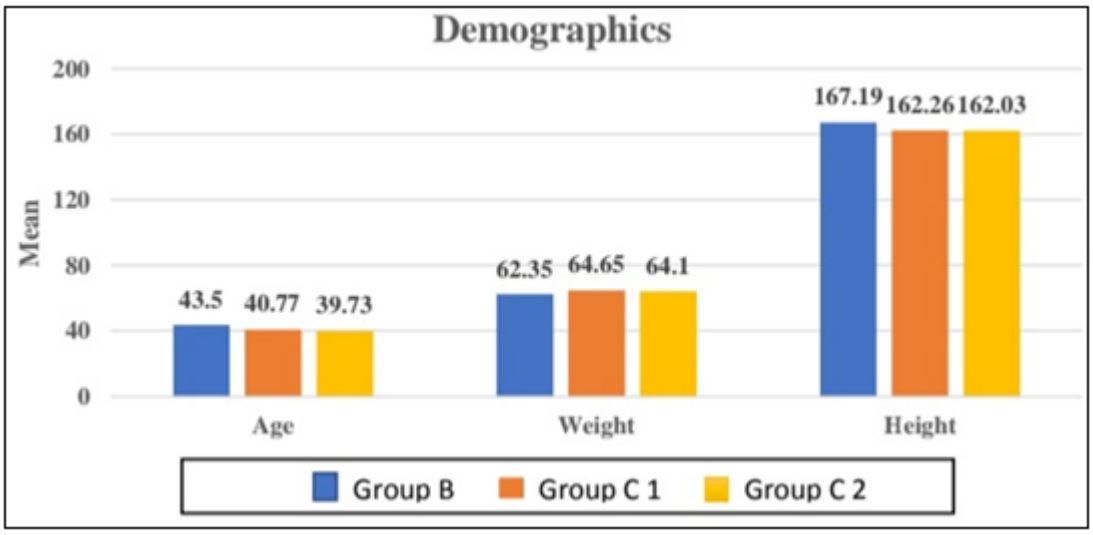
Hypotension was seen in 19.2 % of patients in Group C2 and 7.7 % of patients in Group B and Group C1. Bradycardia was seen in 15.38 % of patients in Group C2 and 7.7% in group C1. Sedation and nausea vomiting seen in 3.8% of both group C1 and C2. There was no clinical or statistical significance in the incidence of side effects among the groups.

Table 1

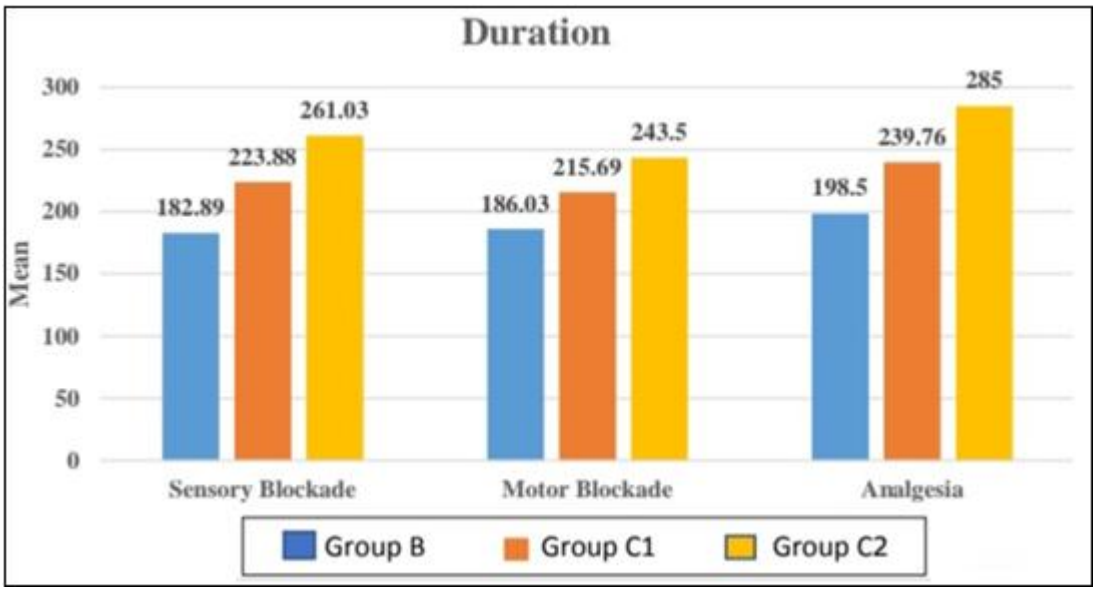
Onset of Blockade (min)	Group B (mean±SD)	Group C1 (mean±SD)	Group C2 (mean±SD)	P value
Sensory	2.29 ± 0.39	2.15 ± 0.32	1.5 ± 0.44	0.001*
Motor	3.33 ± 0.49	2.90 ± 0.31	2.42 ± 0.38	0.001*

