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Original Research Article

Effect of Pre-Operative Discontinuation of Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Antagonists on Intra-Operative Arterial Pressures after Induction with Etomidate

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Abstract

Background: Hypertension is a leading preoperative risk factor among patients of all age groups and dominates in the group aged 50 years and older, continuation of ACEIs/ARBs was associated with an increased risk of intraoperative hypotension.

Aim and Objective: To stud effect of pre-operative continuation of ACEI or ARA therapy on intraoperative blood pressure (BP) in surgical patients after induction of etomidate.

Material and Method: This was a randomized prospective double-blinded study conducted in Department of anaesthesia, of our institute for the period of 6 months in which 50 patients were included after getting informed consent, and followed inclusion and exclusion criteria. Patients were randomized with random number technique into two equal groups, Group A and Group B.

Results: There was no significant difference was observed in mean age group of patients between the groups, also gender distribution and ASA distribution between the groups were statistically not significant. Mean difference of SBP, DBP and MAP between before induction and at 1 minute after induction between the group was not significant, but after 1 min till 15 min it was statistically significant, and later on it was comparable.

Conclusion: Our study found that etomidate is a favourable agent for induction even in patients who continue on ACEI or ARA drugs, but there are less studies are available with etomidate. More studies are required to prove efficacy of etomidate in continuation of ACEI or ARA during surgery.

Keywords: Hypertension, Cardiovascular Complications, ACEIs/ARBs, Etomidate.

Introduction

Hypertension is a leading preoperative risk factor among patients of all age groups and dominates in the group aged 50 years and older [1–3]. Preoperative hypertension

increases the risk of surgical bleeding, stroke, and cardiovascular complications. Tight blood pressure control improves outcome. According to the 2017 American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, blood pressure should be <130/80 mmHg during an antihypertensive drug therapy [4].

Hypertension affects 26.4% of the global population.[5] It is an independent predictive factor of cardiac adverse events in noncardiac surgery.[6] In patients with known coronary artery disease or at high risk for coronary artery disease who are undergoing noncardiac surgery, preoperative hypertension increases risk for death by 3.8 times.[7] Perioperative hemodynamic instability is associated with cardiovascular complications. Interestingly, multiple studies suggest that perioperative cardiac complications are associated with intraoperative hemodynamic instability, rather than acute intraoperative hypertension alone. A decrease of 40% in MAP and an episode of a MAP ≤50 mmHg during surgery are associated with cardiac events in high-risk patients.[10] Even short episodes of intraoperative MAP of ≤55 mmHg are associated with acute kidney injury and myocardial injury after a noncardiac surgery.[8] The threshold and duration at which an association might be found between a perioperative stroke and hypotension are not completely known.[9] Intraoperative hypotension is one of the most encountered factors associated with death related to anaesthesia.[10]

Interactions between angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor antagonists (ARAs) and anaesthesia are controversial. But as first line antihypertensive treatment, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) produce arterial vasodilatation and reduce blood pressure through the inhibition of the renin–angiotensin aldosterone system. Moreover, the use of ACEIs/ARBs exerts many beneficial effects, including improved cardiovascular and renal outcomes in patients with diabetes, decreased mortality in patients with acute kidney injury, and improvement in symptoms and survival in patients with heart failure with reduced ejection fraction. Nevertheless, the current evidence does not provide a definitive answer regarding whether ACEIs/ARBs should be continued or withheld in the perioperative setting. While some studies showed that continuation of ACEIs/ARBs was associated with an increased risk of intraoperative hypotension, other studies argued that different ACEIs/ARBs management strategies did not affect perioperative hemodynamic stability or postoperative outcomes. To date, there is no well-designed randomized controlled trial with adequate power to assess the perioperative risks and benefits of ACEIs/ARBs.

Propofol, used alone at induction of anaesthesia, promotes a significant decrease in arterial blood pressure compared with thiopentone or etomidate.[11,12] Even with reduced doses, propofol is a more hypotensive agent than etomidate.[13] Moreover propofol has a direct effect on vessels: it causes a dose-related decrease of potassium-induced tone in veins at low dose and arterioles at higher dose.[14] Etomidate preserves hemodynamic stability through maintenance of both sympathetic outflow and autonomic reflexes. In patients with severe aortic stenosis, etomidate induces less hypotension than propofol after the induction of anaesthesia.[15]

Hence, we have undertaken this study to the effect of pre-operative continuation of ACEI or ARA therapy on intraoperative blood pressure (BP) in surgical patients after induction of etomidate.

