Cent. Eur. J. publ. Health 10, 2002, No. 1-2, p. 29-31

SMOKERS - VITAMIN C - HYPERCHOLESTEROLAEMIA

Hijová E., Kuchta M., Petrášová D.
Institute of Experimental Medicine, Faculty of Medicine, Šafarik University, Košice, Slovak Republic

SUMMARY

Cigarette smoking is one of the major public health problems of our times. Smokers are damaged by free radicals formed during smoking. The antioxidant capacity of smokers is reduced. Vitamin C (ascorbic acid) deficiency in heavy smokers with a total cholesterol more than 6.7 mmol/l ranges from 35-55 %. It is mediated by smoking, by its low dietary intake by preferential high dietary intake of saturated and unsaturated fats.

Vitamin C is an important water soluble antioxidant, therefore its intake can at least partially reduce the unfavourable effect of smoking caused by the attack of free radicals on the organism when smokers are unable to quit smoking.

Key words: smokers, vitamin C, hypercholesterolaemia, malondialdehyde, body mass index

Address for correspondence: E. Hijová, Institute of Experimental Medicine, Faculty of Medicine, Šafarik University, Tr. SNP 1, 040 66 Kosice, Slovak Republic

INTRODUCTION

Cigarette smoking has been identified as a major source of preventable morbidity and premature mortality (1). Cigarette smoke has two phases - a gaseous phase of smoke and solid phase (tar). Tar is partially retained in the filter, and the gaseous phase passes through the filter. The gaseous phase and tar contain more than 10^{17} radicals per gram. Smokers inhale both phases containing highly effective oxidants, which initiate oxidative stress in the organism, mainly in the lungs (2). Active smoking and exposure to tobacco smoke in the environment (ETS - Environmental Tobacco Smoke) have a negative impact upon the progression of various diseases and atherosclerosis. The impact of smoking is higher in persons suffering from diabetes mellitus and hypertension (3). ETS exposure of non-smokers is often referred to as passive smoking or involuntary smoking. Cigarette smoke contains and induces generation of free radicals. This balance between generation and removal of free radicals produces oxidative stress (4).

The organism has its own defensive antioxidant mechanisms to eliminate the production of free radicals or in case that radicals have already been produced, to decrease any consequences of their negative effects.

Therefore the basic aim of this work was to evaluate the efficacy of the antioxidant defensive system of serum levels of vitamin C (ascorbic acid) at the different risk levels of total cholesterol and values of body weight in middle-aged probands in long-term heavy cigarette smokers and non-smokers.

MATERIAL AND METHODS

Characteristic of Probands

Our study included 212 probands (109 smokers and 103 non-smokers) - employees of different industrial plants from the eastern part of the Slovak Republic. The average age of probands was 49.6 years. Smokers smoked 15 cigarettes and more per day. All of them were active smokers and nobody of them stopped smoking ten years before study. None of the adults used any vitamins supplements for a minimum of five months before the study and in the course of it. Vitamin users were excluded from the study. All probands were divided into risk groups depending on different serum levels of total cholesterol (TCH). The low risk group (control group) included probands with mean serum levels of total cholesterol TCH<4.69 mmol/l and values of BMI<25 kg /m^2. Probands with serum levels of TCH (>4.7 - <5.19 mmol/l) and values of BMI (>25.1 - <27 kg/m^2) represented the group with a borderline risk. Probands from the group with moderate risk had serum levels of TCH (>5.2 - <6.69 mmol/l) and values of BMI (>27.1 - <30 kg/m^2). The high risk group had TCH levels over 6.7 mmol/l and values of BMI >30.1 kg/m^2.

Laboratory Assays

Total cholesterol (TCH) and triacylglycerols (TG) were determined enzymatically using Boehringer sets (Germany). The serum level of vitamin C was spectrophotometrically estimated using Roe and Kuether methods (5). The degree of the oxidative activity was evaluated from the detection of malondialdehyde formation (MDA - TBARs) assayed with thiobarbituric acid using the fluorometric method of Yagi (6). Body mass index (BMI) as a ratio of weight to square height is given in kg/m^2. Statistical processing of data was carried out using the Statgraphics version 4.0. programme; significance of differences of the mean values was tested by multivariat and regression analysis.

