Serum Homocysteine Level in Patients Suffering From Unstable Angina

*Perviz R,[1] Sarkar CR,[2] Zahid AR,[3] Ahmed N,[4] Ali MI [5]

Unstable angina is one of the global fatal problems in both developed and developing countries. There is a link between unstable angina and serum homocysteine. Total serum homocysteine level is increased in unstable angina. This cross sectional study was conducted from July 2010 to June 2011 in the Department of Physiology, Rangpur Medical College, Rangpur. The experimental subjects (diagnosed unstable angina patient) were selected from Cardiology Department, Rangpur Medical College & Hospital, Rangpur. Mean total serum homocysteine level was significantly higher ($p<0.001$) in unstable angina in comparison with the healthy control subjects.

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Key words: Serum Homocysteine, Unstable Angina.

Introduction

Cardiovascular diseases are one of the leading causes of mortality and morbidity in the developed countries. They are also emerging as prominent public health problems in the developing countries. The high burden of mortality from cardiovascular causes in the developing countries was estimated at 9 million in 1990 and is being expected to increase to 19 million by 2020.[1]

Ischemia of heart muscles comprises not only insufficiency of oxygen, but also reduced availability of nutrients and inadequate removal of metabolites. The duration and severity of ischemia is sufficient to cause even death of heart muscle. Ischemic heart disease (IHD) is the syndrome resulting from myocardial infarction, angina pectoris, chronic ischemic heart disease with heart failure and sudden cardiac death. Among them angina pectoris is one common disease. Angina pectoris is a clinical condition in which the ischemia is less severe and does not cause death of cardiac muscle. Two common manifestations of ischemia are unstable and stable angina pectoris. Unstable angina may be defined as angina pectoris which occurs at rest or minimal exertion, usually lasting more than 20 minutes. It is progressively being severe as described frank pain and new onset within one month. It is caused by dynamic obstruction of a coronary artery due to plaque rupture with superimposed spasm. It is the most threatening frequent cause which announces the approach of myocardial infarction.[2 - 5]

1. **Dr. Rebeka Perviz, Senior Lecturer, Department of Physiology, Northern (Pvt.) Medical College, Rangpur.. drzahid63@gmail.com*
2. *Chandra Rani Sarkar, Professor, Department of Physiology, Rangpur Medical College, Rangpur.*
3. *Dr. ATM Zoadur Rahim Zahid , Assistant Professor, Department of Physiology, Rangpur Medical College, Rangpur.*
4. *Dr. Neaz Ahmed, Aassistant Professor, Department of Biochemistry, Rangpur Medical College, Rangpur.*
5. *Dr. Md. Idris Ali , Junior Consultant, Department of Anaesthesiology, Badargang THC, Rangpur.*

* *For correspondence*

Homocysteine is a sulfur containing amino acid. It has atherogenic effect on vascular smooth muscle cell migration and proliferation. It has also prethrombotic properties by inhibition of thrombomodulation activity, reduction of protein C activation. It also stimulates the platelet generation of thromboxane A_2 which is a vasoconstrictor and increases platelet aggregation.[6, 7] Auto oxidation of homocysteine generates superoxide anion radicals which cause oxidative modification of low density lipoprotein. A raised total serum homocysteine level has been found to be an independent risk factor for atherosclerotic disease like unstable angina. [8, 9] An emerging pattern of atherosclerosis due to formation of fibrous plaques and loss of vascular elasticity associated with hyperhomocysteinemia was reported by some author.[10] The elevated total serum homocysteine level is considered cytotoxic and are found in 5 to 10 % of the general population and in up to 40% of patients with cardio vascular disease.[11]

The aim of this study is to evaluate the association between the elevated total serum homocysteine level and unstable angina in the population of Bangladesh. So, the practical recommendation for screening the elevated total serum homocysteine level can be justified and treatment of this modifiable risk factor should be recommended.

