International Journal of Research in Medical Sciences
Sankaranand P et al. Int J Res Med Sci. 2018 Feb;6(2):493-502
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20180287

Original Research Article

Duration of analgesia, sensory and motor blockade and intra operative hemodynamic changes caused by intrathecal bupivacaine, bupivacaine plus clonidine and bupivacaine plus dexmedetomidine in spinal anesthesia: prospective, comparative study

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Received: 10 January 2018
Accepted: 15 January 2018

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ABSTRACT

Background: This is comparative study to differentiate the effects of Dexmedetomidine and clonidine on duration of analgesia, motor and sensory blockade and the intraoperative hemodynamic profile when mixed with Bupivacaine.
Methods: Patients aged 15-45 years having ASA 1 and ASA 2 scheduled for elective orthopedic surgeries under spinal anaesthesia were included and divided into 3 groups equally (50 patients each)' i.e. Group B received only 3.0 ml of 0.5% Bupivacaine (Heavy); Group C received 3.0ml of 0.5% Bupivacaine (Heavy) mixed with Clonidine 30 µg; and Group D administered with 3.0 ml of 0.5% Bupivacaine (Heavy) mixed with 5µg Dexmedetomidine.
Results: Majority of the cases enrolled in the study were knee disorders and the rest being fracture femur, tibia. At preoperative interval mean systolic blood pressure and diastolic blood pressure of Group B was slightly higher than Group C and Group D. At the time when spinal anaesthesia was given, a slight fall in DBP of patients was observed in all Group B, Group C and Group D. Mean heart rate of patients at preoperative interval in patients of Group B, Group C and Group D respectively, with Group C and Group D showing slightly lower mean heart rate as compared with that of the mean heart rate of Group B but the values were not statistically significant. There were no any significant changes in the hemodynamic status.
Conclusions: Both of used combinations provide prolonged sensory and motor blockade, hemodynamic stability, minimal side effects, and excellent intraoperative and postoperative analgesia.

Keywords: ASA grade I/II, Hemodynamic, Spinal anesthesia

INTRODUCTION

In Spinal anesthesia adjuvants, like Clonidine, Dexmedetomidine, midazolam, opioids, neostigmine and Magnesium Sulphate, have been used to prolong the effect of spinal anesthesia.[1-5] Clonidine and Dexmedetomidine have been repeatedly demonstrated to prolong sensory and motor block when used intrathecally with local anaesthetics.[6]

Clonidine and Dexmedetomidine have also been known to affect BP in a complicated manner after intrathecal administration, because of resisting actions at multiple sites. The combination of Clonidine or Dexmedetomidine also allows for a reduction in the total dose of the local

anaesthetic used, which translates into better hemodynamic stability intraoperatively.[7-11] Clonidine and Dexmedetomidine have also been shown to have significant analgesic effect in the postoperative duration much after the regression of the motor blockade which allows for early and pain free ambulation.[9-11]

In the view of these facts, this study is planned to differentiate the effects of Dexmedetomidine and clonidine on duration of analgesia, motor and sensory blockade and the intraoperative hemodynamic profile when mixed with Bupivacaine. This study also aims to ascertain the safety of these drugs for use in routine practice in the hospital.

METHODS

It was a randomized, double blind, prospective, observational study done for a period of one year at Command Hospital Air Force (CHAF), Bangalore in Department of anaesthesiology and critical care. All 150 patients in the age group of 15-45 years having ASA 1 and ASA 2, scheduled for elective orthopedic surgeries under spinal anaesthesia, were considered to be entitled for participation in the study. The sampling of the cases was done by simple randomization according to a machine generated arbitrary number table, without blinding. The patients were arbitrarily divided into three equal groups (50 patients each)' i.e. first group (group B) received only 3.0ml of 0.5% bupivacaine (heavy); second group (group C) received 3.0ml of 0.5% Bupivacaine (heavy) mixed with Clonidine 30µg; and third group (group D) administered with 3.0ml of 0.5% bupivacaine (heavy) mixed with 5µg Dexmedetomidine. These solutions were diluted with 0.9% saline solution to a gross volume of 3.5ml and were prepared a person not involved in the patients' care.