RESULTS

Results of changes in concentrations of total cholesterol, vitamin C, and malondialdehyde between smokers and non-smokers were divided into quartiles in relation to the serum level of total cholesterol and are summarized in Table 1.

Table 1. Changes of parameters between smokers and non-smokers in different groups of total cholesterol risk

Parameters		TCH < 4.69 x ± SD	TCH >4.7 - <5.19 x ± SD	TCH >5.2 - <6.69 x ± SD	TCH > 6.7 x ± SD
TCH (mmol/l)	S	4.43 ± 0.25	5.0 ± 0.15	6.05 ± 0.25	7.48 ± 1.04***
	NS	4.36 ± 0.28	4.97 ± 0.12	5.56 ± 0.26	7.22 ± 0.54
Vitamin C (μmol/l)	S	45.2 ± 11.6	38.0 ± 13.34	35.0 ± 9.29	29.0 ± 9.73
	NS	52.35 ± 19.28	50.2 ± 13.12	47.3 ± 15.6	45.02 ± 18.2
Deficit of vit. C between S and NS	S NS	- 13.5%	- 24.3%	- 26%	- 35.5%
MDA (nmol/l)	S	3.47 ± 0.28	3.46 ± 0.95	4.0 ± 0.65	4.43 ± 0.96**
	NS	3.38 ± 1.08	3.34 ± 1.14	3.71 ± 1.09	4.22 ± 0.89

*** $p < 0.001$; ** $p < 0.01$; S - Smokers; NS - Non-smokers

Table 2. Vitamin C, triacylglycerols and LDL-cholesterol distributed into quartiles of body mass index in smokers and non-smokers

Parameters		BMI < 25 kg/m² x ± SD	BMI >25.1<27 x ± SD	BMI >27.1<30 x ± SD	BMI > 30.1 x ± SD
TG (mmol/l)	S	1.6 ± 0.69	1.9 ± 0.70	2.7 ± 0.80	3.5 ± 1.32**
	NS	1.3 ± 0.48	1.6 ± 0.47	2.0 ± 0.61	1.9 ± 0.70
Vitamin C (μmol/l)	S	35.08 ± 9.29	37.25 ± 9.34	38.06 ± 13.34	37.24 ± 9.32
	NS	49.40 ± 13.12	40.55 ± 12.23	51.54 ± 18.32	52.57 ± 19.57
LDL-CH (nmol/l)	S	2.9 ± 0.41	3.1 ± 0.46	3.4 ± 0.5	3.2 ± 0.83**
	NS	1.8 ± 0.47	2.2 ± 0.39	2.1 ± 0.3	2.4 ± 0.41

** $p < 0.01$; S - Smokers; NS - Non-smokers

Within the group with low risk (control group) the serum levels of lipids and plasma levels of malondialdehyde in smokers and non-smokers did not differ significantly. Vitamin C (ascorbic acid) deficiency in smokers versus non-smokers in the low risk group was 13.5%, and had an increasing tendency in individual risk groups. In heavy smokers with a total cholesterol more than 6.7 mmol/l in comparison with the control group the deficit of ascorbic acid ranged from 35-55 %. In the highest quartile of total cholesterol, oxidative activity measured by MDA is significantly increased ($p<0.01$) in smokers due to the unusual drop of vitamin C serum level.

High BMI values may signalize some health problems, and are asociated with changes in lipid concentrations and a lower vitamin C intake (Table 2).

Triacylglycerols and LDL-cholesterol divided into quartiles of body mass index in smokers are significantly higher in the upper quartile ($p<0.01$), and serum levels of vitamin C did not differ significantly in the two groups, but were relatively lower in smokers.

DISCUSSION

Smoking is a serious world-wide health, social and toxicological problem. The toxic properties of smoking have a negative impact not only on active smokers but also on subjetcts exposed to smoke referred to as a passive smokers. Passive smoking consists of tobacco smoke emitted from the end of a burning tobacco product (sidestream smoke) plus the smoke and the portion of inhaled (mainstream smoke) that is exhaled by the smoker.