Materials and Method

This was a randomized prospective double blinded study conducted in Department of anaesthesia, of our institute for the period of 6 months in which 50 patients were included after getting informed consent, and followed inclusion and exclusion criteria.

Inclusion Criteria

1. Age between 30 years to 60 years
2. ASA of grade II
3. Patients who were receiving only ACEI or ARA for control of hypertension.
4. Preoperative BP at the time of admission ≤140/90 mmHg.

Exclusion Criteria

1. Age less than 30 years and more than 60 years
2. Patients with valvular disease, ischemic heart diseases, cardiac failure
3. Preoperative BP at the time of admission ≥140/90 mmHg.

Randomization: Patients were randomized with random number technique into two equal groups, Group A and Group B.

Group A: Group consisted of 25 patients whose ACEI or ARA drug was stopped the day before surgery.

Group B: Group consisted of 25 patients whose ACEI or ARA drug was continued on the day of surgery.

Method

The pre medication drugs, induction agents, analgesics, muscle relaxants and volatile anaesthetic agents used for maintenance of anaesthesia were the same for all patients. In the operation theatre a large bore intravenous (IV) cannula was put under local anaesthesia. Midazolam 0.02 mg/kg and fentanyl 2.0 µg/kg 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 etomidate 0.2–0.3 mg/kg followed by vecuronium 0.1 mg/kg and were ventilated with 60% of oxygen, 40% of nitrous oxide and 1% of isoflurane. At the end of 3 min, a quick and gentle laryngoscopy and tracheal intubation were done. Throughout the surgical procedure anaesthesia was maintained with the combination of oxygen, nitrous oxide and isoflurane with controlled ventilation maintaining normocapnia and normoxia with oxygen saturation ≥98%. Intraoperative monitoring included continuous electrocardiogram, non-invasive BP monitoring, respiratory gas monitoring and pulse-oxymetry. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressures (MAP) were measured just before induction and after induction at 1, 3, 5, 10, 15, 30, 45 and 60 min. Intraoperative hypotension was defined as SBP <85 mmHg and hypertension as SBP >140 mmHg. Hypotension was treated initially with increasing the infusion rate of IV crystalloids, giving a maximum of up to 1000 ml. Whenever MAP was <60 mmHg, hypotension was treated with IV ephedrine in incremental bolus doses of 6 mg. Those patients who received ephedrine were not included in the study as further BP readings could be affected by the use of ephedrine.

Statistical Analysis:

Collected data were entered in the Microsoft Excel 2016 for further statistical analysis, qualitative data were expressed in frequency and proportion and quantitative data were expressed by using mean and standard deviation. Mean difference between the mean values were assessed by using t-test. P-value<0.05 were considered as statistically significant at 5% level of significance.

Observation and Results

Study included 50 patients for various surgeries, divided into two groups A and B equally having 25 patients in each group and their observation were as bellow

Table 1 : Distribution of Demographic variable between the groups.

Parameters	Group A	Group B	Chi-square test/t-test	P-value
Age				
Mean ± SD	42.12±6.31	39.51±7.21	1.36	0.1795
Gender				
Male	15(60%)	17(68%)	0.3472	0.555
Female	10(40%)	8(32%)		
ASA				
Grade I	21(84%)	19(76%)	0.5	0.479
Grade II	4(16%)	6(24%)		

Above table showed distribution of various demographic variable between the groups and we have observed that there was no significant difference was observed in mean age group of patients between the groups, also gender distribution and ASA distribution between the groups were statistically not significant.

Table 2: Mean difference distribution of SBP between pre-induction and at different interval of time

Time (Min)	Group A		Group B		P-value
	Mean	SD	Mean	SD	
1Min	15.2	11.18	16.21	8.44	0.72
3 Min	11.12	7.14	25.12	7.16	<0.001
5 Min	14.2	18.42	31.13	7.42	<0.001
10 Min	12.14	18.14	28.14	6.85	<0.001
15 Min	8.15	21.36	22.42	6.24	<0.001
30 Min	6.17	14.26	5.94	12.43	0.9518
45 Min	4.63	11.42	5.12	10.63	0.875
60 Min	2.13	15.6	3.14	14.72	0.814

Table showed that Mean difference of SBP between before induction at 1 minute after induction between the group was not significant, but after 1 min till 15 min it was statistically significant, and later on it was comparable.

Table 3 : Mean difference distribution of DBP between pre-induction and at different interval of time.

