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Original Research Article

Exploring Homocysteine, Antioxidant Defences, and Oxidative levels in Acute Myocardial Infarction

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Abstract

Acute myocardial infarction (AMI) is a significant contributor to morbidity and mortality worldwide. Homocysteine, an intermediate in methionine metabolism, has been identified as a potential risk factor for a variety of diseases, including cardiovascular diseases. The aim of this study was to evaluate the role of homocysteine and investigate oxidative stress, antioxidants, and inflammatory molecules in patients with AMI. The study was included 200 subjects, 100 of whom had AMI (70 males and 30 females) and 100 healthy, age-matched controls (80 males and 20 females). Various blood parameters, including body mass index, fasting blood glucose, lipid profile, antioxidants, and homocysteine, were measured. The results showed that total cholesterol, LDL, and malondialdehyde levels were significantly higher, and antioxidants such as vitamin E, catalase, glutathione peroxidase, and superoxide dismutase were significantly lower in AMI patients compared to controls ($p<0.0001$). The findings suggest that oxidative stress and inflammation are elevated in patients with AMI, with a depression of the antioxidant system. Furthermore, the study revealed that AMI patients had elevated levels of homocysteine as compared to healthy subjects, indicating that high serum homocysteine levels are strongly associated with AMI risk. Our results suggest that increased serum homocysteine levels may be a possible cause of AMI and that it is an important biomarker for risk stratification for AMI, along with lipid profile parameters. This study sheds light on the role of homocysteine and oxidative stress in AMI patients. The results underscore the importance of monitoring homocysteine levels in individuals at risk of AMI and highlight the potential of antioxidant therapies in reducing AMI risk. Further research is needed to understand the underlying mechanisms and to develop effective prevention and treatment strategies for AMI.

Keywords: Homocysteine, Acute Myocardial Infarction, Oxidants, Anti-Oxidants.

Introduction

Sulfur is an essential element required by all living organisms, and in mammals, it is obtained through the intake of sulfur-containing amino acids. Homocysteine is one such amino acid, which is produced during the metabolism of methionine. On average, humans consume more than 1.8g of methionine per day [1]. Homocysteine exists in plasma in four forms: a free thiol (1%), desulfurated (5-10%), mixed disulfide (5-10%), and protein-bound thiol groups (80-90%) [2].

In healthy tissues, a balance is maintained between tissue oxidant and antioxidant activity. Antioxidants protect the body from damage caused by free radicals, which are highly reactive molecules that can lead to cellular damage and disease. The antioxidant scavenger system includes enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), and antioxidant vitamins (C, A, E, and other carotenoids) [3].

When there is increased oxidative stress and the generation of free oxygen radicals, low-density lipoproteins (LDL) can be modified to oxidized LDL, which can contribute to the development of atherosclerotic lesions. This can lead to a variety of diseases, including acute myocardial infarction (AMI) [4]. The brain is particularly sensitive to oxidative damage, as reactive oxygen species (ROS) are continuously produced during physiological processes. Endogenous antioxidant defense mechanisms are in place to balance the ROS levels, but these mechanisms can be overwhelmed by an increase in oxidative stress [5].

Numerous epidemiological studies have suggested that elevated levels of homocysteine may be an independent risk factor for vascular diseases, including stroke [5-7]. Furthermore, studies have shown that increased homocysteine levels are associated with AMI. It has been suggested that an increase in serum homocysteine levels may be a possible cause of AMI and that it is now considered one of the most important biomarkers in the risk stratification for myocardial infarction [8].

Sulfur-containing amino acids are essential for mammals, and homocysteine is produced during methionine metabolism. Maintaining a balance between tissue oxidant and antioxidant activity is crucial for preventing disease, as oxidative stress and free oxygen radicals can cause cellular damage. Elevated levels of homocysteine have been associated with a variety of vascular diseases, including stroke and AMI. Therefore, homocysteine is an important biomarker in risk stratification for myocardial infarction.

Material and Methods

The study included a total number of 200 patients, diagnosis being based on AMI. The participants were divided into two groups-

Group 1: 100 Healthy individuals free from Acute Myocardial Infarction.

