# Evaluration of Perioperative Haemodynamic Changes in Hypertensive Patients Treated By Angiotensin Converting Enzyme Inhibitor or Angiotensin II Receptor Blocker, Undergoing Elective Abdominal Surgery Under General Anaesthesia

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#### Abstract:

Aims: Our study is aimed to assess and evaluate perioperative haemodynamic changes in hypertensive patients treated by angiotensin converting enzyme inhibitor or angiotensin II receptor blocker, undergoing elective abdominal surgery under general anaesthesia

**Objectives**: To study the haemodynamic changes on patients continuing/discontinuing Angiotensin Converting Enzyme inhibitor or Angiotensin II Receptor Blocker on the day of surgery.

Methods: In this prospective study, after randomization and double blinding 60 patients going for elective abdominal surgery were selected in the surgery ward of swaroop rani hospital Allahabad. Amongst them, 30 patients (control group –GROUP A) did not consume any ACEI or AR blockers for controlling BP on the day of surgery but the remaining 30 patients (experimental group- GROUP B) used the drugs on the day of surgery. In these groups the effect of antihypertensives on hemodynamic changes before, during and after surgery were studied by heart rate, blood pressure, ST-T segment changes, SpO2 and statistical analysis using Normal test for means and corresponding P values were calculated by Student t test and Fishers exact test.

Results: Pre-induction HR, SBP, DBP and MAP were comparable between groups (pre op "P" value > 0.05). However when the post-induction values were compared with subsequent readings at lmin ("P" value < 0.05), 3min ("P" value < 0.0001), 5min ("P" value < 0.0001), 10min ("P" value < 0.0001), 15min ("P" value < 0.0001), 20min ("P" value < 0.0001) 30min ("P" value > 0.05), 45min ("P" value > 0.05) and 40min ("P" value > 0.05) value value > 0.05) it was found that there was a significant reduction in HR, SBP, DBP and MAP in Group B up to 20 min and needed vasopressors and atropine to maintain it. There was no ST-T changes and SpO2 changes in both groups.

**Conclusions:** Intraoperative haemodynamics can be safely managed when angiotensin converting enzyme inhibitor or angiotensin II receptor blockers are withhold on the day of surgery.

**Keywords:** Angiotensin II receptor blocker, Angiotensin-converting enzyme inhibitors, General anesthesia, Hypotension

### I. Introduction

The use of angiotensin converting enzyme inhibitors(ACE inhibitors)is one of the means available to block renin angiotensin system. Besides being the first line treatment of hypertension those drugs also decrease morbidity and mortality in patients with heart failure, acute myocardial infarction, especially in patients with low ejection fraction and they are also useful on the secondary prevention of strokes. Patients recovering from unstable angina or acute myocardial infarction without elevation of the ST segment and who have concomitant hypertension, diabetes mellitus or heart failure, represent another group that seems to benefit from the continuous use of ACE inhibitors<sup>1</sup>

Preoperative maintenance of drugs such as beta blockers and centrally acting alpha 2 agonists to protect the myocardium during the surgeries, and drugs whose preoperative discontinuation can cause rebound hypertension such as centrally acting alpha 2 agonist is recommended<sup>2</sup>. In contrast the continuation of drugs such as angiotensin converting enzyme inhibitors, ARB II on the day of surgery based on reports of significant hypotension after induction of anaesthesia suggesting a deleterious interaction between ACE inhibitors, ARB II and anaesthestics in general has been questioned<sup>3</sup>

However discontinuation of drugs used for a long time such as antihypertensives can implicate on a higher risk of intraoperative hypertensive peaks with harmful consequences for the patients<sup>2</sup>.

Therefore the indication of angiotensin converting enzymes inhibitors or angiotensin II receptor blockers in patients with hypertension has been well defined. Maintenance or discontinuation of this type of drug on the day of anaesthesia and surgical procedure is controversial.

Hence the present study was conducted to asses and compare the effects of continuation of Angiotensin converting enzyme inhibitors and Angiotensin II receptor blockers therapy on the day of surgery with

discontinuation of Angiotensin converting enzyme inhibitors and Angiotensin II receptor blockers therapy on the day of surgery, on perioperative stability of cardiovascular system in abdominal surgical patients after induction of general anaesthesia, and also to determine the measures to manage the complications.

### **II.** Material And Methods

The study was conducted from August 2014 to august 2015, after obtaining approval from the hospital ethical committee and consent from the patients. The type of study was randomized, prospective and double blinded.

A total of 60 patients who were aged between 30 to 60 years, belonging to ASA grade II, receiving only ACEI or ARB for control of hypertension for at least 1 months were included in the study.