Methods

This is a cross sectional analytical study conducted in the Department of Physiology, Rangpur Medical College, Rangpur during July 2010 to June 2011. The study has been designed to estimate total serum homocysteine level in unstable angina. The ethical committee of Rangpur Medical College, Rangpur approved the study protocol. 35-65 years old diagnosed 35 patients of both sexes of unstable angina patient who were admitted in the Cardiology Department of Rangpur Medical College and Hospital, Rangpur were included as experimental Group B. Age matched apparently healthy 35 subjects of both sexes were selected form the community as control group A. Patients suffering from valvular heart disease, congenital heart disease, kidney diseases, liver diseases, diabetes mellitus, hypertension and obesity were excluded from the study. After selection of subjects, the objectives and procedures of the study were explained to them and their informed written consent was taken. A standard questionnaire was filled after taking history and thorough physical examination. The subjects were instructed to be in overnight (8-10 hours) fasting state. Then next day at 8.00 AM five (5) ml of blood was collected from antecubital vein from each subject under all aseptic precautions by a disposable syringe. The needle was detached from the nozzle and then blood was immediately transferred into a dry sterilized deionized test tube with a gentle push to avoid haemolysis. The test tubes were kept in slanting position till formation of clot. As synthesis of homocysteine continues in the red blood cell after blood drawn so, serum was separated by centrifuging the blood at 3000 rmp for 5 minutes. The clear supernatant was taken and kept in ependorfs. Samples were stored at -70°c. Quantitative measurement of total serum homocysteine was estimated by fluorescence polarization immunoassay (FPIA) in 'AxSYM system'. It was done in the laboratory of the Department of Biochemistry of BSSMU. Data were expressed as mean ± SD. All the data were recorded systematically in a preformed data sheet and statistical analysis were done by computer based software SPSS 15.0 version for windows. Comparison of total serum homocysteine level of unstable angina with control group was done by unpaired 't' test. In the interpretation of results, <0.05 level of probability (P) was accepted as significant.

Results

Total serum homocysteine level was significantly higher (P<0.001) in unstable angina (Group – B) than control subjects (Group – A). (Table 1 and Fig. 1)

Table I: Mean ± SD total serum homocysteine levels

Groups	Number	Total Serum Homocysteine (µmol/L)
A	35	10.83±1.93
B	35	25.07±10.95

A = Control group

B = Unstable angina

A vs B P<0.001

(Normal range of total serum homocysteine level is: 3.36 – 20.44 µmol/L [12])

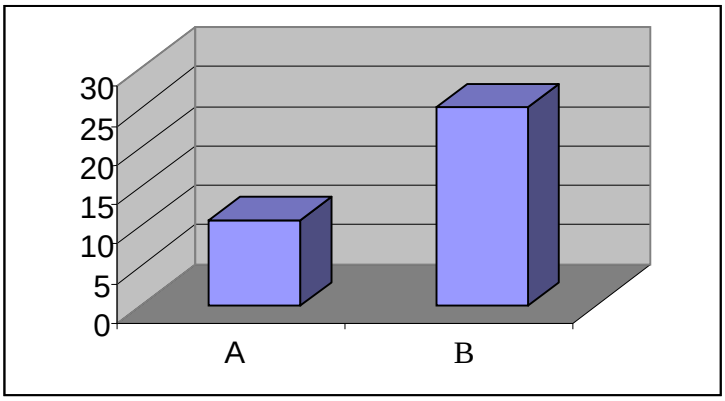

Figure 1. Mean total serum homocysteine levels in Group A and B

Discussion

Many authors of different countries reported significant raised mean total serum homocysteine level in ischemic heart disease (unstable angina).[6 -11, 13 – 21] It might be due to deficiency of vit. B_6, B_{12} and folic acid deficiency. Homocysteine is metabolized by trans-sulfuration and re-methylation pathway. In trans-sulfuration pathway, homocysteine is condensed with serine to form cystathionine. This reaction is catalyzed by vit. B_6 dependent enzyme cystathionine beta synthase. Cystathionine subsequently hydrolysed to form cysteine which is further metabolised to sulfate and excreted through urine. Due to deficiency of vit. B6, this trans-sulfuration pathway is hampered which leads to elevation of total serum homocysteine. In remethylation pathway, homocysteine is remethylated back to methionine by transfer of a methyl group from 5 - Methyltetrahydrofolate in a reaction catalysed by cobalamine (vit B12) dependent enzyme methionine synthase. Remethylation pathway also requires folic acid. Deficiency of vit B12 and folic acid the remethylation of homocysteine is impaired and causes elevation of total serum homocysteine level.

Raised serum homocysteine induces vascular dysfunction, platelet generation of thromboxane A2 and platelet aggregation through oxidative stress and also by inhibiting nitric oxide synthesis. Thromboxane A_2 released from platelet causes coronary vasoconstriction, platelet aggregation and platelet plug formation. Reduced nitric oxide impairs endothelial nitric oxide dependent vasodilation. These events may lead to formation of unstable angina.

Conclusion

Total serum homocysteine is increased in unstable angina may be due to deficiency of Vit B_{12} & Vit $_{B6}$ and folic acid and it can be prevented by supplementation of these vitamins. So, the present study will be helpful to develop awareness about reduced serum Vit B_{12} & Vit $_{B6}$ and folic acid and its relation to unstable angina. It also helps to develop awareness among the community about the importance of these vitamins in the prevention of unstable angina.

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