

INTRATHECAL BUPRENORPHINE, CLONIDINE AND FENTANYL AS ADJUVANTS TO 0.5% HYPERBARIC BUPIVACAINE IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES: A PROSPECTIVE, RANDOMIZED AND COMPARATIVE STUDYRashmi Pal¹, K. K. Arora², N. S. Doneria³**HOW TO CITE THIS ARTICLE:**

Rashmi Pal, K. K. Arora, N. S. Doneria. "Intrathecal Buprenorphine, Clonidine and Fentanyl as Adjuvants to 0.5% Hyperbaric Bupivacaine in Lower Abdominal and Lower Limb Surgeries: A Prospective, Randomized and Comparative Study". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 46, June 08; Page: 8009-8017, DOI: 10.14260/jemds/2015/1164

ABSTRACT: BACKGROUND: Among all the spinal adjuvants, clonidine, an alpha-2 agonist has the ability to alleviate both the somatic and visceral pain and is more potent at spinal site, favoring its neuraxial administration. **OBJECTIVE:** This study was done to compare the onset and duration of sensory and motor blocks, duration of analgesia, haemodynamic and adverse effects of Clonidine, buprenorphine and fentanyl used intrathecally with hyperbaric 0.5% bupivacaine. **SETTINGS & DESIGN:** This prospective, randomized and comparative study included 90 ASA class 1 & 2 patients undergoing lower abdominal and lower limb surgeries under spinal anesthesia after approval from hospital ethics committee with written informed consent of patients. **MATERIALS AND METHODS:** Patients were randomly allocated into three groups (n=30) and received 50µg of clonidine, 25µg of fentanyl and 75µg of buprenorphine respectively in group BC, BF and BB as adjuvants to 15mg of 0.5% hyperbaric bupivacaine (3.0ml). The onset time and duration of sensory and motor block, duration of analgesia, haemodynamic changes and side effects were recorded. **RESULTS:** The onset time of motor block and durations of sensory, motor blockade and analgesia were prolonged in-group BC as compared to group BF and BB (P<.001). There was no significant difference in the onset time of sensory block in three groups (P>.05). Group BC had lower heart rate and mean blood pressure and higher sedation score. **CONCLUSION:** Intrathecal Clonidine in a dose of 50µg is an effective adjuvant to local anesthetics in neuraxial blocks despite mild sedation and haemodynamic variations.

KEYWORDS: α2-adrenoceptor agonist, Bupivacaine, Buprenorphine, Clonidine, Fentanyl.

INTRODUCTION: Spinal anesthesia is the most commonly used technique for lower abdominal and lower limb surgeries. Of all adjuvants, opioids and Clonidine are continuously gaining popularity for their desirable effects and better profile of adverse effects than others. Opioids and local anesthetics administered together intrathecally are known to have synergistic analgesic effects, whereas Clonidine, an alpha-2 receptor agonist has emerged out with its desirable anesthetic properties. Its role is being explored in neuraxial blocks as an adjuvant to local anesthetics for reducing their requirements, improving haemodynamic stability and providing analgesia.^[1-3]

When local anesthetic, bupivacaine is combined with Intrathecal Clonidine, complete surgical anesthesia could be obtained along with relief from somatic as well as visceral pain both intra and post operatively with fewer side effects.^[3-6] This study was conducted to evaluate onset and duration of sensory and motor block, duration of analgesia, haemodynamic and adverse effects of fentanyl, buprenorphine and Clonidine given intrathecally with hyperbaric 0.5% bupivacaine.

ORIGINAL ARTICLE

MATERIALS & METHODS: Ninety patients aged 20-60 years, of American Society of Anesthesiologists (ASA) grade 1 and 2, scheduled for lower abdominal and lower limb surgeries lasting not more than three hours were included in the study. After obtaining approval from the institutional ethics committee and ascertaining selection criteria, informed valid consent was obtained for participation in the study. Exclusion criteria were patient's refusal, coagulation abnormalities, allergy to any drug being used, pre-existing severe bradycardia or ejection fraction <30%, hypovolemia or hypotension, arrhythmias, or cardiac block, raised intracranial pressure, head injury, bronchial asthma, caesarean section or any other contraindication to spinal anesthesia.