Time (Min)	Group A		Group B		P-value
	Mean	SD	Mean	SD	
1Min	10.5	5.42	9.42	5.6	0.49
3 Min	7.63	5.87	14.36	7.5	<0.001
5 Min	4.42	9.42	14.96	6.8	<0.001
10 Min	6.78	10.1	18.42	7.4	<0.001
15 Min	3.45	9.5	4.12	7.9	<0.001
30 Min	0.45	7.42	1.26	4.5	0.659
45 Min	-1.17	6.4	0.23	8.6	0.37
60 Min	0.83	7.1	0.75	7.6	0.969

Table showed that Mean difference of DBP between before induction at 1 minute after induction between the group was not significant, but after 1 min till 15 min it was statistically significant, and later on it was comparable.

Table 4: Mean difference distribution of MAP between pre-induction and at different interval of time.

Time (Min)	Group A		Group B		P-value
	Mean	SD	Mean	SD	
1 Min	14.2	6.9	11.96	7.46	0.27
3 Min	8.9	7.15	19.4	5.87	<0.001
5 Min	12.7	11.96	22.4	5.32	<0.001
10 Min	9.4	14.6	24.6	9.7	<0.001
15 Min	7.6	9.7	28.4	7.6	<0.001
30 Min	1.4	9.21	2.03	8.99	0.8077
45 Min	0.87	8.6	0.79	7.36	0.972
60 Min	0.14	8.9	0.45	8.46	0.9001

Table showed that Mean difference of MAP between before induction at 1 minute after induction between the group was not significant, but after 1 min till 15 min it was statistically significant, and later on it was comparable.

Discussion

Hypotension is significantly associated with postoperative myocardial infarction, acute kidney injury, and death [16–19]. In addition, the duration of hypotension was significantly associated with postoperative stroke for patients undergoing non-cardiac and non-neurosurgical procedures [20]. Randomized studies also confirmed that interventions targeting an optimal blood pressure reduced the risk of organ dysfunction after major non-cardiac surgery [21, 22]. One study by Roshanov PS et al in which 955 patients with coronary artery disease and mean age of 69.7 years undergoing major non-cardiac surgery, perioperative hypotension independently predicts cardiovascular events (myocardial infarction or cardiovascular death) within 30 days after surgery [23]. Older hypertensive patients have impaired autoregulation of blood flow in the vital organs (such as heart, brain, and kidneys) and are at increased postoperative risk, so perioperative blood pressure management is extremely important. Strategies that limit perioperative hypotension contribute to the improvement of postoperative outcomes. There are no firm recommendations on the use of ACEIs/ARBs in the perioperative period, because high level of evidence such as a randomized controlled trial with a large sample size is lacking. Previous observational studies suggested that withholding ACEIs/ARBs was associated with a lower incidence of intraoperative hypotension and a reduced risk of 30-day vascular events and all-cause mortality.

In the present study we have not found any significant difference in age, gender and ASA grading between the groups. In the study by Comfere *et al*.,[24] it was reported that hypotension occurred in about 60% of patients who had last ACEI or ARA therapy less than 10 h prior to anaesthetic induction which was somewhat more than present study. These differences could be due to the fact that in the study by Comfere *et al*., various induction agents were used like thiopentone and propofol. In the present study only, etomidate was used as an induction agent, which gives more hemodynamic stability compared to propofol. [15]

In the study by Bertrand *et al*.[25] statistically significant reduction in SBP was seen during the initial 5-23 min time interval only. But in our study, we have observed hypotension till 15 minutes after induction later on it was stable throughout the surgery. According to the study by Van Diepen *et al.*[26] observed that in the cardiac surgical population, the preoperative administration of an ACEI or ARB has also been associated with intraoperative hypotension, but the

postoperative hemodynamic effects are less clear. In our study we have observed hypotension postoperatively among 20% of the patients.

We were able to maintain MAP above 60 mm of Hg with IV fluids in most of the patients who received ACEI or ARA on the day of surgery, which was supported by Tohmo and Karanko.[27].

In the present study we have used very less ephedrine which is first line treatment of intraoperative hypotension, maximum patients were managed with IV fluids.

Conclusion

From overall observation and discussed with other studies, in this study we can conclude that, continuation of ACEI or ARA into the preoperative setting increases the risk of hypotension after induction, but with proper anaesthetic drug and more safely handling of intraoperative hemodynamic can be reduce risk of hypotension and other risks intraoperatively and also post-operatively. Our study found that etomidate is a favourable agent for induction even in patients who continue on ACEI or ARA drugs, but there are less studies are available with etomidate. More studies are required to prove efficacy of etomidate in continuation of ACEI or ARA during surgery.

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