Alterations in Circulating Adhesion Molecules in Acute Myocardial Infarction before and after Thrombolysis with Streptokinase

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ARTICLE INFO

ABSTRACT

Introduction: The role of adhesion molecules in the development and progression of coronary atherosclerosis is inevitable. It is not clear yet whether these molecules increase or decrease in level after thrombolytic therapy. This study was designed to compare concentrations of soluble forms of adhesion molecules in patients with acute myocardial infarction before and after reperfusion by thrombolysis with streptokinase (SK).

Methods: In this study, in 40 patients with acute myocardial infarction who were admitted in our Emergency Department undergoing thrombolysis with SK, plasma concentrations of six adhesion molecules [soluble L-selectin, P-selectin, E-selectin, intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and platelet endothelial cell adhesion molecule-1 (PECAM-1)] were measured by enzyme linked immunosorbent assay (ELISA), before and 3 hours after intervention.

Results: While soluble E-selectin and PECAM-1 concentrations did not differ within the 3 hours after interventions ($P > 0.05$), the level of P-selectin, L-selectin, ICAM-1, VCAM-1 were significantly reduced after thrombolysis with SK ($P < 0.05$).

Conclusion: Adhesion molecules which mediate the interactions in leukocyte endothelium vary in levels after reperfusion with SK. It was shown that 4 out of 6 adhesion molecules significantly reduced after thrombolysis with SK.

Introduction

Cardiovascular disease is the most prevalent and major cause of death world wide and burdens huge costs on the health care system.[1-4] Mortality due to Ischemic Heart Diseases (IHD) deacreases by early treatment and long term survival in patients increases subsequently.[5] Coronary artery reperfusion is accepted as a method to achieve reduction in size of myocardial infarction.[6] Thrombolysis technique with streptokinase (SK) is a confirmed method for reopening of an occluded vessel in patients with acute myocardial infarction.[6] Cellular adhesion molecules (such as: P-selectin, E-selectin, L-selectin, VCAM-1, PECAM-1, ICAM-1) have an important role to play in progression of atherosclerotic plaque.[7,8]

Besides, those mononuclear cells which are responsible for release of matrix metalloproteinases are activated by adhesion molecules leading to plaque rupture and initiation of acute coronary syndrome. Consequently, it can be concluded that an intervention leadngs to decline in adhesion molecules level could postpone the process of atherosclerotic plaque formation or rupture. On the other hand, it has been shown that patients with high

levels of these adhesion molecules have poor prognosis in future.[9] Some studies imply that adhesion molecules would decrease[10] or increase[11] in level, after reperfusion with different types of thrombolytic drugs.

Here in our hospitals in Iran, the only cost-benefit and available thrombolytic drug for reperfusion of coronary arteries in patients with acute myocardial infarction is intravenous thrombolysis with streptokinase (SK), 1.5 million IU over 60 minutes. The aim of this study was to compare concentrations of six soluble forms of adhesion molecules in patients with acute myocardial infarction before and 3 hour after attempted reperfusion by thrombolysis with streptokinase (SK).

Materials and Methods

From January to June 2011, 40 patients admitted to the emergency department of Rasul-Akram Hospital with the diagnosis of acute myocardial infarction (based on a history of typical chest pain and electrocardiographic changes) and with no contraindication of streptokinase administration were included in this study. The patients were selected using a convenient sampling method.

Blood samples from all 40 patients were taken prior to thrombolysis with SK, and then 3 hours after treatment. Plasma samples werer extracted by centrifugation at 4°C, at 3000 rpm for 10 min. Samples were later stored at −80°C before measurement of plasma levels of the soluble forms sE-selectin, sL-selectin, sPselectin, sICAM-1, sVCAM-1, and sPECAM-1 using commercially available enzyme-linked immunosorbent assays (ELISAs). Results were presented as mean±standard deviation (SD) for serum levels of adhesion molecules before and after thrombolysis with SK. The Statistical test used in this study was Paired-Sample *t*-Test. A $P \leq 0.05$ was considered statistically significant. The SPSS 17 (SPSS Inc., Chicago, Illinois, USA) statistical software package was used for all calculations. Our study was approved by the ethics committee of Iran University of Medical Sciences (IUMS). Informed written consent was obtained from each patient or his or her guardian.

