Serum Homocysteine Levels in Patients with Acute Myocardial Infarction in Jordan

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Abstract

Objective: To examine the homocysteine level in Jordanian patients with acute myocardial infarction.

Methods: Plasma fasting homocysteine levels were measured in 90 patients with acute myocardial infarction and compared to 90 age-, sex-, and smoking habit matched control subjects free of clinical coronary disease.

Results: Homocysteine (mmol/l) levels were significantly higher in patients compared to controls (18.5 ± 7.8 v 12.0 ± 8.4; p=0.002).

Conclusion: The result of this study indicates that homocyteine level is high in patients with acute myocardial infarction and it may be a risk factor for coronary heart disease in Jordanian population. Public health education about homocysteine and its reduction by increasing supplements of folate and vitamin B may reduce the incidence of coronary artery disease in Jordanian population.

Keywords: Homocyteine, Atherosclerosis, Acute Myocardial Infarction, Coronary Heart Disease.

Introduction

Atherosclerotic cardiovascular disease is one of the major causes of death worldwide. Traditional risk factors for atherosclerosis may account for only one half to two thirds of the actual risk. In recent years, it has been suggested that many variables may contribute to atherosclerosis including plasma fibrinogen, lipoprotein (a), estrogen deficiency, C-reactive protein, and homocysteine. [1, 2] Homocysteine is a naturally occurring amino acid, derived from methionine which is present in dietary protein and produced in small amounts by the human body.

Homocysteine exerts adverse effect in human and is, therefore, rapidly metabolized by transsulfuration (which depends on vitamin B6) or remethylation (which depends on folic acid and vit B12). [3]

Deficiency in any of these vitamins may lead to some degree of hyperhomocysteinemia. Some studies have found that homocysteine is an independent, modifiable risk factor for cardiovascular disease and a strong predictor of mortality in patients with coronary artery disease. [4-7]

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In contrast, in neither the American Multiple Risk Factor Intervention Trial (MRFIT) nor the Finnish north Karelia project was any association observed between total homocysteine and coronary heart disease. [8, 9] The above presented discrepancies in literature on the role of homocysteine in coronary artery disease led us to investigate this issue. The aim of this study was to assess the level of homocysteine in patients with acute myocardial infarction and normal person in Jordan.

Methods

Ninety patients who satisfied the World Health Organization criteria for myocardial infarction [11] were recruited from admissions to the coronary care unit at Princess Basma Teaching Hospital. The period of recruitment was between January 2003 and January 2004. Control subjects were recruited randomly from adult visitors to patients with non-cardiovascular illnesses on general medical and surgical wards at Princess Basma Teaching Hospital. All control subjects had a normal ECG.

Exclusion criteria for patients and controls included previous history of ischemic heart disease, deep vein thrombosis, cerebrovascular accident, renal dysfunction (serum createnine > 133 mmol/l), and taking multivitamins.

Informed consent was obtained from all patients and controls. Cases and controls filled in a standard questionnaire about their personal histories, major risk factors, history of ischemic heart disease, and provided blood samples for laboratory analysis.

Venous blood samples were obtained after 12 hr fasting within the first 24 hr of myocardial infarction. Blood was transferred into EDTA tubes. Serum was separated within 15 minutes of collection by centrifugation at room temperatures for 15 minutes at 1000g, and immediately stored at –20C until analysis. Cholesterol, Triglyceride, and High Density Lipoprotein (HDL) were measured by enzymatic colorimetric method. Homocysteine was measured by Enzymatic Immunosorbent Assay (ELIZA).

Statistical Analysis

Data are presented as mean and ± SD. A comparison between groups was performed by mean of an unpaired t test for continuous variables. A p value < 0.05 was considered statistically significant. The analysis was performed using the SPSS statistical package.

Results

The two groups were matched for age, sex, smoking habit (table 1). Patients were more likely to be hypertensive or to have diabetes mellitus.

Table (2) displays homocysteine, total cholesterol, LDL, HDL, and triglyceride blood levels of the patients and the controls. Plasma homocysteine levels (mmol/l) were higher in patients compared to controls (18.5±7.8 vs 12±8.4; p =0.02). The serum total cholesterol, LDL, HDL, and triglyceride levels were significantly higher in patients compared to controls.

Table (1): Baseline demographics of patients and controls.

Variable	patients (90)	Controls (90)	p-Value
Age (years)	55.3 ±6.7	53.0±7.5	NS
Sex (M/F)	72/18	72/18	NS
Smoking (%)	49(54%)	46(51%)	NS
Diabetes mellitus	40(44%)	8 (7.7%)	<0.001
Hypertension	30(32.6%)	6(6.6%)	<0.001

Table (2): Laboratory results.

