Evidence Based Case Series

ASSOCIATION OF HYPERHOMOCYSTINEMIA WITH ACUTE MYOCARDIAL INFARCTION IN YOUNG PATIENTS

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KEY WORDS: Hyperhomocystinemia, Myocardial Infarction, atherosclerosis, thrombosis.

The relative risk of developing coronary artery disease (CAD) in Pakistani population is highest in early ages. The pathogenesis of arterial thrombotic disease involves multiple genetic and environmental factors related to atherosclerosis and thrombosis[1]. Well established genetic and environmental risk factors account for only about two-thirds of cardiovascular events that have lead to on-going search for new markers of cardiovascular risk[2]. In recent years there is rapidly growing literature on the relationship between the hemostatic system and arterial thrombosis. Studies have shown that Homocysteine (Hcy), a recognized thrombophilic marker, may be significant in a subset of patients who are young and lacking conventional risk factors. But, in Pakistan there is paucity of data about the thrombophilia status in young patients with myocardial infarction.

Homocysteine is a simple amino acid that has recently received a great deal of attention as a risk factor for atherothrombotic vascular disease. The increasing interest in mild hyperhomocystinemia as an important risk factor for cardiovascular diseases is based on the observation that a rare inborn metabolic error, homocystinuria, leads to hyperhomocysteinanemia, atherosclerosis, and arterial or venous thromboembolic events in early adulthood. Hyperhomocystinemia, alone or with other thrombophilic risk factors, may be associated with vascular occlusive pathology underlying varied clinical presentations.

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MATERIAL AND METHODS

We are reporting observational study of 12 cases of young patients who presented with documented Myocardial Infarction at Department of Cardiology, Shifa International Hospital, Islamabad, from August 2006 to June 2009. The evidence of myocardial infarction was obtained by ECG, cardiac enzymes, cardiac nuclear scan or coronary angiography. Common conditions causing hyperhomocystinemia like renal disease, cancer, thyroid disorder, use of antifolate drugs were ruled out. Hyperhomocystinemia was categorized as moderate (16-30 umol/L), intermediate (31-100 umol/L) and severe (>100 umol/L)[3]. Fasting homocysteine levels were measured quantitatively on machine Axym Plus System (Abbott).

RESULTS

Of the twelve patients included in this study all had documented myocardial infarction, there were 11 males (91.6%) and 1 female (8.3%). Mean age at the time of MI was 32.2 years ranging from 24 to 37 years. Work up of risk factors of CAD revealed elevated fasting homocysteine levels ranging from 19-59 umol/L (mean 31.9 umol/L). Seven patients (58.3%) had moderate (16-30 umol/L) and five patients (41.6%) had intermediate (31-100 umol/L) hyperhomocystinemia. One patients had hypercoagulable state (protein S deficiency) along with hyperhomocystinemia. One patient had Cerebrovascular Accident (Left MCA infarct) along with Acute Antro-lateral Myocardial Infarction. Smoking as a risk factor was present in 6 (50%)

patients, hypertension in 2 (16.6%) patients, dyslipidemia in 6 (50%) patients, 7 (58.3%) patients were over weight but none was obese, none had diabetes and no patient had positive family history of coronary artery disease. Out of 12 patients 10 underwent coronary angiography; 7 (70%) patients had single vessel CAD, 2 (20%) patients had double vessel CAD and 1 (10%) patient had normal coronaries on coronary angiography (Table-1). The patient who had normal coronaries on angiography had history of Antroseptal Myocardial Infarction and received thrombolytic therapy.

homocysteine induce sustained injury of arterial endothelial cells, proliferation of arterial smooth muscle cells and enhance expression/activity of key participants in vascular inflammation, atherogenesis, and vulnerability of the established atherosclerotic plaque. In fact, the effect of elevated homocysteine appears multifactorial affecting both the vascular wall structure and the blood coagulation system. The proposed pathogenetic mechanisms of vascular injury are oxidative damage of the endothelium through suppression of the vasodilator nitric oxide, increasing the levels of asymmetric dimethylarginine, and

