



## The Role of Bacterial Translocation in Development of Acute Intestinal Obstruction

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### Authors' contributions

This work was carried out in collaboration between all authors. Author SB designed the study and wrote the first the manuscript. Author SK wrote the protocol. Author AA managed the literature searches and evaluated analyses. All authors read and approved the final manuscript.

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### ABSTRACT

**Aim:** Studying of quantity and quality content of intestinal microflora and abdominal cavity exudate in complex treatment of acute intestinal obstruction with addition of enterosorption.

**Materials and Methods:** It was investigated the results of treatment of 63 patients with acute intestinal nontumoral obstruction at the age from 16 up to 83 years old. The patients were divided into 2 groups according to the treatment measures: the group without enterosorption and the group with the using of domestic enterosorbent "Zerotox". The gut microflora and abdominal cavity exudate were investigated.

**Results of Investigation:** The addition enterosorption to the complex of enteral measures permitted of significant improvement of quality and quantity content of intestinal microflora, as well as early stopped of exudation in abdominal cavity and because of it the frequency of postoperative complications decreased from 20% down to 7,9%, and mortality from 8% down to 2,6%.

**Conclusion:** The using of enterosorption in complex of enteral measures permits to significant improves the results of treatment of acute intestinal obstruction.

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## 1. INTRODUCTION

Acute intestinal obstruction (AIO) is one of the actual and most complex problems of urgent abdominal surgery. The high lethality during this pathology, which reaches 17-21% and does not tend to decrease [1,2], according to many authors, is in most cases caused by development of endotoxemia and multiorgan insufficiency [3,4,5].

Pathogenesis of disorders at AIO is, first of all, connected with the change of barrier function of an intestinal wall that leads to the cascade of pathophysiological processes with formation of the syndrome of intestinal insufficiency (SII) with the subsequent multiorgan disorders [5,6].

The syndrome of intestinal insufficiency, which includes disorders of motor, secretory, absorptive, and barrier functions of intestines, begins long before operation. According to a number of authors, the progressing paresis of intestines and disorder of transit of intestinal contents sharply change the quantity and quality of intraluminal and parietal intestinal micro flora, break barrier function of intestines and contribute to translocations of toxins and microorganisms in the bloodstream and peritoneal cavity [7,8,9]. In this regard, the value of the digestive tract (DT) as the initial and potential source of endogenous intoxication of the bacterial and dismetabolic nature becomes obvious [10].

The treatment of the syndrome of intestinal insufficiency in ATO is complex and is defined by its reason, SII stage, endotoxemia severity, and realized when two important stages are performed – elimination of the surgical center and rehabilitation of the intestinal lumen. For intensive removal of an intraluminal intestinal endotoxin and reduction of its receipt in the bloodstream, it is necessary to apply various active methods of an enteral detoxication. One of the most rational of the numerous known and approved methods is the enterosorption based on active binding and removal from a gastrointestinal tract of various endogenous and exogenous substances aggravating or supporting intoxication [2,5,7].

In acute intestinal obstruction, increasing the level of endotoxemia in the body, significant loss of protein may lead to changes in indicators of

both humoral and cellular factors of the immune system. In addition, the affected local defense factors such as increased phagocytosis, the titre of lysozyme and secretory fractions of immunoglobulin A (sIgA) in the exudate of the abdominal cavity. In the pathogenesis of a variety of postoperative complications plays a major role of secondary immunodeficiency.

Based on the foregoing we have set a goal to conduct a dynamic assessment of the quantitative composition of the intestinal microflora and to identify indicators of local factors protect the exudate of the abdominal cavity in complex treatment of acute intestinal obstruction.

In this regard, the research of intestinal microflora and exudate of an abdominal cavity in the conditions of complex treatment of acute intestinal obstruction with inclusion of an enterosorption is obviously important.

## 2. MATERIALS AND METHODS

We studied the results of treatment of 63 patients aged from 16 to 83 years with AIO of non-neoplastic genesis, hospitalized in surgical department of the 3<sup>rd</sup> clinic of the Tashkent Medical Academy in years 2010-2015. 10 patients (15, 8%) were older than 60 years.

The adhesive intestinal obstruction observed in 35 patients (55,6%) was the most frequent cause of AIO, strangulation intestinal obstruction is diagnosed in 18 patients (28,6%), obstructive intestinal obstruction - in 7 (11,1%).

All patient after the statement of the diagnosis carried out a complex of the conservative medical actions directed on elimination of AIO. Unsuccessfulness of these actions within two hours served as the indication to performance of the emergency surgery. The choice of surgery depended on an operational finds and the reason of AIO.

