SERUM ACTIVITY OF ANGIOTENSIN CONVERTING ENZYME AND BLOOD PRESSURE RESPONSE TO ACUTE DYNAMIC EXERCISE

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Abstract

Angiotensin converting enzyme (ACE) plays an important role in blood pressure regulation not only in the state of rest, but also during physical exercise. The aim of this study was to estimate the serum ACE activity in response to acute dynamic exercise.

The study involved a group of young, healthy, male volunteers (average 22 years of age). Exercise testing was carried out on ergometer bicycle according to the protocol of individually adjusted continuous, constant workload (3W/kg). The activity of ACE in serum was measured in venous blood, in the period of rest, in 4th, 8th and 12th minute of exercise and 1st, 3rd and 6th minute of recovery by spectrophotometric method.
Marked inter-individual differences in basal serum ACE activity were determined (range 8, 31 - 63, 72 U/L). Serum ACE activity did not significantly vary during exercise and in the period of recovery. Systolic blood pressure changed during exercise compared to values during rest period in accordance with the applied type of dynamical exercise. Diastolic blood pressure did not vary considerably during exercise. Statistically significant correlation between mean arterial blood pressure and ACE activity in the serum was not found.
The lack of increase of ACE activity in the serum, in spite of changes in blood pressure values, most likely shows the presence of alternative ACE independent pathway involved in the production of vasoactive substances that have important role in the regulation of cardiovascular system response to acute dynamic exercise.

Key words: angiotensin converting enzyme, acute exercise, healthy volunteers, male

Introduction

Angiotensin I converting enzyme, dipeptidyl carboxypeptidase (ACE, kininase II: EC 3.4.15.1, peptidase P) is a part of the renin angiotensin system that plays important role in electrolyte balance and blood pressure regulation not only in the state of rest, but also during physical exercise. ACE is also involved in the calicrein-kinin system. Besides being present in plasma, ACE could be located at luminal surface of vascular endothelial cells in various places in body. The activity of ACE was determined not only in blood serum but also in most of vascularized tissues. (1)
Circulating ACE levels or ACE activities in plasma are highly genetically determined (2.3). There are two forms of ACE gene in humans: D (deletion), or I (insertion), and there are three possible configurations: DD, DI and II. It was demonstrated that I/D dimorphism related to ACE genes concurs with serum and tissue activity of ACE. The ID polymorphism is physiologically important because it was observed that the I allele is accompanied with lower (3, 4), and D allele with relatively higher activity of circulating and tissue ACE (4). This was confirmed in studies conducted in populations of various ethnic groups. The variations in levels of ACE activities related to ID polymorphism of ACE genes probably do not influence the systemic level of angiotensine II and blood pressure (5).
In healthy persons the levels of ACE in plasma can show as much as 5-fold inter-individual variations (6), but intra-individual variations are small, and there are no marked variations in serum activity of ACE during 24 hours (7).
Physiological role of ACE is still not completely revealed. ACE cleaves dipeptide (histidyl-leucine, His-Leu) from the C terminal end of decapeptide chain of angiotensin I and produces angiotensin II, potent vasopressor and aldosterone stimulating peptide. An the same time, ACE deactivates bradykinin in systemic circulation that is potent vasodilator and stimulator of prostaglandin production.
Physical activity stimulates the renin angiotensin system (8, 9). The inhibition of ACE does not inhibit this stimulation completely (10).
There is disagreement in reports about changes of serum ACE activity in response to physical effort. Some of them showed the lack of changes in serum ACE activity (11) while the others reported an increase (6).
Because of the above-mentioned controversial findings, we aimed this study to estimate the serum ACE activity in healthy, male subjects in response to acute dynamic exercise.

Subjects and methods

Subjects

The study involved 14 healthy, young, male volunteers (average 22 years of age). All of them signed written informed consent. The School of Medicine Ethic Committee, Sarajevo approved the study protocol.

Procedure

Before exercise testing each subject underwent the same procedure consisting of clinical history, physical examination, routine laboratory tests, electrocardiogram (ECG) and blood pressure measuring in the period of rest. The results of this procedure showed that these subjects had no evidence of present or past health problems. No subject was taking any medication in the study period.

Exercise test

The exercise testing was conducted in quiet environment with temperature ranging from 22° to 24° C.

