Original Research Paper

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Hyperhomocysteinemia, Hyperglycemia and Hyperlipidemia In Atherosclerosis in Type 2 Diabetic Patients

Medical Science

KEYWORDS : Homocysteine, C-reactive protein (CRP), fibeigen, glucose, lipids, type 2 diabetic patients, atherosclerosis.

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ABSTRACT

Objective:

Increasing evidence has shown that atherogenesis is not only caused by hypercholesterolemia, but several other risk factors like obesity, dyslipidemia, hyperglycemia, bacterial and viral infection. Hyperhomocysteinemia also have been identified recently, all mediated through inflammation,which can lead to atherosclerosis.Several events have also been identified to be involved in the overall inflammation reaction in the blood vessel which include endothelium dysfunction, expression of adhesion molecule, recruitment of leukocytes to the injured endothelium, migration of monocytes to the arterial intima, and transformation of monocytes to macrophages, in order to facilitate the assessment of early risk for atherogenesis.

We have made an effort in this study to identify soluble markers that will allow the detection of these factors and the identification of associated inflammation events. Since early risk for atherogenesis are largely preventable with dietary modification and lifestyle changes. Hyperhomocysteinemia,hyperglycemia and hyperlipidemia shown to be associated with atherosclerosis.

In the present study, we aimed to evaluate the relation of plasma homocysteine levels in atherosclerotic vascular disease with hyperglycemia and hyperlipidemia in type 2 diabetic patients.

Design and methods:

A total number of 100 type 2 diabetic patients were included in the study of these patients, 46 had established atherosclerotic vascular disease and 54 had no evidence of atherosclerotic vascular disease. Homocysteine levels and markers of inflammation, namely C-reactive protein, fibrinogen, glucose regulation and lipid parameters were studied.

Results:

Homocysteine levels C-reactive protein (CRP) fibrinogen, glucose and lipid markers were all significantly elevated in patients with atherosclerotic vascular disease when compared with patients without vascular disease.

Conclusions:

Homocysteine, C-reactive protein (CRP), fibrinogen, glucose and lipid levels are increased in type 2 diabetic patients with atherosclerotic vascular disease.

Introduction

Diabetes is an important risk factor for atherosclerosis, and atherosclerotic vascular disease is a major cause of morbidity and mortality among patients with diabetes mellitus. Numerous factors including hyperglycemia, hyperlipidemia, hypertension, smoking, endothelial dysfunction, and platelet and coagulation abnormalities contribute to the process of accelerated atherosclerosis in diabetes [1,2,3].

Atherosclerosis is considered to be an inflammatory process triggered by response to injury. The increase in the plasma inflammation markers were shown to be related with the risk of vascular disease in non-diabetic individuals [4,5,6,7,8,9,10,11,12,13]. There is evidence suggesting increased inflammatory activity in type 2 diabetic patients [14,15,1617]. C-reactive protein (CRP) and fibrinogen are well known to be increased in inflammatory conditions [6,7,8,11]. Homocysteine (Hcy) is known to take part in the development of atherosclerosis and vascular injury and it has been suggested to contribute to the atherosclerotic process of diabetes mellitus. Several studies have demonstrated that plasma Hcy levels are elevated in diabetic patients [18,19,20,21,22,23,24]. But the relation of inflammatory activity to Hcy levels is not well established. The present study was undertaken to compare plasma inflammation markers and Hcy levels in type 2 diabetic patients with and without atherosclerotic vascular disease and to investigate the possible relationship between inflammatory activity and Hcy levels in these patients.

Subjects and methods

Totally, 100 type 2 diabetic patients were included in the study. Of these patients, 46 had established atherosclerotic vascular disease and 54 had no evidence of atherosclerotic vascular disease. Past history of myocardial infarction, coronary artery by-pass surgery, peripheral arterial disease, stroke or angiographically proven coronary artery disease in a patient with electrocardiography (ECG) findings or angina pectoris were considered to be evidence for atherosclerotic vascular disease. Fasting morning serum and plasma samples were obtained from each patient and hemoglobin A1c (A1c), total cholesterol, triglyceride, high density lipoprotein cholesterol (HDL-C), Fibrinogen levels were measured coagulometrically with Stago Compact analyzer. A1c, HDL-C, triglyceride, total cholesterol, levels were studied with Cobas automatic analyzer using Roche Diagnostic tool kits. Low density lipoprotein cholesterol (LDL-C) was calculated using the Friedwald formula. Plasma Hcy levels were measured using ELISA kits.

Results

Basic characteristics and clinical variables of the study population are given in Table 1. fibrinogen, significantly higher in patients with atherosclerotic vascular disease than in those without vascular disease. Plasma Hcy levels were also significantly elevated in diabetic patients with atherosclerotic vascular disease. After adjustment for age, diabetes duration, Hcy levels persisted to be significantly different between groups.

