

Serum Homocysteine Levels in Patients with Myocardial Infarction in Gorgan (In Northern Iran)

¹Hamid Reza Joshaghani, ²Ahmad Ali Shirafkan and ³Abdoljalal Marjani

¹Department of Medical Laboratory Technology, School of Paramedicine,
Golestan University of Medical Sciences, Gorgan, Iran

²5th Azar Teaching Hospital, Golestan University of Medical Sciences, Gorgan, Iran

³Department of Biochemistry, Faculty of Medicine,
Golestan University of Medical Sciences, Gorgan, Iran

Abstract: Homocysteine is a sulfur-containing amino acid produced by demethylation of methionine. Genetic mutations and deficiency in nutrients may disrupt homocysteine metabolism and cause an increase in plasma homocysteine level. Approximately 10% of the patients with were cardiovascular disease has elevated plasma homocysteine. Blood sample was drawn from 48 patients who have AMI that without a history of using folic acid or vitamin B complex supply and 48 health people without history of MI, diabetes, hyperlipidemia and hypertension. Homocysteine assayed by Elisa method, folic acid and vitamin B12 performed by RIA method. Mean of homocysteine in case group $30.3 \pm 5.3 \mu\text{M L}^{-1}$ and in control group 11.1 ± 3.1 ($p < 0.001$). Mean of serum B12 in patients group $297.1 \pm 208.9 \text{ pM L}^{-1}$ and in control group 261.5 ± 205.3 that not seen significant difference between two groups. Serum folic acid in patients group was $3.9 \pm 2.9 \text{ ng mL}^{-1}$ and in control group was 4.3 ± 3.5 that not significant different in two groups. In this study, level of homocysteine in patients is significantly more than control group. Therefore in this area concentration of homocysteine is very effective in incidence of MI.

Key words: Folic acid, homocysteine, Iran, myocardial infarction, vitamin B12

Introduction

Homocysteine is a sulfur-containing amino acid produced by demethylation of methionine. Homocysteine has been shown to play a critical role in several remethylation and transsulfuration metabolic pathways (Tutuncu *et al.*, 2005). Genetic mutations and deficiency in nutrients may disrupt homocysteine metabolism and cause an increase in plasma homocysteine levels (Gallagher *et al.*, 1996). An elevated plasma homocysteine level is a risk factor for Cardiovascular Disease (CVD) (Bores, 1997). Approximately 10% of the patients with cardiovascular disease, elevated plasma homocysteine level appears to be the major risk factor (Boushey *et al.*, 1997). It has been shown that each 3 mmol L^{-1} increase in plasma homocysteine levels above 7.2 mmol L^{-1} is associated with a 35% increase in the risk of myocardial infarction (Verhoef *et al.*, 1996). Approximately two-thirds of cases of elevated Homocysteine concentration were estimated as being due to low or moderate concentrations of folate (Voutilainen *et al.*, 2004). Of the three important vitamins for homocysteine metabolism, B12 has the most limited distribution in nature; it is biosynthesized by some bacteria. In humans, it supports the activities of two known enzymes, the cytoplasmic methionine synthase and the

Corresponding Author: Hamid Reza Joshaghani, Department of Medical Laboratory Technology,
School of Paramedicine, Building of Falsafi, Hircan Boulevard, Gorgan, Iran
Tel: +98 171 4421663 Fax: +98 171 4421664

mitochondrial methylmalonyl-CoA mutase (Oltean and Banerjee, 2003). Since, the correlation between MI and level homocysteine is contradictory, we decided to assay concentration of homocysteine in patients that suffering from MI and assessment correlation between homocysteine level, folate and B12.

Materials and Methods

In 5th Azar Teaching Hospital in Gorgan (Center of Golestan Province in Northern Iran) from March to August 2004, blood sample after 12 h fasting was drawn from 48 patients with AMI that didn't have a history of folic acid or vitamin B complex supply. Immediately, serum was separated and store in deep freezer. Too, from 48 health people without history of MI, diabetes, hyperlipidemia, hypertension in fasting condition blood sample was drawn.

