
# The role of bacterial translocation in the development of systemic inflammation in patients with cirrhosis of the liver.

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**ABSTRACT**

The study included 52 patients with cirrhosis of the liver and 16 clinically healthy individuals of the control group. In all patients, the excess bacterial growth syndrome was determined using a hydrogen breath test with lactulose, the level of C-reactive protein in blood plasma and duplex scanning of unpaired vessels of the abdominal cavity with determination of their diameter, linear and volumetric blood flow rates, and for arteries - also the resistance index. The expansion of the arteries of the stomach and intestines and the growth of blood flow through them with cirrhosis of the liver are observed only in the presence of the syndrome of excessive bacterial growth. In patients with cirrhosis of the liver without the syndrome of excessive bacterial growth, the indicators of gastrointestinal blood flow practically do not differ from those of clinically healthy individuals. The development of bacterial overgrowth syndrome in cirrhosis of the liver is associated with more frequent development of ascites (OR=3.15) and varicose veins of the esophagus of the 3rd degree (OR=4.99). The blood flow through the splenic artery and vein, as well as the severity of splenomegaly and hypersplenism in cirrhosis of the liver, practically do not depend on the presence of excessive bacterial growth syndrom

**Keywords:** liver cirrhosis, excessive bacterial growth, systemic inflammatory reaction, bacterial translocation, portal blood flow, mesenteric blood flow.

Acute intestinal obstruction (AIO) is a disease characterized by a violation of the passage of intestinal contents through the gastrointestinal tract (GIT). In the first hours of AIO formation, there is increased peristalsis in the intestinal loops of the adductor section and an expansion of the lumen of the intestinal loops. In the walls of the intestine there is a plethora of veins, turning into a stasis of blood. The edema of all layers of the intestinal wall increases, due to the fact that the released tissue kinins and histamine disrupt the permeability of the vascular wall, which leads to interstitial edema of the intestine and its mesentery and fluid leakage, first into the lumen of the intestine, and then into the abdominal cavity [4 ]. Necrosis appears on the mucous membrane. In the mucous and submucosal layers, hemorrhages occur, which have a different shape and size. Changes in oncotic and osmotic pressure both in the intestinal lumen and in the parietal layer lead to disturbances in the composition of the intestinal microbiocenosis : gradually aerobic microorganisms begin to be replaced by anaerobes. Because of this, in acute obturation obstruction, gases, mainly hydrogen sulfide, begin to accumulate above the place of the obstacle, intestinal loops bloat, and absorption processes are disturbed [4 ]. As a result of fermentation

and putrefaction, osmotically active substances accumulate in the afferent loop of the intestine, which enhance the sequestration of fluid, which is also facilitated by the release of histamine, serotonin and other endogenous amines. They are characterized by circulatory and lymphatic disorders , destructive changes in the intestinal mucosa against the background of an active inflammatory process. AIO can develop in patients with various comorbidities, including cirrhosis of the liver (LC) - the terminal stage of a wide range of chronic liver diseases. Recently, in the pathogenesis of systemic complications of liver cirrhosis (LC), much attention has been paid to the phenomenon of bacterial translocation (BT) - the penetration of bacteria from the intestinal contents into its wall, mesenteric lymph nodes, portal and systemic circulation [8 ]. An increase in resistance to portal blood flow in cirrhosis leads to a decrease in blood flow through the portal vein, stagnation of blood in it, its expansion and an increase in pressure in it. This complication triggers a number of successive pathogenetic mechanisms of cirrhosis, such as hyperdynamic type of blood circulation, splanchnic vasodilation , ascites, and esophageal varices (EVVs). It is assumed that BT leads to the development of systemic inflammation, manifested, among other things, by systemic vasodilation , which triggers a cascade of hemodynamic changes - in cirrhosis [ 6,9]. One of the factors contributing to BT in cirrhosis is bacterial overgrowth syndrome (SIBO) in the small intestine [1,2,3]. Violations of the intestinal microflora, as evidenced by numerous literary sources, are found in most patients with liver cirrhosis, and the severity of its clinical manifestations and the development of complications in some cases is associated with changes in the intestinal microecology. Thus, intestinal contamination with pathogenic and opportunistic microflora in patients of this group contributes to promotion permeability walls intestines for bacteria , their toxins, as well as micro- and macromolecules , disorders of parietal digestion , decreased synthesis of B vitamins, disorder of the hepatic- enteric circulation, which ultimately leads to the progression syndrome of hepatocellular insufficiency.

