Serum aldosterone as a predictor of heart rhythm disorders in acute myocardial infarction

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ABSTRACT

Introduction: In addition to the fastest reperfusion procedure of coronary arteries blood flow, identification of patients with increased risk of early and late complications is of the utmost importance in acute myocardial infarction (AMI).

Methods: We included total of 207 patients in the acute phase of myocardial infarction, which were divided into two groups, 127 patients without clinical symptoms of heart failure (HF) and 60 patients with HF symptoms. For all patients serum aldosterone levels were determined 24 hours after acute MI.

Results: In the group of decompensated patients, changes in aldosterone level did not show a statistically significant effect on paroxysmal supraventricular tachycardia (PSVT) occurrence (p > 0.05), while in the group of compensated patients there is statistically significant effect on PSVT occurrence (p = 0.004). Changes in aldosterone level in the group of decompensated (p=0.030) and compensated patients (p=0.024), showed statistically significant influence on the ventricular tachycardia (VT) occurrence. In the group of compensated patients, changes in aldosterone level showed a statistically significant effect on ventricular fibrillation (VF) occurrence (p = 0.024).

Conclusion: Plasma aldosterone level in patients with acute myocardial infarction has a significant influence on the occurrence of cardiac rhythm disorders irrespective of the existence of cardiac decompensation.

Keywords: aldosterone, myocardial infarction, prediction.
served in the developing proarrhythmogenic stimuli such as QT dispersion [13]. A shortened QT interval was found in patients with ischemic heart disease who received spironolactone therapy, which also contributes to the antiarrhythmic effects of aldosterone antagonists [14]. In addition to the fastest reperfusion procedure of coronary artery blood flow, identification of a patient with increased risk of early and late complications is of the utmost importance in patients with acute MI.

MATERIALS AND METHODS

Patients population. The study included 207 patients in the acute MI, who were divided into two groups, 127 patients without clinical symptoms of heart failure (HF) and 60 patients with HF symptoms. At admission after physical examination, the level of aldosterone in the blood was determined. The aldosterone reference ranges are from 8.00 to 172 pg/ml at rest, or 30.0 to 355 pg/ml after exercise (reference values at rest were used).

Statistical analysis. Since the distribution of continuous variables was asymmetrical, we used the median and interquartile range to represent the mean and the scattering measure, and for their comparison nonparametric tests (Mann-Whitney U test, Kruskal-Wallis test). By univariate logistic regression, we examined the effect of aldosterone on the prediction of variables with two outcomes. Ethical approval was obtained from Ethical Committee of Clinical Center University of Sarajevo.

Table 1. Effect of aldosterone level in serum on the appearance of paroxysmal supraventricular tachycardia (PSVT) according to the examined groups

<table>
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<th></th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>Df</th>
<th>p</th>
<th>Exp(B)</th>
<th>95.0% CI for Exp(B)</th>
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<tr>
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<td>0.151</td>
<td>1.019</td>
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<td>0.543</td>
<td>18.102</td>
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<td>0.099</td>
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<tr>
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<td>0.009</td>
<td>8.276</td>
<td>1</td>
<td>0.004</td>
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<td>1.008</td>
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<td>57.487</td>
<td>1</td>
<td>0.0001</td>
<td>0.088</td>
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Table 2. Effect of aldosterone level in serum on the appearance of ventricular ectopy (VES) according to the examined groups

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<th>Df</th>
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RESULTS

Binary logistic regression investigated the quantifiable chances [Exp(B)] for paroxysmal supraventricular tachycardia (PSVT) versus aldosterone levels in the group of compensated and decompensated patients. In the group of decompensated patients, changes in aldosterone levels did not show a statistically significant effect (chance quantification) on PSVT (p > 0.05, NS) while in the group of compensated patients significance was of, p = 0.004. In the group of compensated patients, regression analysis showed that elevation of aldosterone levels by 10 ng/dl increases the chances of developing PSVT by 2.6% in our sample, or 0.8% to 4.4% in the compensated patient (Table 1). In the group of decompensated patients, changes in aldosterone levels showed statistically significant influence on VES, p = 0.047.

