Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublisher.com

Cardiology

Assessment of the Level of Homocysteine in Acute Coronary Syndrome Patients Vis-A-Vis Chronic Stable Angina Patients

Ajay Sharma[1*], Abhinav Nair[2], Rohit Shrivastava[3], Bhoopendra Bhadauriya[4]
[1]Associate Professor, Department of Cardiology, Gandhi Medical College, Bhopal, India
[2]Resident, Department Of Medicine, Gandhi Medical College, Bhopal, India
[3]Consultant Cardiologists, LBS Heart Hospital, Bhopal
[4]Resident, Department Of Medicine, Gandhi Medical College, Bhopal, India

Original Research Article

***Corresponding author**
Ajay Sharma

Article History
Received: 02.03.2018
Accepted: 10.03.2018
Published: 20.03.2018

DOI:
10.21276/sjams.2018.6.3.17

Abstract: Coronary Artery Disease is a major cause of morbidity and mortality in the modern society. The major classic cardiovascular risk factors and such non-modifiable risk factors such as age, sex, and family history cannot fully explain why some people develop CAD, stroke and other cardiovascular diseases while other persons do not. Other factors may also increase the likelihood of developing cardiovascular disease and contribute to thermogenesis. Hyperhomocystinemia is one such recognized risk factor. This particular study was done to assess the homocysteine levels in acute coronary syndrome patient's vis-à-vis chronic stable angina patients with the aim of finding an independent association between homocysteine levels and coronary artery disease in these patients. The study was planned such that patients with a clinical diagnosis of CAD(based on symptoms and/ or stress test, ECG, and routine lab investigations) - acute coronary syndrome or chronic stable angina underwent test for plasma homocysteine and then results were compared among the 3 groups(chronic stable angina, unstable angina and acute myocardial infarction), the conclusion was a higher mean level of plasma homocysteine in patients with a clinical diagnosis of acute myocardial infarction compared to unstable angina or chronic stable angina thereby establishing a role of homocysteine levels as an important predictor of disease severity in CAD patients.

Keywords: AMI (acute myocardial infarction), CSA (Chronic stable angina), USA (Unstable angina), CAD (coronary artery disease), homocysteine.

INTRODUCTION

Among the many risk factors that have emerged for coronary artery disease, elevated plasma or serum levels of homocysteine is of particular interest. Epidemiological studies have shown that moderately elevated plasma homocysteine levels are highly prevalent in the general population and are associated with the increased risk for fatal or non-fatal cardiovascular disease, independent of the classic risk factors. Homocysteine is a sulfur-containing amino acid produced during the catabolism of the essential amino acid methionine. Homocysteine can be metabolized via two major pathways. In most tissues, homocysteine is re-methylated in a process that requires methionine synthase, vitamin B12 as a cofactor, and methyltetrahydrofolate as a cosubstrate. This pathway requires an adequate supply of folic acid and the enzyme methylene tetrahydrofolate reductase (MTHFR) [1]. Genetic and acquired abnormalities in the function of these enzymes or deficiencies in folic acid, vitamin B6, or vitamin B12 cofactors can lead to elevated homocysteine levels. Plasma homocysteine levels are usually measured in the fasting state and can be measured before or after methionine loading, which is a way of stressing the homocysteine metabolic pathways [2], may be more sensitive than measurement of fasting homocysteine levels for detecting mild disturbances in the transculturation pathway that may be caused by vitamin B6 deficiency or partial cystathionine beta-synthase deficiency [2,3], this test may also help to identify patients who have impaired homocysteine metabolism and who may be at increased risk for vascular disease [3]. Experimental evidence suggests that the atherogenic propensity associated with hyperhomocystinemia is caused by endothelial dysfunction and injury, which is in turn followed by platelet activation and thrombus formation. Numerous mechanisms have been suggested by which hyperhomocysteinemia may contribute to atherothrombotic vascular disease, including direct toxic endothelial cell damage. Direct toxic endothelial cell damage has been shown in both in-vitro and in-vivo