Preoperative evaluation was carried out in all patients with detailed history, general physical examination including height and weight, evidence of any special deformity or any neurological disease and mental status of the patient. Pulse rate, blood pressure, respiratory rate and oxygen saturation in room air were noted and systemic examination was performed. The patients were randomly divided in three groups of thirty each using a computer random number sequence.

GROUP BC -3.0ml of 0.5% of hyperbaric bupivacaine (15mg) + 50µg (0.33ml) of Clonidine + (0.17 ml normal saline) = 3.5ml.

GROUP BF -3.0ml of 0.5% hyperbaric bupivacaine (15mg) +25µg (0.5ml) fentanyl= 3.5ml.

GROUP BB -3.0ml of bupivacaine heavy 0.5% (15mg) + buprenorphine 75µg (0.25ml) + normal saline (0.25ml) =3.5ml.

The total volume of solution in all the groups was 3.5 ml and the drug solution was prepared by an anesthesiologist not involved in the study. All patients were familiarized with visual analogue scale (VAS). A preoperative fasting of 6 hour was confirmed and baseline heart rate and blood pressure were noted. Glycopyrrolate 0.2mg was administered intramuscularly to all patients, 30 minutes before procedure. In the operation theatre, an intravenous line was secured and preloading was done with Lactated Ringer's solution at the rate of 10 to 15 ml/kg. No sedatives or analgesics were administered preoperatively. Patient monitoring included non-invasive blood pressure, pulse oximetry and three lead electrocardiograms.

Subarachnoid block was performed in sitting position with midline approach under strict aseptic precautions using 25 Gauze quincke needle. The loaded drug was injected over 10 to 15 seconds, once free flow of cerebrospinal fluid was confirmed. The time at which the injection completed was considered zero time of the study and all the measurements were recorded from this point. Patients were immediately placed in supine position supporting the head and shoulders. Oxygen was given with the face mask at flow rate of 4 l/min.

The highest level of sensory block was sensed by pinprick method in caudal to cephalic direction every two minute, after the procedure of subarachnoid block was complete and the time taken to achieve absence of pinprick response at T 10 level in midclavicular line was taken as onset of sensory block. Motor block was assessed by modified Bromage scale⁷ (Bromage 0: able to move hip, knee and ankle, Bromage 1: not able to move hip but able to move knee and ankle, Bromage 2: unable to move hip and knee but can move ankle, Bromage 3: unable to move any). Time taken to reach Bromage 3 was noted and was considered the onset of motor block. Intraoperative sedation was tested on subjective sedation scale as described by Wilson et al⁸: Grade 1: calm and oriented, Grade 2: drowsy, Grade 3: arousable to verbal command, Grade 4: arousable to mild physical stimulation, Grade 5: unarousable.

ORIGINAL ARTICLE

Satisfactory block was defined as a sensory level of T 10 and modified Bromage score of three. Duration of sensory block was defined from completion of drug injection to the re-appearance of response to pinprick at L-1 level. Duration of motor block was recorded as time from injection of drug into the subarachnoid space to achieve Bromage-0. Both the durations were noted. Duration of surgery was also recorded. Postoperative pain was assessed by visual analogue scale (VAS) using a plain scale measuring 10cms with 1 mm markings, in which 10 corresponded with most extreme pain and point 0 with no pain at all. Duration of analgesia was taken from the time of intrathecal drug administration to the time when patient, first complained of pain. At that point the study was terminated with respect to analgesia and injection paracetamol 15mg/kg was given. Postoperatively the hemodynamic variables and oxygen saturation were recorded until complete recovery of the patients from anesthesia.

Statistical analysis was done using Statistical Package for Social Science (SPSS 20.0 evaluation version). Data were expressed as means and standard deviation (SD). For categorical data chi-square test was used with P value reported at the 95% confidence interval (CI). Continuous data were compared using analysis of variance (ANNOVA). If P value was significant, then Tukey's honestly significant difference (HSD) post- hoc test was applied to see the significance between each pair of groups.