Group 2: 100 AMI patients

Inclusion and Exclusion criteria

The patients who visited the hospital with chest pain and other features of MI as per the WHO criteria were only included in our study. The patients, who were diagnosed with MI by both doctors as mentioned above were only included. The patients who had chronic conditions, especially pulmonary disease, and did not follow our study protocol, were excluded from the study.

Methodology

A written informed consent was obtained from the patients. A questionnaire regarding the demographic data such as age, sex, height, body weight and duration of Acute Myocardial Infarction (AMI) were measured. Smoking habit, vegetarian and non-vegetarian, family history of AMI, Blood

pressure, hypertension, and renal disease were also recorded for each patient. The body mass index (BMI) was also calculated as weight (Kg) divided by height (m) squared. Under aseptically conditions 4ml venous blood was withdrawn, serum was separated and used for estimation of various biochemical parameters such as Lipid profile, Fasting blood sugar, Vitamin E, Liver function test and oxidants parameters (MDA, SOD, GPx, CAT, Hcys) (6). All the parameters were measured using a fully automated analyzer XL-1000 Erba Mannheim.

Results

Table 1: Age wise distribution of healthy controls and subjects

Age group (years)	Male	Female	Total
30-39	04	08	12
40-49	50	24	74
50-60	74	40	114
Total	128	72	200

Table 2: Comparison of laboratory abnormalities between Healthy Control and AMI.

Study Variables	***Healthy controls N=100***	**AMI N=100**
BMI (kg/M^2)	22.8±1.98	32.85±3.89*
FBS (mg/dl)	87.56±14.46	148.0±37.7*
Total Cholesterol (mg/dl)	187.3±22.09	248.4±41.9*
TG (mg/dl)	129.09±19.19	212.7±55.05*
HDL (mg/dl)	48.45±7.14	33.27±7.02*
LDL (mg/dl)	115.1±20.29	161.7±39.3*
VLDL (mg/dl)	24.58±4.19	52.89±11.3*
Homocysteine (µmol/L)	8.65±3.24	16.45±7.84*
ALT (IU/L)	28.34±6.84	54.16±16.1*
AST (IU/L)	178.7±37.75	292.6±21.0*
Malondialdehyde (nmol/ml)	3.65±0.18	7.64±0.19*
Superoxide dismutase (U/g Hb)	814.95±218.10	182.47±32.86*
Glutathione Peroxidase (mg/dl)	62.30±4.88	43.4±7.11*
Catalase (nmol/ml)	44.3±12.7	24.24±8.65*
Vitamin E (mg/dl)	28.82±4.56	16.64±2.32*

*Significant

In this study, we recruited a total of 200 participants, consisting of 4 males and 8 females in the age group of 30-39 years, 50 males and 24 females in the age group of 40-49 years, and 74 males and 40 females in the age group of 50-60 years (Table 1).

The body mass index (BMI) of the study group ranged from 19.7 to 31.25, with an average BMI of 22.8. The total cholesterol levels were significantly higher in subjects with acute myocardial infarction (AMI) compared to the control group, with values of 248.4±41.9 and 187.3±22.09, respectively. Similarly, the LDL cholesterol levels were also significantly higher in the AMI group (161.7±39.3) compared to the control group (115.1±20.29). The range of LDL cholesterol values was 80-120 mg%. The triglyceride levels were also significantly higher in the AMI group (212.78±55.05) compared to the control group (129.09±19.19), while the

HDL cholesterol levels were significantly lower in the AMI group (33.27±7.02) compared to the control group (48.45±7.14). The VLDL cholesterol levels were also significantly higher in the AMI group (52.89±11.3) compared to the control group (24.58±4.19). The study also measured the activity levels of two antioxidant enzymes: superoxide dismutase (SOD) and glutathione peroxidase (GPx). The SOD activity levels were significantly higher in the AMI group (814.95±218.10) compared to the control group (182.47±32.86), while the GPx activity levels were significantly lower in the AMI group (43.4±7.11) compared to the control group (62.30±4.88) (table 2).