Exclusion criteria

Patients less than the age of 15yr. and more than 45yrs., who had comorbid conditions or using α2-adrenergic receptors antagonists, calcium channel blockers, angiotensin converting enzyme inhibitors, patients with psychiatric illness, neurological disease, as well as patients falling under class ASA III-V and patients declining to give consent were also excluded from the study.

Written informed agreement was procured from these patients for enrolling in the study. These patients were presented to a routine pre-anaesthetic evaluation (PA checkup) prior to surgery. Complete medical history and demographic profile was elicited from the patients including the age, weight, height, and history of liquor or drug intake, also history of smoking, postoperative nausea and vomiting (PONV), or motion sickness, and ability to perform normal physical activities of daily living.

Patients were premedicated with Tab Diazepam 5mg PO given at 2200hrs. night before surgery. Before intrathecal injection, patients underwent standard monitoring (GE Dash 3000), including an electrocardiogram (5 lead), noninvasive blood pressure and pulse oximeter; and baseline vital parameters were noted. An intravenous (IV) access with a 16-gauge IV cannula (B. Braun Medical, India Pvt. Ltd) was established and preloaded with 500ml of HES and 500ml of Ringer Lactate. Spinal anesthesia was performed on patient in the sitting position, using a 25-gauge LP needle (B. Braun Medical, India Pvt. Ltd) with a midline start at L3-4 interspace. After intrathecal injection, patients were instantly placed in the prone position with head elevated for 5min and, after which, they were placed in the required position to begin with surgical intervention.

Heart rate and non-invasive arterial BP were measured at 3 to 15minute intervals, and peripheral oxygen threshold was observed constantly by pulse oximeter.

The strength of pain was evaluated using a 10cm visual analog scale (VAS; 0: no pain and 10: worst pain. The patient was asked to point to the position on the line between the faces to signify the amount of pain they were currently feeling. The left endpoint indicated 'No Pain' whereas the right end indicated 'Worst pain ever'. Once the patient had indicated the amount of pain they had, the clinician reviewed the reverse side of the ruler, which indicated a number 0-10. The number that correlated with the spot on the VAS the patient pointed was the pain rating recorded.

During surgery ringer lactate solution was infused depending on the deficit and maintenance required. Supplementary IV fluids (crystalloids, colloids and blood) were regulated as preoperatively dictated by blood loss and hemodynamic volatility. The blood loss of >500ml was substituted with by packed RBCs if hemoglobin was <9.0g/L. We explained clinically applicable hemodynamic volatility as a drop of 30% or more in average arterial pressure from baseline value; we served these patients with 300ml of supplemental IV bolus of 6mg ephedrine (Claris Life sciences, Inc., Gujarat, India) if they remain unresponsive in 5minutes duration.

Statistical methodology

The three groups were compared for their efficacy to achieve maximum sensory and motor blockage, time taken to achieve designated level of blockage, success in achieving designated level of blockage and like variables including intraoperative and postoperative complications and use of analgesics. Chi-square test, ANOVA, "t"-test and paired "t"-test was used for Univariate analysis. The result was measured in terms of significance of association at 95% confidence level i.e. "p" value less than 0.05.

RESULTS

A total of 150 patients were enrolled in this particular study and were arbitrarily divided in to three groups comprising of 50 patients each.

First group (Group B) received only 3.0ml of 0.5% Bupivacaine (Heavy); Second group (Group C) received 3.0ml of 0.5% Bupivacaine (Heavy) mixed with Clonidine 30µg; and Third group (Group D) administered with 3.0ml of 0.5% Bupivacaine (Heavy) mixed with 5µg Dexmedetomidine. Mean age the patients were 30.87+/- 8.5years (ranged from 18 to 45 years); the mean weight of the patients was 66.13+/- 10.4kgs (ranged from 34 to 90kgs) and about 54.7% of the patients included in the study had the ASA score I whereas about 45.3 % patients had ASA II (Table 1).