RESULTS: The three groups were comparable with respect to age, weight, height, ASA physical status and duration of surgery [Table-1]. The characteristics of the subarachnoid blocks in three groups with inter-group comparison are shown in table-2 (Table-2). There was no significant difference in the onset time of sensory block in three groups ($p>.05$), although Clonidine group had fastest onset. There was significant difference in the onset time of motor block, duration of sensory and motor block and duration of analgesia in all the groups ($p<.001$). There was significant difference in VAS score at 4 and 6 hr in all the groups, with lowest score in group BC. Subjective sedation scores also differed significantly in all the groups with a maximum score in group BC followed by BB and BF. Heart rate (Figure-1) and mean blood pressure (Figure-2) were also found to be lower in group BC as compared to group BF and BB. Bradycardia and hypotension were found more in group BC, whereas nausea, vomiting and itching were found in group BF and BB.

DISCUSSION: Antinociceptive action of Clonidine exists for somatic and visceral pain.^[9,10] Clinical efficacy of Intrathecal Clonidine to relieve visceral pain in well-established^[11-12] but Clonidine is also associated with few side effects like bradycardia, hypotension and dry mouth. So, 50 μ g dose of Clonidine was chosen in our study, as higher doses (150 μ g) are also associated with significant risk of hypotension as reported by Chiari et, al.^[13]

Clonidine is a selective partial agonist for α_2 adrenergic receptors and it is the most studied drug used for neuraxial anesthesia.^[14] It is more potent after neuraxial than systemic administration indicating spinal site of action and favoring neuraxial administration.^[15] It is moderately lipid soluble, easily penetrates the blood brain barrier leading to spinal and supra spinal receptor binding and thus provides effective and long lasting post-operative analgesia. Recently, Clonidine has also been shown to increase acetylcholine (Ach) levels in lumbar cerebrospinal fluid, as cholinergic activation imparts analgesia.^[15] It may also cause local vasoconstriction.^[15] Intrathecal α_2 agonists are found to have antinociceptive action for both somatic and visceral pain.^[16]

ORIGINAL ARTICLE

Fentanyl is a lipophilic μ receptor agonist opioid. Intrathecally It exerts its effect by combining with opioid receptor in the dorsal horn of spinal cord and may have a supraspinal spread and action. The effectiveness of Intrathecal opioids depends on their bioavailability,^[17] so opioids can provide good perioperative analgesia. Reuben et al^[18] used different doses (5, 10, 20, 40, 50 μ g) of fentanyl in their study and found that even 20 μ g of fentanyl in combination of 0.5 % of bupivacaine gave good amount of analgesia. So, we have used 25 μ g of fentanyl in our study.

Buprenorphine is another opioid which increases sensory block without affecting motor block and haemodynamic^[19] it also has high lipid solubility and highest affinity for opiate receptors^[20,21,22]. As suggested by Capogna et al,^[21] duration of analgesia is dose dependent and it was found to increase up to 294.0 \pm 17.93 minutes with buprenorphine in our study, which is less than 475 minutes and 430 minutes as stated by Shaikh and kiran et al^[23] and capogna et al,^[22] respectively.

There was no significant difference in onset time of sensory block in three groups (463.8 \pm 54.42 seconds, 477.6 \pm 55.2 seconds, and 477.6 \pm 61.8 seconds in group BC, BF and BB respectively) ($P > 0.5$). This result was supported by studies done by Singh et al^[24] and Strebel et al,^[25] where they concluded that fentanyl as well as Clonidine does not alter the onset of sensory block, whereas onset of sensory block in BB group did not match to a study done by Dixit et al^[26] in caesarean sections in which it was significantly shortened to 1.85 \pm 1.39 min with the addition of buprenorphine to 0.5% hyperbaric bupivacaine (5.35 \pm 1.79 minutes.)

The difference in mean onset of motor block (Bromage 3) was statistically significant in all three groups being 142.66 \pm 33.99 seconds, 222 \pm 52.06 seconds and 274 \pm 56.11 seconds in group BC, BF and BB respectively ($p < .001$). It was lower than onset time for sensory block in all the groups of our study, probably because onset of sensory block was taken as a time for its spread up to T10 level. The value of 274 \pm 56.11 seconds achieved with 75 μ g of buprenorphine in our study was comparable to 198 seconds achieved with 60 μ g of buprenorphine in a study done by Gupta M^[27] et al.