Results

All 40 patients who were included in the study were in the age range of 46 to 83 years old (65.90 ± 10.6 years). There were 30 male patients (75%) and 10 female patients (25%). The levels of 6 adhesion molecules were measured before and 3hours after thrombolysis with streptokinase (1.5 million IU over 60 min). The results has been presented in Table 1.

Discussion

Adhesion molecules are considered to be indicators of activation of leukocytes, platelets and endothelial cells. It has been shown that in patients with acute coronary syndrome, these molecules would increse in atherosclerotic plaque rupturing, ischemic and reperfused areas.[8] We found significantly decreased serum levels for P-Selectin after SK reperfusin. The concentration of L-Selectin was also reduced by 3 hours after SK lysis. VCAM-1 palys an important role in atherosclerosis plaque progression and even rupture of the plaque leading to thrombosis. VCAM-1 is related to the aggregation of leukocytes, on the other hand, adherence of leukocyts to vascular endothelial cells causes endothelium dysfunction.[12] It has also been shown that plasma levels of VCAM-1 were significantly decreased. After thrombolysis in patient with acute myocardial ischemia, it has been shown that both soluble ICAM-1 and PECAM-1 increase in levels within the initial hours after reperfusion.[13,14]

In the present study, we found PECAM-1 to be stable after reperfusion, but significant decline in ICAM-1 level was observed. Endothelial cells are the only source of E-selectin expression and an increase in E-selectin could reveal endothelial activity.[15] Some studies have shown that this molecule rises in patients with myocardial ischemia and hypertension.[16-20] No significant differences were observed in the concentration of E-selectin within the 3 hours after intervention. In a 2001 study by Kerner et al., the concentration af 6 adhesion molecules in 30 patients with acute myocardial infarction was measured and it was seen that E-selectin, ICAM-1, VCAM-1 and PECAM-1 had no significant difference in levels after streptokinase administration; however, L-selectin and P-selectin significantly deacreased after thrombolysis with SK. These findings are not consistent with results of our study.[6]

In other seperated studies by Postadzhiyan[9], Squadrito,[10] Parise,[21] and Zeitler,[22] it has been shown that adhesion molecules would decrease in levels after thrombolytic therapy. These findings have a relative conformity to our findings.

Conclusion

It seems that adhesion molecules vary in levels following reperfusion therapy with streptokinase. Overall, 4 out of 6 adhesion molecules showed significant decline in levels after reperfusion by SK thrombolytic therapy in acute myocardial infarction. The clinical importance of these results should be investigated in further studies. Besides, these results indicate that thrombolysis with streptokinase would decrease adhesion molecule levels and may lead to decline in atherosclerosis progress and recurrence of myocardial infarction.

Table 1. Serum levels of soluble adhesion molecules

	P-Selectin (ng/ml)	L-Selectin (ng/ml)	VCAM-1 (ng/ml)	ICAM-1 (ng/ml)	E-Selectin (ng/ml)	PECAM-1 (ng/ml)
Before reperfusion	127.15 ± 22.84	479.7 ± 148.91	1012.75 ± 402.9	446.35 ± 106.02	87.71 ± 6.13	67.95 ± 15.29
Three hours after reperfusion with SK	108 ± 16.43	389.6 ± 106.24	858 ± 322.9	348.45 ± 75.6	101.32 ± 7.95	67.1 ± 17.81
P	0.002	0.006	0.002	0.0001	0.117	0.681

Limitations

Blood samples of the patients were taken in only two time intervals; once before thrombolysis with SK, and then 3 hours after SK administration due to funding shortage.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Iran University of Medical Sciences.
Conflict of interests: The authors declare no conflicts of interest.

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