Regression analysis showed that elevation of aldosterone levels by 10 ng/dl in decompensated patients increased the chance of ventricular extrasystole (VES) formation by 2.9%, or 0.5% to 5.7% in decompensated patients. In the group of compensated patients, changes in aldosterone levels did not show a statistically significant effect on VES, p = 0.089, NS. (Table 2).

In the group of decompensated patients, changes in aldosterone levels showed statistically significant influence on the ventricular tachycardia (VT), p = 0.030. We showed that elevation of aldosterone levels by 10 ng/dl increased the chance of VT formation by 4.7% in our sample, or from 0.4% to 9% in decompensated population.

| B- standardized model coefficient; S.E.- standard error; Wald- non-standardized coefficient; Df- degree of freedom; p-probability; Exp(B)- Exponent of a standardized coefficient, odd quantity; CI-confidence interval |
In the group of compensated patients, changes in aldosterone values show a statistically significant effect on VT, $p = 0.024$. Increase in aldosterone levels by 10 ng/dl increases the chance of VT formation by 2.6% in our sample, or 0.8% to 4.4% in compensated patients (Table 3).

In the group of decompensated patients, changes in aldosterone values did not show a statistically significant effect on ventricular fibrillation (VF), $p = 0.916$, while in the group of compensated patients we have a different situation with, $p = 0.024$. Regression analysis showed that elevation of aldosterone levels by 10 ng/dl in the group of compensated patients increases the chances of the VF formation by 2.7% in our sample, or 0.9% to 4.5% in compensated patients (Table 4).

**DISCUSSION**

Beygui et al. showed that elevated aldosterone level in blood correlates with increased risk of cardiac death, through the occurrence of ventricular fibrillation and recurrent hospitalization due to heart failure during six months of follow-up [11]. ESC Guidelines for management of acute STEMI also underline that increases in plasma aldosterone levels correlate with increase of cardiovascular events [12]. The renin-angiotensin-aldosterone system (RAAS) through its physiological role plays a key role in promoting and maintaining inflammation. Inflammation is particularly an important mechanism in the development and progression of cardiovascular disease. RAAS has proinflammatory and profibrotic effects at cellular and molecular levels. [13]. Patients with coronary disease in the LURIC study have increased cardiovascular mortality [9]. Guichard et al. underline that increase level of aldosterone is of important prognostic and therapeutic value in patients with coronary pathology [14]. Aldosterone is associated with the occurrence of major intrahospital events following myocardial infarction such as death, reanimated cardiac arrest, life-threatening cardiac arrhythmia or heart failure [15, 16, 17].

Serial measurements of neurohormonal changes in groups of post-infarction patients show that plasma aldosterone is at its highest level at the patient’s admission and falls rapidly over the hours after admission without any signs of rapid activation of the angiotensin converting enzyme inhibitor at that stage [8]. The presented observation is unique in assessing prognostic value of aldosterone in a large group of patients accepted for primary PCI. In the presented study, the highest aldosterone quartile level is associated with poor clinical outcomes, irrespective of age, heart failure, and success or failure of reperfusion [13].

Data from the Beygui et al. study further show that plasma aldosterone concentration, even if within the aforementioned physiological range, but in the upper quartiles values, can cause a significantly increased incidence of infarction complications [3]. In this way, aldosterone pretends to be a major marker of poor cardiovascular outcomes by identifying high risk patients.
in planning for invasive reperfusion in STEMI [3, 11, 12, 17].

In our study, through monitoring the occurrence of PSVT after myocardial infarction, it was shown that only in the group of compensated patients alteration of aldosterone values showed a statistically significant effect on PSVT occurrence with p = 0.004. In the decompensated patient group, we do not have this situation, which is somewhat illogical since the occurrence of PSVT is mainly associated with the development of decompensation, although this rhythm disturbance can be caused by excessive sympathetic stimulation. Although received chance of developing PSVT in a group of decompensated patients was unexpected, sympathetic stimulation could be basically a mechanism for the PSVT in a compensated group. Aldosterone increases sympathetic activity by decreasing the intake of noradrenaline into cardiac muscle, and this aldosterone-stimulated increased sympathetic activity could explain the result obtained.