Each subject, immediately after period of warming up that lasted 3 minutes (workload 1,5W/kg) carried out one exercise test of 12 minutes, in upright, sitting position on bicycle ergometer (LODE-Corival 400) under the protocol of continuous, constant, individually adjusted workload (3 W/kg) and cycling rate of 60 RPM.

Blood pressure was measured using standard cuff method in the period of rest, in the 4th, 8th and 12th minute of exercise and in the 1st, 3rd and 6th minute of recovery.

ECG was continuously monitored during exercise and in the recovery period using Quinton ECG monitoring system Q-5000.

The indications for aborting the test were: unusual changes in ECG or blood pressure reactions, pain in legs, dyspnoea and dizziness.

Serum ACE activity

Blood samples were drawn through a canilla placed into the left cubital vein in the period of rest, in the 4th, 8th and 12th minute of exercise and in the 1st, 3rd and 6th minute of recovery. The ACE activity in serum was determined by spectrophotometric method according to Filipoviæ et al. modification (12) using hippuryl-l-histidyl-l-leucine as a substrate ("Sigma", St. Luis, USA). Spectrophotometer used was "Perkin Elmer" 550 S model. The values of serum ACE activity were expressed in U/L.

Statistical analysis

Values were expressed as mean +/- SEM. In the analysis of changes of serum ACE activity and blood pressure values, we used t test for small dependent samples. Differences were considered statistically significant at the $p < 0,05$. The coefficient of correlation was determined by Pearson's method.

Results

The average values of serum ACE activity in period of rest, during exercise and in recovery period is shown in Table 1.

There were marked inter-individual variations in basal values of serum ACE activity amongst the subjects (range 8, 31 - 63, 72 U/L). No statistically significant changes in serum ACE activities were found either in the exercise period or in the recovery period. The dynamics of blood pressure changes is shown in Figure 1.

Systolic blood pressure (SBP) increased significantly in comparison to the value measured in the period of rest. The dynamics of changes is in accordance with the type of applied dynamic, rhythmic exercise on bicycle ergometer. In the recovery period systolic blood pressure decreased successively, and at the end of this period there were no statistically significant differences in comparison to the value in the period of rest.

During exercise there were no significant changes of diastolic blood pressure (DBP). In the early period of recovery (in the 1st minute) DBP decreased significantly compared not only to the values in the period of rest but also at the end of exercise. At the end of recovery period the value of DBP was statistically significantly lower than in the period of rest. The dynamics of mean arterial pressure changes and serum ACE activity is shown on logarithmic scale in Figure 2.

Our results did not show significant correlation between SBP, DBP or MAP and serum ACE activity either in the period of rest, during exercise or in the recovery period.

