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Evaluation of homocysteine, vitamin B_{12} and folic acid in young patients with myocardial infarction

Ashuma Sachdeva*, Veena Singh, Himanshu Madaan, Kiran Dahiya
Department of Biochemistry, Pt.B.D.Sharma PGIMS, Rohtak, Haryana, (INDIA)
E-mail : ashuma@in.com
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ABSTRACT

In the developing worlds of today, ischemic heart disease (IHD) is responsible for causing more deaths and disability than any other illness and it has been predicted that IHD is likely to be the major cause of death worldwide by the year 2020, surpassing diseases like cancer. Homocysteine (Hcy), a non proteinogenic amino acid is being increasingly recognized as an independent risk factor in the etiology of vascular diseases. Normal Hcy levels in body (3.7-13.9 umol/l) are maintained by adequate supply of vitamin B_{12} and folic acid which aid in metabolism of Hcy. This prospective study was conducted to compare the levels of homocysteine, vitamin B_{12} and folic acid (estimated by Chemiluminescence) in 45 young (30-55years) cardiac patients (who had suffered myocardial infarction) with 40 age matched normal controls. The mean serum homocysteine in the patients with MI was 21.72 µmol/l and 8.34 µmol/l in controls. Vitamin B_{12} deficiency was seen in 25/45 cases and 18/40 controls. However serum folate level was normal in all the subjects. This study shows a positive correlation between hyperhomocysteinemia and acute coronary syndrome. This was also associated with vitamin B_{12} defeciency particularly in vegetarians.So vitamin supplementation could be of help in such cases.

KEYWORDS

Homocysteine;
Folic acid;
Vitamin B_{12};
Myocardial infarction.

ABBREVIATIONS

Hcy, homocysteine
MI, myocardial infarction
IHD, ischemic heart disease

INTRODUCTION

Homocysteine (Hcy) is a toxic, non proteinogenic sulfur containing, highly reactive amino acid that is synthesized during conversion of methionine to cysteine. It is catabolised by vitamin B_6 dependent transsulfuration and remethylaton which relies on folate and vitamin B_{12}. This amino acid is being increasingly recognized as an independent risk factor in vascular diseases. Although the hypothesis of association of hyperhomocysteinemia with atherosclerosis was given in early 60's, it failed to get acceptance at that time.

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But recent studies are now confirming the trend. On the basis of recent retrospective, prospective and epidemiological studies from Europe USA and Canada, it is now widely accepted that hyperhomocysteinemia is an independent risk factor for cardiovascular diseases even after negating the effect of other traditional risk factors. Evidence from these studies has also shown the association between Hcy and ischemic heart disease (IHD) to be equally valid in both men and women. A meta analysis of 17 studies involving 5230 individuals suggest that a 1µmol/l increase in Hcy concentration is associated with 10% increase in IHD risk. A large case control multicentre European trials involving men and women younger than 60 years of age found a 2.2 times higher risk of coronary and other vascular diseases in those with plasma tHcy levels in the top fifths of the normal range as compared to those in the bottom four fifths. This risk was independent of other risk factors but was notably higher in smokers and hypertensives[1]. The risk rose from 3,8% in those with lowest levels (below 9umol/l) to24.7%with the highest level(>15umol/l).

Serum Hcy levels are found to be raised in both folate and vitamin B_{12} deficiency. Studies have shown that at serum folate levels above 15ng/ml ,Hcy levels are at a low normal plateau .Patients taking regular multivitamin supplements have higher folate and vitamin B_{12} levels and lower serum Hcy levels, than those not taking supplements[2].

Mortality due to IHD is 40% higher in Indians as compared to Europeans and this increased mortality is independent of risk factors like cigarette smoking, hypercholesterolemia and hypertension. Indian Asians are reported to have reduced intake of vitamin B_{12} and folate, which increases the Hcy levels and thereby increasing the risk of IHD.

EXPERIMENTAL

45 patients in the age group 30- 55 years, with myocardial infarction were taken up for study. All the patients had electrocardiogram (ECG) changes suggestive of MI. TroponinI ultra levels were estimated in all of them to confirm MI. Serum homocysteine, vitamin B_{12} and folate levels were evaluated and compared with 40 normal controls of the same age group. The normal values for serum homocysteine level was taken as 3.7-13.9 µ mol/l, serum folate as >5.8ng/ml, serum vitamin B_{12} as 215-916pg/ml and serum TroponinI ultra as 0-1.5ng/ml.

Exclusion criterion

Following patients were excluded from the present study:

1 The persons who were smokers and alcoholics.
2 The patients who were on regular multivitamin therapy.
3 Those who had other risk factors for IHD like hypertension, diabetes, and family history of IHD, dyslipidaemia, severe anaemia, hypothyroidism and renal dysfunction.

