National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Comparative study of variations in blood pressure and heart rate among normotensive patients and hypertensive patients receiving angiotensin receptor blockers during surgery under spinal anesthesia

Dinakar K R[1], Narendranath Sanji[1], Ravishankar R B[2], Vidya H K[1], Shashikala G H[1]

[1]Department of Pharmacology, JJM Medical College, Davangere, Karnataka, India, [2]Department of Anesthesiology, JJM Medical College, Davangere, Karnataka, India

Correspondence to: Narendranath Sanji, E-mail: sanji_naren@yahoo.com

Received: August 17, 2018; **Accepted:** September 06, 2018

ABSTRACT

Background: Hypotension is the most common complication associated with spinal anesthesia and more common in patients with a history of hypertension. Regular use of antihypertensive medications can prevent this effect. However, the continuation of the drugs that inhibit the renin-angiotensin-aldosterone system on the day of surgery is still a matter of debate. **Aims and Objectives:** This study aims to study the intraoperative changes of blood pressure (BP) and heart rate in patients on angiotensin receptor blockers (ARBs) undergoing surgery under spinal anesthesia and to compare the data with normotensive patients. **Materials and Methods:** Thirty normotensives (Group A) and 30 hypertensive patients, who were regularly on ARBs and continued the drug on the day of surgery (Group B) was compared. The baseline BP and heart rate were recorded. After spinal anesthesia, the BP and heart rate were noted at predetermined time intervals. Primary parameters evaluated were changed in mean arterial pressure and change in the heart rate. **Results:** The incidence of hypotension ($P = 0.04$) and fall in SBP ($P = 0.01$) was statistically significant in Group B. There was no significant change in the heart rate. The change in diastolic BP was not statistically significant. The usage of rescue medication was more in the study group than in the controls, but it was not statistically significant. **Conclusion:** There is an increased chance of intraoperative hypotension in hypertensive patients continuing ARBs on the day of surgery, but the hypotension can be managed effectively with vasopressor agents.

KEY WORDS: Hypertension; Spinal Anesthesia; Angiotensin Receptor Blockers; Hypotension

INTRODUCTION

Hypotension is the most common complication associated with spinal anesthesia. Incidence of hypotension is more common in patients with a history of hypertension.[1] Although antihypertensive medications decrease this effect by controlling blood pressure (BP), their varying effects on the cardiovascular system can have multiple effects on the hemodynamics during the initial phase of spinal anesthesia.[2] Better knowledge about these agents will help the anesthesiologist to anticipate the hemodynamic changes associated with its usage.

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2018.8.0827106092018	

Most of the general and spinal anesthetic drugs reduce the influence of sympathetic tone on the cardiovascular system. Therefore, under anesthetic influence, there is increased reliance on the renin–angiotensin system (RAS) for the maintenance of BP. Hence, the drugs that antagonize RAS, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs) block the RAS response to hypotension and

increase the risk of hypotension intraoperatively.[3] The chances that these patients requiring inotropic support to bring the BP back to normal levels are high.

Researchers have studied the effects of antihypertensive medications on general anesthesia as well as spinal anesthesia. Studies have also been done to determine the benefits of continuing the calcium channel blockers and beta-blockers on the day of surgery both under general anesthesia[4,5] and spinal anesthesia.[6] There were conflicting reports on the continuation of ACE inhibitors on the day of surgery in patients undergoing surgery in spinal anesthesia.[7,8] The continuation of the drugs that inhibit the renin-angiotensin-aldosterone system is still a matter of debate. This study was done to observe and analyze the effects of ARBs on the BP and heart rate in patients undergoing surgery under spinal anesthesia when they continue ARBs even on the day of surgery.

MATERIALS AND METHODS

The study was done in Chigateri Government Hospital and Bapuji Hospitals attached to JJM Medical College, Davangere. Institutional ethical clearance was obtained before starting the study. 60 patients undergoing surgery under spinal anesthesia were included in the study. Group A or the control group consisted of 30 normotensive patients and Group B or the test group consisted of 30 hypertensive patients on monotherapy with ARBs.

Inclusion Criteria

Patients with essential hypertension and on ARBs to treat hypertension for at least 1 month were included in the study. Patients scheduled for elective surgeries under spinal anesthesia.

Exclusion Criteria

Patients with other coexisting diseases such as diabetes, coronary artery diseases, cardiac diseases, severe hypovolemia, pregnancy, and sepsis were excluded from the study.

