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Original Article

Effects of the Discontinuation of Angiotensin-Converting Enzyme Inhibitors 12 and 24 Hours Before Open-Heart Surgery on Hemodynamics During and After Surgery

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ABSTRACT

Background: Preoperative use of angiotensin-converting enzyme inhibitors (ACEIs) is an independent predictor of the need for inotropic support postoperatively and hypotension during surgery; consequently, some surgeons suggest that ACEIs be discontinued prior to coronary artery bypass graft surgery (CABG). However, the optimal time of ACEI discontinuation before CABG remains controversial. In this study, we compared the effects of ACEI discontinuation 12 and 24 hours before open-heart surgery on the hemodynamic status of patients during surgery.

Methods: This randomized controlled trial was conducted on patients undergoing elective CABG. The patients were randomly divided into 2 groups: in the first group, ACEIs were discontinued 12 hours before CABG and in the second group, ACEIs were discontinued 24 hours before CABG. Hemodynamic evaluations including blood pressure (systolic, diastolic, and mean arterial pressures), the heart rate, and the hemoglobin level were performed.

Results: The trends of changes in systolic blood pressure (P = 0.41), diastolic blood pressure (P = 0.360), the heart rate (P = 0.11), and the hemoglobin level (P = 0.92) were not significantly different between the 2 groups over time. The mean arterial pressure was significantly different between the groups over time (P = 0.038). Likewise, the mean arterial pressure in the 24-hour group was significantly higher than that of the other group until the time of sternotomy, after which time the mean arterial pressure in the 12-hour group was significantly higher.

Conclusions: ACEI discontinuation before CABG had some effects on the hemodynamics of our patients during anesthetic induction, including the prevention of hypotension during surgery; nonetheless, our data did not show the optimal time to stop ACEIs prior to CABG. ***(Iranian Heart Journal 2020; 21(2): 27-33)***

KEYWORDS: Angiotensin-converting enzyme inhibitors, Coronary artery bypass grafting, Hemodynamics, Discontinuation

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Angiotensin-converting enzyme inhibitors (ACEIs) are used widely after myocardial infarction and in the treatment of hypertension and congestive heart failure. [1, 2] ACEIs confer their cardioprotective proprieties through the dilation of the peripheral vessels, leading to ventricular remodeling by inhibiting the generation of angiotensin II, which is a strong vasoconstrictor, and increasing bradykinin availability. [2, 3] In addition, ACEIs play an important role in reducing the occurrence of ischemic events after coronary artery bypass graft surgery (CABG) and, thus, decrease mortality and adverse cardiac events and improve the quality of life. [4]

There are still controversies over the preoperative use of ACEIs in CABG. Several studies have suggested that although the prolonged use of ACEIs results in cardiovascular benefits, it can not only increase the risk of hypotension during CABG by reducing systemic vascular resistance but also increase the need for vasoconstrictors during anesthesia. [4, 5] For this reason, these investigations have suggested that instead of administrating ACEIs up to and including the day of surgery, ACEIs be discontinued before CABG to improve the hemodynamic status of patients during the induction of anesthesia. [4] Be that as it may, there is no consensus on the optimal time of ACEI discontinuation. Some studies have recommended that these drugs be stopped at least 12 hours before surgical anesthesia induction. Moreover, it has been suggested that in patients who cannot tolerate hypotension, ACEIs be discontinued 24 hours before surgery. [6, 7]

Accordingly, we conducted the present study to compare the effects of ACEI discontinuation 12 and 24 hours prior to open-heart surgery on the hemodynamic status of patients during surgery.

METHODS

This randomized controlled trial was conducted on patients undergoing cardiac surgery. The study protocol was approved by our local ethics committee in accordance with the Helsinki Declaration of the World Medical Association (2000). Written informed consent was obtained from all the study participants.

Patients

The inclusion criteria comprised age between 40 and 70 years, candidacy for elective CABG, history of hypertension, consumption of ACEIs, and left ventricular ejection fractions of more than 40%.