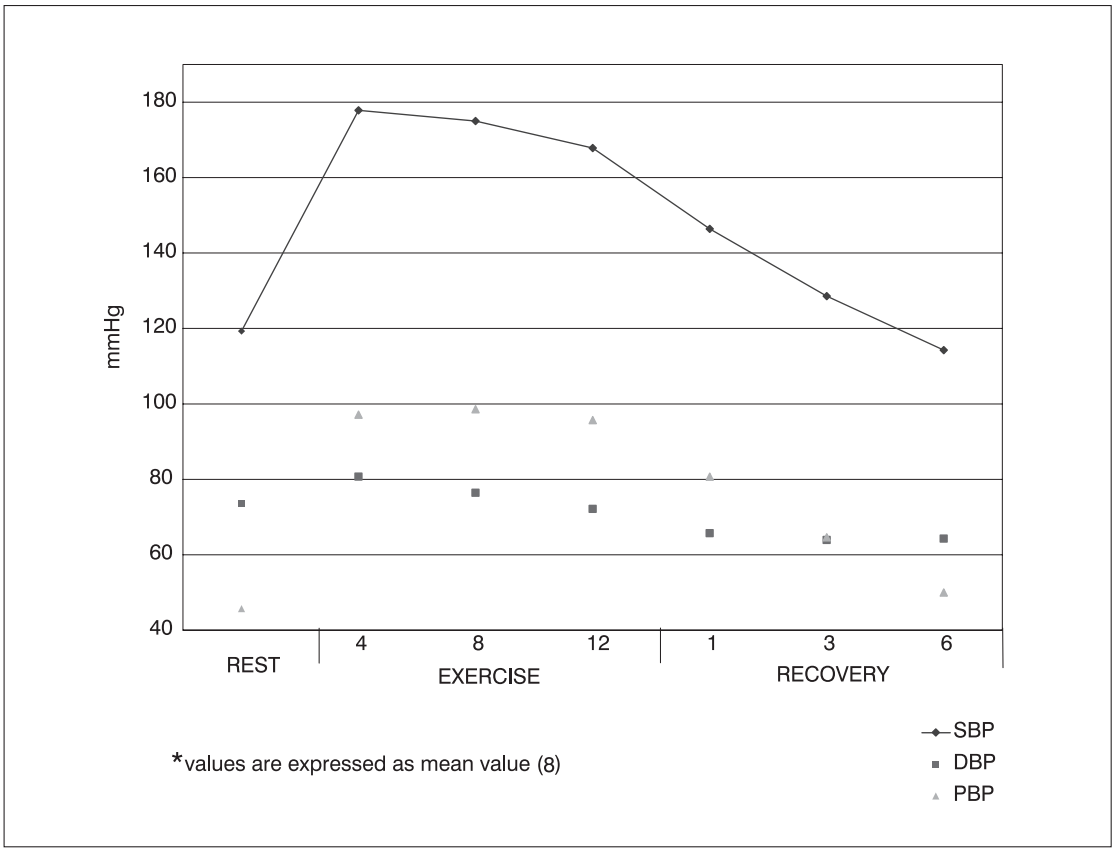
Discussion

Acute physical exercise demands fast adaptation of entire cardiovascular system. The most important hemodynamic changes are due to the need for matching the blood flow with increased metabolic needs of active tissue (13). The increase in cardiac output and changes in peripheral resistance caused by local vasodilatation in active tissues influence arterial blood pressure values.

Both humoral and nerve mechanisms are involved in the regulation of blood pressure (14). They maintain the balance between the needs for increase in arterial blood pressure that is important for obtaining appropriate blood flow through active parts and decrease of arterial blood pressure caused by peripheral vasodilatation (for delivering nutrients and oxygen, and elimination of vaste products and carbon dioxide as well as thermoregulation).

Angiotensin converting enzyme is one of the key molecules in the production of potent vasopressor, angiotensin II, which effectively influences blood pressure values. The values of basal serum ACE activity in subjects involved in our study showed marked inter-individual differences, which is in accordance with the results by Woods et al. (6). They related their results with polymorphism of ACE genes. It was observed that the subjects with DD genotype

Fig. 1. Dynamic of changes in systolic (SBP), diastolic (DBP) and pulse (PBP) blood pressure in period of rest, during exercise and in recovery period



had higher average values of serum ACE activities in basal conditions, while the subjects with II genotype had lower values.

Reports on serum ACE activity in response to acute physical exercise are not consistent. There were problems in comparison of the obtained results due to the use of numerous different protocols of exercise testing (different in the intensity of workload and duration of workload) and different equipment used in exercise (bicycle ergometer or treadmill). The results may also be influenced by the personal characteristics of the subjects (age, gender, ethnicity, level and type of usual physical activity). The important differences in findings of different studies are due to frequency of blood sampling (6, 11) not only in the period of exercise but also in the recovery period.

Table 1. The serum angiotensin converting enzyme (ACE) activity in period of rest, during exercise and in recovery period