Table 1
Clinical characteristics and laboratory data of the patients with and without atherosclerotic vascular disease.

	Patients without vascular disease*n*=54	Patients with vascular disease*n*=46	Statistical significance
Age (years)	56.24±1.49	63.75±1.26	*P*<0.001‡
Diabetes duration (years)	11.00±0.98	16.87±1.12	*P*<0.001‡
A1_ (%)	9.80±0.47	9.55±0.34	
Ccr (ml/min×1.73m^2)	79.37±3.13	62.74±3.3.1	*P*<0.001‡
Cholesterol (mg/dl)	205.42±7.03	205.97±6.97	
Triglyceride (mg/dl)	172.26±14.36	178.24±14.67	
HDL-C (mg/dl)	46.67±1.69	42.63±2.48	
LDL-C (mg/dl)	127.24±6.24	127.97±6.14	
CRP (mg/dl)	0.513±0.11	1.310±0.36	*P*=0.04*
Fibrinogen (mg/dl)	386.122±12.06	457.585±18.27	*P*=0.002†
Homocysteine (µmol/l)	10.725±0.59	13.840±0.95	*P*=0.005a†

Data are means±S.D. HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; a Model 1, adjusted for age; P=0.091, model 2, adjusted for diabetes duration; P=0.012, model 3, adjusted for Ccr; P=0.240.

Parameters found to be significantly correlated with Hcy are shown in Table 2. The correlation coefficients between the variables were not significantly different among patients with vascular disease and in those without vascular disease when analyzed separately. triglyceride levels (r=0.282, P=0.007) and a negative correlation with HDL-C levels (r=−0.400, P<0.001).

Table 2
Correlation coefficients found to be significant by univariate analysis between homocysteine (Hcy) levels, and other cardiovascular risk factors.

	Ccr(ml/m×1.73/m^2)	Triglyceride(mg/dl)	HDL-C(mg/dl)
CRP (mg/dl)	r=−0.263	r=0.282	r=−0.4
	P=0.012	P=0.007	P<0.001
Fibrinogen (mg/dl)	r=−0.273		
	P=0.009		
Hcy (µmol/l)	r=−0.489		
	P<0.001		

HDL-C, high density lipoprotein cholesterol; Ccr, Creatinine clearance; CRP, C-reactive protein; HCY, Homocysteine.

Discussion

Atherosclerosis is substantially more prevalent, appears earlier, and progresses more rapidly in diabetics when compared with normal population. Even if some of the established cardiovascular risk factors exist more frequently in diabetics, they cannot completely explain this increase in the macrovascular disease [1,2,3].

Recent investigations have suggested that atherosclerosis is an inflammatory process that is initiated as a response to injury and there is growing evidence on its relationship to inflammation parameters. The association of inflammation with vascular disease is clearly established in non-diabetic individuals [17,25].

There is evidence suggesting increased biochemical parameters in both type 1 and type 2 diabetic patients, factors such as hyperglycemia, obesity, and hyperinsulinemia are all proposed to affect in atherosclerosis.[11,26.27]

In our study, biochemical parameters all found to be significantly elevated in type 2 diabetic patients with atherosclerotic vascular disease when compared with patients without vascular disease. This finding suggests that biochemical activity is increased in type 2 diabetics with atherosclerotic vascular disease.

Hcy is also suggested to be a causative factor for atherosclerosis. Hcy levels were found to be elevated in patients with vascular disease and were proposed to contribute to atherosclerosis in patients with coronary artery disease, stroke, and peripheral vascular disease [1,19,20,22,24,28]. Hcy-induced vascular pathologies include fragmentation of the internal elastic lamina, disruption of elastic fibers, smooth muscle hyperplasia, and arterial and venous thrombosis[28]. It is clear that hyperhomocysteinemia can promote atherosclerosis. Endothelial cell injury, endothelial dysfunction, increased smooth muscle cell growth, increased platelet adhesiveness, enhanced LDL oxidation and deposition in the arterial wall, and direct activation of the coagulation cascade may all contribute to this process [1,18,28]. Several studies have demonstrated that Hcy levels are increased in diabetes. Elevated Hcy levels were shown to be a stronger risk factor in diabetics than in non-diabetic patients [1,19,20,21,24,29,30].

Plasma Hcy levels were also found to be significantly elevated in our type 2 diabetic patients with atherosclerotic vascular disease when compared with patients without vascular disease. Hcy a mediator role in the unfavorable serum lipid changes seen in type 2 diabetes.Plasma Hcy levels are also affected directly by the renal functions and are increased substantially with the decrease in Ccr values. The presence of nephropathy causes elevated plasma Hcy concentrations because of reduced clearance of Hcy [1,19,21,29]. Patients with significantly elevated creatinine levels were not included in our study. However, even among diabetic patients with relatively good renal functions, Hcy levels were significantly associated with renal functions.

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