Patients were excluded if they had a history of congestive heart failure, valvular disease, severe and chronic pulmonary disease, chronic renal failure, and consumption of other antihypertensive drugs (except for beta-blockers).

Randomization and Interventions

Two days prior to surgery, the study population was randomized into 2 groups via the balanced block randomization with an allocation sequence based on a block size of 8, generated by a computerized random number generator. All the patients were blind to allocation. The patients were randomly divided into 2 groups: in the first group, ACEIs were discontinued 12 hours prior to CABG and in the second group, ACEIs were stopped 24 hours before CABG.

The surgery premedication and anesthesia protocol were the same in both groups. As a premedication, 0.1 mg/kg of morphine and 1 mg of lorazepam were prescribed on the night before surgery and also on the morning of surgery. The standard anesthetic procedure was performed for the whole study population. Induction with 0.5 µg / kg of sufentanil, 0.1 mg/kg of midazolam, and 0.2 mg/kg of cisatracurium was done. Maintenance was performed by 100%

oxygen, 0.5 µg/kg/h of sufentanil, 1 µg/kg/min of midazolam, 0.9 µg/kg/min of cisatracurium, isoflurane 0.4–1%. The study subjects underwent cardiopulmonary bypass (CPB) after receiving 300UI/kg of heparin and having an activated clotting time of over 480 seconds. The temperature was reduced to 31 to 33 °C. In all the patients, surgical access was through a median sternotomy incision. ECG monitoring, arterial line placement, central venous pressure measurement, and pulse oximetry were performed for all the patients.

Outcomes

The study subjects were hemodynamically evaluated (blood pressure [systolic and diastolic pressures as well as the mean arterial pressure [MAP]) and the heart rate) at the following times: before induction, after induction, after intubation, before sternotomy, after sternotomy, before aortic cannulation, at CPB time (every 15 minutes), after CPB, at sternum closure, upon arrival at the ICU, and in the ICU every hour until extubation (up to 6 hours).

During CPB, MAP was maintained between 50 and 80 mm Hg. If MAP was below 50 mm Hg, the patient was administered 20 µ/dose of norepinephrine. If MAP exceeded 80 mm HG, first the depth of anesthesia was increased and then phentolamine was injected. Before and after CPB, 0.5–5µ/kg of TNG in addition to isoflurane was prescribed. Blood pressure monitoring was checked through the arterial line, and the heart rate was monitored with ECG.

In general, hemodynamic changes and the use of TNG, norepinephrine, and phentolamine were compared between the 2 groups.

Statistical Analysis

The statistical analyses were performed with SPSS, version 15 for Windows (SPSS Inc, Chicago, Illinois). A *P* value of less than 0.05 was considered statistically significant. The data were expressed as the mean ± the standard deviation for the interval and the count (%) for the categorical variables. All the variables were tested for normal distributions using the Kolmogorov–Smirnov test. The categorical values were compared using the χ^2 test or the Fisher exact test. The mean of the variables was compared between the 2 groups using the independent *t*-test or the Mann–Whitney *U* test. Repeated measure ANOVA was applied to assess the trend of changes in the dependent variables.

RESULTS

The mean age of the patients was 61.23 ± 9.767 years. Of the 66 patients, 48 (72%) were male and 18 (28%) were female. Thirty-three patients were assessed in each group. Table 1 presents the comparison of the demographic and clinical data between the 2 groups. There were no differences between the groups as regards the demographic characteristics, clinical data, and drugs ($P > 0.05$).

Repeated measure ANOVA was applied to determine the difference in the mean systolic blood pressure over time between the 2 groups. The trend of changes in systolic blood pressure was not significantly different between the patients in the 2 groups over time ($P = 0.41$) (Fig. 1).

