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Vitamin E and serum lipid level in patients with rectal carcinoma

ABSTRACT

Background: *Epidemiological studies indicated connection of the rectal carcinoma with the dietary lipid content, but the identification of the links associating the causes with the consequences are still far from being resolved. On the other hand, it has been experimentally confirmed that vitamin E expresses antitumour effects in some types of malignancies, but these effects strongly depend not only on the vitamin E form employed, but also on the presence of other antioxidants, e.g. selenium (Se).*

Materials and methods: *In this work, we monitored the values of the following parameters in blood of patients diagnosed as having rectal carcinoma: cholesterol, HDL, LDL, triglycerides and vitamin E. The measurements were performed immediately before and after the surgery (rectal resection), as well as 1, 3 and 6 months postoperatively. One group of patients was postoperatively supplemented with dietary antioxidants and the values of the above parameters were monitored by the same schedule.*

Results: *Ratio of vitamin E content and the sum of triglycerides and cholesterol (E/trg+chol) was lower in patients than in the population of adult healthy volunteers, suggesting it to be a more reliable indicator of the risk factor for rectal carcinoma development than the level of vitamin E alone. A decline of both vitamin E level and E/trg+chol ratio was noticed in patients as early as one month postoperatively, while in the group receiving antioxidants, a significant decrease of these parameters was recorded only 6 months postoperatively.*

Conclusion: *The fact that the supplementation postpones reduction of vitamin E level postoperatively suggests that antioxidants could express some beneficial effects on the outcome of a standard therapy.*

Key words: *Vitamin E; Triglycerides; Cholesterol; Rectal Cancer; Antioxidants*

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INTRODUCTION

The data on the role of vitamin E in the etiology of the rectal carcinoma, as well as on the influence of a supplementation therapy on this disease, based on clinical experience, are rather scarce (1). Epidemiological studies indicated connection of the rectal carcinoma with the dietary lipid content, but the identification of the links associating the causes with the consequences are still far from being resolved (2). According to the data accumulated during the past several years, the diet consisting of moderate amounts of lipids and proteins and high amounts of fruit and vegetables, rich in cellulose fibers, represents the primary measure in the prevention of the rectal carcinoma development (3). As a risk of rectal carcinoma is increased by mutagenic action of free radicals, dietary antioxidants such as vitamin E, through reduction of this harmful species should be protective in the case of rectal carcinoma. In the present study, relevant parameters of lipid profile cholesterol, triglycerides, HDL, LDL, as well as content of vitamin E as a liposoluble antioxidant were monitored. The objective of the protocol of this study was allso to examine whether the increase of plasma of vitamin E due to supplementation improve lipid profile in patients with rectal carcinoma.

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MATERIALS AND METHODS

Sample

Blood serums from 42 patients with rectal carcinoma were used in this work. Samples were obtained from Surgical Clinic Belgrade, and taken from patients of both sexes, (age range from 42 to 65 years). Sampling was done before and immediately after the resection of colon, as well as 1, 3 and 6 months after the surgical intervention. A group of 29 patients were supplemented with antioxidants while the ramaining 13 patients served as the control. Supplementation started immediately after the surgical intervention, and blood serum samples were analyzed 1, 3 and 6 months later. Supplemented patients were given organically bound selenium in a dry, inactive biomass of beer yeast with vitamins A, C and E (Oligogal Se®, Galenika Pharmaceutical Works, Zemun Yugoslavia, (4)) 3x1 dose daily for the first 4 months of supplementation, and 1x1 daily beginning with the 5th month of treatment with recommendaton to avoid fatty and salty food.

Formulation of Oligogal Se®

Based on the results of determination of organically bound selenium in a dry, inactive

biomass of beer yeast enriched additionally with selenium ("selenium yeast"), a formulation Oligogal Se® was determined. A single dose consisted of organically bound selenium 100 μg in "selenium yeast", vitamin A 1500 IU, vitamin C 90 mg, and vitamin E 45 IU (4).

