Original Research Article

Study of role of Homocysteine as a risk factor in patients with cardiovascular events

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Abstract

Background: Epidemiological research has shown that increased total homocysteine (tHcy) levels are associated with an increased risk of thromboembolic disease; however, controversy still exists over which subtype of stroke is allied to hyperhomocysteinemia. This study aimed to investigate whether elevated tHcy is an independent risk factor for ischemic stroke

Keywords: Plasma homocysteine, vascular disease, acute vascular event, hyperhomocysteinemia.

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INTRODUCTION

Several studies have postulated that elevated tHcy is a strong and independent risk factor for vascular diseases including ischemic cerebral stroke. Other studies have reported the same results in Turkish and Malay populations with ischemic stroke.[1,2] Furthermore, Biswas *et al.*[3] conducted a study in 120 Indian patients with acute ischemic stroke and showed that there was a significant relationship between HHcy and ischemic stroke (P=0.001). They also found decreased serum concentrations of vitamin B12 and folate in a significant number of their patients and the role of MTHFR 677 C T polymorphisms in hyperhomocysteinemia in some of their patients.[4] Oxidative damage to the vascular endothelium and the proliferation of the vascular smooth muscle create a prothrombotic condition, which contributes to the development of premature atherosclerosis.[5] Moreover, HHcy has been found as a potential risk factor for cardiovascular disease and vascular dementia.[6-9] Some studies have shown that even mildly increased plasma tHcy can also be a significant risk factor for stroke, more specifically ischemic stroke. The aim of this study was to evaluate HHcy as a risk factor for ischemic stroke.

MATERIAL AND METHODS

Present study was prospective, observational study, conducted in department of general medicine, Kanachur Institute of Medical Sciences, Mangalore. Study duration was of 1 year (July 2017 to June 2018). Study was approved by institutional ethical committee.

Inclusion criteria: Patients with age above 18 years, either gender, admitted for Ischemic heart disease, peripheral vascular disease, Deep Vein Thrombosis and Pulmonary Thromboembolism willing to participate in study

Exclusion criteria: Patients associated with diseases such as renal failure, hypothyroidism, psoriasis, any malignancies and psychiatric disorders. Patients taking drugs such as Methotrexate, oral contraceptive pills-dopa, Nicotinic acid and Theophylline. Patients taking folic acid or any vitamin supplement. Patients not willing to participate.

Study was explained and written consent was taken for participation. A detailed history and thorough clinical examination was done as per the proforma and were investigated further, Cardiac enzymes – CKMB, Blood urea, Serum creatinine and Coagulation Profile were done in all patients.

Fasting plasma homocysteine: Estimation was done by Fluorescence polaraization immunoassay (FPIA – ABBOTT –AXSYM- USA). Plasma homocysteine level greater than 15µmoles/L is considered as

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hyperhomocysteinemia. Whenever required Echocardiography, Computed Tomography Head and Thorax, Magnetic Resonance Imaging Brain, Carotid and Vertebral Doppler Study, Doppler of Peripheral Vessel, Angiogram andVenogram were done.

The following parameters were studied:

Smoking: In terms of pack years, smoking index.

Diabetes mellitus: Known diabetics on treatment. Newly detected DM satisfying WHO criteria.

Symptoms of diabetes mellitus with random blood glucose >200 mg%

Fasting plasma glucose > 126 mg%,

2hr plasma glucose > 200 mg%

Hypertension: Known hypertensive on treatment. Newly detected hypertension according to JNC VII criteria.

Family history of Ischemic heart disease

Obesity: Patients were classified as overweight and obese based on body mass index.

BMI = Weight (kg)/height (mt2)

Dyslipidemia: According to NCEP-ATP III guidelines, patients were considered to have dyslipidemia when, Total cholesterol > 200 mg%, HDL < 40 mg%, LDL > 130 mg%, Triglycerides > 150 mg%.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Table 1: General characteristics

Age	Number of cases	Percentage
20-29	4	4
30-39	17	17
40-49	3	3
50-59	56	56
60-69	20	20
Sex		
Male	72	72
Female	28	28
Food habits		
Veg	74	74
Mix	26	26

Table 2: Symptoms at the time of admission

Symptoms	Number of cases	Percentage
Chest pain	39	39
Breathlessness	14	14
Palpitation	01	01
Headache	04	04
Difficulty in speech	23	23
Weakness in limbs	44	44
Others	40	40