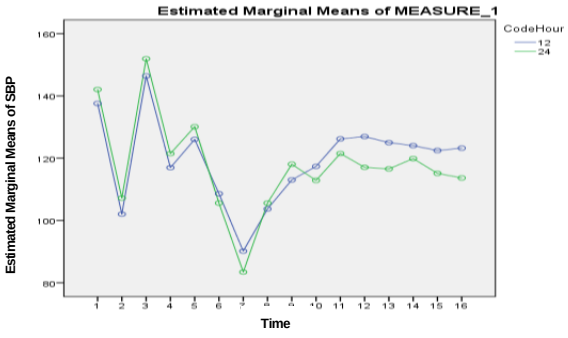

Figure 1: Systolic blood pressure changes over time

There was no significant difference in diastolic blood pressure at different time points between the patients in the 2 groups ($P = 0.360$) (Fig. 2).

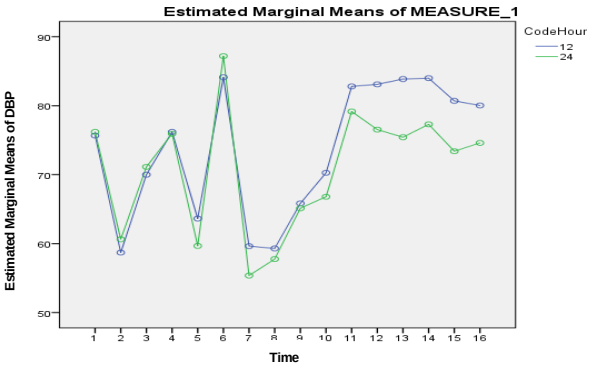

Figure 2: Diastolic blood pressure changes over time

The trend of changes in the heart rate was not significantly different between the patients in the 2 groups over time (P = 0.11) (Fig. 3).

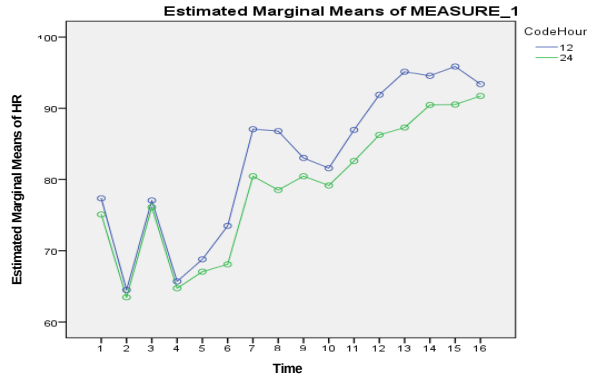

Figure 3: Heart rate changes over time

MAP was significantly different between the groups over time (P = 0.038). MAP was significantly higher in the 24-hour group than in the 12-hour group until the time of sternotomy, after which time it was significantly higher in the 12-hour group (Fig. 4).

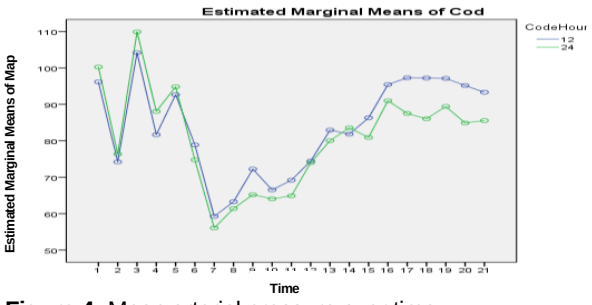

Figure 4: Mean arterial pressure over time

The trend of changes in the hemoglobin level was not significantly different between the 2 groups over (P = 0.92) (Table 2).

DISCUSSION

Although cardiac surgery, particularly CABG, is now deemed a common procedure, clinical strategies to prevent cardiac surgery-associated major cardiovascular complications are few and unsatisfactory. One of the current medical interventions to prevent these cardiovascular complications is the use of ACEIs. [7, 8] The beneficial effects of ACEIs include improvement in hemodynamics resulting from vasodilation and afterload reduction, enhancement of the left ventricular function resulting from neurohormonal effects, and prevention of harmful ventricular remodeling. [9-11]

Lee et al [3] conducted a study on 80 patients and revealed that the cardiac output and the heart rate were significantly higher in patients who did not receive ACEIs prior to CABG. They concluded that the use of ACEIs prior to surgery increased the need for vasoconstrictors to maintain blood pressure. It should be noted, however, that they did not discuss the time of ACEI discontinuation in the control group. Ranger et al [12] assessed the effects of ACEIs on hospital mortality in 4224 patients and found that the use of ACEIs in the early stages of postoperative heart surgery could have a positive effect on the cardiovascular status of patients. They also concluded that a surgical operation without the use of ACEIs could be associated with non-lethal ischemic cardiac events.

