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Estimation of intestine epithelium permeability In patients with colorectal cancer

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Significant role in endotoxemia development belongs to structural and functional state of the gastrointestinal tract and especially to the permeability of the small and large intestine linear epithelium, allowing toxins to go though bloodstream to various organs and tissues. In case of disorders in the barrier function and morphofunctional state of biocaenosis intestine becomes a center of severe toxic-infectious effects on the body as a whole [1, 3]. Disruptions in intestine microflora endoecology lead to multiple structural, functional and metabolic changes which are the base for formation of a different pathophysiological states and, particularly, colorectal cancer. Investigation of the intestine barrier function in patients with gastrointestinal tract tumors outlines a new dimension in the problem of prevention and treatment of cancerogenesis.

The aim was to study the structural and functional state and the barrier function of small and large intestine epithelium in patients with colorectal cancer and its prognostic significance in diagnosis, treatment and prevention of cancer morbidity of the population.

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).

Epithelial barrier function of the small and large intestine was estimated by the method proposed by I.V. Gmoshinsky et al. [2]. Noncoagulated native egg white was eaten by patients on an empty stomach in the morning at the rate of 1g of protein per 1 kg of body weight. The amount of egg protein - ovalbumin (OVA) was measured in blood serum before and 3 hours after ingestion by immunoenzyme method [2, 3]. Statistical analysis of obtained results was performed by the Student-Fischer indexes.

Results of researches and their discussion

Studies of OVA amount in patients serum before and after egg white test according to localization of the tumor process are presented in Table 1.

In the reference group ("conditionally healthy") statistically significant changes in the concentration of OVA according to sex were not detected.

Table 1

The ovalbumin amount in the serum of patients with colorectal cancer before and after egg white test according to the tumor process localization

Localization of the tumor process	OVA concentration (ng/ml), M±m			
	Men		Women	
	before egg white test	after egg white test	before egg white test	after egg white test
RC (n=54)	0,97±0,34	22,6±4,3*	0,86±0,30	23,4±5,6*
CeC (n=27)	0,85±0,28	24,3±4,1*	0,82±0,34	22,8±4,5*
SC (n=62)	0,93±0,32	28,4±5,8*	0,90±0,27	27,9±6,3*
TCC (n=66)	0,86±0,30	23,6±4,7*	0,82±0,29	24,5±4,3*
CoC (n=30)	0,98±0,35	23,2±3,8*	0,92±0,36	22,6±4,1*
Group of "conditionally healthy" (n=43)	0,56±0,13	0,75±0,19	0,52±0,17	0,68±0,21

Note: * - differences are significant both with a group "conditionally healthy" and with the subgroup " before egg white test", p <0.05.

In patients with CRC in comparison with the "conditionally healthy" persons average concentrations of OVA before egg white test in men and women did not differ significantly (large values of the variance).

Comparing indexes before and after white egg test, we can see a significant increase of the OVA amount in the serum of both men and women. Thus, in men OVA concentration increased at RC in 23,3; at CeC – in 28,6; at SC – in 30.5; at TCC – in 27,4 and at CoC – in 23,7 times. In women rising of OVA level at RC was in 27,2 times; at CeC – in 27,8; at SC – in 31; at TCC – in 29,8 and at CoC – in 24,5 times.

It should be noted that in all cases of native protein ingestion, its concentration after 3 hour exposure increased in more than 20 times in patients serum. However, the highest levels of ovalbumin in the serum were found in both men and women with sigmoid colon, cecum and transverse colon cancer. Significant differences in the dynamics of accumulation of OVA between women and men were not revealed (p> 0.05).

Depending on the severity and stage of tumor in all patients it was detected significantly higher concentrations of OVA in the serum after white egg test in comparison with the reference group (Table 2).

Table 2

The ovalbumin amount in the serum of patients with colorectal cancer before and after egg-white test according to the stage of tumor process

Stage of tumor process development	OVA concentration (ng/ml), M±m	
	before white egg test (men, women)	after white egg test (men, women)
I stage (n=6)	0,85±0,12*	18,62±2,15*
II stage (n=34)	0,93±0,14*	23,35±1,76*
III stage (n=161)	0,96±0,17*	27,40±2,37*
IV stage (n=38)	0,99±0,21*	32,56±3,28*
"conditionally healthy" (n=43)	0,54±0,15	0,71±0,20

Note: * - differences are significant both with "conditionally healthy" group and with the subgroup "before white egg test", p <0.05

In patients with CRC at the I stage of disease OVA amount after white egg test in comparison with initial index (before white egg test) has increased in 21.9 times (on 57,4 %), in the II - in 25.1 (on 72,2 %), in the III – in 28,5 (on 77,7 %) and in the IV - in 32.8 times (on 83,3 %). A close relationship between the stage of carcinogenesis and the concentration of OVA in serum should be noted: with increasing severity of the disease the OVA

amount after white egg test was also significantly higher.

Conclusions. Thus, the results of studying the barrier function of small and large intestine epithelium in patients with CRC suggest serious disturbances of structural, functional and metabolic state of the intestine epithelium, which are attended by sharp increasing of its permeability in more than 20 times. It may be one of other motives in the development of organism intoxication by metabolites of digestion and waste products of vital function of microbiocaenosis as well as can be premorbid phase in development of the gastrointestinal tract carcinogenesis. Disease stage and localization of tumor have a high correlation with the disorder of the small and large intestine epithelium permeability. It can be prognostically important index in the diagnosis of the severity and location of colon cancer.

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