Negative correlations of serum total-homocysteine and HDL-c levels in ICU patients

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Abstract

An elevated plasma level of total homocysteine (tHcy) has long been known as an independent predictor of cardiovascular disease (CVD). However, in the absence of a clear mechanism linking tHcy to CVD, there has been an ongoing debate whether this relationship is one of cause and effect or whether an elevated level of plasma tHcy is an epiphenomenon.
The aim of the present study was to evaluate possible correlations between high levels of tHcy and the anti-inflammatory agent HDL-C along with the atherogenic LDL-C and TGs in adult patients with acute cardiovascular events.
Method and Materials: tHcy, TGs, HDL-C and LDL-C levels were measured in 94 patients (51 men, 43 women) 48-66 y aged, who were admitted to ICU of Cardiology Department. tHcy levels were measured using fluorescence polarization immunoassay (FPIA).
Results: Mean serum tHcy was found 16.63±7.55 μmol/l. There was no significant correlation between tHcy and TGs and LDL-C levels. On the contrary, a negative relationship between tHcy and HDL-C concentration was found with Pearson's correlation coefficient (r = – 0.42).
Conclusions: In this study, we detected and evaluated a negative relationship between t-Hcy and HDL-C levels in a hospitalized ICU population from the Greater Metropolitan area of Athens.

Keywords: Total serum Homocysteine (tHcy), high density cholesterol lipoproteins (HDL-C),low density cholesterol lipoproteins (LDL-C),triglycerides (TG), paraoxonase-1 (PON1)

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Introduction

Homocysteine (tHcy) is a sulfur containing aminoacid which is converted into methionine in the presence of folic acid and vitamin B_{12}.[1] Hcy concentration is considered to depend on genetic and environmental factors, such as nutritional habits.[2]

An elevated plasma level of total homocysteine (tHcy) has long been known as

an independent predictor of cardiovascular disease (CVD). However, in the absence of a clear mechanism linking tHcy to CVD, there has been an ongoing debate about whether this relationship is one of cause and effect or whether an elevated level of plasma tHcy is an epiphenomenon, reflecting the presence of some other proatherogenic factor that is actually responsible for the CVD.[3]

Clinical studies of patients with coronary artery disease (CAD) reveal a negative correlation between plasma levels of Hcy and HDL-C. A prospective study evaluating survival of patients with angiographically defined CAD found increased mortality and decreased HDL-C in patients with the highest Hcy levels. Thus high Hcy predicts all-cause mortality in CAD, independent of traditional risk factors. [4]

Recent studies have provided supporting data showing that plasma Hcy is negatively correlated with HDL-C levels in patients with myocardial infarction and CAD. [5,6]

On the basis of the above mentioned data we measured levels of tHcy, LDL-C, HDL-C and triglycerides (TG) in the sera of adult patients of ICU in a Cardiology Department of a Hospital of Athens in order to calculate possible correlations between these parameters.

Materials and Methods

The present study was approved by the Greek Ethics Committee, according to Helsinki declaration (1989).

Blood was drown immediately after the admittance of the patients. Blood was centrifuged and kept to -20°C, in order to avoid false release of Hcy. All determinations were performed on the same day.

Determination of Hcy was performed using fluorescence polarization immunoassay (FPIA) and IMX analyzer. Sensitivity of the method was 0.50 μmol/l.

Levels of TG, HDL-C and LDL-C were measured in by using enzymic and chromatometric methods in a biochemical analyzer Olympus AG640 Medicon.

Statistical evaluation of the results was performed by using non parametric method (Mann-Whitney) and correlation factors Pearson were evaluated for all parameters measured.

Results

a. Descriptives

94 patients (51 men, 43 women) 48-66 years aged took part in our study. All patients a sample population from the Greater Metropolitan area of Athens, suffered from acute cardiovascular events were admitted to the Intensive Care Unit (ICU), Cardiology Department , Sotiria Hospital of Athens.

b. Statistics

Mean value of tHcy was 16.65±7.55 μmol/l well above the normal range of 9.9-10.6 μmol/l given in bibliography.[7,8] Mean value of tHcy for men was 16.8±8.09 μmol/l and for women 16.45±6.35μmol/l.