Table 3: Comparison of risk factors among patients

Risk factors	Cases	Percentage
Diabetes mellitus	41	41
Hypertension	50	50
Smoking	53	53
Alcohol	14	14
Family h/o CAD	20	20
Dyslipidemia	62	62

Table 4: Homocysteine levels

Homocysteine	Number of cases	Range (µmol/L)
Moderate	47	15-30
Intermediate	23	30-100
Severe	02	>100
Total	**72**	

Table 5: Mean plasma homocysteine in patients

Risk factor	Mean value
Homocysteine (5-15µmol/L)	11.13±3.09µmol/L
>15µmol/L	32.0±19.5µmol/L

P value – 0.000 highly significant

Table 6: Comparison of mean plasma homocysteine among smokers and non-smokers

High risk factors		Plasma homocysteine level	Family h/o CAD
Smoking	Smokers	30.9±22.3µmol/L	0.008
	Non-smokers	20.8±12.9µmol/L	
Alcohol	Non-alcoholic	24.85±17.56µmol/L	0.087
	Alcoholic	34.27±26.12µmol/L	
Diabetes mellitus	Diabetic	23.71±14.58µmol/L	0.286
	Non-diabetic	27.88±21.66µmol/L	
Hypertension	Hypertensive	24.96±14.95µmol/L	0.531
	Non-hypertensive	27.37±22.60µmol/L	
Lipid abnormality	Dyslipidemia	26.88±18.0µmol/L	0.635
	Normal	25.0±20.94µmol/L	
BMI	Normal	25.50±15.78µmol/L	0.679
	Overweight	27.12±23.26µmol/L	
Family h/o CAD	No family history	27.77±20.30µmol/L	0.093
	Family h/o CAD	19.74±11.56µmol/L	

Table 7: Percentage of Homocysteine in Acute Vascular Event

Acute vascular event	Cases	Percentages
CAD (MI and US)	42	42
CVD	51	51
PAD	4	4
DVT and PTE	3	3

Chi-square – 75.600 p value – 0.000

DISCUSSION

Over the last decade, convincing evidence has been gathered on the relation between moderate elevation of plasma tHcy and ischemic stroke. Several studies have reported that HHcy is associated with two to threefold increased risk of ischemic stroke.[9] In 1995, Boushey *et al.*[9] reported the results of the first meta-analysis of 27 observational studies on Hcy and atherosclerotic vascular disease, of which 11 studies addressed the association between Hcy and risk of stroke. Nine case-control studies provided support for the hypothesis that Hcy is an independent risk factor for stroke, while 2 prospective studies reported negative results. Several Asian studies have shown the independent role of HHcy in increasing the risk of ischemic strokes.[10] However, some of these studies have had the confounding effects of nutritional deficiencies (such as vitamin B12, vitamin B6, and folate). Omrani *et al.*[11] conducted a study in 93 Iranian patients with acute ischemic stroke and concluded that HHcy was a risk factor for ischemic stroke. They did not study the relationship between HHcy and ischemic stroke subtypes, but showed that there was a significant relationship between HHcy and smoking in their patients group. Novel risk factor like homocysteine is elevated among the patients with acute vascular disease when compared to normal levels. In the present study higher level of homocysteine is found in smokers, which is highly significant. However, there is no significant association between hyperhomocysteinemia and other conventional risk factors like alcohol, dyslipidemia, Diabetes mellitus, Hypertension and family history of CAD. Although acute coronary, cerebrovascular, and peripheral vascular events share the same underlying pathologies, risk factors, and preventive treatments, they are rarely studied concurrently. Only about two-thirds of all episodes of symptomatic atherothrombotic vascular disease in developed countries

can be attributed to established genetic and environmental vascular risk factors.[12] An additional causal vascular risk factor may be raised plasma levels of homocysteine (hyperhomocysteinaemia). Although 30 years have elapsed since hyperhomocysteinaemia (and homocystinuria) were first associated with an increased risk of atherothrombotic vascular disease,[13] it is only recently that sufficient evidence has mounted to suggest that the association is independent and dose-related, and it remains to be established whether it is causal and modifiable. WHO and World Bank data indicate that in India deaths attributed to Coronary and Cerebrovascular disease have increased markedly with the expanding population and will continue to increase.[10] Further large scale randomized multicentered studies are yet to be done to understand the proper association between homocysteine and conventional risk factors in an individual with acute vascular event.

CONCLUSION

Plasma homocysteine should be evaluated in all patients of vascular disease especially in the absence of traditional risk factors and it should be considered as an independent risk factor for the development of future acute vascular event.

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