Majority of the cases enrolled in the study were knee disorders and the rest being fracture femur, tibia (Table 2). The patients included in the study, underwent Arthroscopy and associated procedures, CRIF and associated procedures, ORIF and associated procedures, patellar procedures and miscellaneous procedures.

Table 1: Demographic profile of patient i.e. age (in year) and weight (kg) of the patients.

		No. of patients	Mean ±SD (range)	Bupivacaine N=50 Mean ±SD (range)	Clonidine N=50 Mean ±SD (range)	Dexmeditomedine N=50 Mean ±SD (range)
Age		150	30.87±8.5 (18-45)	32.9±7.8 (18-44)	27.6±7.2 (19-45)	31.9±8.9 (18-45)
Weight		150	66.13±10.4(34-90)	64.21±9.4(34-78)	66.29±11.2(46-90)	68.40±10.4 (48-90)
ASA	I	82	54.7 %	29 (58%)	27 (54%)	26 (52%)
	II	68	45.3 %	21 (42%)	23 (43%)	24 (48%)

Table 2: Diagnosis of the operated patients.

Type of surgery	No. of patients	(%)
Femur fracture	28	18.7
Fracture tibia	26	17.3
Knee disorders	69	46.0
Miscellaneous	27	18.0

Of the three group of patients, Group D (Dexmedetomidine) showed longest duration of mean motor blockade followed by Group C (Clonidine) whereas the Group B (Bupivacaine) had least duration mean motor blockade, among the three (p >0.001) (Table 3). Group D (Dexmedetomidine) also showed longest duration of mean sensory blockade followed by Group C (Clonidine) whereas the Group B had least duration mean sensory blockade, among the three (p > 0.001) (Table 3).

Mean heart rate of patients at preoperative interval was 79.3±2.5, 77.9±4.4 and 77.8±3.4 in patients of Group B, Group C and Group D respectively. Mean heart rate of patients at preoperative interval were showing significant intergroup difference (p=0.010). Mean heart rate of patients of Group B, were slightly higher than that of Group C and Group D. At spinal, a group D showed minimum fall in mean heart rate as compared to Group B, Group C (Appendix 1; Figure 1).

Table 3: Comparison of duration among groups.

	Bupivacaine Mean ±SD (range)	Clonidine mean ±SD (range)	Dexmeditomedine mean ±SD (range)	P value	T value
Motor block	166.48±46.5(84-278)	243.84±58.10 (111-398)	408.0±82.9 (245-678)	0.000	
Sensory block	166.32±46.7(84-278)	254.30±50.2(164-389)	466.68±83.6 (259-596)	0.000	
Rescue analgesia	235.6±24.6(189-307)	346.8±43.1(287-415)	484.9±19.8 (390.8-539.8)	0.000	
Highest pain score	6.8±2.2 (4-8)	5.3±1.8 (3-6)	4.6±1.1 (2-5)	0.000	

At preoperative interval mean systolic as well as diastolic blood pressure of Group B was slightly higher than Group C and Group D. At the time when spinal anaesthesia was given, a slight fall in SBP /DBP was observed in all the Groups (Appendix 02/03; Figure 2/3).

Mean heart rate of patients at preoperative interval was 78.8 ±3.2, 76.3±3.3 and 76.1±2.1 in patients of Group B, Group C and Group D respectively, with Group C and Group D showing slightly lower mean heart rate as compared with that of the mean heart rate of Group B but

the values were not statistically significant (Appendix 04; Figure 4).

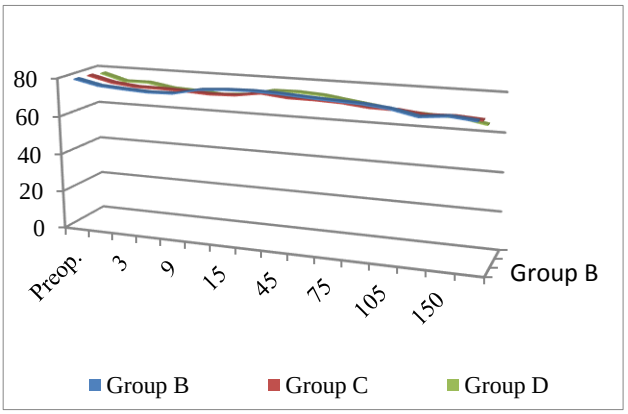

Figure 1: Comparison of heart rate (bpm) between three groups at different time intervals.