Depending on the used medical actions, patients were divided into 2 groups. The control group was made by 25 patients without enterosorption, the main group included 38 patients at whom the enterosorbent zerotox on the basis of a hydrolytic lignin of cotton seeds peel was applied (production of Uzbek Scientific-Research

Chemical- Pharmaceutical Institute named after A. Sultanov). Distinctive feature of this preparation is that due to the porous structure it occludes toxic substances of exogenous and endogenous origin. Existence on a surface of oxygen-containing groups promotes course of processes of a hemosorption due to which there is an active adsorption of pathogenic micro flora with its subsequent destruction [9].

In patients of control group, the treatment was carried out by the traditional technique accepted in clinic: in the early postoperative period the active intestines decompression (ID) and the intestinal lavage (IL) through the two-channel naso- intestinal probe established during operation. IL was carried out by drop introduction of 1500 ml of salt solution (identical in the electrolytic with the composition of the small intestine chyme) through a small gleam of a naso-intestinal probe, with an exposition of 30 minutes and the subsequent active aspiration.

On patients of the main group, besides a traditional complex of medical actions, an Enterosorption was carried out. For this purpose a suspension at the rate of 100 g of zerotoks powder on 1000 ml of 0,9% of solution of chloride of sodium was prepared. Enterosorption was begun after active aspiration of contents of a small intestine with drop introduction to a naso-intestinal probe of an enterosorbent. The single volume of a sorbent made 500 ml. After injection of a preparation, an exposition within 30 minutes was created, then active aspiration from a big gleam of a probe was carried out. Further series of an Enterosorption were performed each 8 hours (3 times per day) in the office of intensive therapy or in recovery room. In the rest of the time, the naso-intestinal probe was in the DK mode. Duration of series of an Enterosorption was 3-5 days depending on the level of the endogenous intoxication (EI), a state of motor-evacuation function of the gastrointestinal tract, the general health of patients. In process of restoration of motor-evacuation function of the gastrointestinal tract and eliminations of manifestations of SII, it was changed to enteral probe food or the gentle oral food.

The standard clinical, laboratory, microbiological and instrumental methods (an electrocardiogram, ultrasonography, a X-ray analysis) were applied for the assessment of efficiency of the carried-out treatment, confirmations of SII and a syndrome of endogenous intoxication. Special attention was paid on feature of a course of a disease and the postoperative period.

Before operation and also in the early postoperative period, for an objective assessment of a condition of patients, the degree of EI was estimated based on the leukocyte index of intoxication (LII) by a technique of Kalf-Kalifa, concentration of toxins of molecules of average weight (MAW) by N. I. Gabrielyan's technique and cowriter in modification A. S. Vladyki and cowriters. (1986) and to the level of products of a nitrogenous exchange (urea, creatinine).

For studying of a phenomenon of a bacterial translocation in patients with AIO, the specific structure of intestinal contents micro flora and exudate of an abdominal cavity is studied. Material was taken away during operation and in the 1-, 3-, 5- and 7 days of the postoperative period. A quantitative assessment of the content of microorganisms in various environments of an organism with the use of the sector Gould method on high-selective nutrient mediums was carried out. (Feldman Yu.M. etc. // Lab. business. 1984).

Considering numerous data of literature on a pathogenic role of opportunistic flora, pathogenicity factors were defined in the allocated representatives of intestinal micro flora. For this purpose standard methods were used by which defined hemolytic features, plasma-coagulation ability, fibrinolytic, lecithinase, hyaluronidase activity [5]. The cultures possessing two and more factors of pathogenicity were considered the most probable agents in realization of potential pathogenicity.

The level of lysozyme in the exudate was determined by the method proposed genome S. R. Aliev (1994), which included the use of sterile paper disks. Phagocytic activity of neutrophils in the exudate was evaluated by the method of A. V. Antonova (1996). The method for determination of immunoglobulin A secretory fraction (slgA) based on the method of Mancini.

### 3. RESULTS AND DISCUSSION

Patients of both groups experienced disorders of hemodynamics, huge losses of water and electrolytes, and a picture of hemoconcentration in the beginning. These indicators and also results of a biochemical blood test testified to initially serious condition of patients. A stage-by-stage aspiration of contents of gastrointestinal tract was carried out intraoperatively during installation of naso-intestinal probe. The average size of gastrointestinal tract reached  $1860\pm 34$  ml.