Smokers' health is damaged by free radicals formed during smoking. The free radicals are characterized as extremely reactive atoms, molecules or their fragments named oxidants. They participate in the process of serious diseases such as atherogenesis, cancers, different metabolic and neurodegenerative diseases. Long-term smokers are endangered by development of bronchial carcinoma and cardiovascular disorders. Smoking may accelerate aging.

Smoke induced decrease of the serum level of vitamin C and carotene, is caused mainly by antioxidant-consuming radicals in tobacco smoke (7, 8, 9). The vitamin E intake is inversely correlated to the risk of peripheral arterial disease independent of smoking. α-tocopherol and β-carotene are stored in adipose tissue lipids. After transfer of free fatty acids to the adipocytes including the flux of those they are storing, and this results in a decrease of their levels in the circulation. They are released from depots through activation of β_2- adrenergic receptors, which are stimulated by catecholamines, free fatty acids are released

from adipose tissue and this is one of the ways of their removal from the circulation and depots. It is an extraordinary phenomenon that smokers have a poor intake of vitamin C. Results of our examined group, where vitamin C deficiency was between 35 to 55 % in heavy smokers with hypercholesterolaemia confirmed this statement. This deficit is in close relation with depletion of the ascorbic acid pool due to preferential dietary intake of saturated and unsaturated fats with a prevalence of saturated fats which represent about 40 % of total energy intake. Dietary habits of probands were evaluated using questionnaires. The interaction between vitamin C and vitamin E may not only be restricted to the vital recycling of vitamin E by vitamin C, but also to complementary antioxidant actions in different compartments. Insufficiency of vitamin C increases adhesion of monocytes to the endothelium in smokers, but oral supplementation of vitamins can normalize this adhesion (10).

A review of the epidemiological literature indicates that smokers, especially males, usually ingest less antioxidants in food than non-smokers, and the fact that cigarette smoke contains known mutagens and carcinogens, smoking may have adverse effects on male reproduction (11, 12, 13). There is some evidence suggesting that paternal smoking is associated with congenital anomalies and childhood cancer. Oxidative stress caused by smoking does affect not only the lungs, but the whole organism. Particles smaller than 5 μm in smoke cause respiratory burst reaction - RBR, which can damage the DNA. Lung inhibitors of elastase are inactivated due to smoke and this can after years lead to development of emphysema.

The free radicals abundantly increase lipoperoxidation, the mean levels of malondialdehyde and LDL-cholesterol are higher in elderly smokers. Antioxidants (vitamins C and E) protect the organism against lipoperoxidation and lipoperoxidation in smokers is lower till vitamin C is exhausted (14).

Because oxidants play the principal role in the pathogenesis of pulmonary diseases caused by smoking, administration of exogenous antioxidants (vegetables, fruits) is recommended, which may help to improve the oxidant/antioxidant balance. Humans, like other primates and guinea pigs, must ingest vitamin C because they lack L-gluconolactone oxidase, which is the enzyme required for the final step in the de novo synthesis of ascorbate from glucose. Vitamin C (ascorbic acid) is a major watersoluble vitamin in the human plasma. It participates in hormone and neurotransmitters' synthesis, in conversion of cholesterol to bile acids, affects immunity functions, decreases tumour formation in the gastrointestinal tract by blocking nitrosamines. It has a very wide spectrum of biological effects, and its intervention cannot be located into one place. We are unable to determine the precise answer to the question of an optimum daily dose of vitamin C for the human organism (15). Smokers may compensate a statistically significant deficit of vitamin C by a daily dose of 40-68 mg. This is the officially recommended daily dose in the most countries. Levine et al. recommended an intake of 200 mg/day. The allowance should be taken in food adhering to the principle "vegetables or fruits 5 times a day". Administration of antioxidants is very important for smokers because according to WHO prognoses, there are up to 20 million new cases of oncological diseases expected each year up to year 2020. Among them, lung cancer is the most frequent cause of the death in males, and holds the third position in females, therefore it has the first position in the total number of deaths from malignancies in world-wide statistics.

