Homocysteine: Often Neglected but Common Culprit of Coronary Heart Diseases

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ABSTRACT

Hyperhomocysteinemia is an independent risk factor for ischemic heart disease and stroke. We report in absent risk factors the clinical correlation between severe acute coronary syndrome and hyperhomocysteinemia. A 38-years-old nonsmoker, nondiabetes, normotensive, and strict vegetarian with positive family history of ischemic heart diseases had acute myocardial infarction with raised serum homocysteine level.

Keywords: Acute myocardial infarction, family history of ischemic heart disease, homocysteine

INTRODUCTION

Cardiovascular diseases and strokes are the major contributors to mortality and disability in South Asia.1 Coronary heart disease (CHD) in India rose to 1.17 million in 1990-2.03 million in 2010. Studies conducted in the past decade confirmed that the poor have a higher risk of heart attack than the rich.2 Serum homocysteine level 15 μmol/L is an independent risk factor for cardiovascular diseases.3 Indian population and those migrated in UK fasting homocysteine concentrations 6% higher in Indian Asians than Europeans. Hyperhomocysteinemia may contribute to twice as many as CHD in Indian Asians.4 In Indian rural and urban vegetarians population, hyperhomocysteinemia is attributed to low concentration of vitamin B12.4,5 Hyperhomocysteinemia is an independent risk factor involved in CHD and stroke, yet no study has demonstrated an association of hyperhomocystemia and CHD in Indian scenario.3 Increased serum cysteine levels are due to rapid metabolism of homocysteine via the transsulfuration pathway in B12 deficiency state.6 Typical Asian Indian diet is predominantly vegetarian that is always deficient in vitamin B12.3,7 We report in absent risk factors the clinical correlation severe acute coronary syndrome and hyperhomocysteinemia.

CASE REPORT

On 3rd September 2012, a 38-years-old man of 60 kg weight, nonsmoker, nondiabetic, normotensive attended outpatient department at 8.45 am with complaints of severe agonizing chest pain radiating to both arms and to back, he sweated profusely since last 30 min. He gave a history of the recurrent backache, and both arms pain was diagnosed due to cervical spondylosis though magnetic resonance imaging was normal. He consumed antacids for burning sensation in the chest since last 1 week. His family is a strict vegetarian. His father died 1 year before due to massive myocardial infarction and cardiac arrest. He denied any history of chest pain, angina and was not investigated for ischemic heart disease. He denied of any medication in a recent past. On arrival to the hospital, he was in an agony due to chest pain, extremities were cold, pulse 68/min low volume, blood pressure 130/92 mmHg; oxygen saturation with nasal oxygen 3 L/min was 99%. Heart sounds were muffled, there was no murmur. Electrocardiogram (ECG) showed hyper-acute T waves in the chest leads with reciprocal changes in inferior wall leads. ST segment
elevated 4 mm in V1 and 1 mm in aVR suggestive of proximal left anterior artery block (Figure 1a). His hemoglobin concentration was 14.8 gm/dl, lipid profile was normal, creatine phosphokinase MB 46.12. Blood was sent for homocysteine, B12, and folic acid detection at Mumbai. Lipid profile was within normal limit.

He was given clopidogrel 600 mg, aspirin 300 mg, nitroglycerine 6 µg/min drip. Pain killer pentozocin was closely monitored on multipart monitor. He was given tenectplase 30 mg intravenous bolus preceded by 3 mg low molecular weight heparin. Within 2 h, acute ECG (Figure 1b) changes regressed, he was chest pain-free and hemodynamically settled. At the end of 4 h of admission, he again complained of severe backache and left shoulder pain. ECG showed marked ST elevation with left anterior hemi block with right bundle branch block. Repeat intravenous bolus of low macular weight heparin regressed the acute ECG changes.

He had undergone rescue angiography at tertiary care hospital Mumbai. Angiography showed three vessels diereses with left anterior descending (LAD) 100% block (Figure 2a), and other vessels had diffuse lesion. He denied coronary bypass surgery and hence, stent was put in LAD and balloon angioplasty in the left circumflex (Figure 2b). Total expenses were 5.5 lacks ($8461.53). At tertiary care hospital, he was investigated in details including hepatitis and HIV antigen except homocysteine level and was given prasugrel 10 mg, carvedilol and atorvastatin 40 mg with antacids. By this time, we received report from Mumbai, which showed plasma homocysteine 80.98 μmol/L (normal 5.46-16.22), serum B12 <83 pg/ml (normal 174-878), folic acid 4.2 ng/ml (normal 3-17). He was advised with oral vitamin substitute.

