The level of latent presence of markers of intestinal infectious agents in HIV patients

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HIV infection is now the most important medical and social problem in the Russian Federation. Activation of opportunistic infections is one of the most frequent causes of death of HIV-infected patients. Intestinal infectious agents side by side with other microorganisms determine the characteristics of the course and prognosis of the disease. The latent presence of pathogens intestinal infections markers has not been studied in patients with HIV infection.

The aim was to study the frequency of detection and levels of LPS/O-antigens (LPS/O-ag) and of Shiga toxin antigen (ShT-ag) in feces and in circulating immune complexes (CIC) in blood of HIV patients.

Materials/methods. 123 HIV-infected patients with stage IV without diarrhea were surveyed in 2012-2014. The average age of patients was 36,8±7,8 years. The control group - 40 blood donors. We tested the paired stool samples and CIC (in blood) In the qualitative coagglutination reaction on slides for LPS/O-ag as markers of main intestinal infections pathogens, and for ShT-ag in the semiquantitative agglutination reaction on the plates and the level of IgG-immune complexes in feces. Specially prepared natural highly specific hyperimmune rabbit antiserum to LPS/O-ag and Shag and test systems for determination of antigens on the glass and plates were made in Federal research centre of epidemiology and Microbiology by name N. F. Gamalei. Statistical analysis was performed using conventional methods.

Results. For the first time it was revealed that HIV-infected patients with stage IV without diarrhea and without seeding of pathogenic enterobacteria have a high frequency of detection of LPS/O-antigens of Shigella, Salmonella, Yersinia, Campylobacter in stool samples. It was found the excess of detection rate and titers of antigen Shiga toxin in stool of patients with HIV, compared with donors, an increase of these indicators in mixed infection (in the presence of LPS/O-antigens of several pathogens in feces) (p≤0.01).

Detection frequency of LPS/O-antigens of intestinal infections pathogens in feces in HIV infection patients at the IV stage.

LPS/O-antigens	Detection frequency
S.sonnei	23,5%
S.flexneri 1-5	
S.flexneri 6	
C.jejuni, C.coli, C. lari	3,9%
Salmonella sgr.B	19,6%
Salmonella sgr.C1	
Salmonella sgr.C2	
Salmonella sgr.D	
Salmonella sgr.E	
Y.pseudotuberculosis I	25,5%
Y.pseudotuberculosis III	
Y.enterocolitica O3	
Y.enterocolitica O9	
Total (abs.,%)	72,5%

It has been established disturbance of production of specific antibodies in blood to Shiga toxin in HIV infection patients with IV stage and decrease level of specific Shiga toxin CIC.

Detection frequency of Shiga toxin antigen in feces and CIC in HIV disease dynamics.

Patients (n=121)	№ sample	Shiga toxin in feces (≥ 1:8)	Shiga toxin in CIC (≥ 1:4)
General group	1	56,8%	9,1%*
	2	55%	9,5%*
Total	1+2	56,1%	9,3%*

Notes: * -the reliability of differences in comparison with stool analysis (p≤0,01)

The frequency of detection and levels of Shiga toxin antigen and IgG-immune complexes in feces of HIV patients (IV stage, without diarrhea)

LPS/ O-ag	ShT-ag		IgG-immune complexes	
	1	2	1	2
mono (n=78)	50% 0,88± 0,1*	40% 0,65± 0,1*	1,76± 0,1*	1,99± 0,2*
mixt (n=45)	68,2% 0,92± 0,1*	75,7% 1,37± 0,1*#	1,92± 0,2*	1,80± 0,2*
Control	8% 0,04±0,03		2,97±0,04	

The reliability of differences: * -with blood donors; # - with mono and 1 sample (p≤0,01)

Conclusion. Detection of mono- and mixed-O-antigens in the feces of patients with HIV infection indicates the presence of latent agents of intestinal infections that are undetected by bacteriological methods and do not manifest clinically as a diarrhea. In conjunction with increase in titer and frequency of Shiga toxin antigen detection testifies pronounced intestinal dysbiosis. Disturbance of production of Shiga specific antibodies in HIV patients with stage IV and increasing of Shiga toxin level in the presence of mixt O-antigens of enteric pathogens in feces indicates "disruption" of the formation antishigatoxic immunity, which, in turn, can help sustain intoxication syndrome and reduce the effectiveness of antiretroviral therapy.

Concomitant pathology in HIV patients depending on the presence of LPS/O-antigens and Shiga toxin

	mono O-ag		mixt O-ag	
	1 group Shiga+ (≥1:8)	2 group Shiga - (≤1:4)	3 group Shiga+ (≥1:8)	4 group Shiga - (≤1:4)
Chronic diseases of the GIT	170%	160%	204%*	214%*
Diarrhea	40%	33,3%	41,4%	50%
Liver cirrhosis	40%	33,3%	104%*	50% #
Hemorrhagic syndrome	0	13,3%	24,1%*	14,3%
Lympho-proliferation	30%	60%	79,3%*	71,4%
1+3 groups	82 %			
2+4 groups	63 %			

Notes: The reliability of differences in comparison:
*- with mono infections; # - with the 3-rd group;
& - between groups ShT-ag (+) and (-).
-GIT- gastro-intestinal tract
- IV stage – IV stage of secondary diseases according to V.Pokrovskii et al, 2003

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