The time taken for regression of sensory block to L-1 was statistically significant being 306.67 \pm 60.47 minute, 267 \pm 30.18 minute and 174.33 \pm 23.44 minute in group BC, BB and BF respectively ($p < .001$). The duration of sensory block in group BC is supported by study of Elia et al,^[28] who concluded that time taken for two segment regression was prolonged with 150 microgram dose of Clonidine although associated with hypotension. This value of 306.67 \pm 60.47 sec. was again supported by a dose response study done by Strebel et al,^[25] where the time for L1 regression was 325 \pm 69 min with 75 μ g Clonidine, Which was slightly higher than the dose used in group BC of our study. The mean time of sensory regression to L-1 in group BF i.e. 174.33 \pm 23.44 min is slightly lower to the regression time to S1 level i.e. 179 \pm 47 min in a study done by Ghanem S M et al.^[29] The mean time to regression of sensory block to L1 in group BB was 267 \pm 30.18 with 75 μ g of buprenorphine and is comparable to 225 \pm 64.49 minutes with 60 μ g of buprenorphine as found in study of Gupta M et al.^[27] This difference in duration could be due to larger dose used (75 μ g) in our study, as this effect is dose dependent with opioids. There was significant difference in the durations of motor Block in all three groups. ($p < .001$).

The duration of motor block in group BF (151.27 \pm 12.02 min) shows that fentanyl does not prolong it as supported by the study of Singh et al ^[24] however, Clonidine significantly prolongs the duration of motor block up to 254.67 \pm 72.05 minutes as supported by the studies of Elia et al^[28] and Jain et al.^[29] However this was in contrast to the study of kabbachi et al ^[30], who concluded that the addition of 2 μ g/kg Clonidine (= 100 μ g) to hyperbaric 0.5 % bupivacaine does not prolong the duration

ORIGINAL ARTICLE

of motor block. The duration of motor block in group BB (222.66 ± 24.34 min) was comparable to 205.17 ± 63.0 minutes achieved with $60 \mu\text{g}$ of buprenorphine, in a study done by Gupta M. et al.^[27]

The difference in duration of analgesia was also significant in all the 3 groups ($p < .001$) being longest in group BC (353.19 ± 7.69 min) and lowest in group BF (195.83 ± 7.30 min). The durations of analgesia in group BC and group BF in our study were comparable to 386.8 ± 13.56 min. with clonidine $60 \mu\text{g}$ and 289.83 ± 15.4 min. with fentanyl $50 \mu\text{g}$, respectively in a study done by Strebel et al.^[25] The duration of analgesia with buprenorphine in our study i.e. 294 ± 17.93 minutes was quite comparable to 289.66 ± 64.94 minutes as in the study done by Gupta M et al.^[27]

Haemodynamic variations were more pronounced in group BC as compared to group BB and BF. Respiratory depression also did not occur in any of the group. The decrease in blood pressure in group BC was supported by the study of Elia et al.^[28] who reported that there were more episodes of hypotension with $150 \mu\text{g}$ of Clonidine. This is in contrast to the study done by strebel et al.^[25] that relative hemodynamic stability was maintained with $150 \mu\text{g}$ of Clonidine in combination with 0.5% hyperbaric bupivacaine. VAS score was also significantly lower in group BC than in group BB and BF as supported by the study of Jain et al.^[29] and Grandhe et al.^[31] Sedation score in group BC was higher than in group BF and group BB. Absence of control group to compare the effects of drugs separately has been the limitation of our study.

CONCLUSION: It can be concluded that although Intrathecal Clonidine ($50 \mu\text{g}$) is associated with mild hemodynamic instability and sedation, it provides quicker onset and prolonged duration of sensory and motor blocks simultaneously increasing the duration of analgesia when compared to fentanyl ($50 \mu\text{g}$) and buprenorphine ($75 \mu\text{g}$) and can be used as optimal dose as an Intrathecal adjuvant.