At the preanesthetic clinic, after a written informed consent, detailed history was taken from the patients regarding their antihypertensive medications, duration of treatment, other coexisting diseases, and concomitant medications.

On arrival in the operating room, all the patients were preloaded with 10 mL/kg of Ringer lactate (RL) solution. Standard monitoring included continuous electrocardiography, pulse rate, oxygen saturation with a pulse oximeter, and automated non-invasive BP (NIBP). Baseline values were taken as the reading during the rest period after the infusion of fluids.

Lumbar puncture was performed with all the aseptic precautions in the L_3–L_4 space. When free flow of the cerebrospinal fluid was established, 3 mL of 0.5% hyperbaric bupivacaine was administered over a 10 s period. The patient was put in a supine position. NIBP and pulse rate were recorded every 2 min for the first 10 min and every 5 min till the end of the surgical procedure that is at 2 min, 4 min, 6 min, 8 min, 10 min, 15 min, and 20 min.

Hypotension was defined as a decrease of mean arterial pressure (MAP) of more than 30% from baseline within a 20 min interval, and relevance was defined as a therapeutic intervention with fluids or pressors within 20 min.[1] Hypotension, if occurred, was treated with injection mephentermine 6 mg/dose and IV fluids 5 mL/kg until both systolic arterial pressure (SBP) and MAP increased above the threshold level. The time to rescue dose and the total dose of rescue medication was recorded.

Bradycardia, defined as heart rate <50 beats/min, not responding to intravenous fluids (IVF) was treated with injection atropine 0.6 mg IV stat. Maintenance infusion of RL was continued throughout the surgery and the total IV fluid administered throughout the surgery was recorded.

The administration of all rescue drugs was at the discretion of the anesthetist.

Statistical Analysis

Baseline data were analyzed using descriptive statistics. The changes of SBP, diastolic BP (DBP), MAP, and heart rate were analyzed as follows:

The changes of the parameter within the group were first analyzed using one-way ANOVA, and the variation within the different time intervals was analyzed with the *post hoc* tests to know which is the group with maximum variability compared to baseline.

Intergroup comparison at the 2 min, 4 min, 6 min, 8 min, 10 min, 15 min, and 20 min from the data of controls and cases, respectively, was done by unpaired *t*-test.

$P \leq 0.001$ was considered very highly statistically significant, a value of ≤0.01 was highly statistically significant, a value of ≤0.05 was statistically significant, and a value >0.05 was statistically insignificant.

RESULTS

Patient Disposition and Baseline Characteristics

Patients were enrolled between March 2013 and September 2014 from the Bapuji Hospital and Chigateri district hospitals attached to the JJM Medical College, Davangere. 60 patients undergoing surgery under spinal anesthesia were

included in the study. Group A or the control group consisted of 30 normotensive patients and Group B or the test group consisted of 30 hypertensive patients on monotherapy with ARBs. All the patients were taken up for the surgery after the physician and anesthetist regarded them fit for surgery. The demographic characteristics of both the groups were comparable as summarized in Table 1.

There was no significant difference in the sex distribution in the two groups. The mean body weight was comparable in both the groups. The average height of the block after spinal anesthesia was at the 7–8th thoracic level. The baseline SBP was on an average 14.5 mm of Hg higher in the hypertensive group than the normotensive group. The baseline DBP was on an average 4.4 mm of Hg higher in the hypertensive group than the normotensive group. The baseline MAP was on an average 9.9 mm of Hg higher in the hypertensive group than the normotensive group. The baseline heart rate was almost the same in both the groups, i.e., 80 bpm.

In Group B, the average duration of use of antihypertensive medication, i.e., ARBs were 1.3 years and the most common ARB were telmisartan 40 mg once per day.

Table 1: Baseline patient characteristics

Characteristic	Groups (n=30)	
	Group A	Group B
Age in years	44±15	54±8
Sex (M: F)	16:14	17:13
Weight in kg	53±10	61±11
Average height of block	T7–T8	T7–T8
Baseline SBP in mm of Hg	124.7±12	139.2±17.8
Baseline DBP in mm of Hg	77±5.3	81.4±8.07
Baseline MAP in mm of Hg	92.7±5.7	102.6±9.7
Baseline heart rate in beats per minute	80.83±10.07	79.6±9.2