Controversy still persists regarding the role of ACEIs in patients undergoing CABG. Some surgeons have attributed the beneficial effects of ACEIs to their antihypertensive and antiatherogenic properties, while some other surgeons do not agree. In a study by

Devbhandari et al, [13] a questionnaire was used to enquire about the opinion of 167 surgeons regarding the use of ACEIs prior to CABG. The majority (63%) of them indicated that ACEI drugs caused vasodilatation, which led to an increase in the intake of fluids, inotropes, and vasoconstrictors. Forty (39%) of these surgeons believed that ACEIs should be discontinued before CABG, and 40 (38) were opposed to the discontinuation of ACEIs. Twenty (20%) of the respondents believed that there was no difference between taking and discontinuing these drugs.

Table 1: Comparisons of the demographic and clinical data

	12 Hours (n=33)	24 Hours (n=33)	*P* value
Age (y)	59.73±9.94	62.73±9.51	0.20
Sex (male)	23(76.7)	22(73.3)	0.76
BMI	26.09±3.00	25.26±3.59	0.55
DM	11(36.7)	12(40)	0.79
Smoking	11(36.7)	13(43.3)	0.59
EF %	49.50±6.97	46.43±6.29	0.06
Pump time (min)	77.67±29.70	84.17±29.18	0.29
Surgery time (min)	215.83±62.06	225.00±57.55	0.33
Drug dose TNG (mg)	12.37±4.91	13.57±6.39	0.56
Norepinephrine (μg)	110.00±111.92	116.82±135.87	0.74

BMI, Body mass index; DM, Diabetes mellitus; EF, Ejection fraction

Table 2: Trend of changes in the hemoglobin level (g/dL) between the 2 groups over time

	12 Hours	24 Hours
Before induction	13.40±1.51	13.35±2.17
After intubation	8.94±1.02	9.01±1.42
At CPB commencement	12.09±2.41	12.17±1.89
At CPB warming	10.64±2.15	10.55±1.94
After CPB	10.07±2.51	9.94±1.77
***P* value**	0.92	

CPB, Cardiopulmonary bypass

Several studies have suggested that the preoperative use of ACEIs is an independent predictor of the need for inotropic support postoperatively and hypotension during surgery; they, therefore, suggest that ACEIs be stopped prior to CABG. Still, the optimal time of ACEI discontinuation before CABG remains controversial.

Some studies have recommended that these drugs should be discontinued at least 12 hours before surgical anesthesia induction. In patients who cannot tolerate hypotension, ACEIs should be discontinued 24 hours before surgery.

In our study, we found no difference in terms of systolic and diastolic blood pressures and the heart rate between the patients for whom ACEIs were discontinued 12 hours before CABG and those for whom ACEIs were stopped 24 hours before CABG. MAP was the only parameter that was significantly higher in the 24-hour group than in the 12-hour group until the time of sternotomy; nonetheless, after sternotomy, MAP was significantly higher in the 12-hour group.

Bertrand et al [14] randomly divided 37 patients into 2 groups. In the first group, ACEIs were discontinued on the day before surgery and in the second group, ACEIs were stopped 1 hour before surgery. They showed that the patients who had received the drug on the morning of treatment had

more severe episodes of hypotension than did those for whom ACEIs were discontinued from the day before. Additionally, Bertrand and colleagues also reported the need for vasoconstrictors.

CONCLUSIONS

Although the discontinuation of ACEIs before CABG had some effects on the hemodynamics of our patients during anesthetic induction (eg, prevention of hypotension during surgery), our data did not show the optimal time for ACEI discontinuation prior to CABG. Further studies with larger sample sizes in each group are warranted.

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