The serum sample of all the patients was taken up and evaluated for all the parameters by chemiluminescence using ADVIA CENTAUR CP (Siemens).

RESULTS

This study included 15.55% females and 84.5% males. Whilst in control group 27.5 % were females and 72.5% were males. Most of the patients (37.7%) were in the age group of 46 -50 years (TABLE 1 & 2).

The mean serum homocysteine in the patients with MI was 21.72 µmol/l and 8. 34 µmol/l in controls. Hyperhomocystinemia was observed in 68.4% males and 42.8 % females in the cases. Whilst in the control group none of females had hyperhomocystinemia as against 6.89% of males (TABLE 3).

Vitamin B_{12} deficiency was seen in 25/45 cases and 18/40 controls (TABLE 4).

Mean B_{12} levels in case group was 284.52pg/ml and in control group it was 564.16pg/ml.

However serum folate level was normal in all the subjects.

DISCUSSION

The mean Hcy level in cases was 21.72µmol/l and in the control group it was 8.3472µmol/l and the difference was statistically significant. Out of the 40 controls, only 2 (5 %) had high Hcy levels, one in the age group 41-45 years and the other in the age group of

TABLE 1 : Association of age with serum homocysteine (µmol/l) in cases

Age in years	Serum Homocysteine(µmol/l)		Total
	Abnormal	Normal	
30-35	2	1	3
36-40	4	2	6
41-45	9	4	13
46-50	10	7	17
51-55	4	2	6

TABLE 2 : Association of age with serum homocysteine (µmol/l) in controls

Age in years	Serum homocysteine(µmol/l)		Total
	Abnormal	Normal	
30-35	-	7	7
36-40	-	12	12
41-45	1	11	12
46-50	-	6	6
51-55	1	2	3

TABLE 3 : Sexwise distribution of hyperhomocysteinemia (µmol/l)in cases and controls

Sex	Cases		Controls	
	Abnormal	Normal	Abnormal	Normal
Male	26	12	2	27
Female	3	4	-	11
Total	29 (64.5%)	16 (35.5 %)	2 38 (5%)	(95%)

TABLE 4 : Correlation between serum homocysteine and vitamin B_{12} levels in cases and controls

		Cases		Controls	
		Males	Females	Males	Females
Hcy	(abnormal)	26/38 (68.42%)	3/7 (42.85%)	2/29 (6.89%)	0/11
	(normal)	12/38 (31.57%)	4/7 (57.14%)	27/29 (93.1%)	11/11 (100%)
Vit B_{12}	(abnormal)	23/38 (60.52%)	2/7 (28.57%)	13/29 (44.82%)	5/11 (45.45%)
	(normal)	15/38 (39.47%)	5/7 (71.42%)	16/29 (55.17%)	6/11 (54.54%)

51 to 55 years, while the remaining 38 (95%) had normal values. In a study conducted by Jagdish et al [3], young patients <40 years had significantly higher Hcy levels than older patients (>40yrs) while there was no significant difference between the control groups. Studies of healthy men and women indicate that certain acquired and genetic determinants can affect Hcy levels. Women tend to have lower basal levels than men, and neither contraceptive nor hormone replacement therapy seems to significantly alter the levels. Studies done by Mayer et al.[4] and Stein et al also showed the similar finding of higher levels of Hcy in males as compared to females.

Vitamin B_{12} deficiency was seen in 25/45 cases and 18/40 controls. Most of the patients who had abnormal Hcy levels in case group were deficient in B_{12} also. Only 3 cases with high homocysteine had normal B_{12} levels. Out of 18 controls that had low vitamin B_{12} levels, 2 had hyperhomocysteinemia. None of the controls with normal B_{12} levels had hyperhomocysteinemia (TABLE 3). Amongst those who were deficient in B_{12} in cases 67.3% were vegetarians whilst in control group 46.7% were vegetarians. The CRISIS Cohort of Yajnik·s showed that low vitamin B_{12} concentration and hyperhomocysteinemia was common in Indian men, particularly in vegetarians[5].

Serum folate was normal in all cases, 60% of such cases had high Hcy levels 2 controls with high Hcy level had normal serum folate. This was not statistically significant.

Thus, a significant correlation was found between high Hcy levels in recent acute coronary syndrome that also had low vitamin B_{12} levels. Vegetarians had relatively high Hcy and low B_{12} levels. Hence vitamin supplementation could have some important role in reducing homocysteine level. Malinow et al.[6] reported no effect of folate supplements on the plasma Hcy of coronary artery disease patients.In contrary Schorah et al.[7] found that an additional folic acid supplement resulted in a significant fall in the plasma Hcy.Wald et al.[8] and Rydlewicz et al.[9] in 2002 demonstrated that atleast 400µg/day of folic acid was necessary to elicit an optimal reduction of plasma Hcy in patients with IHD.

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