Serum glucose, triglyceride and cholesterol performed by enzymatic method (Man Company-Iran) by clinic II instrument. Homocysteine assayed by Elisa method (IBL kit), folic acid and vitamin B12 performed by RIA method (MP Biomedicals Company).

Results

Thirty six of case group were man and 12 of them women. In control group were 29 men and 19 women. Mean age of patients was 52.5 years (51.5±9.3 men, 55.5±8.1 women) versus 48.6±6.8 years in control group (49.0±7.0 men, 48.1±6.7 women). The mean of homocysteine in patients group was 30.3±5.3 $\mu\text{M L}^{-1}$ and in control group 11.1±3.1 ($p < 0.001$). The mean of serum B12 in patients group was 297.1±208.9 pM L^{-1} and in control group 261.5±205.3, there wasn't significant difference in two groups. Serum folic acid in patients group was 3.9±2.9 ng mL^{-1} and in control group was 4.3±3.5, there wasn't significant difference in two groups. Concentration of homocysteine, B12 and folic acid in two groups to separate genus to be shown in Table 1.

Table 1: Mean of concentration of homocysteine, B12 and folic acid in case and control group according to genus

Groups		Homocysteine	B12	Folic acid
Case	Men	31.3±5/0	286.5±187.7	3.7±3.1
	Women	27.1±5.1	328/8±270.0	4.5±2.1
Control	Men	11.3±3.5	216.8±158.7	3.8±2.1
	Women	10.7±2.3	329.6±250.7	4.9±5.0

Discussion

Cardiovascular Disease (CVD) is the most common cause of death in the world. CVD are related to cigarette, hypercholesterolemia and obesity. For the first time McCully and Wilson in (1975) presented the hypothesis of correlation between CVD and hyper homocysteinemia. Qujeq and his colleagues to show correlation between increase of homocysteine with MI in Babol- Iran (25.05±2.44 in patients versus 12.75±1.2 in control group) (Qujeq *et al.*, 1996). Verhoef *et al.* (1996) reported that homocysteine concentration in CVD patient was 11% more than control group. In this report, level of B6 and folate in case group significantly decrease than control group, but for B12 the difference between two groups was not significant. In this study, level of homocysteine in patients is significantly more than control group. Therefore, in this area concentration of homocysteine is very effective on the incidence of MI. Contradiction between reports indicated necessary correlation MI and homocysteine assessment in every place.

In this study, there wasn't significant difference between folate and B12 in two groups. Pinto *et al.* (2005) reported that the administration of 500 µg folate per day in 2 weeks caused decrease of homocysteine level. Therefore; administration of folate for high risk patients can be useful. The results one research in Singapore by Ng *et al.* (2002) is contrary with this study, they didn't observe correlation between MI and homocysteine. In other case-control study by Christensen *et al.* (1999) in Norway, level of homocysteine in case group was more than control group, but concentration of folate in cases was less than controls. These researchers believed other factors for example cigarette and alcohol causes this contrary. In Iran, the information about use of alcohol is unreliable. For this reason, we did not question about use of alcohol.

Until recently, the measurement of homocysteine in serum and plasma was limited to laboratories equipped with highly specialized instrumentation such as gas chromatography-mass spectrometry or HPLC (Huijgen *et al.*, 2004). Many methods, mostly by HPLC, have been reported for measuring homocysteine. These methods are relatively complex and require highly specialized equipment (Zhang *et al.*, 2004). Since in our university we haven't HPLC instrument, we assayed homocysteine by Elisa method. This method (Elisa) performed similarly for patient and control samples, therefore results are reliable for comparison in two groups.

We recommend a study to be performed on all patients of province that suffering from MI for homocysteine level, vitamins B status and Cystathionine β-synthase and methylene tetrahydrofolate reductase polymorphism.

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