Patients were randomized by sealed envelope technique into two equal groups, Group A and Group B. Group A consisted of 30 patients whose ACEI or ARA drug was stopped on the day of surgery. Group B consisted of 30 patients whose ACEI or ARA drug was continued on the day of surgery. Patients with valvular and ischemic heart diseases, cardiac failure, Respiratory disorders, carcinoid tumors, pheochromocytoma or thyrotoxicosis ,were excluded.

Anesthetic management was standardized by a study protocol. The pre medication drugs, induction agents, analgesics, muscle relaxants and volatile anesthetic agents used for maintenance of anesthesia were the same for all patients. In the pre operative room intravenous (IV) cannula was put under local anesthesia.Inj. Midazolam 0.02 mg/kg and Inj.fentanyl 2.0  $\mu$ g/kg ,Inj.glycopyrrolate0.2mg were given IV slowly. A crystalloid infusion 10 ml/kg was given to all patients before induction followed by 5 ml/kg/h until the end of surgery.

All patients were induced with Inj. propofol 2.0-2.5 mg/kg, Inj. succinylcholine 1.5-2 mg/kg body weight i.v. and tracheal intubation was performed with cuffed endotracheal tube. Anaesthesia was maintained with 60%:40% (N2O:O2) with intermittent isoflurane (0.5-1%) on soda lime closed breathing circuit . Muscle relaxation was maintained with loading dose of inj. vecuronium (0.04-0.07mg/kg) i.v. followed by supplementary doses (0.01-0.02mg/kg) i.v. as and when required.

After completion of anaesthesia, residual paralysis was reversed with neostigmine (0.05 mg/kg) i.v. and glycopyrrolate (0.01mg/kg) i.v. Extubation is done after thorough suctioning of oral cavity.

Following parameters was observed for hemodynamic response and monitored perioperatively, just before induction and after induction at 1, 3, 5, 10, 15,20, 30, 45 and 60 minute and post operative ward after 15 minutes of extubation.

### A:- Heart Rate

### B:- Blood Pressure

- a. Systolic Blood Pressure
- b. Diastolic Blood Pressure
- c. Mean Arterial Blood Pressure

# C: ST-T Segment Changes

### D:- Pulse Oximetry Spo2

- 1. Hypotension was defined as SBP < 20% of baseline value.<sup>4</sup>
- 2. Bradycardia was defined as HR < 60 beats/ minute.<sup>5</sup>
- 3. Tachycardia was defined as HR > 25% of baseline value<sup>6</sup>.
- 4. Hypertension was defined as SBP >20% of baseline value<sup>7</sup>.

Hypotension was treated initially with increasing the infusion rate of IV crystalloids (Ringer lactate), giving a maximum of up to 500 ml within 5-7 minutes followed by , IV ephedrine in incremental bolus doses of 10 mg. Whenever MAP was <60 mmHg, it was treated immediately with inj.vasopressin $^80.5$ -1U Bolus followed by infusion0.03- 0.06U/minute i.v.

Bradycardia was treated with inj. atropine 0.6 mg i.v.

Hypertension and tachycardia was treated with inj. Esmolol 250-500 microgram/kg i.v. bolus over 1-2 minutes then 50 -300 microgram /kg/minute infusion

Statistical analysis was performed using Microsoft Excel 2010 and online statistical calculation website. Student t-test (paired & unpaired), Fisher's exact test and Two Propotional Z test was used to test the significance of data. Data were presented as mean  $\pm$  S.D. A 'P' value of <0.05 was considered significant.

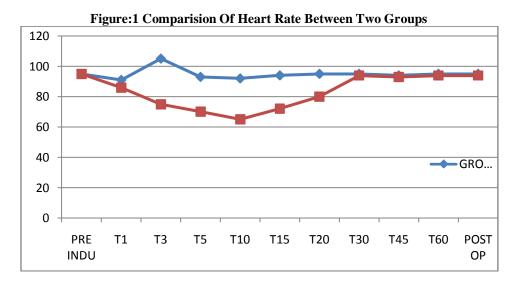
### III. Results

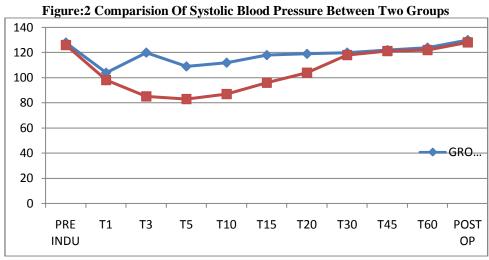
Both groups were comparable with respect to, demographic profile i.e. age, weight, height & preinduction baseline vital parameters i.e. H.R. ,S.B.P., D.B.P.,M.A.P and  $SPO_2$  were statistically similar between both groups.