Table 2

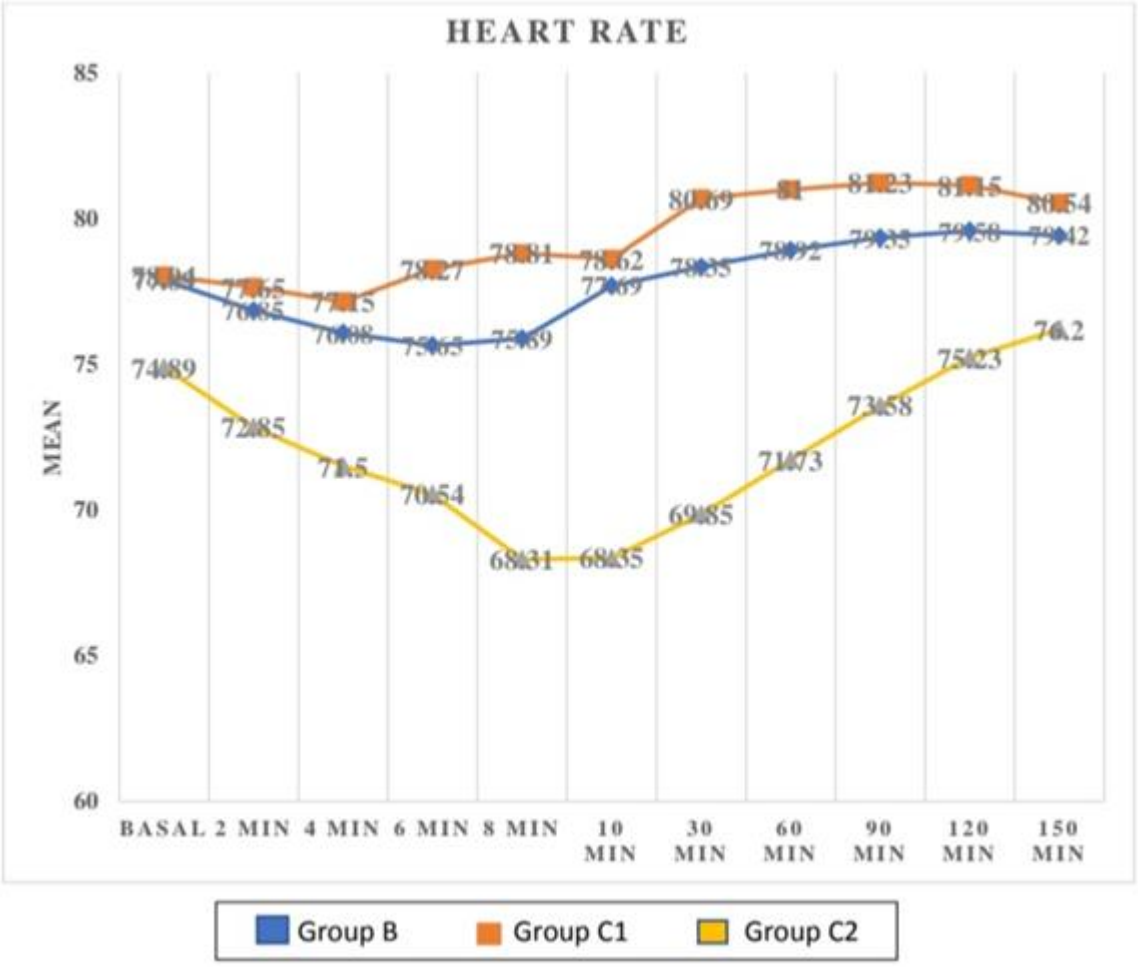
Duration (min)	Group B (mean±SD)	Group C1 (mean±SD)	Group C2 (mean±SD)	P value
Sensory Blockade	182.89 ± 12.02	223.88 ± 24.79	261.03 ± 18.78	0.001*
Motor Blockade	186.03 ± 18.45	215.69 ± 21.50	243.50 ± 18.73	0.001*
Analgesia	198.50 ± 13.09	239.76 ± 16.60	285.00 ± 17.40	0.001*