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure

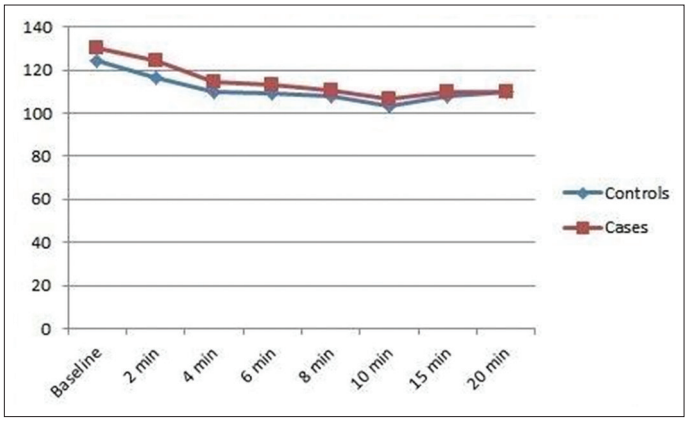

Figure 1: Variations in the systolic blood pressure (SBP). The changes from the baseline of SBP in the first 20 min after spinal anesthesia. X-axis - duration, Y-axis - SBP in mm of Hg. The maximum fall of SBP is seen at 10 min in both the groups

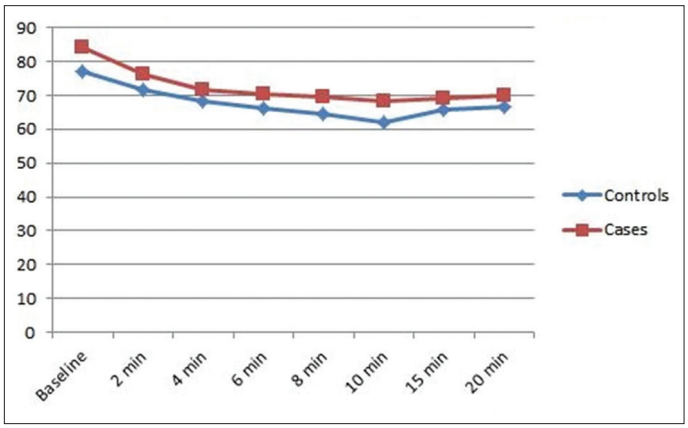

Figure 2: Variations in the diastolic blood pressure. The changes from the baseline of DBP in the first 20 min after spinal anesthesia. Xaxis - duration, Y-axis - DBP in mm of Hg. The maximum fall of DBP is seen at 10 min in both the groups

BP

Automated NIBP was used to monitor all patients of both the groups before spinal anesthesia and after spinal anesthesia intraoperatively. Readings were recorded at 2 min, 4 min, 6 min, 8 min, 10 min, 15 min, and 20 min. The administration of either vasopressors or hypotensives during the surgery was at the discretion of the anesthetist. After 20 min, any variation in the BP was considered to be due to surgical causes like blood loss as the level of anesthetic block gets fixed at the particular dermatome.

SBP

The mean SBP was 124.7 mm of Hg and 130.2 mm of Hg in the Group A and Group B, respectively, at the baseline before the patient was administered spinal anesthesia. The SBP dropped after spinal anesthesia [Figure 1]. In both the cases and controls, the fall was maximally seen at 10 min post-spinal anesthesia. The fall of SBP in the controls or cases was not statistically significant over the time periods when compared with baseline of the same group as analyzed by one-way ANOVA followed by a *post hoc* analysis. The unpaired *t*-test did not show any difference statistically when the changes in the SBP were compared between Group A and Group B at the respective time intervals.

DBP

The mean DBP was 77.06 mm of Hg and 84.4 mm of Hg in the Group A and Group B, respectively, at the baseline [Figure 2]. The DBP dropped after spinal anesthesia in both the cases and controls and the fall was maximally seen at 10 min post-spinal anesthesia. The fall of DBP in the controls or cases was not statistically significant over the time periods when compared with baseline of the same group. The unpaired *t*-test showed that the fall was greater in the control

group than the cases at 2 min, 6 min, 8 min, and 10 min (P = 0.02, 0.04, 0.01, and 0.01, respectively).

MAP

The change seen in MAP was similar to the SBP and DBP. The baseline mean of MAP was 92.7 mm of Hg and 102.6 mm of Hg in the control and case group, respectively. There was a fall in the MAP following spinal anesthesia [Figure 3], but the fall was not statistically significant within the group. When the MAP of Group A was analyzed against the data obtained from Group B, there was a significant drop of more than 30% in patients of Group B (P = 0.04).