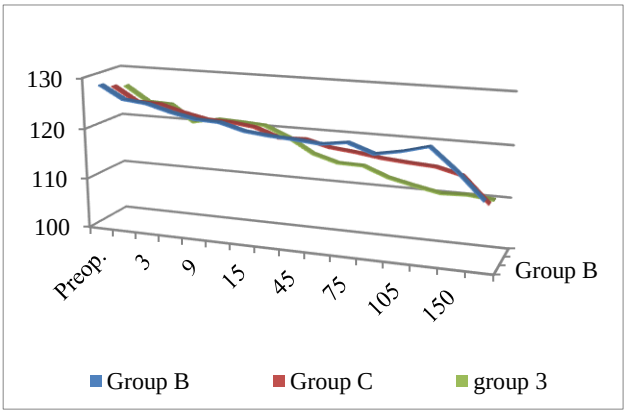

Figure 2: Comparison of systolic blood pressure mm Hg between three groups at different time intervals.

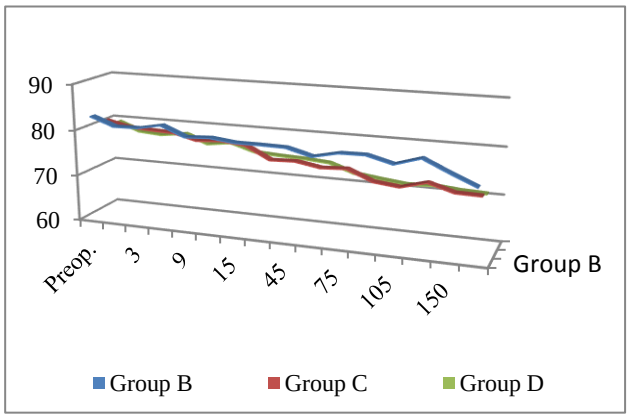

Figure 3: Comparison of DBP (mm Hg) between three groups at different time intervals.

Mean systolic blood pressure of patients at immediate post-operative interval was 126.1±3.2, 123.8±4.6 and 122.9±5.2 in patients of Group B, Group C and Group D respectively, with Group C and Group D showing slightly lower mean systolic blood pressure as compared with that of the mean systolic blood pressure of Group B but the values were not statistically significant (Appendix 5; Figure 5).

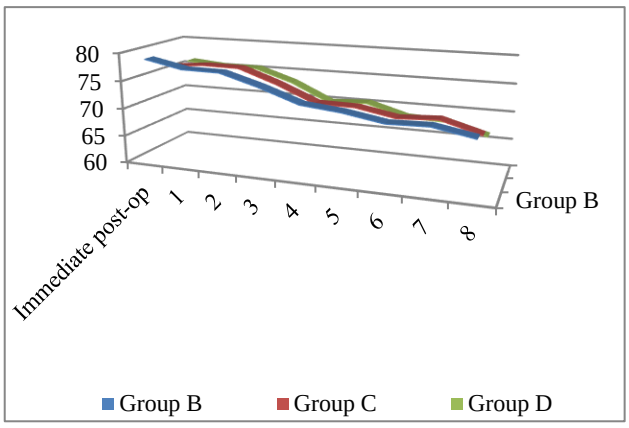

Figure 4: Comparison of post-operative heart rate (bpm) between three groups at different time intervals.

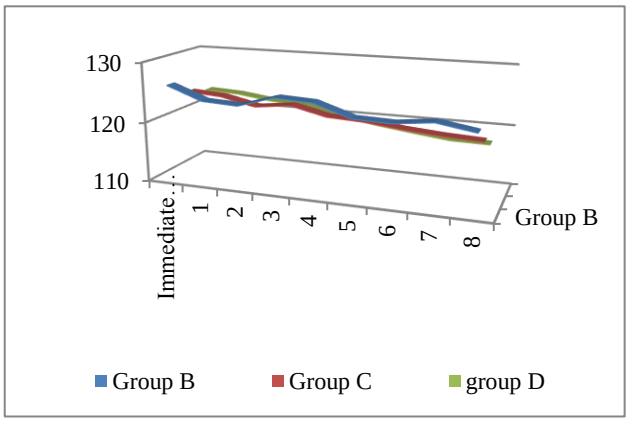

Figure 5: Comparison of post-operative systolic blood pressure (mm Hg) between three groups at different time intervals.