In the present study, At T1 minute post induction mean HR(P>0.05) of group B was not significantly lower than group A but, mean SBP (P<0.05), DBP (P<0.05) and MAP (P<0.05) were significantly lower than group A . In group B mean HR, SBP., DBP and MAP at T3(P<0.0001), T5(P<0.0001), T15(P<0.0001), T20, (P<0.0001) minute post induction were significantly lower than group A .At T30, T45, T60 minutes mean H.R., S.B.P., D.B.P., and M.A.P were statistically similar between both groups (P>0.05). There was statistically no significant difference (P>0.05) in  $SpO_2$  level between the groups from T1 to T60 minute . There were no ST-T changes in both the groups from T1 to T60 minutes.

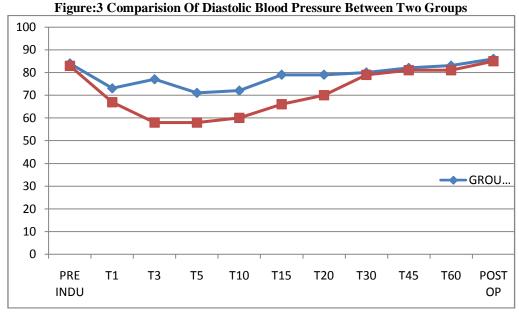
In our study patients who took ACE inhibitor or ARB(group B) associated with 100% hypotensive (<20% of baseline blood pressure)episodes(P<0.0001) than group A in post induction period upto 20 minutes, 50%(15 patients) within 1 minute and 100%(30 patients) at 3 min. In group B, 20 patients required Ringer lactate and i.v. ephedrine to maintain systolic blood pressure within 20% of baseline and in ten patients (33.33%)we used vasopressin to maintain mean arterial pressure more than 60mmHg (out of five patients who took enalapril on the day of surgery four patients needed vasopressin to maintain mean arterial blood pressure more than 60mmHg and all the patients who took ARB on the day of surgery needed vasopressin to maintain mean arterial pressure >60 mmHg) . In 15 patients(50%) out of 30 patients (GROUP B)we used atropine to maintain heart rate more than 60/min. It was also statistically significant (P<0.0001)compare to group A where there was no bradycardia episodes.

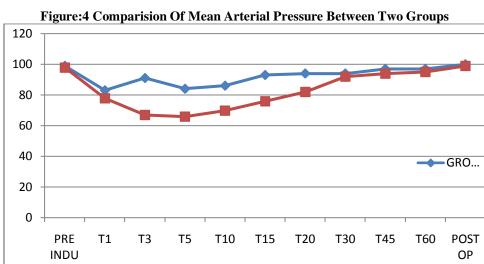
In group A hypotensive episodes occurred at 1minute in 9 patients (30%) and it was managed with Ringer lactate within 3 min. In group A, 1 patient (3.3%) had hypertensive(> 20% of baseline) and 1patient(3.3%) had tachycardia( > 25% of baseline) episodes required esmolol to control it and it was statistically insignificant(P>0.05) compare to group B. Mean HR, SBP, DBP, MAP, SPO2 were comparable between the groups (P>0.05) at post - operative period. There were no ST-T segment changes in both groups





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Analysis of complications after induction of anaesthesia

GROUP	HYPOTENSION	HYPERTENSION	BRADYCARDIA	TACHYCARDIA	ST-T CHANGES	SPO <sub>2</sub> CHANGES
A	9(30%)	1(3.33%)	0(0%)	1(3.33%)	0(0%)	0(0%)
В	30(100%)	0(0%)	15(50%)	0(0%)	0(0%)	0(0%)
P	< 0.0001	>0.05	< 0.0001	>0.05	-	-

## IV. Discussion

The present study results comparable with several studies in the past, which had also reported intraoperative hypotension with the use of ACEI and ARA in the surgical setting.[8,9,10,11,12,13, 14, 15,].

In the study done by Coriat, et al., showed, In hypertensive patients chronically treated with ACEIs, maintenance of therapy until the day of surgery may increase the probability of hypotension at induction. Our study results also suggest all the patients who took ACE inhibitors on the day of surgery to control blood pressure were associated with 100% hypotensive episodes, needed ephedrine to maintain systolic pressure within 20% of baseline and in four patients who took enalapril on the day of surgery required vasopressin to maintain mean arterial pressure more than 60mmHg

This study result consistent with a study conducted by Brabant SM.,et al <sup>[9]</sup> which has shown hypotensive episodes occur more frequently after anesthetic induction in patients receiving Angiotensin II receptor subtype-1 antagonists under anesthesia than with other hypotensive drugs. They are less responsive to the vasopressors ephedrine or phenylephrine. The use of a vasopressin system agonist was effective in restoring blood pressure when hypotension was refractory to conventional therapy

In the study by Comfere *et al.*,<sup>[11]</sup> it was reported that hypotension occurred in about 60% of patients who had last ACEI or ARA therapy less than 10 h prior to anesthetic induction. But in our study, all the patients who had ACEI or ARA on the day of surgery developed hypotension. The difference may be due to various induction agents like thiopentone and propofol were used by Comfere *et al.*,<sup>[11]</sup>. In our study,we used only propofol as an induction agent, and also patients took ACEI and ARB on the day of surgery morning which could have caused more frequent hypotensive episodes . Malgorzata *et al.*<sup>[16]</sup> also found more profound hypotension with propofol induction when compared with etomidate induction in the patients who had received ACEI.