Determination of vitamin E content in blood serum

Vitamin E (R, R, R-α-tocopherol) in blood serum was determined by gas chromatography (5).

The exact volume of blood serum (ranged from 1 ml to 5 ml) was extracted with an equal volume 1:1 of hexane p.a. Merck 2-3 times in glass cuvettes. After extraction the samples were centrifuged at 3000-4000 rpm, 15-20 min. n-hexane extracts were separated and n-hexane evaporated up to the volume of 0.1 ml by nitrogen streaming. BHT (2,6-bi-terc-butyl-4-methyl phenol) was added to the samples and concentration of vitamin E was determined by Varian gas chromatograph, using super DB 5 column, 5 m long, with 0.33 mm radius.

The conditions of analyses: temperature of the detector was 300°C (flame ionization detector); temperature of the injector 200°C; temperature program and speed 50-285°C; 15°C/min; caring gas - nitrogen; and -gases for combustion - oxygen, hydrogen.

Vitamin E concentration was calculated using the standard curve as reference. Normal values were from 15-24 mmol/L (4-6).

Determination of triglycerides, cholesterol, HDL and LDL

Triglycerides, cholesterol, HDL and LDL were determined by using standard biochemical procedures incorporated in Randox tests. The values up to 1.95 mmol/L for triglycerides, 3.1-6.5 mmol/L for cholesterol, 0.78-1.95 mmol/L for HDL and 1.55-4.53 mmol/L for LDL were taken as normal.

Statistical analyses

For statistical analyses of data standard Student's t-test was performed (7).

RESULTS

Our results show (Table 1) that in patients with rectal carcinoma the preoperative value of vitamin E ranges within normal scope of values. Ratio (μM/mM) of vitamin E content and the sum of triglycerides and cholesterol (E/trg+chol) was lower (R =2) in patients than in the population of adult healthy volunteers (R=4) (Figure 1), suggesting it to be a more reliable indicator of the risk factor for rectal carcinoma development than the level of vitamin E alone.

Table 1. Serum vitamin E, TG, CHL, HDL and LDL concentrations in patients before and after the colon resection - the effect of supplementation

			Non-supplemented			Oligogal Se®		
	Before	After	1	3	6	1	3	6
Vit E	15.96±3.14	13.60±3.10	1.52±1.26*	5.52±1.54*	2.65±1.50*	15.09±6.07	10.67±3.28	4.01±1.44*
TG	1.56±0.10	0.89±0.08	1.52±0.18	1.99±0.45	1.96±0.46	1.68±0.11	1.43±0.08	1.77±0.15
CHL	5.82±0.2	3.68±0.14	4.91±0.56	5.52±0.54	5.89±0.40	5.69±0.20	5.77±0.21	6.07±0.25
HDL	1.44±0.07	1.03±0.05	1.48±0.19	1.77±0.24	1.76±0.20	1.34±0.06	1.49±0.08	1.81±0.12
LDL	3.77±0.18	2.23±0.15	2.74±0.51	2.84±0.66	3.28±0.43	3.57±0.18	3.62±0.20	3.51±0.19

* $p<0.005$

Units for vitamin E are μmol/L, and for TG, CHL, HDL and LDL mmol/L. The results were expressed as means ± S.E