REFERENCES:

1. Bloor BC, Flacke WE. Reduction in halothane requirement by Clonidine, an alpha-adrenergic agonist. *Anesth Analg* 1982; 67; 741-5.
2. Ghignone M, Calvillo O, Quintine L. Anesthesia and hypertension; the effects of Clonidine on perioperative haemodynamics and halothane requirements. *Anesthesiology* 1987; 67(1); 3-10.
3. Gordh T. Epidural Clonidine for treatment of postoperative pain relief after thoracotomy. A double-blind placebo-controlled study. *Acta Anaesthesiol Scand* 1988; 32(8): 702-9.
4. Kirno K, Lundin S, Elam M. Epidural Clonidine depresses sympathetic nerve activity in humans by supraspinal mechanism. *Anaesthesiology* 78(6): 10217.
5. Mendez R, Eisenach JC, Kashtan k. Epidural Clonidine analgesia after caesarean section. *Anaesthesiology* 1990; 73(5); 842-52.
6. Motsch J, Graber E, Ludwig K. Addition of Clonidine enhances postoperative analgesia from epidural morphine: a double-blind study. *Anaesthesiology* 1990; 73; 1066-73.
7. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anaesthesiol Scand Suppl.* 1965; 16: 55-69.[PubMed]
8. Wilson E, David A, Mackenzie N, Grant IS. Sedation during spinal anaesthesia: Comparison of propofol and midazolam. *Br J Anaesth* 1990; 64: 48-52.
9. Danzebrink RM, Gebhart GF. Antinociceptive effect of intrathecal adrenoceptor agonists in a rat model of visceral nociception. *J Pharmacol Exp Ther* 1990; 25(3): 698-705.

ORIGINAL ARTICLE

10. Harada Y, Nishioka K, Kitahata LM. Contrasting actions of intrathecal morphine or enkephalin or intravenous U50, 488H on the visceromotor response to colorectal distension in rat. *Anaesthesiology* 1995; 83; 336-43.
11. Hunt CO, Naulty JS, Bader AM. Perioperative analgesia with subarachnoid fentanyl-bupivacaine for caesarean delivery. *Anesthesiology* 1989; 71; 535-40.
12. Coutney MA, Bader AM, Hartwell. Perioperative analgesia with subarachnoid sufentanil administration. *Reg Anaesth* 1992; 17; 274-8.
13. Chiari AZ, Lorber C, Eisenach JC, Wildling E, Krenn C, Zavrsky A. Analgesia and haemodynamic effects of intrathecal Clonidine as a sole agent during first stage of labour: a dose-response study. *Anaesthesiology* 1999; 91: 388-96.
14. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: defining the role in clinical anesthesia. *Anaesthesiology* 1991; 74(3): 581-605.
15. Eisenach JC, De Kock M, Klimscha W. Alpha-2-adrenergic agonists for regional anesthesia. A clinical review of Clonidine (1984-85). *Anaesthesiology* 1996; 85(3): 655-74.
16. Al-Ghanem SM, Masood IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Quatawneh AM. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine to spinal block characteristics in gynecological procedures. A double-blind controlled study. *Am J Appl Sci* 2009; 6: 882-7?
17. Justins DM, Francis D, Houlton PG, Reynolds F. A controlled trial of extradural fentanyl in labour. *Br J Anaesth*.1982; 54: 409-14.
18. Reuben SS, Dunn SM, Duprat KM, O'Sullivan P. An intrathecal fentanyl dose-response study in lower extremity revascularization procedures. *Anesthesiology*.1994; 81(6): 1371-5.
19. Saxena AK, Arva S. Current concepts in neuraxial administration of opioids and non-opioids: An overview and future perspective. *IJA* 2004; 48: 13-24.
20. Lanz E, Suke G, Theiss D, Glocke MH. Epidural buprenorphine: a double-blind study of postoperative analgesia and side effects. *Anesth Analg* 1984; 63: 593-98.
21. Capogna G, Celleno D. Spinal buprenorphine for postoperative analgesia after caesarean section. *Acta Anaesthesiol Scand*.1989; 33:236-238.
22. Capogna G, Celleno D. Intrathecal buprenorphine for postoperative analgesia in the elderly patients. *Anaesthesia* 1988; 48:128-30.
23. Shaikh SI, Kiran M. Intrathecal buprenorphine for postoperative analgesia: A prospective randomized double blind study. *J Anaesth Clin Pharmacol*.2010; 26:35-8.
24. Singh H, Yang J, Thornton K, Adolf H. Study on the effects of intrathecal fentanyl on the onset and duration of hyperbaric bupivacaine. *Can J Anaesth*.1995; 42(11): 987-91.
25. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small dose intrathecal Clonidine and isobaric bupivacaine for orthopedic surgery: a dose-response study. *Anaesth Analg* 2004; 99: 1231-8.
26. Dixit S. Postoperative analgesia after caesarean section: An experience with intrathecal buprenorphine. *IJA* 2007; 51(6): 515-18.
27. Gupta M, Shailaja S, Hegde KS. Comparison of intrathecal dexmedetomidine with buprenorphine as adjuvant to bupivacaine in spinal anesthesia. *J Clin Diagn Res*. 2014; 8(2): 114-17.