One of the indicators of elimination of SII and safe postoperative period during AIO was the emergence of intestinal peristalsis. Thus, in patients with mild endotoxemia, peristaltic waves appeared on the 3rd day after surgery and with severe degree with favorable condition – only on 5-6th days of the postoperative period.

Intraoperative aspiration of contents of swollen intestine loops with the help of a naso-intestinal probe, also its continuation in the early postoperative period in combination with IL promoted early appearance of intestinal peristalsis. Thanks to these actions, indicators of an endotoxemia (Table 1) authentically decreased.

Results of studying of quantitative parameters of microorganisms in intestines contents in patients with AIO without enterosorbent are presented in the Table 2. It is apparent from the table that dysbiosis is observed in intestinal microflora during operation whose characteristic is reliable reduction of quantity of anaerobic flora and essential increase in facultative flora. Thus, the number of bifidobacteria and lactobacilli is sharply reduced in anaerobic flora. At the same time in facultative flora the greatest quantitative changes affected lactosonegative escherichias, enterococcus, proteas and fungus.

In 24 hours after operation, dysbiotic processes in intestines became severe. Thus, the quantity of lactobacilli was  $lg\ 2,60\pm 0,10$ , CFU/ml while the norm is  $7,6\pm 0,20$  CFU/ml, i.e. it decreased by 5. In facultative group of microbes, escherichias underwent the biggest grow change -  $4,50\pm 0,11$  CFU/ml, while the norm is  $1,50\pm 0,10$  CFU/ml, i.e. it increased by 3.

On the 3<sup>rd</sup> day after the operation, the positive changes affecting both anaerobic and facultative group of microbes were registered in flora of intestines.

On the 5-7th days after the operation in flora of intestines the positive changes arose, which became most expressed on the 7th day. During

these terms, we see elimination of staphylococcus and a protea. It is known that exactly these microbes provide development of pyoinflammatory complications because of their enzymes of pathogenicity.

From the Table 2 it is visible that intestinal microflora considerably improved after the use of an enterosorbent on the 5th days after carrying out operation. Thus, the quantity of aerobic bacteria considerably decreases in the background of the increase in quantity of anaerobic bacteria. On the 7th day the indicators of anaerobic and aerobic microorganisms became closer to norm. Staphylococci, streptococci and proteas were not found.

In exudate of an abdominal cavity during microbiological research during operation lactobacilli, peptostreptococci, an Escherichia, staphylococcus, enterococci, proteas and Candida sort of fungus were found in the indigenous representatives of the intestinal microflora. It testifies that the walls of intestines become permeable for microorganisms during AIO (a horizontal bacterial translocation).

During microbiological research of exudate on the 1st day after the operation, all above-mentioned types of microflora of exudate were found, however the quantity of this flora was slightly more than at the previous examination. The quantity of lactobacilli decreased twice.

On the 3<sup>rd</sup> day after operation a considerable change of a microbic landscape, anaerobic and aerobic bacteria were found in the studied exudate during microbiological research. The number of peptostreptococcus considerably changed ( $2,0\pm 0,11$  and  $1,30\pm 0,10$ ;  $p<0,05$ , respectively). The same regularity is found in staphylococcus ( $2,6\pm 0,12$  и  $1,30\pm 0,1$ ;  $p<0,05$ ) and streptococci ( $1,85\pm 0,1$  и  $1,00\pm 0,0$ ;  $p<0,05$ ). Insignificant reduction of quantity of enterococcus, escherichias, protea and fungus was noted. Growth of lactobacilli is not found.

**Table 1. Indicators of severity of endotoxemia in patients with AIO after operation**

Term of research, days	LII		MAW		Urea	
	Control gr.	Main gr.	Control gr.	Main gr.	Control gr.	Main gr.
Initially	7,4±0,91	7,8±0,78	1,6±0,11	1,5±0,12	13,9±1,3	12,4±1,5
1	6,8±0,84*	6,1±1,2*	1,6±0,32*	1,4±0,38*	13,1±1,1*	11,2±1,3*
3	3,2±0,82*	2,5±0,94*	1,2±0,17*	0,9±0,18*	8,9±0,81*	8,2±0,88*
5	1,2±0,66	1,4±0,46	0,76±0,18*	0,7±0,17*	7,2±0,78*	7,6±0,72*
7	1,05±0,05	1,03±0,05	0,58±0,15	0,52±0,14	7,7±0,38	7,8±0,56