In addition to smoking itself, prognoses of many diseases are deteriorated by insufficient saturation with vitamin C and obesity. Increased requirements of vitamin C in smokers and lipid disorders accelerate atherosclerosis and its complications. Prevention is more effective than cure of consequences of diseases caused by smoking. Therefore support of non-smoking is necessary.

REFERENCES

1. **Peto, R., Lopez, A. D., Boreham, J., Thun, M., Heath, C., Doll, R.:** Mortality from smoking worldwide. Brit. Med. Bull. 52, 1999, 12-21.
2. **Pryor, W. A., Stonne, K.:** Cigarette smoke radicals and the role of free radicals in chemical carcinogenicity. Environ. Hlth Persp. 105, 1997, 875-882.
3. **Maritta, S., Samet, M. Jaakkola and Jonathan:** Occupation exposure to environmental tabacco smoke and health risk assessment. Environ. Hlth. Persp. 107, 1999, 829-835.
4. **Gutteridge, J. M. C.:** Lipid peroxidation and antioxidants as biomarkers of tissue damage. Clin. Chem. 41, 1995,1819-1828.
5. **Roe, J. H., Kuether, C. A.:** Determination of ascorbic acid in whole blood and urine through the 2,4-dinitrophenylhydrazine derivate of dehydroascorbic acid. J. Biol. Chem. 147, 1943, 399-406.
6. **Yagi, K.:** Assay for blood, plasma or serum methods in enzymology. Meth. Enzymol. 105, 1984, 328-331.
7. **Kollár, J., Petrášová, D., Rozdobuďková, V., Koprovičová, J., Šipulová, A., Hijová, E.:** Antioxidative efficacy in heavy smokers. 13. World Congress of Cardiology, April 26-30, 1998, Rio de Janeiro, Brasil, 83-92.
8. **Frei, B.:** Ascorbic acid protects lipids in human plasma and low-density lipoprotein against oxidative damage. Amer. J. Clin. Nutr. 54 (Suppl.), 1991, 1113S-1118S.
9. **Kalra, J., Chadhary, A. K., Prasad, K.:** Increased production of oxygen free radicals in cigarette smokers. Int. J. Exp. Path. 72, 1991, 1-7.
10. **Weber, Ch., Erl, W., Weber, K., Weber, P. C.:** Increased adhesiveness of isolated monocytes to endothelium is prevented by vitamin C intake in smokers. Circulation 93, 8, 1996, 1488-1492.
11. **Sofikitis, N., Miyagawa, I., Dimitriadis, D., Zavos, P.. Sikka, S.. Hellstrom, W.:** Effects of smoking on testicular function, semen quality and sperm fertilizing capacity. J. Urol. 154, 1995, 1030-1034.
12. **Vine, M. F.:** Smoking and male reproduction: a review. Int. J. Androl. 19, 1996, 323-337.
13. **Birkett, N. J.:** Intake of fruits and vegetables in smokers. Publ. Hlth. Nutr. 2, 1999, 217-222.
14. **Mulholland, C. W., Strain, J. J., Trinick T. R.:** Serum antioxidant potential and lipoprotein oxidation in female smokers following vitamin C supplementation. Int. J. Food Sci. Nutr. 47, 1996, 227-231.
15. **McCall, M. R., Frei, B.:** Can antioxidant vitamins materially reduce oxidative damage in humans? Free Radic. Biol. Med. 26, 1999, 1034-1053.
16. **Levine, M., Conry-Cantilena, C., Wang, Y. H., Wech, R. W., Washko, P. W., Dhariwal, K. R., Park, J. B., Lazarev, A., Graumlich, J. F., Cantilena, L. R.:** Vitamin C pharmacokinetics in healthy volunteers: Evidence for a recommended dietary allowance. Proc. Nat. Acad. Sci.(USA) 93, 1996, 3704-3709.

Received October 18, 2000