Over the past years, the importance of RAAS in the pathophysiology of atrial fibrillation has been recognized. There is more and more evidence that MR antagonism can influence atrial electrophysiology, i.e. atrial fibrillation-induced electrical remodelling, whereby the molecular mechanisms of this process are almost unknown. Also, retrospective studies have reported an increased incidence of this arrhythmia in patients with primary aldosteronism [16, 17, 18].

In a separate group of experiments conducted in vitro using an atrial cell line, Taiwanese researchers showed that MR receptor expression correlates with an uninterrupted electric depolarization field and that cell exposure to aldosterone activates Ca 2+ / K + current [13, 16]. In these in vitro experiments, co-incubation with spironolactone weakens the changes caused by the exposure of atrial cells to aldosterone, indicating the involvement of MR dependent pathway. These results represent an important step in the understanding of cellular and electrophysiological mechanisms that may be the cause of spironolactone effects in the prevention of atrial fibrillation [17, 18]. A similar model is found in Laszla and associates study, which suggests that selective MR antagonism can affect atrial ionic (Ca 2+ /K +) currents and their tachycardia induced remodelling effects. [18, 19].

In the groups of decompensated subjects, changes in aldosterone values showed a statistically significant effect on VES p = 0.047. In decompensated patients there are numerous factors that have been implicated in the pathogenesis of VES, namely hypoxia, hemodynamic abnormalities, abnormalities of acid-base status, increased automation and re-entry mechanism, however, what could be fundamentally statistically significant for aldosterone on VES in decompensated patients is a combined effect of alterations in electrolyte homeostasis and aldosterone potentiated myocardial fibrosis, which is one of the most commonly reported effects of aldosterone on myocardial infarction. Similar observations have also been made in LURIC study, stating that apart from left ventricular hypertrophy due to pro-fibrous effects, aldosterone stimulates diffuse accumulation of connective tissue, predisposing the development of ventricular arrhythmias by increasing electrical inhomogeneity in the implementation and impaired gap junction function. Finally, aldosterone mediated MR activation may alter the expression of different ion channels, leading to disruption of cardiac activity potentials. These arguments were further reinforced by observing the impressive reduction of ventricular extrasystoles and QT interval after MR blockade [19, 20].

In the group of both decompensated (p = 0.030) and compensated (p = 0.024) subjects, changes in aldosterone values had a statistically significant effect on occurrence VT. The result is expected with regard to the mechanisms of the occurrence of aforementioned rhythm disorders, and that some of these mechanisms are encountered in both groups of respondents. It has already been reported that aldosterone leads to disturbances in electrolyte homeostasis, induces autonomic dysfunction (activates sympathetic and parasympathetic inhibitors), potentiates the effects of catecholamines, slows epinephrine into the myocardium and disrupts the function of baroreceptors, which are some of the predetermined mechanisms for the formation of VT [21].

Other mechanisms, however, may also be of significance. Discovery that transcardiac extraction of aldosterone may be reduced by blockade of aldosterone in patients with myocardial infarction may affect intracellular potassium and tendency for ventricular arrhythmias.

Recent meta-analysis involving seven trials and 8635 patients with heart failure or coronary artery disease has been studying the effects of antagonist aldosterone, spironolactone and eplerenone on ventricular arrhythmia. This meta-analysis has shown that these drugs reduce the rate of ectopic ventricular beats, the risk of VT, and ultimately the risk of sudden cardiac deaths in these patients [17].

In the group of compensated subjects, alteration of aldosterone values showed a statistically significant effect on the appearance of VF p = 0.024. This observation is in line with previous studies. Already mentioned study done by Beygui et al. has shown that elevated levels of aldosterone in the blood correlate with the onset of ventricular fibrillation [20]. This linkage of aldosterone and the appearance of VF, as one of the most serious
complications of myocardial infarction in our study, is independent of heart decompensation as well as of mechanisms that put heart decompensation into the pathophysiological substrate of VF after acute myocardial infarction.

CONCLUSION

The level of plasma aldosterone in patients with acute myocardial infarction has a significant influence on the occurrence of cardiac rhythm disorders irrespective of the existence of cardiac decompensation.

DECLARATION OF INTEREST

The authors declare no conflicts of interest.

REFERENCES