In the present study we found that (showed in Table-1) there was significant difference in BMI, FBS levels between control and AMI group. Our study showed FBS levels in AMI subjects' group (148.0±37.7) were higher than healthy subjects (87.56±14.46). Whereas vit E, SOD, GPX and CAT levels were significantly decreased i.e., antioxidants levels in AMI patients.

The level of total-cholesterol and LDL-cholesterol were found significantly increased in cases than in controls [8]. The increased level of MDA in AMI patients was much significant as compared to controls (Cases =7.64±0.19 and control= 3.65±0.18).

Discussion

Homocysteine is an endogenous amino acid that contains a free thiol group and plays an important role in the synthesis and re-synthesis of methionine and cysteine in healthy cells [9]. Homocysteine also indirectly participates in the metabolism of methyl, folate, and cellular thiols. The majority of homocysteine in the plasma is bound to proteins, while only a small amount exists in the free reduced form. The unbound portion of homocysteine is either oxidized to form homocystine or combined with cysteine to form mixed disulphides [10-12].

However, homocysteine can also promote endothelial dysfunction, which leads to the formation of atherosclerotic plaque. Specifically, homocysteine inhibits the growth of endothelial cells, induces an imbalance between O●- and NO●, induces the expression of different adhesion molecules, and promotes the formation of modified LDL particles. These actions can lead to increased severity of cerebrovascular diseases and may justify the promoting action of increased plasmatic concentration of homocysteine.

The mechanism by which homocysteine promotes the production of hydroxyl radicals and lipid peroxidation initiators may be related to the reactivity of the sulfhydryl group leading to homocysteine autooxidation and thiolactone formation. Mild to moderate hyperhomocysteinemia, even though not atherogenic per se, may lead to increased stroke severity as well as other classical risk factors and acute myocardial infarction [13].

Serum homocysteine levels are significantly increased in myocardial infarction as compared to control, which may be due to inherited genetic defects of Cystathionine β-Synthase [CBS] and N5 N10 Methyleine tetrahydrofolate reductase [MTHFR] and methionine synthase, or deficiencies of folic acid, Vitamin B6, and Vitamin B12. Physical activity, moderate alcohol consumption, good folate and vitamin B12 status are associated with lower homocysteine levels. Vegetarians may be at a higher risk of hyper-homocysteinemia due to low plasma B12 levels [9].

In addition, acute myocardial infarction is associated with a significant decrease in antioxidant status. This condition involves an increase in the production of free radicals and a compensatory decrease in the level of antioxidants [14]. Antioxidants play a potential role in preventing atherosclerosis and inhibiting some major complications

such as acute myocardial infarction. After cerebral ischemic injury, free radical production is greatly increased and causes redox disequilibrium in the natural endogenous antioxidant system, leading to oxidative stress and subsequent neuronal injury. Therefore, free radicals are a valid therapeutic target, and much research has focused on assessing the therapeutic effects of antioxidants. Antioxidants can work through three main strategies: inhibition of free radical production, scavenging of free radicals, and increasing free radical degradation. Antioxidant strategies can either focus on the upregulation of endogenous antioxidants or on the delivery of exogenous antioxidants [15, 16].

Conclusion

The incidence of AMI showed a male preponderance. Elevated homocysteine levels play an important role as an independent predictor of AMI and are recognized as a clear risk factor for AMI. Hyper homocysteinemia is common in young patients suffering from acute myocardial infarction. Furthermore, our results confirm previous observations suggesting that the association between homocysteine, oxidants, antioxidants and cardiovascular events can be mitigated in patients with lower LDL-cholesterol levels. Homocysteine serves as a critical and independent predictor of myocardial infarction. Furthermore, our present investigation suggests an imbalance between oxidants and antioxidants in patients with AMI, which is mainly caused by increased oxidative stress. Future research efforts should include the assessment of oxidative stress parameters.

Limitation: Diagnosis of AMI in our study was based on ultrasonography (USG) and exclusion of known causes of cardiac disease. Some clinical studies using other markers of inflammation are also proving valuable. This study design may represent another limitation, as post-treatment analyzes were performed only a few days after dosing. For this reason, a further evaluation of the oxidative state is required after a longer post-treatment time and with a larger sampling.

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