Heart Rate

The mean heart rate at the baseline was 80.8 bpm in controls and 79.6 bpm in cases. The heart rate also reduced after spinal anesthesia [Figure 4] with a maximum fall at 10 min in Group A and 6 min in Group B. In both the groups, there was an increase in heart rate after the maximal drop, but the increase in Group B was greater than the increase in Group A. Statistically the heart rate variation was not significantly different both within the groups and in between the groups.

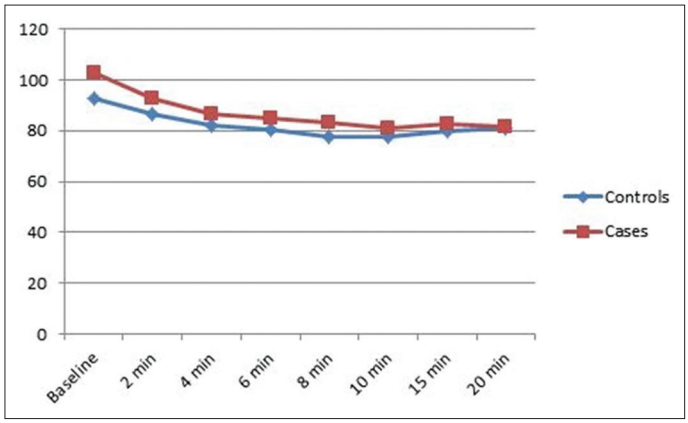

Figure 3: Variations in the mean arterial pressure. The changes from the baseline of MAP in the first 20 min after spinal anesthesia. X-axis - duration, Y-axis - MAP in mm of Hg. The maximum fall of DBP is seen at 10 min in both the groups

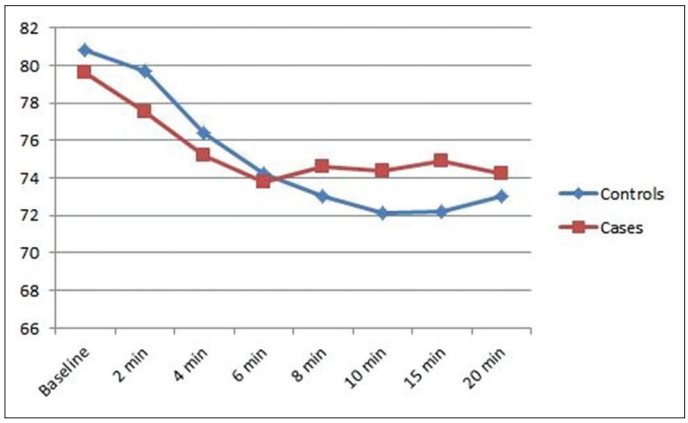

Figure 4: Variations in the heart rate. The changes from the baseline of heart rate in the first 20 min after spinal anesthesia. X-axis - duration, Y-axis - heart rate in beats per minute. The fall in heart rate is maximum at 10 min in Group A and at 6 min in Group B. The increase in heart rate following the maximal drop is seen to a greater degree in Group B than in Group A

The total number of cases that had significant drop (30% from baseline) of MAP was 1 and 6 in Groups A and B, respectively. The difference was statistically significant (P = 0.04) showing the incidence of hypotension was significant in hypertensive patients who were regularly on AT 1 antagonists and continued it even on the day of surgery [Table 2]. On evaluating the SBP, 8 patients in Group A and 17 patients in Group B had a drop of 30% from baseline. There was a statistically significant difference between Groups A and B (P = 0.01). A 30% drop in DBP was also seen in 5 and 9 patients in Group A and B, respectively. However, Chi-square test between groups did not reveal any statistical significance. The use of vasopressors in response to hypotension was necessary in 8 controls and 15 cases. The difference was not statistically significant (P = 0.06). The incidence of bradycardia (HR <50 bpm) was seen in 4 patients each of both the groups and the rescue therapy was injection atropine in all cases except one where injection glycopyrrolate was used. The use of IVF was almost similar in both the groups. The average use of IVF per patient was 1.25 L in Group A and 1.30 L in Group B.