DISCUSSION

In the present report, we confirmed that serum homocysteine 15 μmol/L is independent and significant risk factor for acute myocardial infarction. Vegetarians are more prone for hyperhomocystenemia. Harvard physician McCully was the first physician to propose the homocysteine “hypothesis of atherosclerosis.” He speculated the cause of atherosclerosis in a case of homocystinuria. The autopsy of hyperhomocysteinemia patient showed massive generalized atherosclerosis. He further hypothesize that even slightly elevated homocysteine level could cause atherosclerosis in adults. Wilcken and Wilcken provided the first evidence of a relationship between abnormal homocysteine metabolism and coronary artery disease in the general population.

Homocysteine is a sulfur-containing amino acid produced in the metabolism of the essential amino acid methionine. For to convert homocysteine back to methionine and transsulfuration subsequently converting the homocysteine to cysteine and taurine required folate and vitamin B12. Normal homocysteine level range is between 5 μmol/L and 15 μmol/L. While 16-30 μmol/L, 31-100 μmol/L and >100 μmol/L are classified as mild, moderate, and severe homocysteinemia, respectively. Deficiency of folic acid, vitamin B6, and vitamin B12 are responsible for the majority of cases of elevated homocysteine in the general population including adults and old. Increase in homocysteine level 3 μmol/L above the normal accompanied with 49 higher risk of ischemic heart disease and reversed by taking folic acid and vitamin B12.
Severity of CHD in a hyperhomocysteinemia was not related to the serum B12 and folic acid level. Ample literature is available on homocysteine and coronary artery risk. A rise in homocysteine above 90th or 95th percentile of control accompanied with increased risk of fatal and nonfatal atherosclerotic coronary artery disease (odd ratio 1.7; 95% confidence interval 1.5-1.9) and venous thrombosis.

Homocysteine stimulates atherosclerosis by causing oxidative endothelial damage, altering the coagulation of blood, and destruction of vascular matrix, thus promoting the thrombus-embolic diseases. Indian and those migrated abroad have raised the level of circulating homocysteine as compared to other ethnic group.

Incidence of acute myocardial infarction due to thrombus in coronaries is not uncommon with raised homocysteine level. Thrombosis rather than atherosclerosis is the main culprit for vascular complications associated with raised homocysteine level. Raised homocysteine in Indian is related to a deficiency of vitamin B12, B6, and folic acid due to faulty dietary habit.

Clinical and epidemiological studies have proved that hyperhomocysteinemia is an independent risk factor for coronary artery disease, peripheral artery disease, and venous thrombosis. Homocysteine plays an important role in the formation of thrombosis by inhibiting vasodilatatic and antithrombotic functions of nitric oxide. Hyperhomocystenemia is a contributing factor for incidence of thrombotic events in patients with systemic lupus erythematosus.

Serum homocysteine level is weakly related to the extent of coronary artery disease but often strongly correlated to acute myocardial infarction and coronary thrombosis. Homocysteine may interact with serum cholesterol by rising low-density lipoprotein oxidation, a predisposing to atherosclerosis.

Supplement with B vitamins is controversial, did not lower the risk of recurrent myocardial infarction but paradoxically promotes atherothrombosis. Folic acid enhances endothelial cell growth, proliferation of vascular smooth muscles and matrix formation resulting in stent re-stenosis and atherosclerotic plaque progression. Thus, vitamin B12, B6, and folic acid supplement may result more harm than good. However, chronic raised level of homocysteine due to vitamin deficiency but a compensatory mechanism probable develops where by this does not lead to increase in the incidence of CHD in resident of Indians.

Strict vegetarians had times higher risk of low vitamin B12 concentration and were prone for hyperhomocysteinemia and acute stroke and myocardial infarction. 60% vegetarians had raised level of homocysteine as compared to 24.1% in control group (P < 0.001) decreased intake of vitamin B12 and folic acid due to prolonged cooking of vegetables, a routine practice in Indian household, recurrent chronic infections and consumption of antibiotics and strict sanitation and use of bacterial filters at common water supply seen in higher educated and income group. Lowering of homocysteine concentrations by fortification of food with vitamin B12 and folic acid benefits for reduction of risk of vascular disease. Indian living abroad also have low vitamin B12 concentration ascribable to low dietary intake due to vegetarian food habits.

### CONCLUSION

Avoidance of strict vegetarian diet, fortification of routine food with vitamin supplements may help to reduce the homocysteine level, a common risk factor for acute myocardial infarction.

### REFERENCES