Parameter	Patients (90)	Controls (90)	P
Cholesterol (mg/dl)	225.4±50.7	189.4±42.1	.00
LDL (mg/dl)	161.4±28.5	115.3±30.4	.00
Triglyceride (mg/dl)	200.2±65.4	112.3±55.6	.00
HDL (mg/dl)	40.5±18.6	55.8±20.4	.00
Homocysteine (μmol/l)	18.5±7.8	12±8.4	.002

All values are expressed as mean±SD

Discussion

In this study, the level of homocysteine in patients is significantly more than the control group. Our results are consistent with many studies. [3-7] The European study from 19 centers concluded that increased plasma homocysteine level is an independent risk factor for vascular disease similar to that of smoking or hyperlipidemia. [12] A meta-analysis also concluded that a 5 μmol/l homocysteine increment elevates coronary artery disease risk by as much as a 0.5 mmol/l (20 mg/dl) increase of cholesterol. [13] There are multitude of mechanisms by which hyperhomocysteinemia can cause atherothrombosis. Homocysteine, in elevated amounts, is toxic to endothelial cells causing intimal injury that is essential for atherosclerotic process. [14-17] Researchers in at least three large studies have examined the complex association between hyperhomocysteinemia and atherosclerotic vascular disease. [18-20] According to Duell, between 10-40% of patients with acute myocardial infarction or stroke may have hyperhomocyteinemia in the absence of traditional cardiac risk factors. [21] High homocysteine level at the admission of myocardial infarction is associated with increased thrombin formation and high mortality. [22, 23] Plasma homocysteine concentrations are minimally influenced by acute phase variations with reliable measurements obtained on admission in patients with acute myocardial infarction. [24] Given these findings, the next step is to establish a direct association between decrease homocysteine level and reduction in risk of cardiovascular disease morbidity and mortality.

In healthy volunteers, and in patients with coronary heart disease, vitamin B supplementation is associated with an improvement in endothelium dependent dilatation, and in serum markers of endothelial injury. [25-28]

However, HOPE 2 TRIAL demonstrates that homocysteine lowering with folic acid and Vitamins B did not reduce the risk of major cardiovascular events in patients with coronary vascular disease. [29] In patients who had an acute myocardial infarction, homocysteine-lowering treatment with Vitamins B did not lower the risk of recurrent cardiovascular disease. [30]

Conclusion

The result of this study indicates that plasma homocysteine level is high in patients with acute myocardial infarction and it may be a risk factor for coronary heart disease in Jordanian population. Homocysteine screening is advisable in patients at high risk for coronary heart disease and coronary artery disease with no major cardiac risk factors. Public health education with increase intake of folate, vitamin B6, and vit B12 to reduce plasma homocysteine may slow or even reverse atherosclerotic damage that may reduce the prevalence of atherosclerotic vascular disease in Jordan.

References

1. Braunwald E. Shattuck Lecture-cardiovascular medicine at the turn of the millennium: triumphs, concern, and opportunities. N Engl J Med 1997; 337:1360-1369.
2. Eikelboom JW, Lonn E, Genest Jr, Hankey G, Yusuf S: Homocysteine and cardiovascular disease: a critical review of epidemiological evidence. Ann Intern Med 1999; 131:363-375.