One of the patients in the Group B had hypotension following spinal anesthesia that did not respond to three successive 1 ml doses of injection mephentermine (6 mg/mL). Hence,

Table 2: The incidence of hypotension, bradycardia, IVF usage, and the rescue medication usage in the study

Parameter	Groups		*P* value
	Controls	Cases	
MAP with 30% drop			
n (%)	1 (3.3)	6 (20)	0.04
SBP with 30% drop			
n (%)	8 (26.6)	17 (56.6)	0.01
DBP with 30% drop			
n (%)	5 (16.6)	9 (30)	0.2
Vasopressor			
n (%)	8 (26.6)	15 (50)	0.06
Fluids			
Average	1.25 L	1.30 L	>0.05 (NS)
Bradycardia			
n (%)	4 (13.33)	4 (13.33)	>0.05 (NS)
Atropine			
n (%)	4 (13.33)	4 (13.33)	>0.05 (NS)

Chi-square test with P<0.05 considered statistically significant.
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, NS: Not significant

his surgery was canceled after 6 min of administering spinal anesthesia.

DISCUSSION

In our study, we identified patients on antihypertensive medications, without any coexisting illnesses. We enrolled 30 patients in each group. Group A or the control group consisted of 30 normotensive patients and Group B or the test group consisted of 30 hypertensive patients on monotherapy with ARBs. Hypotension, defined as a 30% drop in MAP, the most important predictor of morbidity[1], was seen in one patient of Group A and six patients of Group B. This was statistically significant showing that the incidence of hypotension is higher in patients of Group B. There was a significant drop in the SBP in patients of Group B compared to patients of Group A; 8 patients in Group A and 17 patients in Group B had a drop of 30% from baseline. There was a statistically significant difference between Groups A and B ($P = 0.01$). This was considered by the treating anesthetist as significant hypotension and those patients received mephentermine. A 30% drop in DBP was also seen in 5 and 9 patients in Groups A and B, respectively. This was not considered criteria for rescue medication. Of the patients in Group A, 8 patients and 15 patients in Group B received vasopressor support. As mentioned earlier, the rescue medication was given solely under the anesthetist's discretion and it was based on the SBP. Hence, although 17 patients had a drop of 30% in SBP, only 15 received mephentermine. The other two patients had SBP of more than 100 mm of Hg even with a drop of 30% SBP. The difference in rescue medication usage among groups was not statistically significant probably indicating that though the incidence of intraoperative hypotension is high in hypertensive patients on ARBs and has continued their medication on the day of surgery under spinal anesthesia, the need for vasopressor support is not significantly higher than normotensives. There was no statistically significant change of DBP in the test and control groups in the first 20 min. The baseline DBP of the Group A was about 7 mm of Hg lower than the baseline DBP of Group B. This difference existed in nearly at all the time intervals 4.7, 3.2, 4.1, 4.8, 6.1, 3.6, and 3.5 (in mm of Hg) at 2 min, 4 min, 6 min, 8 min, 10 min, 15 min, and 20 min, respectively, where the DBP of Group B was higher than Group A, statistically significant at 2 min, 6 min, 8 min, and 10 min. These values did not have any clinical implication and did not warrant a rescue therapy. The heart rate, in our study, decreased after administration spinal anesthesia till about 10 min in Group A and 6 min in Group B. Then, the heart rate increased gradually but did not reach the mean baseline. Although the heart rate increased in both the groups, the increase was much earlier and more in Group B. This is probably due to the fact that heart rate and BP are inversely related.[9] The excessive fall in BP in Group B might have resulted in earlier increase in heart rate.

Hypotension is the most common physiologic effect of spinal anesthesia, but it is most often misinterpreted as a complication. Clear distinction must be made between physiologic effects of an anesthetic technique and complications that may harm the patient. Rooke *et al*.[10] found out that an exaggerated decrease in BP occurs in elderly patients. He also opined that in people with cardiovascular disease also the decrease is significant and is about 25% decrease in systemic vascular resistance and a 10% decrease in cardiac output. Singla *et al*.[11] found out that following variables were independently associated with an early fall in BP following anesthesia: Age, female sex, body mass index ≥ 30 kg/m^2, history of hypertension, diabetes, anemia, baseline heart rate, baseline SBP and DBP, pulse pressure, vascular overload index, and sensory level of blockade higher than or equal to T_6. The average age in patients of Group B was approximately 10 years more than Group A. This may be one of the reasons for the excessive fall in MAP in patients of Group B. Samad *et al*.,[5] Sear *et al*.,[4] and Hohne *et al*.[8] have all studied the influence of antihypertensive medications on patients undergoing surgery under both general and spinal anesthesia, respectively, and have all opined that a fall in 25% of BP might be hazardous to the patients as it can compromise arterial supply in the coronary and cerebral circulations. Sear *et al*.[4] reported that the pressor responses to laryngoscopy and intubation are unaffected by concurrent medication in mild-to-moderate hypertensive patients, but there was exaggerated hypotension in patients who were receiving ACE inhibitors. Coriat *et al*.[12] reported that the chances of hypotension following induction were high in hypertensive patients who were chronically receiving ACE inhibitors. The data regarding effects of the AT-1 antagonists on spinal anesthesia are not available. However, in our study, following spinal anesthesia, there was no statistically significant impairment of patient hemodynamics needing intervention.

