PLASMA HOMOCYSTEINE CONCENTRATIONS IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Abstract

INTRODUCTION: Most studies indicate that increased plasma homocysteine level is a risk factor for coronary artery disease. However, data concerning the role of homocysteine in young patients with acute myocardial infarction (AMI) is scanty. The aim of this study was to study the possible association between homocysteine plasma levels and early-onset AMI.

METHODS: This case-control study included 83 AMI patients and 83 healthy controls. Biochemical parameters were determined and homocysteine was measured by enzyme immunoassay. Multivariate logistic regression analysis was used to test the association of homocysteine with the occurrence of AMI.

RESULTS: Homocysteine concentration in patients with AMI was higher than in controls (19.54±13.3 and 15.54±8.9 µmol/l, respectively, P=0.002). Hyper-homocysteinemia was associated with early myocardial infarction (odds ratio=5.05). Hypercholesterolemia (OR=4/21), opium addiction (OR=4/78) and age (OR=1/24) also had associations with AMI.

CONCLUSIONS: Our results showed that homocysteine levels are elevated in young patients with AMI, and hyperhomocysteinemia is associated with early myocardial infarction; hence it should be evaluated in all young patients with AMI.

Keywords: Homocysteine, Acute myocardial infarction, young, risk factor.

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Introduction

Acute myocardial infarction (AMI) is uncommon in young adults and mostly afflicts men.[1] It strikes an individual during the most productive years of life. These patients also have different risk factor profiles compared to older patients.[2,3]

Homocysteine is a novel atherosclerosis risk factor; it derives from the metabolism of methionine, an essential amino acid found primarily in dietary animal protein.

Homocysteine concentrations are determined by genetic and nutritional factors, and deficiencies of vitamin B6, B12 and Folic acid are associated with hyperhomocysteinemia.[4] Low blood levels of folate appear to be a particularly strong environmental determinant of homocysteine levels in many populations.[5]

Numerous clinical and epidemiologic trials have suggested that hyperhomocysteinemia is a risk factor for coronary artery disease (CAD).[6,7] In addition, prospective studies have found increased risk of myocardial infarction among patients with moderate hyperhomocysteinemia.[8,9] Although, an elevated plasma homocysteine concentration has been hypothesized as a risk factor for AMI, not all studies have shown such a relationship.[10] Furthermore, data concerning the role of homocysteine in young patients with AMI in a Southwest Asian population (Iran) are rare. The aim of this study was to study a possible association between homocysteine plasma levels and early-onset AMI. We also investigated other risk factors in AMI patients.

Materials and methods

This case-control study was carried out at the Shafa Hospital, Kerman, Iran, between April 2004 and May 2005. The sample consisted of 83 patients with first ST-segment elevated AMI and 83 controls. Subjects from different clinics who were free of any cardiovascular disease were included as control group.

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The diagnosis of AMI was confirmed based on history, serial electrocardiogram changes and cardiac enzymes elevation. A young patient was defined as one aged 40 years or less upon admission. Risk factors of CAD were defined as:

1. Overweight (body mass index >27)
2. Smoking (more than 10 cigarettes daily for at least 5 years)
3. Family history (any first-degree relatives with confirmed CAD)
4. Diabetes mellitus (FBS >126mg/dl, using insulin or oral hypoglycemic agents)
5. Hypertension (systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg or using antihypertensive drugs)
6. Hypercholesterolemia (total cholesterol >200 mg/dl)
7. Hypertriglyceridemia (triglyceride >200mg/dl)
8. Hyperhomocysteinemia (>15 μmol/L)

In patients with AMI, blood samples were obtained on the seventh day after admission for measurement of homocysteine

Blood was drawn after fasting for 12 hours and biochemical parameters were determined. Samples were centrifuged for 10 minutes before measurement of homocysteine. After centrifugation, plasma was decanted and stored at -70 ºC until use. Homocysteine was measured by enzyme immunoassay (Axis-shield, Dundee, United Kingdom) according to the kit manual. We included the groups (case/control) as dependent variable in the model and other potential risk factors as independent ones. Univariate logistic regression was performed for calculating crude odds ratio (OR), and multivariate analysis was performed to calculate adjusted OR. All of these analyses were done by Stata v.8 software.

Results

Plasma homocysteine in patients (19.54±13.3 μmol/l) was significantly higher than in controls (15.54±8.9 μmol/l). Patients were about 24% as likely to have hyperhomocysteinemia as controls (OR 2.88, CI 95%: 1.5-5.5). In univariate analysis, all classic coronary risk factors in patients (except for gender) were significantly higher than in controls (Table 1).

