

SHORT COMMUNICATION

Homocysteine and vitamin C

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*Institute of Preventive and Clinical Medicine, Bratislava, Slovakia. Kudlackova@upkm.sk***Abstract**

Homocysteine has a pro-oxidative activity. This amino acid, a lipid-independent vascular disease risk factor, might cause atherosclerosis by damaging the endothelium either directly or by altering the oxidative status. Levels of plasma homocysteine and vitamin C concentrations were determined in the adult majority population of Southern Slovakia (n=146) and in the ethnic Romany minority (n=119) in this region. Average homocysteine and vitamin C values in Romanies are similar to those in the majority group (non-significantly changed) with an equal finding of hyperhomocysteinemia, as well as with similar frequency of deficient, suboptimal and optimal vitamin C values. Under the condition of sub-optimal (23–50 $\mu\text{mol/l}$) and optimal ($>50 \mu\text{mol/l}$) vitamin C levels, homocysteine values in connected groups are significantly lower with comparison to the value at deficient vitamin C level ($<11.5 \mu\text{mol/l}$), reduction from 10.74 $\mu\text{mol/l}$ to 9.35 and 9.17 $\mu\text{mol/l}$. Multiple regression showed a negative linear correlation of homocysteine and folic acid, vitamin B12 (determinants of homocysteine metabolism), vitamin C (antioxidative effect) together (n=265, r= -0.282, p<0.00008). The significance for vitamin B12 alone, was p=0.0199, for folic acid p=0.0046, for vitamin C p=0.0499. The results express a significant effect of vitamin C in prevention of vascular damage. (Tab. 1, Fig. 1, Ref. 19.)

Key words: homocysteine, vitamin C, relationship, Romany, majority population.

Due to the production of intracellular and extracellular reactive oxygen species, oxidative stress may play the major part in the pathogenesis of cardiovascular and other diseases. Since homocysteine (Hcy) and other thiols have pro-oxidative activity, the oxidative stress hypothesis can be explained by the damaging effects of Hcy on vascular cells and tissues (McCully, 1996; Loscalzo et al, 1998). Hyperhomocysteinemia is a lipid independent risk factor for coronary artery disease, cerebrovascular disease and peripheral vascular disease (Refsum et al, 1998;

Cattaneo, 1999). Each 5 $\mu\text{mol/l}$ increment of total fasting plasma Hcy concentration was shown to be associated with a 60–80 %

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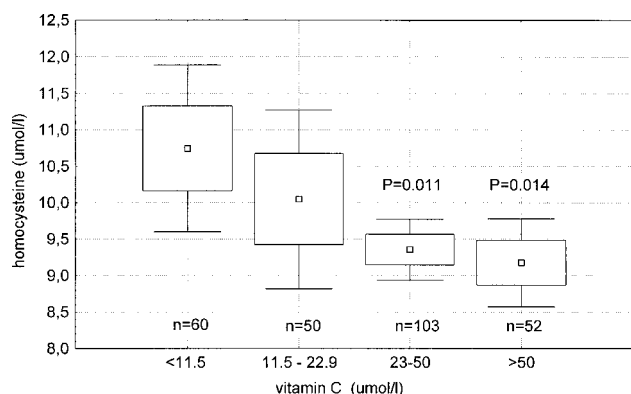


Fig. 1. Homocysteine values in various vitamin C levels: <11.5 µmol/l – severe deficit, 11.5–22.9 µmol/l – deficit, 23–50 µmol/l – suboptimal, >50 µmol/l – optimal (results are expressed as mean±1.00 SEM and ±1.96 SEM).

higher risk of coronary artery disease, a 50 % higher risk of cerebrovascular disease, and a 6-fold higher risk of peripheral vascular disease (Boushey et al, 1995). Hcy might cause atherosclerosis by damaging the endothelium either directly or by altering the oxidative status. Although the mechanism for endothelium damage is not completely understood, it has been suggested that hyperhomocysteinemia may promote the production of hydroxyl radicals, known lipid peroxidation initiators through Hcy autooxidation and thiolactone formation (Heinecke, 1988; Stamler et al, 1993). The blood is not without a potent build-in antioxidative protective system, that includes also ascorbic acid (vitamin C).

The aim of the study was to assess the relationship between Hcy plasma concentration and vitamin C plasma level in the adult population.

Material and methods

Groups of volunteers consisted of 146 subjects by healthy persons of the majority population and 119 subjects by healthy Romany probands from rural regions of Southern Slovakia (village Zlate Klasy, area Zitny ostrov). The subjects with the diagnoses of cardiovascular and oncological diseases, diabetes, renal disease and disease of thyroid gland were excluded. The characteristics of the groups are presented in Table 1.