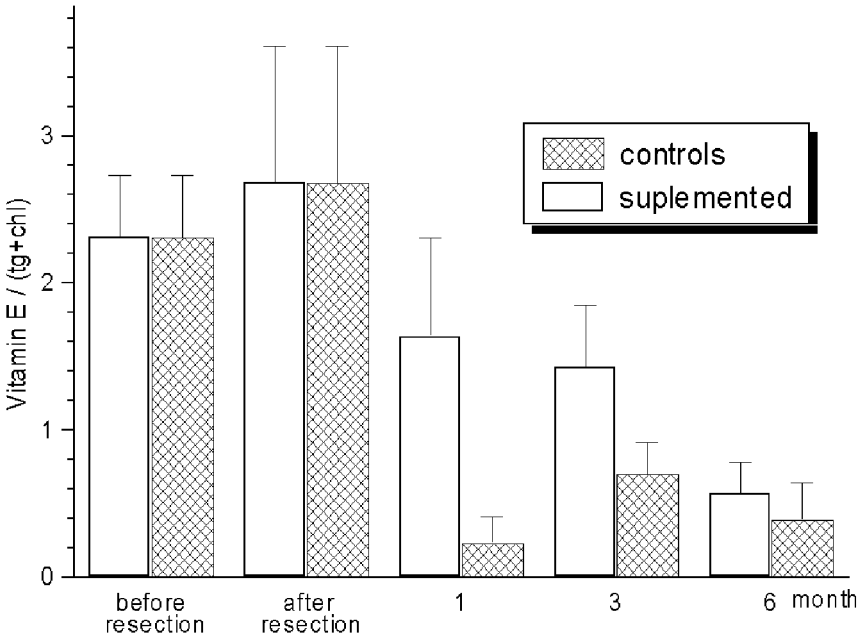

Figure 1. The vitamin E/(TG+CHL) ratio in patients before and after the colon resection - the effect of supplementation. Ratio (μM/mM) for health voluntiers was 4 . The results were expressed as means ± S.E. Statistical significance: * - $p<0.005$ in respect to group before or after the colon resection.

A decline of both vitamin E level and E/trg+chol ratio was noticed in non-supplemented patients as early as one month postoperatively, while in the group receiving antioxidants, a significant decrease of these parameters was recorded only 6 months postoperatively. No significant differences in the content of both HDL and LDL were observed neither when the patients were compared with healthy controls, nor when supplemented patients were compared with non-supplemented ones.

DISCUSSION

Constant oxidative stress in the induction of malignancies is significant from several aspects. First of all, a constant oxidative stress can permanently activate transcription factors and induce the expression of proto-oncogenes such as c-*fos*, c-*jun* and c-*myc* as reported by several authors (11-14). On the other hand, reactive oxygen species (ROS) can damage specifically different protease inhibitors such as α_1-proteinase inhibitor, α_2-macroglobulin and α_2-plasma inhibitor by oxidizing methionine residues in their active centers. Inactivation of these protease inhibitors affects the activities of the proteases, e.g. elastase and plasmin, thus accelerating tumour invasion and development of metastases (15). Recent studies revealed disturbed blood plasma oxidative status in patients with gastric carcinoma. Altered lipid peroxidation was accompanied by a significant decrease of vitamin E, ascorbate, β-carotene, urates and glutathione levels and an increased cerulloplasmin copper content (14).

Numerous studies were focused on the monitoring of antioxidants in body liquids because their antimutagene and antitumour effects have been clearly demonstrated (16). It

has been shown that even vitamin E supplementation does not lead to restitution of its blood level in patients with rectal carcinoma, very probably because of the disturbance associated with the mechanism maintaining adequate vitamin E content in the cell membranes. Our results show that decline of both vitamin E level and E/trg+chol ratio occured in patients as early as one month postoperatively, while in the group receiving antioxidants, a significant decrease of these parameters was recorded only 6 months postoperatively. In 1986, Traber et al. (17) observed a decreased efficiency of vitamin E absorption in the case of its increased intake, which can be of great importance when supplementation of this vitamin is recommended. In this study vitamine E was supplemented in daily dose of 130 U together with other antioxidants. It has been suggested that polyunsaturated long chain fatty acid-rich triglycerides and retinoic acid can lead to a significant decline in the extent of vitamin E absorption (17). Polyunsaturated long chain fatty acids were shown to accelerate vitamin E oxidation under *in vivo* conditions and the observed inhibition of its absorption can be of a special clinical in-terest (18).

As different antioxidants appear to act synergistically, supplementation with vitamin E might be more effective if combined with other micronutritients (19), as it was in our study. It is evident that this way of supplementation delays the postoperative decrease in vitamine E content and ratio VitE/ trg+chol thus reducing this risc factor (19).

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