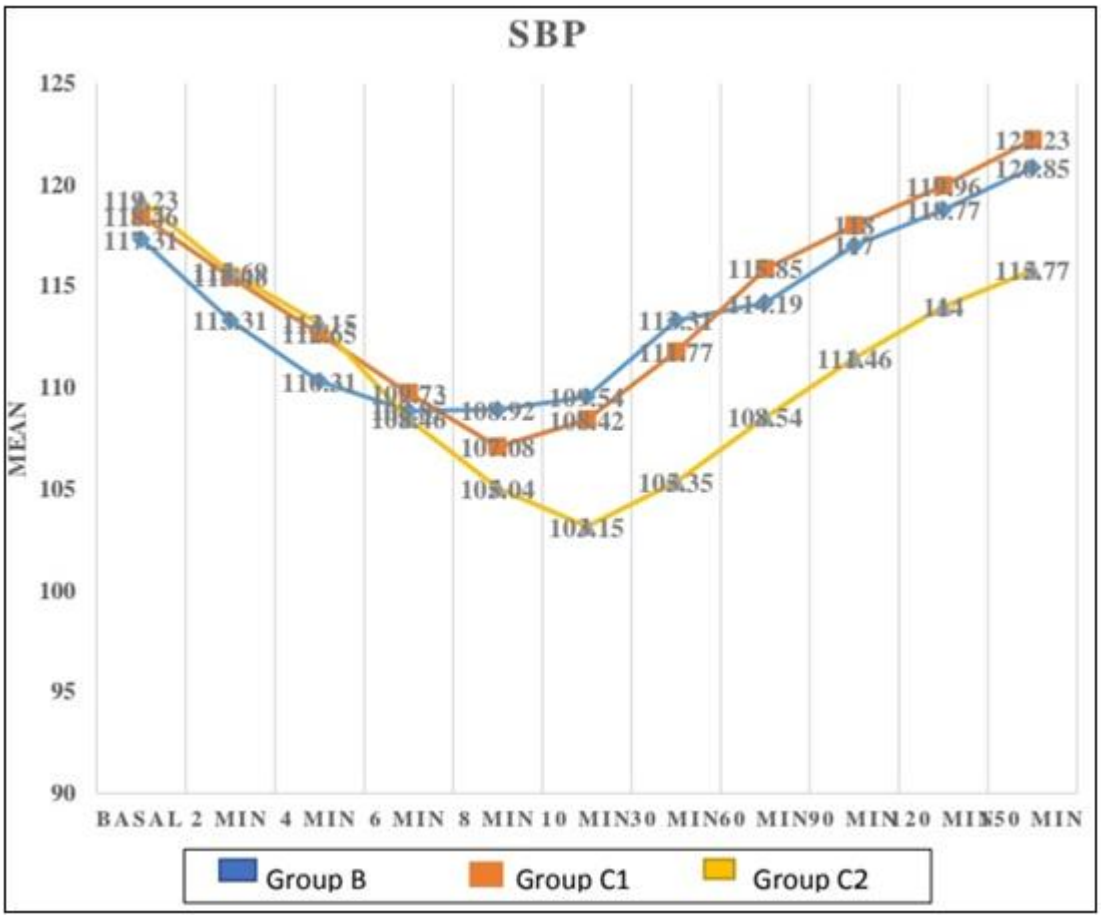
Graph 1



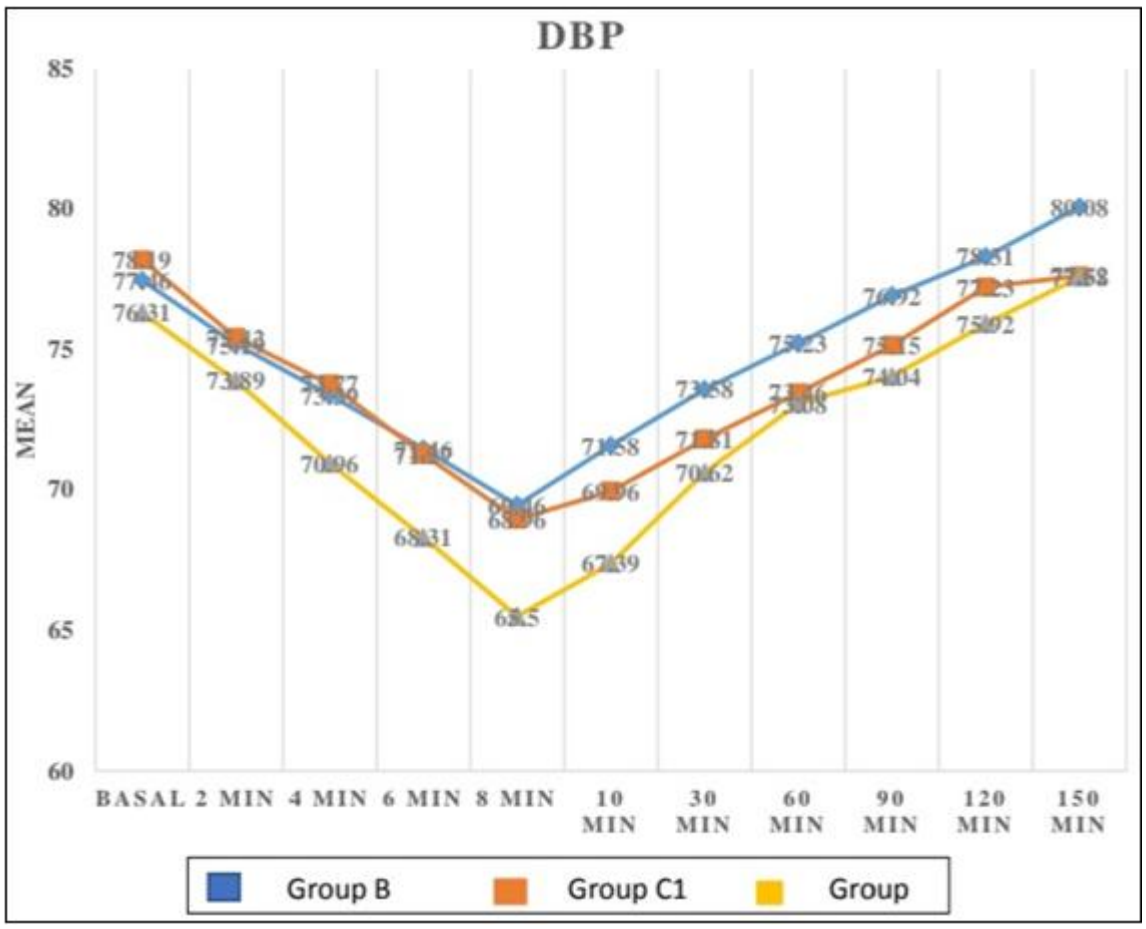
Graph 2



Comparison of Heart rate between study groups



Comparison of SBP between study groups



Comparison of DBP between study groups

5. Discussion

Local anesthetics injected intrathecally in spinal anesthesia produce varied level of analgesia at cost of some side effects. Hyperbaric bupivacaine is more commonly used local anesthetic for these procedures due to potency of producing analgesia at lower neurological side effects. To reduce amount of side effects and to achieve higher grade of analgesia many adjuvants have been added to local anesthetics.

Clonidine act as agonist of α2 adrenoreceptor in the dorsal horn of spinal cord to decrease afferent pain transmission and also by blocking conduction of C and Aδfibers. This action has lead to its use as adjuvant to local anesthetics in spinal anesthesia with better safety and side effects compared to other adjuvants. However intrathecal clonidine at doses of 1-2 µg/kg produce bradycardia, relative hypotension, and sedation. So the much lower doses of clonidine were used in studies as adjuvant but it has shown varying results.

In our study, majority of patients were middle aged in all the groups. Mean age in group B was 43.50 + 9.70 years, in group C1 40.77 + 9.70 years and in group C2 was 39.73±10.62 years with p value of 0.326 which is statistically not significant.

