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HOMOCYSTEINE VARIATIONS IN PATIENTS WITH ISCHEMIC HEART DISEASE

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ABSTRACT

Age, sex, hyperlipidemia, hypertension (HT), smoking, diabetes (DB) and familial causes are considered as the major risk factors of ischemic heart disease (IHD). High levels of plasma homocysteine (Hcy) might be a main involvement in cardiovascular disorders, but lowering the plasma levels of Hcy has not been found as the cure for the cardiac diseases. In view of the controversies related to role of Hcy in IHD it was planned to conduct a study to investigate a precise role of Hcy in IHD patients with various risk factors. The patients were selected after thorough clinical history assessments. They were categorized according to their age and the risk factors they had. The age-matched controls were selected from healthy volunteers. Results for smoking data showed no significant Hcy variations while compared with normal (N) controls. The data of the patients showing the risk factor of hypercholesterolemia (HC) showed significant elevation of Hcy levels for age ranges <30, 30-40, and 60-70. The data of hypertension (HT) gave significant change for age range <30, 30-40, and >70. Whereas N vs DM showed significant variation for age range <30, and 30-40. These results showed that the patients with <30 and 30-40 years age range had significant elevation in Hcy concentration for all risk factors except smoking in the current study.

Key words: Ischemic heart disease, homocysteine, risk factors.

INTRODUCTION

Ischemic heart disease occurs usually due to atherosclerosis of coronary arteries, and it is the most common cause of death world over (WHO, 2004; Ferdinand, 2006). Age, sex, hyperlipidemia, hypertension, smoking, diabetes and familial causes are considered as the major risk factors of ischemic heart disease (Mitchell *et al.*, 2007). These might be the main risk factors (McGill *et al.*, 1997; Wilson *et al.*, 1998; Smith, 2006) of coronary heart disease, but there are CHD patients with no identifiable risk factors (Smith, 2006).

High levels of plasma homocysteine have been considered as a main involvement in cardiovascular disorders, but lowering the plasma levels of homocysteine has not been found as the cure for the cardiac diseases (Marti-Carvajal *et al.*, 2009). Various studies show association between elevated homocysteine levels and the known CHD risk factors, such as sex (Ueland *et al.*, 2001), hypertension and smoking (HSC, 2002).

Homocysteine appears as a nerve and vessel toxin, promoting mortality, cardiovascular disease (CVD), stroke, Alzheimer's Disease, birth defects, recurrent pregnancy loss, and eye disorders. Homocysteine (Hcy) is an amino acid that is produced by the body, usually as a byproduct of consuming meat. It is a thiol aminoacid synthesized during the metabolism of methionine. Increased plasma levels of Hcy can be the result of mutations in the enzymes responsible for Hcy metabolism, particularly cystathionine-beta synthase (CBS) and 5,10-methylenetetrahydrofolate reductase (MTHFR). Furthermore, nutritional deficiencies in B vitamin cofactors required for Hcy metabolism, including folic acid, vitamin B6 (pyridoxal phosphate), and/or vitamin B12 (methylcobalamin), can induce hyperhomocysteinemia (Pezzini *et al.*, 2007).

There has been much interest in Hcy as an important risk factor for vascular diseases independent of the long-recognized factors like hyperlipidemia, hypertension, diabetes mellitus, and smoking (Arrastia, 2000) although its association was described many decades ago (Mc Kully, 1969).

In view of the studies (Mc Kully, 1969; Alfthan *et al.*, 1994; Graham *et al.*, 1997; Stein and McBride, 1998), related to role of homocysteine in ischemic heart disease, it was planned to conduct a study to investigate a precise role of homocysteine in patients with ischemic heart disease with various risk factors.

MATERIALS AND METHODS

The patients with ischemic heart disease were selected after thorough clinical history assessments. They were categorized according to their age and the risk factors they had. The patients with multiple established risk factors such as hypercholesterolemia, diabetes, hypertension, and smoking in combination were excluded in the present study. The age-matched controls were selected from healthy volunteers.

The detailed history, including history of hypertension, diabetes, smoking, and drug history were recorded in all individuals. The selected patients had CT scan/MRI, trans-thoracic echocardiography, detailed lipid profile along with routine biochemistry. Trans-esophageal echocardiography was done in select group of patients. Five milliliters of blood was drawn and collected in a tube. The sample was immediately kept in ice pack and later centrifuged within 30 min to avoid false elevation of Hcy levels due to its release from RBC. Plasma samples were then refrigerated and stored at -80°C till the analysis done.

Regarding ethical consideration, venepuncture is a minimally invasive procedure used frequently as part of the investigation procedure. The patients were informed about the study and the benefit thereof. After taking consent, blood was withdrawn. Descriptive values were expressed as mean ± SD or SEM. Further analysis was done using students ' t ' test. The ' p ' value of < 0.05 was considered statistically significant.