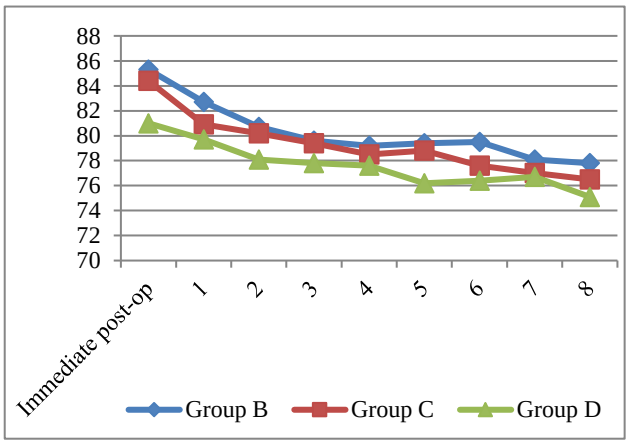

Figure 6: Comparison of post-operative diastolic blood pressure (mm Hg) between three groups at different time intervals.

Mean diastolic blood pressure of patients at immediate post-operative interval was 85.3±1.6, 84.4±3.8 and 81.0±3.4 in patients of Group B, Group C and Group D respectively, with Group C and Group D showing slightly lower mean diastolic blood pressure as compared with that of the mean diastolic blood pressure of Group B but the values were not statistically significant (Appendix 6; Figure 6).

Of the three group of patients, Group D (Dexmedetomidine) showed longest duration of mean time of rescue analgesia followed by Group C whereas the Group B had least duration of mean time of rescue analgesia, among the three ($p > 0.001$) (Table 3). Group D (Dexmedetomidine), showed least mean score on VAS followed by Second group (Group C) whereas the First group (Group B) which received only 3.0ml of 0.5% Bupivacaine (Heavy) had largest mean VAS score, among the three. Moreover, the difference in duration of mean VAS score among the three ($p > 0.001$) (Table 3).

All the three group of patients did not show any significant changes in the hemodynamic status which required any intervention.

Figure 7: Visual analogue scale (VAS).

DISCUSSION

The mechanisms of the analgesic action of α2-agonists have not been completely illuminated. The activation of inwardly improving G1-protein-gated potassium channels results in membrane hyperpolarization decreasing the firing rate of excitable cells in the central nervous system (CNS). This is considered a remarkable mechanism of inhibitory neuronal action of α2-adrenoceptor agonists.[12] Another prominent physiologic action assigned to α2-adrenoceptors is their depletion of calcium conductance into the cell, thus inhibiting neurotransmitter release. These two mechanisms represent two very different ways of effecting analgesia: in the first, the nerve is prevented from ever firing, and in the second, it cannot propagate its signal to its neighbor.[12] Activation of the receptors in the brain and spinal cord inhibits neuronal firing causing hypotension, bradycardia, sedation, and analgesia.[13] In general, presynaptic activation of the α2-adrenoceptor inhibits the release of norepinephrine terminating the propagation of pain signals. Postsynaptic activation of α2-adrenoceptors in the central nervous system inhibits sympathetic activity and thus can decrease blood pressure and heart rate.[14]

Administration of anα2-agonist via an intrathecal or epidural route provides an analgesic effect in postoperative pain without serious sedation.[15] This effect is due to the sparing of supraspinal CNS sites from uncontrolled drug exposure, resulting in strong analgesia without heavy sedation. Most of the clinical experience gained in the use of intrathecalα2-adrenoceptor agonists has been reported with Clonidine. The use of intrathecal Clonidine has a well-established synergetic effect with local anesthetics.[16-19] Clonidine prolongs the time span of intrathecally managed local anesthetics and has robustantinociceptive properties.[20-25] Although such prolongation of the effects of local anesthetics has been described for oral and IV Clonidine administration, the intrathecal route is more effective in prolonging Bupivacaine spinal anesthesia.[23,25-28]