3. McCully K. Chemical pathology of homocystein. Atherogenesis. Anal Clin Lab Sci. 1993; 23(6):477-493.
4. Mayer EL, Jacobsen D, Robinson K. Homocysteine and coronary atherosclerosis. J Am Coll Cardio. 1996; 27:517-527.
5. Fallest-Strobl PC, Koch DD, Stein JH, McBride PE. Homocysteine: a new risk factor for atherosclerosis. Am Fam Phys. 1997; 56(6):1607-1612.
6. Stampfer MJ, Malinow MR, Willett WC, Newcomer LM, Upson B, Ulmann D, Tishler PV. A prospective study of plasma homocysteine and risk of myocardial infarction in US physicians. JAMA. 1992; 268(7):877-882.
7. Graham IM, Daly LE, Refsum HM, Robinson K, Brattstrom LE, Ueland M. Plasma homocysteine as a risk factor for vascular disease: the European concerted action project. JAMA. 1997; 277 (277):1775-1781.
8. Evans RW, Shaten BJ, Hempel JD, Cutler JA, Kuller LH. Homocysteine and risk of cardiovascular disease in multiple risk factor intervention trial. Arterioscler Thromb Vasc Biol 1997; 17:1947-1953.
9. Alfthan G, Pekkanen J, Jauhianen M et al.: Relation of serum homocystein and lipoprotein (a) concentrations to atherosclerotic disease in a prospective Finnish population based study. Atherosclerosis 1994; 106:9-19.
10. Selhub J, Jacques PF, Wilson PWF, Rush D, Rosenberg IH. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. JAMA 1993; 270:2693-2698.
11. WHO (report of the joint international society and federation of cardiology/ World Health Organization Task Force on standardization of clinical nomenclature). Nomenclature and criteria for diagnosis of ischemic heart disease. Circulation 1979; 59:607-609.
12. Graham IM, Daly LE, Refsum HM et al.: Plasma homocysteine as a risk factor for vascular disease. JAMA 1997; 277:1775-1781.
13. Boushey H, Ueland PM, Nygard O, Vollset SE. Homocysteine and cardiovascular disease. Ann Rev Med 1995; 274:1049-1057.
14. Hughes S, Robinson K. Homoscystine: an emerging risk factor for coronary heart disease. Lipid Nurse task force 1998; 4(1): 1-2.
15. Stein JH, Mc Bride PE. Hyperhomocysteinemia and atherosclerotic vascular disease. Arch Intern Med 1998; 158:1301-1306.
16. harjai KJ. Potential new cardiovascular risk factors: left ventricular hypertrophy, homocysteine, lipoprotein (a), triglycerides, oxidative stress, and fibrinogen. Ann Intern Med. 1999; 131:376-386.
17. Domagala TB, Undasa A, Libura M, Szczekik A. Pathogenesis of vascular disease in hyperhomocysteinemia. J Cardiovasc Risk 1998; 5:239-247.
18. Stampfer MJ, Malinow MR, Willett WC et al.: A prospective study of plasma homocysteine and risk of myocardial infarction in US physicians. JAMA. 1992; 268:877-881.
19. Chasan-Taber L, Selhub J, Rosenberg IH et al.: Prospective study of folate and vitamin B6 and risk of myocardial infarction in US physicians. J Am Coll Nutr 1996; 15:136-143.
20. Bostom AG, Rosenberg IH, Silbershatz H et al.: Nonfasting plasma total homocysteine levels and stroke incidence in elderly persons: the Framingham study. Ann Intern Med. 1999; 131:352-355.
21. Duell PB. The relationship between hyperhomocyteinemia and risk of cardiovascular disease. Prev Cardiol 1998; 1:17-21.
22. Al-Obeidi MK, Phillippou H, Stubbs PJ et al.: Relationships between homocysteine, factor v11a and thrombin generation in acute coronary syndromes. Circulation 2000; 101:372-377.
23. Stubbs PJ, Al-Obeidi MK, Conroy R et al.: The effect of plasma homocysteine concentration on early and late events in patients with acute coronary syndromes. Circulation 2000; 102:605-610.
24. Al-Obaidi MK, Stubbs PJ, Amersey R, Noble MI. Acute and convalescent in plasma homocysteine concentrations in acute coronary syndromes. Heart 2001; 85(4):380-384.
25. Chambers JC, Ueland PM, Obeid OA, Wringley J, Refsum H, Kooners JS. Improved vascular endothelial function after oral B vitamins; an effect mediated through reduced concentrations of free plasma homocysteine. Circulation 2000; 102:2479-2483.
26. Woo KS, Chook P, Lolin YI, Sanderson JE, Metreweli C, Celermajer DS. Folic acid improves arterial endothelial in adults with hyperhomocysteinemia. J Am Coll Cardiol 1999; 34:2002-2006.
27. Bellamy MF, McDowell IF, Ramsey MW, Brownlee M, Newcombe RG, Lewis MJ. Oral folate enhances endothelial function in hyperhomocysteinemic subjects. Eur J Clin Invest 1999; 29:659-662.

28. Voutilainen S, Virtanen H, Rissanen G et al.: Serum folate and homocysteine and the incidence of acute coronary events. Am C Clin Nutr 2004; 80:317-323.

29. Lonn E, Yusuf S, Amold MJ et al.: Homocysteine lowering with folic acid and B vitamins in vascular disease. N Engl J Med 2006; 354:1567-1577.

30. Kaare HB, Inger N, Per magene U et al.: Homocysteine lowering and cardiovascular events after acute myocardial infarction. N Engl J Med 2006; 354:1578-1588.

مستوى الهوموسستين في الدم عند مرضى احتشاء عضلة القلب

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الملخص

هدفت الدراسة إلى معرفة مستوى الهوموسستين في الدم عند مرضى احتشاء عضلة القلب في الأردن، واشتملت عينة الدراسة على 90 مريضاً بإحتشاء عضلة القلب الحاد، ومقارنة مستوى الهموسستين عند مرضى لا يعانون من احتشاء عضلة القلب الحاد.

وبعد تحليل النتائج تبين أن مستوى الهوموسستين عند مرضى احتشاء عضلة القلب الحاد هو أعلى من مستواه عند المجموعة الأخرى التي لا تعاني من احتشاء عضلة القلب، حيث كان المستوى 7.8 ± 18.7 م.مول مقارنة مع 8 ± 12 م. مول.

خلصت الدراسة إلى أن مستوى الهوموسستين قد يكون أحد العوامل التي تزيد احتمالية الإصابة بتصلب شرايين القلب. ومن هنا فإن زيادة معرفة الناس بالهموسستين وطرق خفضه قد تقلل من نسبة الإصابة بتصلب شرايين القلب.

<u>الكلمات الدالة</u> : الهموسستين، تصلب الشرايين، احتشاء عضلة القلب الحاد.