Table - 1: General characteristics of patients

Sr. No	Age (yr)	Sex	MI	Hcy umol/L	Comorbids						Coronary Angio/Nuclear scan
					FH	HTN	DM	LIP	Smoking	BMI	
1	35	M	IWMI	20.2	-	-	-	+	+	27.54	SV-CAD (RCA)
2	35	F	ILMI	19.6	-	+	-	-	-	24.7	SV-CAD (RCA)
3	36	M	AWMI	19.46	-	-	-	+	-	22.34	2V-CAD (LAD & CIRC)
4	34	M	AWMI	40.1	-	-	-	+	+	23.3	Tc-MIBI Scan Scar antroseptal area+apex of LV
5	29	M	AWMI	22.9	-	-	-	-	-	28.37	SV-CAD (LAD)
6	29	M	ASMI	48.08	-	-	-	-	+	28.39	Normal coronaries
7	32	M	AWMI	59	-	+	-	-	-	19.48	SV-CAD (LAD)
8	24	M	ALMI	21.43	-	-	-	+	+	21.2	Not done
9	37	M	NSTMI	19	-	-	-	-	+	27.6	2V-CAD (CIRC-RCA)
10	35	M	AWMI	41.45	-	-	-	-	-	25.8	SV-CAD (LAD)
11	25	M	AWMI	>50	-	-	-	+	+	27.7	SV-CAD (LAD)
12	36	M	AWMI	21.8	-	-	-	+	-	22.9	SV-CAD (LAD)

Yr = year; M = male; F = female; MI = Myocardial Infarction; IWMI = Inferior Wall Myocardial Infarction; ILMI = Infro-Lateral Myocardial Infarction; AWMI = Anterior Wall Myocardial Infarction; ASMI = Antroseptal Myocardial Infarction; ALMI = Antro-lateral Myocardial Infarction; NSTMI = Non ST-Elevation Myocardial Infarction; Hcy = Homocysteine; FH = Family History; HTN = Hypertension; DM = Diabetes Mellitus; LIP = Lipids; BMI = Body Mass Index; SV = Single Vessel; 2V = Double Vessel; CAD = Coronary Artery Disease; RCA = Right Coronary Artery; LAD = Left Anterior Descending Artery; CIRC = Circumflex Artery; LV = Left Ventricle.

DISCUSSION

Experimental evidence suggests that an increased concentration of homocysteine may result in vascular changes through several mechanisms. High levels of impaired methylation, vascular smooth muscle proliferation, promotion of platelet activation and aggregation, and disruption of the normal procoagulant-anticoagulant balance favoring thrombosis.[1]

There is consistency in the mean homocysteine level in patients with coronary artery disease from Pakistan and India of about 19 umol/l.[4-9] This finding is significant because the South Asian population has the highest known rate of CAD, which is widespread, early onset, and aggressive.[10] They have higher propensity for clinical events compared with other populations even after adjusting for all known risk factors and the degree of atherosclerosis.[11]

The mean homocysteine level in our case series was 31.9 umol/L, much higher than the standard level. Omenn et al provided a best estimate for the increased risk of coronary artery disease associated with elevated plasma homocysteine levels. The authors compared relative risks in between homocysteine levels of more than 15 umol/L and less than 10 umol/L after adjustment for other cardiovascular risk factors and suggested that such risk difference is similar to that between total serum cholesterol levels of 7.1 and 4.9 umol/L (275 and 189mg/dl).[12]

In our case series positive relationship is noted between hyperhomocysteinemia, smoking and dyslipidemia. These pronounced interactive effects with conventional risk factors, especially with smoking and dyslipidemia, suggests that hyperhomocysteinemia may further enhance the cardiovascular risk in these patients. These observations regarding homocysteine and smoking may have a major implication in Pakistani society which has a high prevalence of smoking habit.

Hence hyperhomocystinemia, a thrombotic marker which is being classified as a proximate risk factor, may act synergistically with other classical risk factors to accentuate the risk of CAD in young population. This observation needs further validation with large scale studies to justify for early screening of Homocysteine levels as it is a potentially modifiable risk factor with little economic burden.

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