

THE STUDY OF THE CONTENT OF RETINOL AND TOCOPHEROL IN SERUM OF PATIENTS WITH COLORECTAL CANCER AND THEIR PROGNOSTIC VALUE FOR THE SUBSTANTIATION OF PATHOGENETIC THERAPY.

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Diet and lifestyle factors play an important role in the etiology of colon cancer, and a large proportion of colon cancer incidence might be prevented by a healthy lifestyle [1]. Among dietary factors, vitamins A, C, and E have been hypothesized to reduce the risk of colon cancer because of their anticarcinogenic properties: vitamin A regulates nuclear receptors that suppress tumor formation, induces cell apoptosis [2], and enhances immune function [3]. Vitamin C has antioxidant properties and enhances the immune system [4]. Vitamin E inhibits lipid peroxidation in cell membranes, prevents oxidative damage of DNA by scavenging free radicals, and inhibits carcinogen production [5, 6].

A limited number of observational studies have investigated the associations between intakes of vitamins A, C, and E and risk of colon cancer, and the results for each vitamin have been inconsistent [7–14]. A pooled analysis of nested case-control studies from five cohorts reported a modestly lower risk of colorectal cancer [15] comparing the highest quartile of serum alpha-tocopherol (vitamin E) concentration to the lowest. On the other hand, a meta-analysis of seven clinical trials that tested effects of different combinations of β -

carotene and vitamins A, C, and E on recurrence of colorectal adenomas (precursors of colorectal cancer) found no significant beneficial effects for supplementation with these nutrients [16]. Two recent clinical trials of vitamin E supplementation that were not included in the meta-analysis also found no beneficial effects of vitamin E supplementation compared with a placebo on colorectal cancer incidence [17, 18]. Some studies [19, 20], but not all [21], have found that use of multivitamin supplements, a good source of vitamins A, C, and E, and others, was associated with lower risk of colorectal cancer.

Whether vitamins A, C, and E provide protection from colon cancer is of considerable public health importance; however, this remains as an open question because of inconsistent findings from previous studies, and randomized trials may have been of insufficient duration to reach definitive conclusions. In this analysis, we examined whether intakes of vitamins A, C, and E from foods and supplemental sources and use of multiple vitamin supplements were associated with risk of colon cancer by reanalyzing the primary data from 13 prospective cohort studies from Europe and North America.

The aim of the study of vitamin A (retinol) and E (tocopherol) in serum of patients with colorectal cancer and their prognostic significance in the pathogenesis of the disease and treatment optimization.

Materials and research methods

239 patients at the age from 35 till 76 years with the established diagnosis of colorectal cancer (CRC) were examined and treated using clinical tools and clinical-morphological methods. According to localization of pathological process the rectum cancer (RC) was diagnosed in 54 patients (29 men, 25 women), cancer of the sigmoid colon (SC) – in 62 patients (37 men, 25 women), a cecum cancer (CeC) – in 27 patients (15 men, 12 women), cancer of the transverse colon (TCC) – in 66 patients (48 men, 18 women), a colon cancer (CoC) – in 30 patients (17 men, 13 women). The first (I) stage of cancer was detected in 6 patients, the second (II) – in 34, the third (III) – in 161 and the fourth (IV) – in 38 oncologic patients (inoperable forms of large intestine cancer). The comparison group included 43 conditionally healthy persons of similar age and sex (23 men, 20 women).

Tocopherol, -carotene and retinol concentrations were determined by high-performance liquid chromatography (HPLC) assay (Milne & Botnen, 1986) within 2-4 y after serum collection. A reversed-phase column was used for the simultaneous determination of the vitamins by using isocratic elution with methanol as the single eluant. A diode-array detector was used to monitor the elution at 292 nm for -tocopherol, at 325 nm for retinol, and at 450 nm for -carotene. The peak heights were used in the calculations. All manipulations were carried out in yellow light in order to avoid photo-isomerisation of the compounds. The between-run coefficients of

variation were 2.2% for -tocopherol, 3.6% for -carotene and 2.4% for retinol.