models to be related to 1) the generation of potent reactive oxygen species [4-8, 2] impaired production of endothelium derived nitric oxide and endothelial dysfunction [9, 3] stimulation of smooth-muscle cell proliferation [10,4] lipid abnormalities including elevated plasma triglyceride levels and increased susceptibility to oxidation of low density lipoproteins[11,12]. A potentially unifying hypothesis of the vascular damage associated with hyperhomocysteinemia relates to the formation of oxygen-free radicals, which cause oxidative vascular damage, proliferation of smooth-muscle cells, alteration in endothelial function and structure, and increased thrombogenecity that ultimately leads to athero-thrombosis [13]. In view of the studies, eight cohort studies reported a statistically significant positive associations between elevated homocysteine levels and cardiovascular disease, a large prospective cohort study from tromso, Norway [14], reported a relative risk for coronary artery disease of 1.41(CI 1.16-1.71) for each increase of 4µmol/l in plasma homocysteine levels, there was no threshold level below which homocysteine was not associated with risk for coronary artery disease. After 5 years of follow up, the Physicians Health Study [15] found an adjusted relative risk for fatal or non-fatal myocardial infarction of 3.4 for persons whose homocysteine levels were in the highest 5% compared with those whose homocysteine levels were in the lowest 90%. The Rotterdam study reported odds ratio of 2.53 for stroke and 2.43 for myocardial infarction in persons whose plasma homocysteine was in the highest fifth. Emerging evidence from epidemiological studies supports a strong, dose –dependent, positive association between plasma homocysteine levels and risk for cardiovascular disease. This association seems to be independent of other known risk factors associated with elevated total homocysteine levels and other cardiovascular risk factors. A substantial body of epidemiological evidence suggests an association between cardiovascular risk and moderately increased plasma homocysteine levels. Henceforth there is enough evidence for an association between serum homocysteine and CAD, and this particular study was done to assess whether acute coronary syndrome patients have higher levels of homocysteine compared to chronic stable angina patients.

METHODS AND MATERIALS

The patients between the age of 30 and 70 years with a clinical diagnosis of CAD (based on symptoms and/ or stress test, ECG, and routine lab investigations) - acute coronary syndrome or chronic stable angina underwent test for plasma homocysteine levels after an informed consent were selected for the study in the department of cardiology at Gandhi Medical College, Bhopal and LBS heart hospital, Bhopal from April 2013- March 2014. The study was approved from the ethics committee of the Institute and informed consent were obtained from patients. Patients with renal failure, hypothyroid patients and patients on antiepileptic drugs, niacin etc. were excluded from the study. Blood for plasma homocysteine measurement was drawn from patients after 6 hours of fasting, plasma homocysteine levels were assessed by HPLC method and then a comparison was made between CSA (chronic stable angina), and USA (unstable angina) and AMI (Acute myocardial infarction) based on the mean levels of plasma homocysteine

STATISTICAL ANALYSIS

The results were expressed as mean + SD unless stated otherwise, a probability value of $p<0.05$ was taken as statistically significant and coefficient of correlation was also assessed.

RESULTS AND DISCUSSION

After measurement of the plasma homocysteine levels in the 3 groups of patients with clinical diagnosis of CAD, the mean values were calculated of each group and a comparison was made. The mean homocysteine level in patients with stable angina was 18.6±6.4µmol/l, in unstable angina it was 21.7±13.6µmol/l and in patients with acute myocardial infarction, the mean homocysteine levels were 29.6±19.2µmol/l(table 1)

Table-1: homocysteine levels

Variable	CSA	USA	AMI
Homocysteine(µmol/l)	18.6±6.4	21.7±13.6	29.6±19.2

Thus, it was observed that the highest mean value of plasma homocysteine levels was seen in the AMI group, followed by the USA group and the CSA group, which establishes the role of higher levels of plasma homocysteine as an independent risk factor in the severity of CAD as the values were higher in patients with acute coronary syndrome compared to chronic stable angina, our findings matched with those of malinow *et al*. [2].

