Angiotensin Converting Enzyme Inhibitors, to Continue or Discontinue on the Morning Day of Surgery

Sabah Noori Al-saad , Arkan Muhammed Mahdi

ABSTRACT:

BACKGROUND:

Angiotensin converting enzyme inhibitors(ACEI) play a pivotal role in the management of hypertension[11]. whether to continue or discontinue them before surgery is an everyday encountered question of both surgeon & patient, this issue is continuously submitting to debate & controversy.

OBJECTIVE:

To compare between the incidence of intra-operative hypotension in hypertensive patients who continue to take ACEI. & those who discontinue, & are undergoing general anesthesia for non-cardiac surgery.

PATIENTS AND METHOD:

A comparative study consist of 40 patients presented to the Medical City, Baghdad Teaching Hospital & Surgical specialty Hospital between July 2011,to March 2012.the age of patients range from 38-70 years old, they were 10 (25 %) men and 30 (75 %) women , they were divided into two groups; according to mode of medication, cases (who were continued taking medication) and control (who were discontinued medication),twenty patient each, all patients underwent different surgical interventions under general anesthesia, they were studied & monitored intra-operatively regarding development of hypotension, this was done at time interval of 5 minutes & at starting point prior to induction of general anesthesia until 20 minutes after.

RESULTS:

By comparing the mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) in between both groups of patients, those who were continued ACEI (group A) or those who were discontinued(group B), it had been found that no significant differences in mean SBP neither pre-operatively nor at different time intra-operatively. P.value in all comparisons was > 0.05.

CONCLUSION:

Continuing or discontinuing ACEI before non-cardiac surgery under general anesthesia has no statistical significance regarding concern of developing intra-operative hypotension.

KEYWORDS: angiotensin,angiotensin converting enzyme inhibitor,intraoperative hypotension.

INTRODUCTION:

There have been several reports and small studies suggesting that intraoperative hypotension after the induction of anaesthesia is more common in patients who receive rennin angiotensin aldosterone system (RAAS) antagonist therapy on the day of surgery. The available literature on this topic is scant, and no guidelines have yet been published on the appropriate use of RAAS antagonists in the surgical patient. In addition, the introduction of new agents that modulate RAAS, such as the direct renin inhibitor aliskiren, will add further complexity to this important clinical question. The current medication guideline used at the perioperative clinic recommends that both ACEI and angiotensin II receptor blocker be discontinued on the morning of non-cardiac surgery ·There are no national or international guidelines that delineate a standard of care in the use of these agents in the perioperative period. The literature supporting this practice relates to the frequency and degree of intraoperative hypotension observed with concomitant use of RAAS antagonists [1].

Continuation of the use of anti-hypertensive medication till the day of surgery can lead to large fluctuations in the blood pressures because of various reasons. One of the many causes is an unpredictable drug interaction between anaesthetic agents and the anti-hypertensive drugs especially the ACEI. With chronic ACEI therapy, there is certainly an abnormal hypotensive response to anaesthesia, which in some patients may prove to be resistant to conventional vasoconstrictors [2]. The Pigott study suggests that the degree of hypotension is less on discontinuation of ACEI, with vasoconstrictor requirement significantly

Baghdad Teaching Hospital, Medical City.

reduced, in the context of cardiopulmonary bypass. A previous study by Colson et al in a similar group of patients, has indicated that patients in whom ACEI are continued to the time of surgery experienced 'significantly' greater reduction in blood pressure and cardiac index, post-induction, than those in whom the ACEI were withdrawn [3]. Noble and Kehlets1 make good general points about the risks of interrupting drug treatment before surgery but there have been case reports of patients treated with ACEI and angiotensin II receptor antagonists becoming profoundly hypotensive and bradycardic during induction and maintenance of anaesthesia[4,5].Complicating matters further, recent pharmacogenomic studies of the RAAS have demonstrated variable genetic susceptibility to RAAS antagonists via single-nucleotide polymorphisms in the genes that encode angiotensinogen, angiotensin receptor I and angiotensin receptor II [1,6].

ACTIONS OF ANGIOTENSIN-II:

Angiotensin-II has several effects . It is a potent vasoconstrictor [7].Vasoconstriction about 40 times more intense than that caused by norepinephrine. Vasoconstriction occurs predominantly in arterioles and, to a lesser degree, in veins [8] In addition, A-II stimulates the sympathetic nervous system via direct and indirect methods to increase norepinephrine and epinephrine release [9,10].

Angiotensin Converting Enzyme Inhibitors:

ACEI are used for the treatment of hypertension and cardiac failure. Their principal mechanism of action is inhibition of A-II formation, but effects on the kallikrein-kinin system are also important. All ACEI reduce arteriolar tone, peripheral resistance and arterial pressure directly by decreasing both AII-mediated vasoconstriction and sympathetic nervous system activity [7].