This study result also consistent with a study conducted by Schirmer U, et al. [14], that continuation of ACEI on the day of surgery associated with significant reduction in post induction heart rate, SBP, DBP, MAP and more hypotensive and bradycardia episodes compared to the discontinuation group.

This study result also consistent with a study conducted by Rajan et al. [15] that continuation of ACEI or ARB on the day of surgery associated with significant reduction in post induction blood pressure. In our study post induction hypotension upto 20 minutes only because of vasopressors support.

### V. Conclusion

Continuation of ACEI or ARB on the morning of day of surgery produces undesirable hypotension and bradycardia after induction of general anaesthesia.

The number of complications were more in patients with continuation of antihypertensive drugs, however they were manageable.

These drugs should be withheld on the day of surgery and sequele arising can be easily managed. It is concluded that patients taking ACEI or ARB should withheld these drugs on the day of surgery.

### References

- [1]. Yusuf S, Sleight P, Pogue J et al. Effect of angiotensin converting enzyme inhibitor, ramipriloncardiovascular events in high risk patients. New England J Med, Jan 20,2000;342(3):145-53
- [2]. Schmidt GR, Schuna A A. Rebound hypertension after discontinuation of transdermal clonidine. clin pharm ,1988;7:772-774 [3]. Ryckwaert F; Colson P. Haemodynamic effects of anaesthesia in patients with ischemic heart failure chronically treate
- [3]. Ryckwaert F; Colson P. Haemodynamic effects of anaesthesia in patients with ischemic heart failure chronically treated with angiotensin converting enzyme inhibitors. Anesth&analg, May 1997;84(5):pp945-949.
- [4]. Jakola ML, Ali-Melkkila T, Kanto J, Kallio A, Scheinin H, Scheinin M. Dexmedetomidine reduces intraocular pressure, intubation response andanaesthetic requirements in patients undergoing ophthalmic surgery. BrJAnaesth 1992;68:570-5.
- [5]. Kallio A, Scheinin M, Koulu M, Ponkilainen R, Ruskoaho H, Viinamaki O, et al. Effects of dexmedetomidine, a selective alpha-2 adrenoceptor agonist, on haemodynamic control mechanism. ClinPharmacolTher 1989;46:33-42.
- [6]. Nathaniel H. Greene, B.S., Craig Weldon, M.D., Terri G. Monk, M.D., M.S. There Are No Consistent Definitions of Hemodynamic Aberrations in the Anesthesia Literature Anesthesiology, Duke University School of Medicine, Durham, North Carolina, 2008.
- [7]. Wheeler AD, Turchiano J, Tobias JD A case of refractory intraoperative hypotension treated with vasopressin infusion. J ClinAnesth. 2008 Mar; 20(2):139-42.
- [8]. 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.
- [9]. Brabant SM, Bertrand M, Eyraud D, Darmon PL, Coriat P. The hemodynamic effects of anesthetic induction in vascular surgical patients chronically treated with angiotensin II receptor antagonists. AnesthAnalg. 1999;89:1388–92.
- [10]. Bertrand M, Godet G, Meersschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? AnesthAnalg. 2001;92:26–30.
- [11]. Comfere T, Sprung J, Kumar MM, Draper M, Wilson DP, Williams BA, et al. Angiotensin system inhibitors in a general surgical population. AnesthAnalg. 2005;100:636–44.
- [12]. Park KW. New therapeutic targets and modalities in cardiovascular medicine. IntAnesthesiol Clin.2005;43:23–37.
- [13]. Khodaparast O, Kheterpal S, Shanks A, Tremper KK. Chronic treatment with ACE inhibitors or ARAs and intra-operative hypotension. Anesthesiology. 2006;105:A44.
- [14]. Schirmer U, Schürmann W. Preoperative administration of angiotensin-converting enzyme inhibitors. Anaesthesist. 2007;56:557–61.
- [15]. Rajan S, Rajagopalan R, SapruK ,Paul J: Effect of preoperative discontinuation of angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists on intraoperative arterial pressure after induction of general anaesthesia. Anesthesia Essays and Researches.Jan-Apr 2014: 8(1): 32-35.
- [16]. Malinowska-Zaprzałka M, Wojewódzka M, Dryl D, Grabowska SZ, Chabielska E. Hemodynamic effect of propofol in enalapril-treated hypertensive patients during induction of general anesthesia. Pharmacol Rep.2005;57:675–8.