In decompensated cirrhosis, when the barrier functions of the intestine and liver are reduced, the development of SIBO leads to a more significant bacterial translocation , which causes a more pronounced systemic inflammatory response, aggravating the condition of patients with AIO. The available data indicate a pathogenetic relationship between bacterial translocation , systemic inflammation, arterial vasodilation , and hyperdynamic circulation in cirrhosis and subhepatic portal hypertension. Hence, the compensated function of the liver is not only a prerequisite for maintaining homeostasis, but also a key point in situations that require excessive expenditure of the body in the intra- and postoperative periods.

Therefore, the study is of particular importance to confirm the above patterns and clarify the possibility of correcting hyperdynamic circulation using selective intestinal decontamination , β- blockers and phlebotropic therapy in patients with AIO.

The **aim** of this study was to study the effect of SIBO on blood flow through the unpaired vessels of the abdominal cavity in patients with cirrhosis.

**Material and research methods .** The study included 52 patients with cirrhosis and 16 clinically healthy individuals. The degree of cirrhosis compensation was assessed using the Child - Pugh scale [6]: compensated cirrhosis — class A, decompensated cirrhosis — classes B and C. All patients underwent standard biochemical, coagulation , and hematological tests, and an ultrasound examination of the abdominal cavity and retroperitoneal organs was performed. In order to determine SIBO, a hydrogen breath test was used [5] . C-reactive protein (CRP) was used as a marker of the systemic inflammatory response ( SIR).

Duplex scanning of the portal and splenic veins, as well as own hepatic, superior mesenteric and splenic arteries and celiac

trunk was performed in the morning on an empty stomach with the patient lying on his back during a short breath-hold at the height of inspiration. The splenic vein was examined in the region of the hilum of the spleen. For veins, the following were determined: the inner diameter and the maximum linear velocity ( MaxLS ) of blood flow. Next, the mean linear velocity ( AvVV = MaxVV x 0.57 ) of blood flow and the volumetric velocity ( VVV = AvVV x vessel cross-sectional area x 60) of blood flow were calculated. The cross-sectional area of the vessel was determined by the formula for the area of a circle [π x (diameter) $^2$ /4].

**Research results and discussion.** Patients with cirrhosis and clinically healthy individuals included in the study were comparable in age, body mass index (BMI) and gender. LC was compensated ( Child - Pugh class A ) in 19 patients, decompensated in 31 patients, including class B in 19, class C in 12 patients with SIBO was detected in 26 (52%) patients with cirrhosis, which made up the SIB group P( +), in contrast to patients with cirrhosis without SIBO included in the - SIBO(-) group. SIBO was detected in 52.6% (10 of 19) of patients with compensated cirrhosis and in 51.6% (16 of 31) of patients with decompensated cirrhosis. In patients with cirrhosis, as well as according to the data of previous studies [5], the diameter of the portal vein was larger, and the LA of the blood flow was less than in clinically healthy individuals, while the differences in the total volume of the blood flow were insignificant. In the splenic vein, the LA of blood flow did not change significantly, which, with an increase in its diameter, led to an increase in volumetric blood flow. As described earlier [6], in patients with LC, the diameter of the - splenic and superior mesenteric arteries was increased, and the linear blood flow was also increased in the former, which led to an increase in volumetric blood flow through these vessels. An increase in the diameter of the portal vein found in patients with cirrhosis did not depend on the presence of SIBO. In patients with cirrhosis without SIBO, the LR of the blood flow was lower than in healthy individuals, but the volumetric blood flow did not differ significantly due to the larger diameter of the vessel . Nevertheless, portal vein volume flow in patients with cirrhosis with SIBO was higher than in healthy individuals, which was not observed in patients with cirrhosis without SIBO . In patients with compensated cirrhosis with the development of SIBO, the resistance index (IR) of the vessel decreased from 0.79±0.04 to 0.71±0.05 (p=0.004) and became almost the same as in clinically healthy individuals ( p=0.997). This was not observed in decompensated cirrhosis: IR in patients with SIBO was 0.76 ± 0.02, without SIBO - 0.75 ± 0.06 ( p = 0.264), the difference from IR in clinically healthy individuals was statistically significant (p < 0.001 and p=0.05, respectively) Since vasodilation , a decrease in vascular resistance, and an increase in volumetric blood flow are observed in SVR, it is assumed that SIBO exerts its influence on intra-abdominal hemodynamics in this way. To confirm this hypothesis in patients with cirrhosis, we studied the level of CRP in the blood. In patients with cirrhosis without SIBO, the concentration of CRP in blood plasma was 0.62÷2.8÷9.1 mg/l, in patients with cirrhosis with SIBO 1.2 ÷10.5÷16.5 mg/l (p=0.028) .