RESULTS

The patients in the present investigation were categorized into several groups on the basis of their age and major risk factors involved (Table 1). Hypertension, diabetes, high cholesterol and smoking were the major risk factors in these patients. The comparison of results for homocysteine (Hcy; µmol/l) for various risk factors is given in Table 2. The abbreviations N, S, HC, HT and DM respectively were shown in Tables for normal, smoking, hypercholesterolemia, hypertension and diabetes mellitus.

Table 1: Homocysteine variations in patients with ischemic heart disease.

Age group (years)	N	S	HC	HP	DM
<30	5.05±2.41 (18)	6.39±2.53 (20)	8.87±2.70 (18)	6.97±2.91 (20)	8.35±2.87 (19)
30-40	6.23±2.67 (21)	6.89±2.88 (20)	8.22±3.12 (20)	8.33±3.23 (19)	8.70±3.45 (20)
40-50	6.90±2.14 (22)	7.21±3.33 (20)	7.83±3.61 (24)	6.34±2.34 (20)	7.24±3.13 (20)
50-60	9.02±3.52 (21)	9.56±3.54 (20)	10.67±3.51 (20)	9.36±3.01 (18)	9.55±3.34 (22)
60-70	10.23±3.92 (20)	12.22±4.00 (20)	13.39±3.99 (24)	7.98±4.21 (21)	9.58±3.97 (20)
>70	12.33±4.12 (20)	12.56±4.11 (20)	14.50±4.57 (20)	9.71±3.49 (20)	11.28±4.01 (23)

The figures in parentheses denote the number of subjects studied; N, S, HC, HT and DM respectively denote normal, smoking, hypercholesterolemia, hypertension and diabetes mellitus.

Table 2: Comparison of homocysteine variations in patients with ischemic heart disease

Age group (years)	N vs S	N vs HC	N vsHP	N vs DM
<30	t=1.667; p=0.1042	t=4.478; p=0.0001	t=2.201; p=0.0343	t=3.777; p=0.0006
30-40	t=0.761; p=0.4510	t=2.198; p=0.0340	t=2.249; p=0.0304	t=2.571; p=0.0141
40-50	t=0.362; p=0.7191	t=1.050; p=0.2993	t=-0.810; p=0.4226	t=0.414; p=0.6809
50-60	t=0.490; p=0.6271	t=1.502; p=0.1411	t=0.321; p=0.7499	t=0.507; p=0.6151
60-70	t=1.589; p=0.1203	t=2.637; p=0.0117	t=-1.769; p=0.0847	t=-0.521; p=0.6054
>70	t=0.177; p=0.8606	t=1.577; p=0.1230	t=-2.170; p=0.0363	t=-0.846; p=0.4027

N, S, HC, HT and DM respectively denote normal, smoking, hypercholesterolemia, hypertension and diabetes mellitus.

The results for smoking data showed no significant Hcy variations ($p>0.05$). The data of the patients showing the risk factor of HC showed significant elevation of Hcy levels for age ranges <30, 30-40, and 60-70. The data of HT (Table 2) gave significant change for age range <30, 30-40, and >70. Whereas N vs DM (Table 2) showed significant variation for age range <30, and 30-40. These results showed that patients with <30 and 30-40 years age range had significant elevation in Hcy concentration for all risk factors except smoking in the current study.

DISCUSSION

There has been much interest in Hcy as an important risk factor for vascular diseases with the long-recognized factors like hyperlipidemia, hypertension, diabetes mellitus, and smoking (Arrastia, 2000). Its association, however, was described even many decades ago (Mc Kully, 1969). This is quite interesting that if the effect of Hcy is more pronounced in the presence of specific risk factors, it may provide us clues about the association of Hcy and that specific risk factor/ factors. This evidence of the involvement of Hcy with IHD in specific conditions may lead us to manage IHD patients in a better way. Although the normal range for Hcy level is already known, a large number of studies have documented increased risk of vascular disease within this range. Hence, the present report explains the sensitivity levels of Hcy according to underlying discomfort and risk factors.

Various studies show association between elevated homocysteine levels and the known CHD risk factors, such as sex (Ueland *et al.*, 2001; HSC, 2002) and smoking (HSC, 2002). Our present study provides similar information but with more precise influence of risk factors at different age groups. Furthermore, our previous reports on the role of homocysteine in ischemic stroke (Naz *et al.*, 2009), modifiable risk factors in ischemic disorders (Khan *et al.*, 2009; Khan and Hussain, 2008; Hussain, 1991), renal ischemia (Yasmeen *et al*., 2008), hypercholesteremia (Fatima *et al.*, 2007) and ischemic disorders in diabetes mellitus (Hussain *et al.*, 2007a,b) agree with the present results.

The condition of hyperhomocysteinemia has a multifactorial origin incorporating nutritional, genetic, pharmacological, and pathological factors. Considering the differences in dietary, genetic, and ethnic factors, the data published from the West might not be applicable to our population. It is difficult to propose a definite cut off value for Hcy levels to be taken as significant and would require a larger population analysis. Hence, the results of present investigation provide newer and potential information for further studies.

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