In our study we compared the duration of sensory and motor block in the three groups of patients, Group B was given Intrathecal Bupivacaine alone, Group C was given intrathecal Bupivacaine plus Clonidine and group D was given intrathecal Bupivacaine plus Dexmedetomidine. As compared to group B, we found that the Group C patients hadprolonged motor and sensory blockade ($p < 0.05$). These results were similar to the findings reported by Seah YS et al and Racle JP et al.[29,30] In either of the groups we did not observe any hypotension either during or after anaesthesia. Further even though there was statistically significant bradycardia ($p = 0.03$) it was not significant enough to warrant treatment with iv Atropine. But this is in contrary to what has been observed by Seah YS et al and Racle JP et al.[29,30] In the studies done by Seah YS et al and Racle JP et al, higher incidence of side effects such as hypotension and bradycardia were reported in the clonidine group and such patients were treated with iv Ephedrine and iv Atropine respectively.[29,30] This higher incidence of side effects

may be attributed to the higher dose (150 microgram) of clonidine received by the patients in these studies as compared to a lower amount (30 microgram) received by patients in our study. Chiari A et al have substantiated the fact that higher incidence of side effects such as hypotension and bradycardia increase with the increase in the dose of clonidine (> 100 micrograms).[31]

Fewer studies are available which compare a combination of intrathecal Dexmedetomidine and local anesthetics. Fukushima et al administered 2µg/kg epidural Dexmedetomidine for postoperative analgesia in humans but did not report neurologic deficits.[30] In our study, the Group D patients reported longest duration of sensory and motor block (mean 466.68 and 408.00min). This is similar to observations reported by Kanazi GE et al.[2] Further Group D patients had stable haemodynamics intra-operatively and post operatively. This is similar to that reported by Gupta R et al.[32]

Of the three groups of patients, Group D showed longest duration of mean time for rescue analgesia (484.90 min) followed by Group C (346.80 min) whereas the Group B required rescue analgesia earliest (235.6 min). Of the three groups of patients, group D showed least mean score on VAS (4.6) followed by Group C (5.3) whereas the Group B had the highest mean VAS score (6.8). These finding are in conformity with the reported pattern of observations in other similar studies.[32,33]

CONCLUSION

5µg Dexmedetomidine seems to be an attractive adjuvant to spinal Bupivacaine, even better than Clonidine in surgical procedures. Clonidine can be considered a good choice as adjuvant, if its dose is kept at a lower level range (<100microgram). Both of these combinations provide prolonged sensory and motor blockade, haemodynamic stability, minimal side effects and excellent intraoperative and postoperative analgesia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sankaranand P, Krishna Prasad GV. Duration of analgesia, sensory and motor blockade and intra operative hemodynamic changes caused by intrathecal bupivacaine, bupivacaine plus clonidine and bupivacaine plus dexmedetomidine in spinal anesthesia: prospective, comparative study. Int J Res Med Sci 2018;6:493-502.

Annexure

Annexure I: Comparison of heart rate (bpm) between three groups at different time intervals.