Thus, the development of SIBO in cirrhosis leads to an increase in SVR. Also, in patients with cirrhosis , an increase in the severity of SVR is accompanied by an increase in the diameter of the superior mesenteric artery and blood flow through it, the diameter of the celiac trunk and blood flow through the proper hepatic artery, as a result, blood flow to the portal system increases and favorable - conditions are created for the development of ascites. In patients with cirrhosis with SIBO, ascites was detected more frequently than in patients with cirrhosis without SIBO (69.2% vs 41.7%; OR = 3.15; p = 0.046).

Based on our data, the pathogenesis of the resulting changes can be explained in such a way that the development of SIBO increases the penetration of bacteria through the epithelium of the small intestine into its wall, then into the portal circulation and systemic

circulation. As a result of the penetration of bacteria into the internal environment of the body (BT), SVR occurs. Since SIBO is observed in the small intestine, which is supplied with blood by the superior mesenteric artery, during its development, BT is accompanied by the formation of a local inflammatory process in the wall of the small intestine, which induces the expansion of arterioles in it, and it is so pronounced that it leads to a decrease in IR of the upper small intestine that feeds the small intestine. mesenteric artery. An increase in resistance to portal blood flow in cirrhosis leads to a decrease in blood flow through the portal vein, stagnation of blood in it, expansion of this vein, and an increase in pressure in it. A decrease in the volumetric blood flow in the portal vein, together with an increase in its diameter, leads to a decrease in the LS blood flow through it. The increase in portal pressure is accompanied by retrograde blood flow through the veins of the lesser curvature of the stomach, which have anastomoses with the esophageal veins belonging to the superior vena cava system, which contributes to the progression of esophageal varicose veins (EVV).

**Conclusions.**

1. Bacterial overgrowth syndrome, with the development of the phenomenon of bacterial translocation in cirrhosis, increases the penetration of bacteria through the epithelium of the small intestine into its wall, then into the portal circulation and systemic circulation, contributing to the development of systemic inflammation syndrome.
2. The data obtained indicate the presence of a pathogenetic relationship between bacterial translocation , systemic inflammation, arterial vasodilation , and hyperdynamic circulation in cirrhosis.
3. An increase in resistance to portal blood flow in cirrhosis leads to a decrease in blood flow through the portal vein, stagnation of blood in it, expansion of this vein, and an increase in pressure in it.
4. The data obtained suggest that the use of drugs that affect the intestinal flora (antibiotics, probiotics ) and vascular tone ( phlebotonics ) can become an alternative therapy before and after AIO surgery in patients with liver cirrhosis.

**Literature.**


1. Ардатская М.Д., Бельмер С.В., Добрица В.П. и др. Дисбиоз (дисбактериоз) кишечника: современное состояние проблемы, комплексная диагностика и лечебная коррекция. Экспе-риментальная и клиническая гастроэнтерология. 2015; 5: 13-50.
2. Жаркова М.С., Маевская М. В., Ивашкин В. Т. Современный взгляд на бактериальные осложнения при циррозе печени. Рос журнал гастроэнтерологии, гепатологии , колопроктологии. 2010;20(6): 61-69
3. Жаркова М.С.,Маевская М. В.,Ивашкин В. Т. Влияние синдрома избыточного бактериального роста и бактериальной транслокации на течение заболевания у больных циррозом печени. Рос журн гастроэнтерол гепато-колопроктол 2012;22(5):56-63
4. Шибитов В.А. Энтеральный дистресс синдром при острой кишечной непроходимости различного происхождения. Автореф., дис. … докт. Мед. наук. Саранск 2018. -С.18-35.
5. Яковенко Э.П., Агафонова Н.А., Яковенко А. В. и соавт. Синдром избыточного бактериального роста в кишечнике - клиническое значение и вопросы терапии. Consilium medicum. 2006. Экстравыпуск. 3-8.
6. Bernardi M. et al. Mechanisms of decompensation and organ failure in

cirrhosis: From peripheral arterial vasodilation to systemic inflammation hypothesis. J Hepatol 2015; 63: 1272-84.
7. De Franchis R. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol 2015;63(3):743-52
8. Giannelli V.,Di Gregorio V., Iebba V. et al. Microbiota and the gut-liver axis: bacterial translocation, inflammation and infection in cirrhosis. World J.Gastroenterol 2014;20(45):16795-810.
9. Zhang Y., Feng Y., Cao B., Tian Q. The effect of small intestinal bacterial overgrowth on minimal hepatic encephalopathy in patients with cirrhosis. Arch Med Sci 2016;12(3):592-6.
10. Yao J., Chang L., Yuan L., Duan Z. Nutrition status and small intestinal bacterial overgrowth in patients with virus-related cirrhosis. Asia Pac J Clin Nutr 2016;25(2):283-91.