Moreover, after adjusting OR for significant classic risk factors, only hyperhomocysteinemia, age, opium addiction, and hypercholesterolemia remained in the model significantly.

The adjusted OR for hyperhomocysteinemia was 5.05 (CI 95%: 1.7-14.9) (Table 1).

About 32 patients (38.55%) had inferior-lateral MI and the others had anterior MI. In both types of MI, hyperhomocysteinemia in patients was significantly higher than in controls (OR 2.95, 2.84, respectively).

Discussion

In the present study, we confirmed that plasma homocysteine in young patients with AMI was significantly higher than in the control group; in addition, increased plasma homocysteine had a significant association with AMI by multivariate logistic regression analysis including conventional coronary risk factors. This is in agreement with previous investigations in other populations. Recently, Nikfardjam et al. showed an association between myocardial infarction and hyperhomocysteinemia.[11] Ogawa et al. also found hyperhomocysteinemia to be associated with early myocardial infarction.[12] However in a study performed in a Southeast Asian population (Singapore), plasma homocysteine levels were not associated with AMI.[10] This inconsistency may partly be explained by racial and dietary differences in the studied

TABLE 1. Crude and adjusted Odds Ratio (OR) for different potential risk factors for acute myocardial infarction (AMI)

Risk factors	Case (n=83)	Control(n=83)	Crude [P value]	Adjusted [P value]
Male (%)	77 (92.8)	79 (95.2)	0.65 [0.517]	----
Hypertension (%)	6 (7.2)	0	----	----
Age (M±SD)	35.9 ± 4.27	29.2 ± 6.02	1.25 [<0.001]	1.24 [<0.001]*
overweight(%)	24 (28.9)	8 (9.6)	3.81 [0.003]	2.45 [0.16]
Cigarette Smoking (%)	55 (66.3)	33 (39.8)	2.98 [0.001]	0.87 [0.8]
Opium Addiction (%)	38 (45.8)	12 (14.5)	4.10 [<0.001]	4.78 [0.009]*
Family history of CAD (%)	15 (18.1)	5 (6.0)	3.44 [0.02]	2.99 [0.15]
Diabetes (%)	17 (20.5)	6 (7.2)	3.31 [0.02]	1.03 [0.9]
Hypercholesterolemia (%)	59 (71.1)	20 (24.1)	7.73 [<0.001]	4.21 [0.006]*
Hypertriglyseridemia (%)	42 (50.6)	15 (18.1)	4.64 [<0.001]	1.99 [0.19]
Hyperhomocycteinemia (%)	41 (49.4)	21 (25.3)	2.88 [0.002]	5.05 [0.003]*

M±SD: Mean ± Standard Deviation.
Only significant variables remain in model for multivariate logistic regression. * indicated independent risk factors for AMI.

groups. We should note that the prevalence of hyperhomocysteinemia is high in the Iranian population.

In a cross-sectional population-based study in healthy Iranian adults, the prevalence of mild hyperhomocysteinemia was 47.6%,[13] which was higher than in other populations.[14,15] In the present study, the hyperhomocysteinemia rate in patients with AMI was 49.4%. These observations are important for primary prevention of AMI in Iran.

The mechanisms that may explain how homocysteine can increase the risk of AMI include its effect on the vascular endothelium, platelets and its role in increasing the risk of thrombosis.[16,17]

Most reported data show that smoking is the commonest risk factor encountered in young patients with AMI in Iran;[18,19] smoking was common in patients and considered as a risk factor for AMI in univariate analysis, but not in multivariate analysis.

For the first time, we reported opium addiction to be independently related to the risk of AMI in young patients. There are no surveys on the effect of opium as a risk factor for AMI in young patients. However, these findings have yet to be confirmed by other studies.

We also found that hypercholesterolemia was an independent risk factor for AMI. Hypercholesterolemia was present in 71% of the patients, while it was reported to be 28.3% in an Italian study.[20] AMI was the predominant disease of men and females represented only 7.2% of patients; this may be due to the low prevalence of coronary heart disease in young women.

Conventional risk factors like positive family history and diabetes mellitus were not common in AMI patients and fewer patients had a history of hypertension.

Our findings showing the low prevalence of hypertension and diabetes mellitus in young patients with AMI are in keeping with other investigations.[20,21]

A limitation of our study is that in patients with AMI, blood samples for homocysteine measurement were obtained on the seventh day after admission; this was based on earlier reports of Egerton et al. and others.[22,23]

Our results showed that homocysteine levels are elevated in young patients with AMI, and hyperhomocysteinemia is associated with early myocardial infarction, hence all young patients with AMI should be evaluated for hyperhomocysteinemia.

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