Time interval (min)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	N	Mean	SD	N	Mean	SD	"t"	"p"
Preop.	50	79.3	2.5	50	77.9	4.4	50	77.8	3.4	0.511	0.010
At spinal	50	76.5	4.1	50	74.8	4.0	50	74.2	4.2	-2.379	0.019
3	50	75.6	4.5	50	74.4	6.1	50	74.3	5.0	-1.094	0.076
6	50	74.9	4.0	50	74.3	5.4	50	72.1	4.8	-5.423	0.031
9	50	75.2	5.1	50	73.9	4.9	47	71.5	5.0	0.293	0.070
12	50	78.0	4.3	50	73.2	5.4	46	70.5	5.3	0.524	0.021
15	50	78.9	4.4	49	73.6	5.5	43	71.4	5.2	0.519	0.005
30	49	79.2	4.6	47	75.5	5.6	45	74.4	5.1	1.364	0.075
45	47	78.8	4.4	46	74.1	5.1	47	74.6	4.4	1.964	0.052
60	46	77.9	4.7	38	74.0	5.5	46	73.8	4.9	1.715	0.190
75	38	77.2	4.8	33	73.5	5.4	38	71.9	4.5	1.798	0.076
90	33	76.6	4.1	31	72.1	5.3	35	70.1	4.2	2.172	0.033
105	31	75.2	4.1	28	71.9	5.2	33	68.3	5.2	2.450	0.017
120	28	72.4	4.7	19	70.4	5.6	29	67.6	4.7	2.215	0.031
150	19	73.7	4.5	17	70.9	5.7	25	67.5	4.9	2.420	0.020
180	17	72.4	5.1	15	70.0	5.9	10	65.0	5.3	1.955	0.057

Annexure II: Comparison of systolic blood pressure mm Hg between three groups at different time intervals.

Time interval (min)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	n	Mean	SD	n	Mean	SD	"t"	"p"
Preop.	50	128.5	5.3	50	127.4	5.1	50	126.6	5.7	-0.528	0.099
At Spinal	50	125.9	3.6	50	124.6	3.2	50	123.6	4.1	-1.205	0.001
3	50	125.4	5.8	50	124.4	4.6	50	123.4	3.6	-1.002	0.091
6	50	124.1	4.5	50	123.1	4.9	50	120.1	5.8	-1.181	0.031
9	50	123.1	4.9	50	122.1	4.5	47	121.1	5.0	-1.099	0.038
12	50	122.9	5.0	50	121.9	5.2	46	120.9	5.5	-1.284	0.052
15	50	121.6	5.3	49	121.3	4.2	43	120.6	5.2	-1.640	0.010
30	49	121.1	4.3	47	119.6	4.1	45	118.6	3.3	-0.488	0.099
45	47	120.8	4.7	46	119.8	4.7	47	115.8	4.7	-0.696	0.089
60	46	120.4	4.6	38	118.6	3.8	46	114.4	4.9	-0.456	0.043
75	38	121.1	3.9	33	118.1	4.7	38	114.3	5.7	-0.879	0.039
90	33	119.4	5.7	31	117.4	4.0	35	112.4	5.0	-0.998	0.023
105	31	120.3	4.3	28	117.0	3.9	33	111.3	4.9	-1.481	0.046
120	28	121.6	6.1	19	116.7	5.1	29	110.3	5.8	-1.399	0.097
150	19	117.5	4.7	17	115.5	5.0	25	110.5	5.7	-0.528	0.099
180	17	112.6	4.6	15	110.6	2.8	10	110.0	3.0	-1.205	0.052

Annexure III: Comparison of DBP (mm Hg) between three groups at different time intervals.

Time interval (min)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	N	Mean	SD	N	Mean	SD	"t"	"p"
Preop.	50	82.9	2.5	50	80.9	4.4	50	79.5	4.3	0.511	0.017
At spinal	50	81.0	4.1	50	79.8	4.0	50	77.6	3.7	-1.379	0.019
3	50	81.1	1.8	50	79.5	3.8	50	77.2	3.4	0.730	0.077
6	50	82.1	1.6	50	79.3	3.0	50	77.9	3.2	-1.825	0.071
9	50	80.0	1.7	50	78.0	2.6	47	76.0	2.6	-1.418	0.017
12	50	80.3	1.5	50	78.4	3.1	46	76.7	3.1	-0.903	0.069
15	50	79.7	2.0	49	77.9	2.7	43	75.1	2.7	-2.550	0.013
30	49	79.7	1.9	47	75.2	2.5	45	74.8	3.5	-0.874	0.100
45	47	79.6	1.9	46	75.4	2.5	47	74.6	3.5	-0.299	0.021
60	46	78.2	2.0	38	74.5	2.5	46	74.2	2.5	-1.344	0.022
75	38	79.4	1.9	33	74.8	2.7	38	72.4	2.1	-0.488	0.091
90	33	79.5	1.4	31	72.6	3.0	35	71.7	2.9	-1.607	0.012
105	31	78.1	2.6	28	72.0	2.1	33	71.1	2.5	-1.745	0.001
120	28	79.8	2.3	19	73.5	2.7	29	71.4	2.0	-1.200	0.059
150	19	77.3	2.5	17	71.9	4.4	25	70.9	3.4	0.511	0.010
180	17	75.0	4.1	15	71.8	4.0	10	70.7	4.6	-1.379	0.019