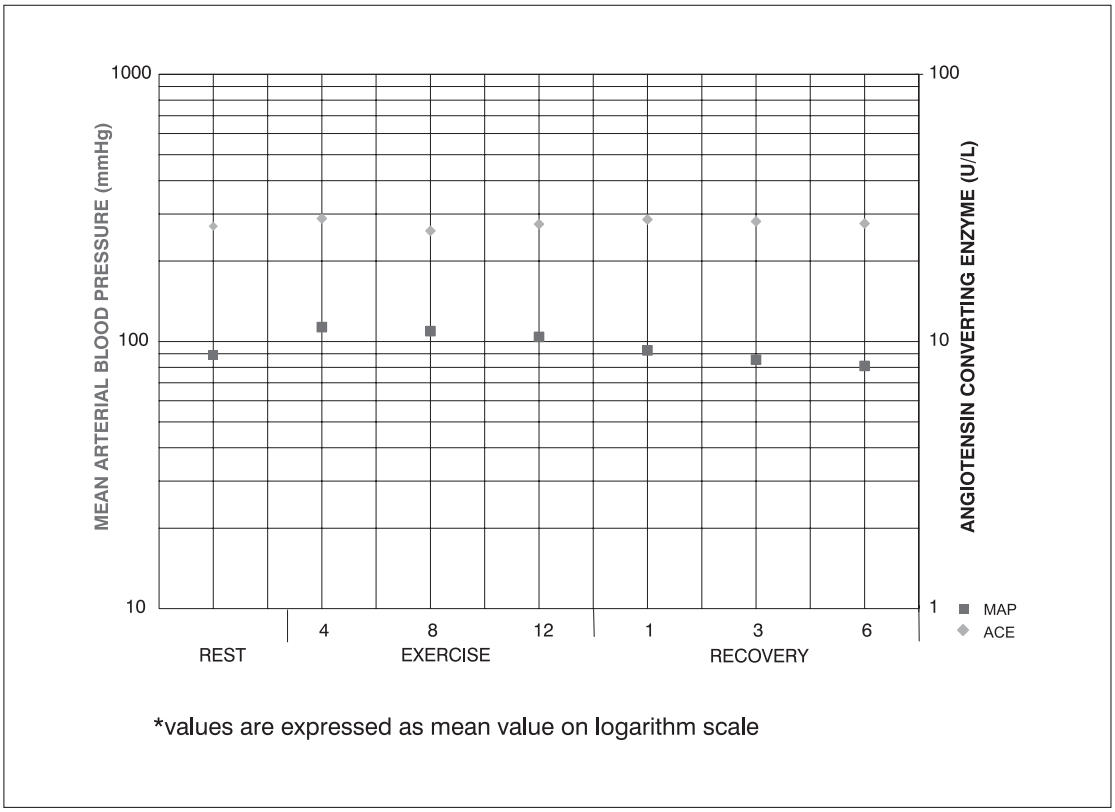
Type of activity		Serum ACE activity (U/L)	
Period of rest		40.04	4.76
Exercise (min)	4	38.51	2.58
	8	37.08	2.51
	12	36.14	1.90
Recovery (min)	1	40.87	3.47
	3	37.44	3.05
	6	38.15	3.84

* Values are expressed as mean value 8 SEM
n (number of subjects) = 14

Our results show that there were no significant changes in serum ACE activity either during exercise or in the recovery period in comparison to the basal values in the period of rest. Miura et al. (11) also found no changes in serum ACE activity during acute dynamic exercise lasting 30 minutes. Nevertheless, they found that concentration of angiotensin II in serum increased significantly. They presumed that this is due to the presence of "kinine-tensine system" that is involved in the production of angiotensin II independently of serum ACE. They also found that there were no statistically significant changes in concentrations of ACE (U/L) at the end of exercise in comparison to basal values. Their results suggested the presence of alternative pathway of angiotensyn II production during acute physical exercise where one or more enzymes from the serine protease group are involved.

As opposed to that, Woods et al. (6) found significant increase in serum ACE activity compared to basal values not only immediately after 20 minutes of exercise at the

Fig. 2. Dynamic of serum angiotensin converting enzyme (ACE) activity and changes in mean arterial blood pressure (MAP) in period of rest, during exercise and in recovery period



level of 70 % of VO2 max, but 40 minutes later as well. In this study, the basal values of serum ACE activity were significantly higher in subjects with DD genotype (45, 5+/-2 nmol His/Leu/ml/min) than in subjects with II genotype (24, 9 +/- 1, 8 nmol His/Leu/ml/min) although the whole group showed an increase in serum ACE activity.
Our results are difficult to compare with the results of the above-mentioned studies because of differences in the design of the studies. The differences are, primarily, in the duration of acute exercise, type of workload, dynamics of blood sampling not only in the period of exercise but also in the recovery period. We found marked differences in basal values of serum ACE activities amongst the subjects included in our study which concurs with Woods et al (6). However, the Miura et al. (11) results are more in accordance with ours and we can accept their presumption that the lack of increase in serum ACE activity during acute exercise is due to the presence of ACE independent pathway in the production of vasoactive agents during acute dynamic exercise.

Conclusion

Acute dynamic exercise does not cause an increase in serum ACE activity in healthy, young male subjects.
Statistically significant correlation between serum ACE level and systolic, diastolic or mean arterial blood pressure either in the period of rest, during exercise or in the recovery period was not found.
The lack of increase in ACE activity in the serum, in spite of changes in blood pressure values, most likely indicates presence of alternative ACE independent pathway involved in the production of vasoactive substances that have important role in the regulation of cardiovascular system response to acute dynamic exercise.

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