In our study mean time of onset of sensory block in group B was 2.29±0.39 minutes, 2.15±0.32 minutes in group C1 and 1.5±0.44 minutes in group C2. The mean time of onset of motor blockade in group B was 3.33±0.49 minutes, 2.90±0.31 minutes in group C1 and 2.42±0.38 minutes in group C2. There was statistically significant difference observed with regard to the onset of sensory and motor blockade between the groups with onset of blockade significantly faster in group C2 compared to group B and group C1.

Our study results were comparable to the study done by **H Saxena et al**[6], who compared three different doses of clonidine (15 mcg, 30mcg and 37.5 mcg) added to intrathecal hyperbaric bupivacaine in 80 adult patients undergoing below umbilical surgeries. They concluded that mean time of onset of sensory and motor blockade was significantly lower in all clonidine groups in a dose dependent manner compared to control group and was lowest in group with 37.5 mcg of clonidine.

A similar study was conducted by **Anil Thakur et al** [8], in 75 adult patients of ASA I & II posted for elective inguinal herniorrhaphy surgeries. They compared low doses of clonidine (15mcg and 30 mcg) added as adjuvant to intrathecal hyperbaric bupivacaine and concluded that mean time of onset of sensory and motor blockade was similar between both clonidine groups but a faster onset was seen in clonidine groups compared to the control group.

Another study conducted by **AgretaGecaj-Gashi et al**[15], with low dose of clonidine added as adjuvant to intrathecal isobaric bupivacaine in 66 patients posted for transurethral surgeries, concluded that the mean time of achievement of sensory block up to level T9 and motor block was significantly shorter in clonidine group compared to bupivacaine alone.

6. Conclusion

Our study revealed that addition of low dose clonidine to intrathecal hyperbaric bupivacaine causes significant prolongation of duration of sensory and motor blockade as well as postoperative analgesia. In our study with addition of low dose clonidine (15 mcg and 30 mcg) to intrathecal hyperbaric bupivacaine we found that clonidine in the dose of 30 mcg added to bupivacaine for subarachnoid block provides maximum benefit with minimum side effects. Though incidence of hypotension and bradycardia is more with 30 mcg of clonidine compared to 15 mcg, but it can be easily managed with routine clinical measures. Therefore clonidine in the dose of 30 mcg can be used as ideal adjuvant with hyperbaric bupivacaine in subarachnoid block for long duration surgical procedures. However prolonged duration of motor blockade with clonidine may be undesirable in short term surgical procedures or ambulatory surgeries.

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