ORIGINAL ARTICLE

28. Elia N, Culebras X, Mazza C, Schiffner E, Tramer MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. *Reg Anaesth Pain Med*.2008; 33(2); 159-67.
29. Jain PN, Gehdoo RP, Priya V. Study of intrathecal Clonidine for postoperative pain relief. *Indpain* 2003; 17(2): 1233-36.
30. Kabbachi O, Ben Rajeb A, Mebazza M, Sifi H, Jelel C. Spinal anesthesia in children: Comparative study of hyperbaric bupivacaine with or without Clonidine. *Br J Anaesth* 2006; 33(2): 159-67.
31. Grandhe RP, Wig J, Yaddanapudi LN. Evaluation of bupivacaine-Clonidine combination for unilateral spinal anesthesia in lower limb orthopedic surgery. *J Anaesthesiol Clin Pharmacol* 2008; 24(2): 155-8.

Variable	Group BC	Group BF	Group BB
Age (years)	39.33±13.46	41.17±13.22	37.27±14.50
Height (cm)	153.20±3.33	155.10±2.57	154.35±4.30
Weight (kg)	56.60±7.23	58.23±5.21	57.42±6.30
ASA ½	16/14	15/15	13/17
Sex (M/F)	16/14	15/15	17/13
Duration of surgery (min)	148±20.53	147±12.46	149±18.65

Table 1: Demographic Profile

ASA= American society of anesthesiology, F=Female, values are mean ±standard deviation (SD), BC= Bupivacaine Clonidine, BF= Bupivacaine fentanyl, BB= Bupivacaine buprenorphine

Variable	Group BC	Group BF	Group BB	P Value BC/BF	P Value BC/BB	P Value BF/BB
Onset of sensory block (sec.)	463.8±54.42	477.6±55.2	477.6±61.8	.614†	.614†	1.000†
Onset of motor block (sec.)	142.66±39.99	220±52.06	274±56.11	.000*	.000*	.000*
Duration of sensory block(min.)	306.67±60.47	174.33±23.44	267±30.18	.000*	.018*	.000*
Duration of motor block(min.)	254.67±72.05	151.27±12.02	222.66±24.34	.000*	.001*	.000*
Duration of analgesia (min.)	353.19±7.69	195.83±7.30	294.00±17.93	.000*	.000*	.000*

Table 2: Comparison of various spinal block characteristics

ORIGINAL ARTICLE

Data shown as mean \pm standard deviation (SD), BC= Bupivacaine Clonidine, BF= Bupivacaine fentanyl, BB= Bupivacaine buprenorphine, *=significant, † =insignificant.

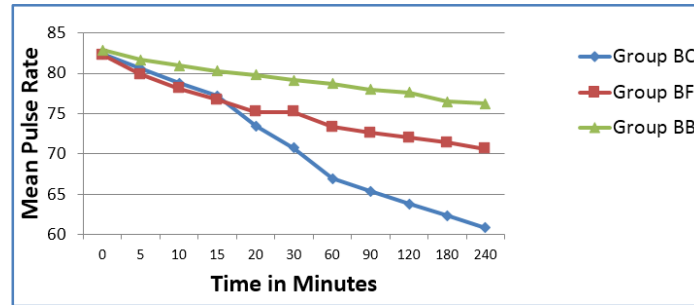


Fig. 1: Variations in Pulse Rate

Heart rate (HR) values are mean \pm standard deviation (SD). No significant differences were noted between the groups