CONCLUSION

According to our study, we conclude that hyperhomocystinemia is a significant and independent risk factor for CAD, and patients with hyperhomocystinemia present more often with unstable coronary syndrome and more severe CAD. Therefore we advocate a careful selective screening for those with a strong family history or suspected elevated levels of homocysteine.

REFERENCES

1. Finkelstein JD. The metabolism of homocysteine: pathways and regulation. European journal of pediatrics. 1998 Mar 1;157(2):S40-4.
2. Bostom AG, Jacques PF, Nadeau MR, Williams RR, Ellison RC, Selhub J. Post-methionine load hyperhomocysteinemia in persons with normal fasting total plasma homocysteine: initial results from the NHLBI Family Heart Study. Atherosclerosis. 1995 Jul 1; 116(1):147-51.
3. Graham IM, Daly LE, Refsum HM, Robinson K, Brattström LE, Ueland PM, Palma-Reis RJ, Boers GH, Sheahan RG, Israelsson B, Uiterwaal CS. Plasma homocysteine as a risk factor for vascular disease: the European Concerted Action Project. Jama. 1997 Jun 11; 277(22):1775-81.
4. Harker LA, Ross R, Slichter SJ, Scott CR. Homocystine-induced arteriosclerosis. The role of endothelial cell injury and platelet response in its genesis. The Journal of clinical investigation. 1976 Sep 1; 58(3):731-41.
5. Harker LA, Slichter SJ, Scott CR, Ross R. Homocystinemia: vascular injury and arterial thrombosis. New England Journal of Medicine. 1974 Sep 12; 291(11):537-43.
6. Wall RT, Harlan JM, Harker LA, Striker GE. Homocysteine-induced endothelial cell injury in vitro: a model for the study of vascular injury. Thrombosis research. 1980 Apr 1; 18(1):113-21.
7. Starkebaum G, Harlan JM. Endothelial cell injury due to copper-catalyzed hydrogen peroxide generation from homocysteine. The Journal of clinical investigation. 1986 Apr 1; 77(4):1370-6.
8. Blundell G, Jones BG, Rose FA, Tudball N. Homocysteine mediated endothelial cell toxicity and its amelioration. Atherosclerosis. 1996 May 1; 122(2):163-72.
9. Stamler JS, Osborne JA, Jaraki O, Rabbani LE, Mullins M, Singel D, Loscalzo J. Adverse vascular effects of homocysteine are modulated by endothelium-derived relaxing factor and related oxides of nitrogen. The Journal of clinical investigation. 1993 Jan 1;91(1):308-18.
10. Tsai JC, Wang H, Perrella MA, Yoshizumi M, Sibinga NE, Tan LC, Haber E, Chang TH, Schlegel R, Lee ME. Induction of cyclin A gene expression by homocysteine in vascular smooth muscle cells. The Journal of clinical investigation. 1996 Jan 1;97(1):146-53.
11. Frauscher G, Karnaukhova E, Muehl A, Hoeger H, Lubec B. Oral administration of homocysteine leads to increased plasma triglycerides and homocysteic acid—additional mechanisms in homocysteine induced endothelial damage?. Life sciences. 1995 Jul 14;57(8):813-7
12. Bokhari SW, Bokhari ZW, Zell JA, Lee DW, Faxon DP. Plasma homocysteine levels and the left ventricular systolic function in coronary artery disease patients. Coronary artery disease. 2005 May 1; 16(3):153-61.
13. Welch GN, Loscalzo J. Homocysteine and atherothrombosis. New England journal of medicine. 1998 Apr 9; 338(15):1042-50.
14. Arnesen E, Refsum H, BØNAA KH, Ueland PM, FØRDE OH, Nordrehaug JE. Serum total homocysteine and coronary heart disease. International journal of epidemiology. 1995 Aug 1; 24(4):704-9.
15. Ullmann D, Tishler MD, Hennekens MD. A prospective study of plasma homocyst (e) ine and risk of myocardial infarction in US physicians. Jama. 1992; 268:877-81.