The variation of plasma concentrations of a novel, adipocyte derived protein, adiponectin, in patients with acute myocardial infarction


A diponectin is a new member of adipocyte derived proteins belonging to the soluble defence collagens. Plasma adiponectin concentrations in obese subjects are decreased in spite of an adipose specific expression. More interestingly, the patients with chronic coronary artery disease exhibited lower plasma adiponectin concentrations compared to body mass index (BMI) matched control subjects. On the other hand, adiponectin accumulates in the vascular subendothelial space when the endothelial barrier is damaged. In vitro, adiponectin suppresses the expression of adhesion molecules in the vascular endothelial cells and cytokine production from macrophages. Therefore, the molecule may be involved in the inflammation and tissue repairing processes.

Acute coronary syndrome is often precipitated by acute thrombosis. It is commonly accepted that the rupture or the erosion of plaques by the inflammatory process leads to coronary thrombosis and acute myocardial infarction (AMI). The C reactive protein (CRP) concentrations in the acute phase are suggested to reflect pre-existing coronary plaque instability associated with the onset of AMI. The significance of adiponectin in acute coronary syndrome has never been investigated. In the present study, we examined the serial change in plasma adiponectin concentrations and its relation to plasma CRP concentration in patients with AMI.

METHODS

Thirty four consecutive patients with AMI, who were admitted within six hours after the onset of symptoms, were included in this study. They underwent emergency coronary angiography for coronary thrombolytic treatment with recombinant tissue type plasminogen activator, percutaneous transluminal coronary angioplasty, and/or coronary stent placement immediately after they were diagnosed as having AMI. The successful recanalisation of the infarct related artery was achieved in all AMI patients. The control group consisted of 35 subjects who had atypical chest pain at rest, or with some exercise, but had no significant coronary artery stenosis (< 25% of luminal diameter) and no coronary spasm. The control group was selected from patients undergoing elective cardiac catheterisation, who had been matched for age, sex, and BMI with the AMI group. The criterion for exclusion in this study was the presence of inflammatory diseases (that is, collagen disease, advanced liver disease, malignant disease, septicemia, arthritis, or other inflammatory or infectious diseases), except for ischemic heart disease.

In the patients with AMI, blood samples were obtained immediately after admission to measure plasma adiponectin and CRP concentrations. Venous blood samples were also taken in the same manner on days 3 and 7 and at four weeks after admission, from the antecubital vein early in the morning, to measure the plasma concentration of adiponectin. In the control subjects, blood samples were obtained at coronary angiography for plasma adiponectin and CRP concentrations, and other biochemical assessment. Plasma adiponectin concentrations were determined by enzyme linked immuno sorbent assay. Plasma CRP concentrations were measured with a clinically validated high sensitivity assay (Dade Behring, Marburg, Germany).

RESULTS

There were no significant differences between the two groups in regard to the following variables: age, sex, the presence of hypertension, diabetes mellitus, smoking habit, BMI, serum total cholesterol concentration. Plasma adiponectin concentrations in the patients with AMI on admission (8.1 (4.8) µg/ml) were significantly lower than those in the control subjects (10.9 (5.5) µg/ml, p = 0.04). Plasma CRP concentrations in the patients with AMI on admission were higher than those in the controls (0.14 (0.12) mg/dl v 0.05 (0.07) mg/dl, p = 0.01).

We studied the sequential changes of plasma adiponectin concentrations after admission in the patients with AMI. The plasma adiponectin concentrations declined significantly at 24 hours (6.2 (3.6) µg/ml, p = 0.004) and at 72 hours (5.8 (3.4) µg/ml, p = 0.0001) compared to the concentrations on admission. They nearly returned to the concentration on admission on day 7 (7.5 (4.1) µg/ml) and at four weeks (7.2 (4.1) µg/ml) after the onset of AMI, but did not reach the concentration on admission (fig 1A). We also examined the relation between plasma CRP concentrations on admission and the reduction of plasma adiponectin concentration at four weeks from the concentration on admission. The reduction of plasma adiponectin was closely correlated with plasma CRP concentrations on admission (fig 1B).

DISCUSSION

The precise mechanism of the decreased plasma adiponectin concentrations immediately after the onset of AMI remains unclear. Plasma adiponectin concentrations may decrease as the result of the rupture of coronary plaques. Adiponectin is detected in the injured vessels but not in the intact vascular walls in humans and rodents. It is possible that adiponectin targets the ruptured plaques resulting in their consumption in the circulating plasma. An alternative explanation is that the inflammatory process may be accelerated in subjects with low plasma adiponectin before the onset of AMI. The process has been believed to facilitate the rupture of the atherosclerotic plaques leading to coronary thrombosis. Active inflammation

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; CRP, C reactive protein; TNFα, tumour necrosis factor α
and accumulation of activated monocyte derived macrophages secreting cytokines, chemokines, growth regulating molecules, and metalloproteinases were observed at the site of coronary plaque rupture in acute coronary syndrome. Adiponectin also suppresses the activity of human monocyte macrophages including TNFα production and foam cell formation. Therefore, adiponectin may play some role in an inflammatory process in vascular walls.

The reduction of plasma adiponectin during the course of myocardial infarction significantly correlated with the plasma CRP concentrations immediately after the onset of AMI. The strong inflammatory activity in the coronary vulnerable plaque may induce the reduction of plasma adiponectin. The decrease of plasma adiponectin concentration will accelerate the inflammatory process, resulting in a vicious cycle.

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REFERENCES

ERRATUM
The second co-author’s name is MacWalter RS, not Mac Walter RS.