Mean value of HDL-C was 40.9±10.78 mg/dl in all patients (38.7±9.8 mg/dl in men and 43.6±11.4 mg/dl in women). Mean value of TG was 133.5±73.5 mg/dl (131.7±72.5 mg/dl in men and 135.7±75.6 mg/dl in women).

Mean value of LDL-C was 128.4±36.9 mg/dl in all patients (126.0±37.2 mg/dl in men and 131.3±36.8 mg/dl in women (Table 1).

Statistically significant correlation was not found between levels of tHcy and TG or LDL-C.

On the contrary, we found negative correlation between tHcy and HDL-C. Pearson coefficient was r=-0.42 (r=-0.46 for men and r=-0.39 for women) (Table 2).

Table 1. Mean ± SD serum tHcy, HDL-C, LDL-C and TG levels in patients

Patients	tHcy	HDL-C	LDL-C	TG
MEN	16.80 ± 8.09 (μmol/l)	38.70 ± 9.80 (mg/dl)	126.0 ± 37.20 (mg/dl)	131.70 ± 72.50 (mg/dl)
WOMEN	16.45 ± 6.35 (μmol/l)	43.60 ± 11.40 (mg/dl)	131.30 ± 36.80 (mg/dl)	135.70 ± 75.60 (mg/dl)

Table 2. Pearson coefficient values between HDL-C and tHcy levels in patients

Patients	R	P
MEN	- 0.46	0.001
WOMEN	- 0.39	0.001

Discussion

Cardiovascular disease is the first cause of death in Greece, with increasing incidence, from 218 to 304 per 100000 during 1980-1987. [9] Alteration in plasma lipoprotein subclass distributions affect mainly atherosclerosis risk. Low plasma HDL-C (hypo-a-lipoproteinemia) is well documented as a risk factor for atherosclerosis. HDLs have several properties that may contribute to their antiatherogenic potential. The best known of these relates to their ability to promote the efflux of cholesterol from cells, including macrophages in the artery wall. [10] HDLs may also protect by virtue of antioxidant, antithrombotic and anti-inflammatory properties. The antioxidant properties of HDLs involve activity of compounds such as paraoxonase1 (PON1).[11-15] that cotransport with HDLs, although apoA-I has also been shown to have antioxidant properties.

Antiinflammatory effects of HDLs include an ability to inhibit both the cytokine induced and the CRP-induced expression of adhesion proteins in endothelial cell. They also correct endothelial dysfunction probably by inducing the synthesis of nitric oxide and most recently have been shown to promote endothelial repair. [16]

On the other hand PON1, a multifunctional antioxidative factor, is the major component of HDL-C, which protects from the oxidation of LDL-C [11-13] and was found significantly decreased as HDL-C in stroke patients. [16]

As already stated an extra atherogenic risk factor which is not directly related to fat consumption is homocysteine

Whatever mechanism is the dominating procedure early findings suggest that a low concentration of HDL-C may explain why people with elevated levels of homocysteine are at increased risk of developing cardiovascular disease.

The relationship between high levels of serum homocysteine and the manifestation of cardiovascular disease is confirmed by the results of the present study, as the significant percentage of ICU patients found with high levels of tHcy (Table 1).

As also shown in Table 1, there was found no statistically significant difference between tHcy levels in men and women.

No statistically significant correlation between TG, LDL-C and tHcy was found, while a negative correlation (r=-0.42) between tHcy and HDL-C levels is detected. This negative correlation is more evident in the group of men vs women (r=-0.46) (Table 2).

Conclusions

1. A negative statistically correlation was evaluated between serum tHcy levels and the concentration of HDL-C in ICU patients
2. No statistical correlation found between the level of serum tHcy and LDL-C and TG serum concentrations
3. A slight but evident difference is detected in the negative correlation (HDL-C and tHcy) between men and women.

Present preliminary findings emphasize once more the need for preventive control of tHcy levels along with the routine lipoprotein fraction determination.

These assays should not be restricted only to high risk age groups, but be also performed in healthy individuals as early as possible. A more detailed investigation within the same group of patients is under way including the HDL-C protein component PON1 as an extra useful biochemical marker.

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