ACE inhibitors in Hypertension*:*

ACEI are indicated for hypertension of all grades. Because these agents do not cause sodium and water retention, they can often be used as monotherapy without a diuretic. [11].

PATIENT AND METHODS:

PATIENTS:

A comparative study conducted at Baghdad teaching hospital & surgical speciality hospital, medical city,Iraq, during the period between July 2011 to March 2012, 40 patients who were presented to the hospitals were selected to participate in this study, their ages were ranged from 38-70 years and they were 10 (25 %) men and 30 (75 %) women , patients were divided into two groups; according to mode of medication, cases (who were continued taking medication) and control (who were discontinued medication), twenty patient each. all patients underwent different surgical interventions under general anesthesia.they were studied & monitored intraoperatively regarding development of hypotension.this was done at time interval of 5 minutes & at starting point prior to induction of general anesthesia until 20 minutes after.

No. of criteria should present for the patient to be included in this study,these are:

- ❖ Patient should be essentially hypertensive, i.e. no obvious secondary cause of hypertension present.
- ❖ Patient should be categorized ASA I or ASA II & compliant to drug.
- ❖ Patient has no history of cardiac ischemia , not in state of CHF& not diabetic.
- ❖ Patient should not be on antihypertensive other than ACEI..
- ❖ One of three types of ACEI are used ,captopril,enalpril or lisinopril.
- ❖ Patient should be in state of controlled hypertension.
- ❖ Those patients who presented for emergency surgical operation were excluded.

METHODS:

Cases group were asked to continue their ACEI, they took drugs at 5 a.m.(i.e. 3-4 h before surgery), intravenous fluid (normal saline) is given before induction of general anesthesia & endotracheal intubation, euvolemia is maintained throughout anesthesia.

Propofol in a dose decided by approximate body weight,1.5-2.5mg/kg is used as induction agent ,together with midazolam 2mg & fentanyl 50mcg. Atracurium 0.5mg/kg as a muscle relaxant is used & halothan at a MAC 0.75% as maintenance agent.B.P. is measured & recorded before induction & then every 5 minutes to a total of 5 times. Automated occlusive device (non-invasive) is used as a measuring & monitoring tool. hypotension was defined by SBP less than 90 mmHg.Other 20 controls were asked to discontinue ACEI drugs on the day of surgery. Same induction procedure & measurement method & tool are used to this group of patient.

Data collection:

Questionnaire was consisted of two parts first part collecting data about the social characteristics of the participants (Age, weight and gender), while the second part inquiring about the clinical characteristics (Medications, chronic illnesses , type of operation and the ASA class) of the participant.

Statistical analysis :

A computerized software for windows were used for the entering and analysis of participants' data , SPSS (statistical package for social sciences) for widows version 18,IBM,US,2007, and Microsoft excel software were used.

All data were entered and analyzed, appropriate statistical test were performed and multiple contingency tables had been conducted.

Chi square was used for comparison of frequencies and percentages of different variables while the independent two samples student's t test was used for comparison of different means in between groups(cases and controls), within groups to compare means at different measurement time points, ANOVA test was used.

Descriptive statistics were presented as (mean ± standard deviation) or frequencies and percentages. Level of significance (P) of ≤ 0.05 two tailed, was assumed. Results finally were presented in tables and /or graphs.

RESULTS:

There were 40 patients with a mean age of (54.5 ± 9.8) year with a range of (38-70) year , they were 10 (25 %) men and 30 (75 %) women , they were divided into two groups; according to mode of medication, cases (who were continued taking medication) and control (who were discontinued medication) (20) patient each ,on the other hand the distribution of cases in both groups by age groups and gender was shown by table .

Table 3. 1: Distribution of patients by age groups and gender (N=40).

Age group	Gender		Total
	Men	Women	
31 - 40	1	4	5
	10%	13.3%	12.5%
41 - 50	0	12	12
	0%	40%	30%
51 - 60	2	10	12
	20%	33.3%	30%
> 60	7	4	11
	70.0%	13.3%	27.5%
Total	10	30	40
	100%	100%	100%

Regarding the medications, 4 patients was on Enalapril 10 or 20 mg once a day, 9 patients on single dose of Lisinopril and the other 27 patients were on captopril with different doses and frequencies. By comparing the mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) in between both groups of patients, those who were continued ACEI (group A) or those who were discontinued(group B), it had been found that no significant differences in mean SBP neither pre operatively nor at different time intra operatively. P.value in all comparisons was > 0.05.

Table 3.2: A comparison mean systolic blood pressure(SBP).