Statistical analyses

Cox regression models were used to estimate the association between dietary antioxidant vitamins and carotenoids, and serum concentrations of -tocopherol, -carotene and retinol and the risk for colorectal cancer. Our analysis used follow-up time starting from randomisation and ending at diagnosis of colorectal cancer, at death, or at the end of follow-up (30 April 1995). Dietary variables were log-transformed and energy-adjusted according to the Willett residual method (Willett & Stampfer, 1986). Dietary and serum variables were entered into the models as indicator variables defined by the second through fourth quartiles among the entire cohort, with the lowest quartile as the reference group. An ordinal score variable was also created to test for dose-response relationships across levels of dietary and serum variables.

Results of researches and their discussion

The study of vitamins in the blood serum of patients with colorectal cancer showed a reduction in vitamin "A" and "E" in both men and women, compared with a control group of observation (Table 1). Vitamin "A" has been reduced in men by 3.1 times in women by 3.9 times, respectively, and vitamin "E" decreased in the serum of 9.2 and 8.3 times. Despite the fact that the total content of vitamins in patients was reduced, the difference in concentration between men and women were statistically unreliable.

Table 1

The content of vitamins in the serum of patients with colorectal cancer according to gender.

Localization of the tumor process	Indicators, gender M±m			
	Vitamin "A" (mkg/100ml)		Vitamin "E" (mkg/100ml)	
	Men	Women	Men	Women
CRC (n=87)	22,4±6,3*	17,4±8,4*	9,2±4,4*	8,3±2,7*
Group of "conditionally healthy" (n=21)	70,8±9,2	67,2±7,4	25,6±5,8	21,4±6,3

Studies of vitamins in the blood serum, depending on the localization of colorectal cancer, revealed a decrease in their concentration in all forms of colorectal cancer. Concentrations of vitamin "A" drops as the 3, 3.4, 2.9 and 4.3 times for the RC, SC, CeC, TCC, CoC. It should be noted that the reduction of the vitamin was observed to

a greater extent in cancer of the sigmoid colon, and to a lesser extent with the CRC.

Was somewhat different dynamics of the reduction, vitamin "E", and less pronounced in almost all forms of colorectal cancer. Thus, vitamin "E" decreased by 3.2, 2.7, 2.6 and 2.2 times for the RC, SC, CeC, TCC.

Table 2

The content of vitamins in the serum of patients with colorectal cancer, depending on the localization process.

Localization of the tumor process	Indicators, gender M±m	
	Vitamin "A" (mkg/100ml)	Vitamin "E" (mkg/100ml)
CRC (n=43)	22,7±3,2*	7,4±3,1*
CeC (n=27)	20,4±4,7*	8,6±2,9*
SC (n=62)	23,6±6,4*	9,2±4,3*
TCC (n=66)	16,1±4,5*	10,6±4,8*
Group of "conditionally healthy" (n=21)	69,4±7,8	23,7±6,5

Analysis of the content of vitamins in the serum of patients with colorectal cancer, depending on the severity of the disease found a clear link between their lower stage of development and carcinogenesis. Vitamin "A" reduced. Tocopherol was reduced in

similar stages of disease at 1.3, 1.6, 2.9 and 4.4 times.

Thus, the results suggest that in patients with colorectal cancer observed hypovitaminosis "A", "E", which involves a violation of proliferation and differentiation of tissues and updated quickly dividing

cells. In this case, there may be a violation of an active absorption from the intestine of various substances, mucosal barrier function of the respiratory, digestive and genito-urinary system, the inhibition of nonspecific resistance to infection, the synthetic activity of the liver, leading to hypoproteinemia, the suppression of the synthesis of steroid hormones, and others have surveyed the group of patients CRC observed inhibition of the antioxidant system, the disease is often accompanied by muscular dystrophy, decreased stability of the cytoplasmic membrane, an increase in hemolysis of red

blood cells and the development of hypochromic anemia, which indicates the involvement of retinol and tocopherol in the mechanisms of development of colorectal cancer and the formation of secondary manifest symptoms characteristic of colon cancer pathology. In this regard, the complex medical and rehabilitation measures for the implementation of the pathogenetic therapy should include fat-soluble vitamins A and E, as antioxidants, stabilizers, accelerators, and membrane processes of differentiation and proliferation of tissues.

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