Time of Observation	Group BC		Group BF		Group BB	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
0 min.	82.4	6.36	82.3	8.77	82.9	2.39
5 min.	80.56	6.48	79.86	9.73	81.7	2.68
10 min.	78.8	6.52	78.1	9.31	80.96	2.78
15 min.	77.2	6.68	76.73	8.77	80.26	2.86
20 min	73.5	6.44	75.23	9.65	79.8	2.75
30 min	70.73	6.29	75.23	8.35	79.16	2.90
60 min	66.96	3.49	73.4	8.20	78.73	3.93
90 min	65.43	3.46	72.6	8.21	78	2.91
120 min	63.83	3.80	72.06	8.20	77.63	2.90
180 min	62.43	3.29	71.43	7.65	76.46	2.38
240 min	60.83	2.80	70.63	7.24	76.26	2.39

Table 3: Showing Variations in Pulse Rate (supporting table for figure-1)

Data shown as mean \pm standard deviation Table (SD), BC=Bupivacaine Clonidine, BF= Bupivacaine fentanyl, BB= Bupivacaine buprenorphine

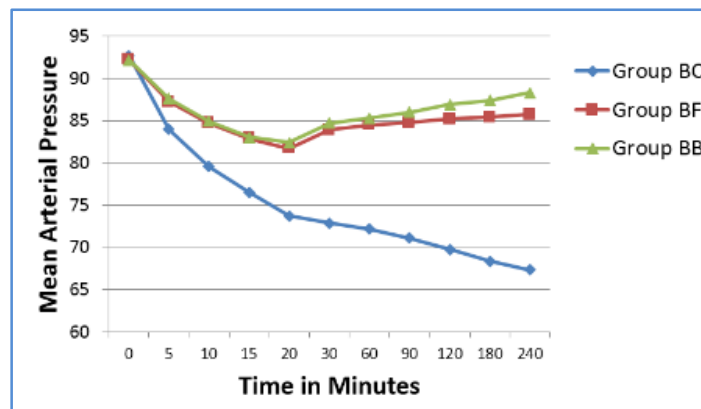


Fig. 2: Variations in Mean Arterial Pressure

ORIGINAL ARTICLE

Mean arterial pressure (MAP) values are mean \pm SD. No significant differences were noted between the groups.

Time of Observation	Group BC		Group BF		Group BB	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
0 min.	92.7	3.79	92.23	2.92	92.2	1.73
5 min.	84	8.51	87.26	5.52	87.63	2.68
10 min.	79.56	8.95	84.7	5.20	84.93	2.70
15 min.	76.51	8.55	82.93	5.29	83.06	2.88
20 min	73.76	8.10	81.7	5.20	82.4	3.28
30 min	72.9	7.57	83.9	6.37	84.7	2.95
60 min	72.2	6.46	84.5	6.14	85.33	2.91
90 min	71.1	5.62	84.76	6.45	86	3.15
120 min	69.76	5.99	85.23	6.43	86.93	2.92
180 min	68.4	6.23	85.4	6.73	87.4	2.99
240 min	67.36	5.98	85.76	7.06	88.33	2.82

Table 4: Showing Variations in Mean Arterial Pressure (supporting table for figure-2)

Data shown as mean \pm standard deviation (SD), BC= Bupivacaine Clonidine, BF= Bupivacaine fentanyl, BB= Bupivacaine buprenorphine.

AUTHORS:

1. Rashmi Pal
2. K. K. Arora
3. N. S. Doneria

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, M. G. M. Medical College, Indore, Madhya Pradesh.
2. Professor & HOD, Department Anaesthesiology, S. S. Medical College, Rewa, Madhya Pradesh.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

3. Post Graduate Student, Department Anaesthesiology, M. G. M. Medical College, Indore, Madhya Pradesh.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rashmi Pal,
28, Chameli Villa,
Bicholi Mardana,
Indore-452001,
Madhya Pradesh.
E-mail: rashmidrpal@gmail.com

Date of Submission: 18/05/2015.
Date of Peer Review: 19/05/2015.
Date of Acceptance: 30/05/2015.
Date of Publishing: 06/06/2015.