In our study, the surgery of one of the patients in the control group was canceled as he had refractory hypotension following spinal anesthesia. Such an entity, called vasoplegic syndrome, has been described with drugs inhibiting RAS and general anesthesia but not with spinal anesthesia.

Our study enabled us to observe the natural course postanesthesia as per anesthetist's judgment. The parameters to be evaluated were defined based on previous studies in such a way that the patient's well-being was not compromised. However, the small sample size of 30, any undiagnosed cardiovascular and concomitant conditions in the patients involved in the study are limitations.

CONCLUSION

The incidence of hypotension in the first 20 min following spinal anesthesia in patients who receive AT-1 antagonists on the day of surgery was relatively higher than normotensives, but the hypotensive episodes could be effectively managed

without any serious hazards to the patient. The heart rate increased to compensate the fall in BP by baroreceptor mechanism. Anesthetists, however, should anticipate and be adequately prepared for any untoward consequences.

REFERENCES

1. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, *et al*. The incidence and risk factors for hypotension after spinal anesthesia induction: An analysis with automated data collection. Anesth Analg 2002;94:1521-9.
2. Saddler JM. Anesthesia and Hypertension-Update in Anesthesia Issue 2 Article 3. UK: Royal Devon and Exeter Hospital; 1992.
3. Shear T, Greenberg S. Vasoplegic syndrome and renin-angiotensin system antagonists. J Anesth Patient Saf Found 2012;27:18.
4. Sear JW, Jewkes C, Tellez JC, Foex P. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy and intubation. Br J Anesth 1994;73:303-8.
5. Samad K, Khan F, Azam I. Hemodynamic effects of anesthetic induction in patients treated on beta and calcium channel blockers. Middle East J Anesthesiol 2008;19:1111-28.
6. Kaimar P, Sanji N, Upadya M, Mohammed KR. A comparison of hypotension and bradycardia following spinal anesthesia in patients on calcium channel blockers and β-blockers. Indian J Pharm 2012;44:193-6.
7. Cozanitis DA. The importance of inhibiting angiotensin convertase inhibitor treatment before spinal anesthesia-a controlled case report. Anesthesiol Reanim 2004;29:16-8.
8. Hohne C, Meier L, Boemke W, Kaczmarczyk G. Angiotensin convertase inhibitor inhibitors do not exaggerate the blood pressure decrease in the early phase of spinal anesthesia. Acta Anesthesiol Scand 2003;47:891-6.
9. Cardiovascular regulatory mechanisms. In: Barrett KE, Barman SN, Boitano S, Brooks HL, editors. Ganong's Review of Medical Physiology. 24th ed. New Delhi: McGraw-Hill; 2012. p. 589-92.
10. Rooke GA, Freund PR, Jacobson AF. Hemodynamic response and change in organ blood volume during spinal anesthesia in elderly men with cardiac disease. Anesth Analg 1997;85:99.
11. Singla D, Kathuria S, Singh A, Kaul T, Gupta S, Mamta. Risk factors for development of early hypotension during spinal anesthesia. J Anesth Clin Pharmacol 2006;22:387-93.
12. Coriat P, Richer C, Douraki T, Gomez C, Hendricks K, Giudicelli JF, *et al*. Influence of chronic angiotensin converting enzyme inhibition on anesthetic induction. Anesthesiology 1994;81:299-307.

How to cite this article: Dinakar KR, Sanji N, Ravishankar RB, Vidya HK, Shashikala GH. Comparative study of variations in blood pressure and heart rate among normotensive patients and hypertensive patients receiving angiotensin receptor blockers during surgery under spinal anesthesia. Natl J Physiol Pharm Pharmacol 2018;8(12):1581-1586.

Source of Support: Nil, **Conflict of Interest:** None declared.