Increased Circulating Angiotensin II as a Prognostic Factor in Acute Coronary Syndrome

M. Momtahen, MD; M. Nayebpour, PharmD, PhD and S. Sadighi, MD

Abstract

Background- Angiotensin II promotes atherogenesis and modulates plaque vulnerability mainly by stimulating inflammatory mechanisms. The aim of this study was to investigate changes in the plasma level of angiotensin II in acute coronary syndrome.

Methods- The plasma level of angiotensin II was measured using the radioimmunoassay method in 81 patients with acute coronary syndrome, consisting of 34 patients with unstable angina and 47 patients with acute MI, and in 80 non-ischemic patients (control group).

Results- The plasma level of angiotensin II was significantly higher in the acute MI patients than that in the control group (11.3±7.50 pg/ml versus 9.72±8.30 pg/ml, P value<0.05) ***(Iranian Heart Journal 2005; 6 (3): 39-41).***

Key words: acute coronary syndrome Ë angiotensin II

It has been shown that angiotensin II (Ang. II) promotes atherogenesis in all its pathophysiological stages mainly by stimulating inflammatory mechanisms.[1,2,3] Plaque vulnerability and the potential for acute atherosclerotic events are also modulated by Ang.II.[3] Components of the renin-angiotensin system (RAS) have been demonstrated to increase in cardiac tissue and culprit coronary lesions of patients with acute coronary syndrome.[4,5,6,11]

Determining circulatory Ang. II, however, has revealed conflicting results. [4,7,8] To test the hypothesis that circulatory Ang. II increases in unstable ischemic heart disease as a inflammatory marker, we examined the differences between plasma Ang. II in patients with acute coronary syndrome (ACS) and a control group.

Methods

Study population

Between July 2004 and Jan. 2005, 81 patients with ACS, comprising 34 patients with unstable angina (UA) and 47 patients with acute MI (AMI) (with or without ST elevation) were investigated. The control group consisted of 80 non-ischemic patients.

The patients were treated with ACE inhibitors or beta-blockers in the two weeks preceding the study, and the patients who had clinical heart failure, pulmonary edema, hypotension or threatening arrhythmia on admission were excluded.

Study design and procedure

Blood was withdrawn from the recumbent patients early in the morning on the 1st day after admission.

To prevent *de novo* formation of Ang.II from angiotensinogen by plasma ACE, pre-chilled EDTA venipuncture tubes were used to collect blood samples.

Bestatin solution was immediately added to the blood samples to inhibit angiotensinase and to prevent *in vitro* destruction of Ang.II.

Measurement of Ang. II

Plasma Ang.II was measured by a double antibody radioimmunoassay method using a modification of the technique reported by

Corresponding author: M.Momtahen, MD, Associate Professor in Cardiology, Shahid Rajaie Cardiovascular Medical Center, Mellat Park, Vali-Asr- Ave., Tehran, Iran. E-mail: Mahmoudm @ rhc.ac.ir

Briefly, extracted EDTA blood samples, calibrators and controls are preincubated for 16 hours with an anti-Ang. II antibody. I^{125} Ang. II is added and competes with Ang. II present in samples, calibrators and controls for the same antibody binding sites in a second 6-hour incubation step. After incubation, a solid-phase second antibody is added to the mixture. The antibody-bound fraction is precipitated and counted in a gamma counter.

Statistical analysis

Data are expressed as means±SD. Comparison between the groups was performed using ANOVA. $P<0.05$ was considered statistically significant.

Patient characteristics

The baseline clinical characteristics of the study population are shown in Table I.

Table 1. Characteristics of case and control groups.

Characteristics	Controls (N=80)	ACS (N=81)
Men/Women	38/41	58/23
Age	52±16	57±12
Smoking (%)	32	40.7
Hyperlipidemia (%)	25	33.3
Diabetes (%)	23	33.3
Hypertension (%)	19	25.9
LVEF (%)	48±6.9	43±7.7

Results

Plasma Ang. II level was significantly higher in patients with acute myocardial infarction than that in the controls (11.3±7.50 pg/ml versus 9.72±8.30 pg/ml, $P<0.05$). There was no significant difference in plasma Ang. II between patients with UA and the controls (9.23±4.20 pg/ml versus 9.72±8.30 pg/ml, $P=0.497$).

Discussion

The results of this study demonstrate an increased plasma level of Ang. II in AMI patients but not in UA patients. It seems that more severe and more extensive ischemia characterized by myocardial necrosis is associated with increased plasma levels of Ang. II. Ang. II is a known mediator of inflammation,[1,2,9] and increased circulating levels of Ang. II in AMI patients may actually reflect a more intense local and systemic inflammatory response in AMI than in UA and controls. In addition to the local effects of inflammation at the level of the atherosclerotic lesion itself, systemic aspects of the inflammatory response may alter thrombotic risk.[9,10] Fibrinogen and plasminogen activator inhibitors (PAI) circulate at higher concentration in inflammatory states.[9,10] Ang. II particularly has been shown to alter fibrinolytic balance by augmenting PAI expression.[2,10,12] A given plaque disruption could have a greater chance to produce an occlusive thrombus under the influence of Ang. II and other mediators of inflammation.[9,10] Indeed, it has been shown that all patients with myocardial infarction preceded by UA have elevated CRP (an inflammatory marker) on admission.[9] Similarly, elevated circulating Ang. II can be used as an independent inflammatory marker in acute coronary syndrome to predict an unfavorable course independently.

Finally, it should be noted that an increased circulating level of Ang. II reflects only the activation of systemic RAS, and its absence does not reject activity of tissue RAS in UA.

Conclusion

We concluded that circulatory Ang. II increased in acute coronary syndrome as an inflammatory marker and that this increment was associated with more severe myocardial ischemia and necrosis. Therefore, it can predict hospital course and prognosis.

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