Annexure IV: Comparison of post-operative heart rate (bpm) between three groups at different time intervals.

Time interval (hours)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	N	Mean	SD	N	Mean	SD	"t"	"p"
Immediate post-op	50	78.8	3.2	50	76.3	3.3	50	76.1	2.1	0.622	0.109
1	50	77.4	6.7	50	76.9	6.1	50	75.5	2.8	0.524	0.019
2	48	77.3	5.1	44	76.8	2.1	50	75.5	3.2	0.519	0.093
3	47	75.3	3.2	44	74.4	6.1	50	73.3	2.8	0.605	0.024
4	47	72.9	6.7	42	71.5	2.1	50	70.1	3.2	0.175	0.031
5	47	72.2	5.1	41	71.4	2.8	47	70.5	5.0	0.293	0.070
6	45	71.0	2.3	40	70.1	3.2	46	68.5	6.1	0.524	0.001
7	45	71.2	5.7	38	70.5	6.7	43	68.3	2.1	0.519	0.005
8	42	69.9	4.6	37	68.5	5.6	45	66.3	2.8	1.364	0.075

Annexure V: Comparison of post-operativesystolic blood pressure (mm Hg) between three groups at different time intervals.

Time interval (hours)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	N	Mean	SD	N	Mean	SD	"t"	"p"
Immediate post-op	50	126.1	3.2	50	123.8	4.6	50	122.9	5.2	-0.696	0.043
1	50	123.9	5.8	50	123.4	4.9	50	122.6	4.3	-0.466	0.039
2	48	123.6	4.5	44	122.1	4.5	50	121.8	4.7	-0.779	0.023
3	47	125.4	4.9	44	122.8	5.2	50	121.4	4.8	-0.998	0.024
4	47	125.1	5.0	42	121.4	2.1	50	120.1	4.7	0.175	0.011
5	47	123.1	5.2	41	121.1	2.8	47	119.1	5.0	0.293	0.070
6	45	122.9	4.3	40	120.4	3.2	46	118.3	2.5	-0.388	0.001
7	45	123.6	4.7	38	119.9	6.7	43	117.6	3.6	-0.696	0.005
8	42	122.6	4.8	37	119.6	5.6	45	117.5	5.8	-0.466	0.075

Annexure VI: Comparison of post-operative diastolic blood pressure (mm Hg) between three groups at different time intervals.

Time interval (hours)	Group B (n=50)			Group C (n=50)			Group D (n=50)			Significance of difference	
	N	Mean	SD	N	Mean	SD	N	Mean	SD	"t"	"p"
Immediate post-op	50	85.3	1.6	50	84.4	3.8	50	81.0	3.4	-1.094	0.076
1	50	82.7	1.7	50	80.9	3.0	50	79.7	3.2	-5.423	0.081
2	48	80.7	1.5	44	80.2	2.6	50	78.1	2.6	0.293	0.070
3	47	79.6	2.0	44	79.4	3.1	50	77.8	3.1	0.524	0.001
4	47	79.2	1.9	42	78.5	2.7	50	77.6	2.7	0.519	0.005
5	47	79.4	1.9	41	78.8	2.5	47	76.2	3.5	1.364	0.075
6	45	79.5	2.0	40	77.6	2.5	46	76.4	3.5	1.964	0.052
7	45	78.1	1.9	38	77.0	2.5	43	76.7	2.5	1.715	0.190
8	42	77.8	1.4	37	76.5	2.7	45	75.1	2.1	-1.094	0.076