Blood samples were collected in the standard way. EDTA was used as an anticoagulant. Total Hcy in plasma was assessed by the HPLC method with fluorescence detection and SBD-F as a derivation agent (Vester and Rasmussen, 1991). The plasma level of vitamin C was measured by HPLC method (Cerhata et al, 1994). The survey was carried out in spring. Chi-square test and multiple regression analysis were used for statistic evaluation.

Results and discussion

Experimental evidence suggests that Hcy may promote atherogenesis through its toxic effects on the vascular endothelium, as it has already been introduced (Wall et al, 1980; Stamler et al, 1993). The toxic effects are likely mediated through oxidative stress (Loscalzo, 1996). Folic acid, alone or combined with other B vitamins, is safe and effective in lowering plasma Hcy levels (Brattstrom et al, 1988; Ubbink et al, 1994). Moreover, antioxidant vitamins, such as vitamin C and E, may have an adjunctive role in preventing Hcy – mediated oxidative vascular injury (Chambers et al, 1999). Intakes of folate, vitamin C and fruits and vegetables were inversely associated with Hcy levels (Tonstad et al, 1997), as were serum folate and vitamin B12 (Krajcovicova-Kudlackova et al, 2001) – correlation Hcy – folic acid levels $p < 0.01$; correlation Hcy – vitamin B12 levels $p < 0.01$. Mix of fruits and vegetables, with a moderate folate content, decreases plasma Hcy concentrations in humans (from 13.9 to 12.1 µmol/l), as it was introduced in the study of Broekmans et al (2000). That compared “high diet” (folate content 228 µg, vitamin C content 173 mg) with “low diet” (folate content or daily intake 131 µg, vitamin C content 65 mg).

Mean Hcy plasma concentration in Romanies is similar to Hcy value in the majority group – non-significant change (Tab. 1) with equal finding of normal values (below 10 µmol/l), other levels 10–15 µmol/l (continual concentration with substantial risk) and over 15 µmol/l – hyperhomocysteinemia (Ueland et al, 1993). The frequency of hyperhomocysteinemia corresponds with the published general population data (Krajcovicova-Kudlackova et al, 2000). The average vitamin C level is also equal in both groups – non-significant change (Tab. 1) with similar finding of severe deficit (<11.5 µmol/l), deficit (11.5–22.9 µmol/l), suboptimal values (23–50 µmol/l) and optimal values (overthreshold 50 µmol/l) with antioxidative effect on reduction of free radical diseases (Gey, 1995). The results allowed a connection of both investigated groups.

Tab. 1. Group characteristics, homocysteine and vitamin C levels.

	Majority population	Romany
n (m+w)	146 (56+90)	119 (48+71)
age span (y)	19-60	19-60
average age (y)	36.2±0.9	35.2±1.0
BMI (kg/m ²)	25.0±0.4	28.7±0.6***
homocysteine (µmol/l)	9.61±0.24	9.92±0.34
<10	63 %	63 %
10-15	34 %	34 %
>15	3 %	3 %
vitamin C (µmol/l)	30.6±1.9	32.7±2.2
<11.5	23 %	23 %
11.5-22.9	21 %	17 %
23-50	40 %	38 %
>50	16 %	22 %

Standard error of mean *** $p < 0.001$

A new group was used for the determination of Hcy relationship to vitamin C levels. Figure 1 expresses the Hcy levels at continual increasing plasma vitamin C values from deficit to optimal. Under the condition of suboptimal and optimal plasma vitamin C levels, the Hcy values are significantly lower as compared to Hcy value at deficit vitamin C levels. Hcy reduction was from $10.74 \pm 0.58 \mu\text{mol/l}$ (vitamin C $< 11.5 \mu\text{mol/l}$) to 9.35 ± 0.21 and $9.17 \pm 0.30 \mu\text{mol/l}$ (vitamin C 23–50 and $> 50 \mu\text{mol/l}$).

In the previous study, it was shown that there was significant positive linear correlation between folic acid and vitamin C (Krajcovicova-Kudlackova et al, 2001). Therefore the contribu-

tion of vitamin C to the reduction of toxic Hcy effect is doubtful. Multiple regression analysis expresses a negative linear correlation of Hcy and vitamins B12, folic acid, vitamin C together, regression coefficient $r = -0.282$, $p < 0.0008$. The significance for vitamin B12 alone was $p = 0.0199$, for folic acid $p = 0.0046$ and for vitamin C $p = 0.0499$.

The results document a significant effect of vitamin C together with folic acid and vitamin B12 on the inhibition of toxic Hcy influence on vascular endothelium. Folic acid or vitamin B12 represent a reducing Hcy level effect, and vitamin C removes free radicals formed from Hcy, mainly in hyperhomocysteinemia.

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