Note. \* -  $P < 0,05$  compared with the previous observed day

**Table 2. Intestinal microflora indicators in patients with AIO before and after operation (lg (M±m) CFU/ml)**

Group of microbes	Quantity of microbes in 1 ml									
	Norm	During operation	Days after operation							
			1		3		5		7	
			Control	Main	Control	Main	Control	Main	Control	Main
Total number of anaerobes	10,2±0,30	7,30±0,2	6,15±0,3	6,25±0,3	6,30±0,4	6,90±0,4	7,80±0,5	7,80±0,5	9,00±0,4	9,50±0,4
Lactobacilli	7,6±0,20	4,10±0,3	2,60±0,1	3,10±0,1	5,10±0,3	5,20±0,3	4,30±0,2	5,30±0,2	5,80±0,2	6,90±0,2
Bifidobacteria	8,8±0,30	5,20±0,3	3,30±0,1	3,80±0,1	4,60±0,2	4,80±0,2	5,30±0,3	5,30±0,3	6,70±0,3	7,50±0,3
Peptostreptococcus	1,3±0,10	1,60±0,1	2,85±0,1	2,05±0,1	2,00±0,1	1,80±0,1	2,00±0,1	1,00±0,1	2,15±0,1	0
Total number of aerobes	7,6±0,25	8,10±0,4	8,20±0,4	8,00±0,4	7,80±0,5	7,85±0,5	6,30±0,5	7,90±0,5	7,00±0,4	7,00±0,4
LP Escherichia	6,5±0,15	2,30±0,1	2,60±0,1	3,60±0,1	3,15±0,2	3,85±0,2	3,00±0,1	5,00±0,1	5,10±0,3	6,10±0,3
LN Escherichia	1,5±0,10	4,60±0,2	4,50±0,1	3,40±0,1	2,60±0,1	2,20±0,1	3,30±0,2	2,00±0,2	3,00±0,1	1,00±0,1
Staphylococcus	2,1±0,14	3,15±0,1	4,0±0,15	4,00±0,15	4,15±0,2	3,15±0,2	3,00±0,1	2,00±0,1	0	0
Streptococci	1,2±0,10	2,60±0,1	2,30±0,1	2,10±0,1	2,00±0,1	1,50±0,1	2,00±0,1	0	1,60±0,1	0
Enterococci	4,3±0,20	5,10±0,3	4,15±0,2	4,05±0,2	4,30±0,2	4,50±0,2	4,60±0,2	4,60±0,2	4,00±0,2	4,60±0,2
Proteas	2,1±0,10	4,60±0,2	3,45±0,2	3,00±0,2	3,00±0,1	2,80±0,1	2,80±0,1	1,80±0,1	0	0
Fungus. Candida	2,0±0,10	3,60±0,2	3,00±0,1	3,20±0,1	3,10±0,1	3,00±0,1	3,15±0,1	2,15±0,1	3,00±0,1	2,00±0,1

**Table 3. The characteristic of microflora of abdominal cavity exudate in patients with AIO before and after operation**

Microorganisms	Quantity of microbes in 1 ml exudate									
	Norm	During operation	Days after operation							
			1		3		5		7	
			Control	Main	Control	Main	Control	Main	Control	Main
Lactobacilli		2,00±0,10	1,0±0,1*	1,0±0,1*	0	0	0			
Peptostreptococcus		1,00±0,01	2,0±0,11*	1,8±0,11*	1,30±0,10*	1,00±0,10*	0			
Escherichia		3,00±0,11	2,00±0,1*	2,00±0,1*	0	1,30±0,10*	0			
Staphylococcus	No exudate	3,15±0,12	2,60±0,12	2,20±0,12	1,30±0,10*	0	1,0±0,01	No exudate	No exudate	No exudate
Streptococci		2,60±0,10	1,85±0,1	1,65±0,1	1,00±0,01*	0	0			
Enterococci		2,15±0,11	1,60±0,10	1,40±0,10	1,00±0,01*	0,90±0,01*	1,10±0,1			
Proteas		1,00±0,01	1,30±0,1	1,30±0,1	1,10±0,10	1,10±0,10	0			
Fungus. Candida		1,00±0,01	1,15±0,1	1,10±0,1	1,00±0,10	0,90±0,10	1,15±0,1			

Note. \*— P<0,05 in comparison with indicators in day of operation

**Table 4. The performance of the local factors of protection in the exudate of the abdominal cavity in patients with AIO before and after surgery, M±m**