Time	Mean ± SD		P.value
	Group A	Group B	
Pre operative SBP	124.6 ± 13.8	127.5 ± 14.1	0.51
SBP at 5th minute	124.4 ± 16.8	122.9 ± 16.5	0.78
SBP at 10th minute	124.9 ± 16.5	121.6 ± 16.3	0.54
SBP at 15th minute	121.2 ± 14.6	118.4 ± 13.2	0.53
SBP at 20th minute	120 ± 12.7	119.4 ± 11.9	0.87

Table 3.3 : A comparison of Pre and intraoperative Diastolic blood pressure(DBP).

Time	Mean ± SD		P.value
	Group A	Group B	
DBP Preoperative	79 ± 9.5	77 ± 7.6	0.47
DBP at 5th minute	77.85 ± 9.8	75.7 ± 11.1	0.51
DBP at 10th minute	77.8 ± 8.9	74.6 ± 9.6	0.28
DBP at 15th minute	76.2 ± 9.7	72.9 ± 8.8	0.28
DBP at 20th minute	76.1 ± 8.1	74 ± 6.4	0.37

* SD = standard deviation

Table3.4 : Distribution of cases by type of operation.

Type of operation	Group		Total
	Group A	Group B	
Laparoscopic Cholecystectomy	10	1	11
Herniatomy	1	5	6
L.N.Biopsy	3	3	6
Bone fracture reduction & fixation	0	6	6
Open Cholecystectomy.	1	2	3
Wound Debridement.	0	2	2
mastectomy	5	1	6
Total	20	20	40

DISCUSSION:

Intraoperative hypoptension induced by angiotensin converting enzyme inhibition is sometimes so profound that necessitate administration of vasopressors. ***McCarthy et al*** studied the effect of two doses of sublingual captopril (12.5 mg and 25 mg) versus placebo administered 25 min before tracheal intubation in 40 patients. The patients receiving captopril were more likely to develop hypotension than those receiving placebo ($p<0.05$) within 3 min of intubation; however, there was no significant difference between the two captopril doses [12] .***coriat et al*** randomised 56 patients undergoing non-cardiac surgery chronically treated for hypertension with captopril (n=36) or enalapril (n=20) into two groups, one in which the ACEIs were administered on the morning of surgery and the other in which it was withdrawn. In the former group, all of the patients who received enalapril and 64% of those who received captopril required ephedrine to treat post-induction hypotension[13] .***Shirmer and Schurmann*** randomised 100 patients receiving chronic antihypertensive therapy with ACEIs in a double-blind study of ACEI discontinuation in non-cardiac surgery. Fifty patients were allocated to receive ACEIs on the morning of surgery and 50 to have it withdrawn. After induction of anaesthesia, the BP and heart rate were significantly lower in the group of patients receiving ACEIs than in the withdrawal group, and the use of supportive adrenergic agonists was required more often (17 of the 50 patients who took ACEIs versus five of the 50 patients in the withdrawal group, $p<0.05$). The authors concluded that patients chronically treated with ACEi should receive the last dose on the day before surgery[14]. As part of their Resource, the ***American College of Physicians*** supports the cautious continuation of RAAS antagonists on the morning of surgery, with the caveat that euvolaemia should be maintained[15]. recently ***Ryckwaert and Colson*** reported that ACEI treatment in patients with infarction-induced myocardial dysfunction does not increase the incidence of severe hypotension after induction of anesthesia. In all, the overwhelming opinion is to continue all antihypertensive medication including the day of surgery and resumption of such therapy postoperatively [16]. A number of studies have shown an improvement in outcome when therapy

is continued versus a worsening in outcome when either ACE i or β blockers have been withdrawn [8]. It was considered that, in certain cases, the preoperative use versus discontinuation of these agents should be factored into the overall risk & benefit equation, as certain groups of patients may benefit from its continuation (eg, systolic dysfunction, uncontrolled hypertension).[1] In my study,there was only one patient (from group A,continued treatment) had developed significant hypotension (SBP<90) for the first 10 minutes after induction of anesthesia.it was rapidly & successfully treated with elevation of leg above level of the heart & rapid infusion of 500 ml normal saline. Another patient from group A had developed hypertension with SBP>160 & DBP>90;in cotrast to the expected,Only one patient out of 20 patients who asked to stop treatment had developed short-lived high BP,SBP >160 for the 1st 15 minutes. The result of no statistical significance of this comparative study might be attributed to inclusion & exclusion criteria were put to select participants.

Meticulous attention was directed to maintain euvolemic status throughout operation.

CONCLUSION:

Continuing or discontinuing ACEI before non-cardiac surgery under general anesthesia has no statistical significance regarding concerns of developing intraoperative hypotension .

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