Indicators of local protective factors	Rate (biol. liquid)	During surgery	The number of bacteria in 1 ml of exudate					
			Day after surgery					
			1st		3rd		5th	
			Control	Main	Control	Main	Control	Main
The titre of lysozyme mg/%	10,1±0,2	13,5±0,1	3,0±0,20*	4,0±0,10*	5,0±0,1*	9,5±0,12	8,3±0,12*	no exudate
Phagocytosis index,%	37,8±2,1	40,3±1,2	18,0±1,3*	20,5±1,3*	20,5±1,3*	29,0±1,5*	30,0±1,5*	
slgA, g/l	1,30±0,1	2,5±0,1	0,7±0,10*	0,8±0,10*	0,7±0,1*	1,2±0,1*	1,0±0,1*	

Note. \*—  $P < 0,05$  in comparison with indicators in day of operation

In the exudate withdrawn on the 5th day after the operation, microorganisms almost were not observed. In 5 examined patients the corresponding growth of quantity of staphylococcus, enterococcus, and Candida sort of fungus was noted ( $1,00 \pm 0,01$ ,  $1,10 \pm 0,10$ ,  $1,15 \pm 0,10$ , respectively).

On the 7th day after operation exudate was not found.

It should be noted (Table 3) that exudate was not present in observed patients after using an enterosorbent on the 5th day.

In the study of fluid, the abdominal cavity in patients with acute intestinal obstruction revealed a significant impairment of local protective factors to the most pronounced at the height of intestinal obstruction, and early postoperative period (Table 3). Moreover, the progression of intestinal dysbiosis accompanied by more significant violations of local immunity. On the 3<sup>rd</sup> day, when indicators of dysbiosis several improved, in parallel positive developments and local factors of protection. In healthy people the contents of the exudate of the abdominal cavity the performance of the local factors of protection (titre of lysozyme, increased phagocytosis and the level of sIgA, compared with the bodily fluids (blood, saliva) other body parts have changed slightly.

However, with the development of acute intestinal obstruction, these figures are due to inflammation and translocation of the intestinal microflora significantly increased, which is evident from the exudate taken during surgery. At the same time 24 hours after surgery in the exudate of the abdominal cavity, there comes a pronounced immunodeficiency in all indicators of local factors of protection because of the stressful situation and using narcotic drugs.

It is interesting to note that three days after the operation clearly shows that in the exudate of the abdominal cavity have been positive developments, since most of the indicators of local factors tended to a significant increase. On the 5th day after surgery in the exudate of the abdominal cavity of patients with acute intestinal obstruction the performance of the local factors of protection was slowly restored.

The analysis of results of patients' treatment in control group showed that in 5 patients (20%) generally with severe degree of an endotoxemia, postoperative complications were observed. The

reason, in our opinion, consisted in a bacterial translocation and slow decrease level in the EI in these patients, despite the ID and IL which were carried out in the postoperative period. The general condition of patients, especially those with initially heavy endotoxemia, improved slowly. The lethality made 8%, 2 patients died because of multiorgan insufficiency.

Additional use of an enterosorption in patients of the main group allowed to reduce the frequency of postoperative complications to 7,9% (3 patients), and a lethality to 2,6% (one patient died of myocardial infarction). A considerable improvement of qualitative and quantitative composition of intestinal microflora, and also the early termination of an exudation in an abdominal cavity was noted in this group.

#### 4. CONCLUSION

Thus, on the basis of the conducted microbiological researches of flora of intestine contents and exudate of an abdominal cavity in patients with AIO, it is possible to draw the following conclusions:

1. In patients suffering from AIO, dysbiosis develops in intestines, and in all patients, the microbic contamination is noted in exudate from an abdominal cavity, especially in the presence of peritonitis. It testifies to process generalization, namely to a bacterial translocation. This mechanism plays large role in development of a syndrome of intestinal insufficiency and leads to degenerate and dystrophic changes of tissues of organs with their subsequent insufficiency.
2. In patients with acute intestinal obstruction in the exudate of the abdominal cavity significantly increase the performance of local defense factors, such as the titre of lysozyme, increased phagocytosis and the level of secretory immunoglobulin A which is associated with the development of the inflammatory process. After 24 hours noted significant immune deficiency all indicators of local factors of protection. Since 3 days, in the exudate of the abdominal cavity, there are positive shifts in all parameters of local protection, and on the 5th day, these shifts in approach to indicators on the day of surgery.
3. The use of an Enterosorption in a together with the enteral actions allows to considerably improve qualitative and

quantitative composition of intestinal microflora, promotes earlier termination of an exudation after operation that leads to considerable reduction of number of postoperative complications and lethal outcomes.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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