Research Article

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Intestinal Microbiocenosis Disorders Correction with Intestinal Lavage in Patients with Acute Poisoning

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BACKGROUND In acute poisoning, accompanied by a violation of microbiocenosis, the problem of its correction has not been studied enough.
AIM OF STUDY Evaluate the possibility of correcting violations of microbiocenosis using intestinal lavage in cases of poisoning with psychopharmacological preparations and cauterizing substances.
MATERIAL AND METHODS 50 male (76.4%) and female (23.6%) patients aged 42 (36; 52) years with psychopharmacological drugs and cauterizing substances poisoning were examined, the composition of the fecal microflora was studied. A total of 100 studies of up to 10 species of microorganisms were conducted. In order to correct violations of the species composition of microbiocenosis, 30 patients underwent intestinal lavage. The comparison group included 20 patients who did not use intestinal lavage.
RESULTS In patients with these poisonings, violations of the specific microbial composition of feces were detected. Intestinal lavage, in contrast to standard therapy, had a corrective effect on fecal microbiocenosis.
CONCLUSION With the help of intestinal lavage, it is possible to correct violations of microbiocenosis in acute poisoning in a short time.
Keywords: acute poisoning, violations of microbiocenosis, intestinal lavage
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GIT, gastrointestinal tract
IL, intestinal lavage
NEA, normal enzymatic activity
PCA, poisoning with cauterizing agents
PPPD, poisoning with psychopharmacological drugs
SES, saline enteral solution

INTRODUCTION

The ecological system formed in the process of phylogenesis, which components include a human per se, his inhabiting microflora and the environment, is in dynamic equilibrium, which can be easily disturbed by the impact of unfavorable factors. The effects of normal microflora on maintaining human health is indisputable and have been proven by a large number of scientific studies. The most important interrelated functions of normal flora to maintain homeostasis of the body include the barrier, regulatory, metabolic,

detoxification, and immunobiological ones. The impact of exogenous or endogenous damaging factors causes a shift in the microecological balance, thus leading to an impairment of these functions. These processes are characterized primarily by a decrease in the number of native microflora elements in the bowel, and a simultaneous increase of opportunistic microorganisms [1, 2]. In cases when the population of opportunistic microorganisms significantly increases, their gene apparatus rearranges the genes in such a way that their virulence and invasiveness increase [3, 4]. An increasing pathogenic aggressiveness and the deterioration of the intestinal wall protective function leading to the intestinal translocation and enterogenic intoxication with subsequent infection of the internal environment of the body serve as a prerequisite for the development of infectious complications and a multiple organ failure [5, 6]. All these complicate patient's condition, worsen the disease prognosis, increase the period and cost of treatment, so the correction of intestinal microbiome disorders in urgent conditions makes an urgent task.

Coping with the intestinal microbiocenosis disorders can be achieved by acting in two directions of targeted effect on the microflora: by suppressing the growth of undesirable microorganisms (using antibiotics, bacteriophages) and creating favorable environmental conditions for beneficial microorganisms by using meta- and prebiotics.

In the context of emergency care for acute poisoning, due to the disadvantages of using antibiotics (with their negative impact on the microbiocenosis, an increase in the number of resistant strains), probiotics (entailing the difficulty of selecting drugs and their doses), and phagotherapy (associated with narrow bacteriofage specificity, and rapid appearance of phage-resistant strains), the use of meta- and prebiotics seems more comprehensive and justified. However, it takes a long time — 2-3 weeks or more to achieve a therapeutic effect with these drugs, which limits their use in critical conditions [7, 8].

The review of literature sources has shown that the problem of microbiocenosis disorders in patients with acute poisoning has not been extensively studied. According to the existing paradigm, this category of patients has all the prerequisites for the development of disorders in the intestinal microflora composition. Factors that can cause such disorders include psychoemotional stress in suicidal patients, the direct effect of exo-and endotoxicants on the intestinal flora, and also shock, hypoxia, the gastrointestinal tract (GIT) paresis, and side effects of medications used in the treatment of acute poisoning and its complications. Sporadic studies have shown that in cases of poisoning with psychopharmacological drugs (PPPD), the intestinal dysbacteriosis of various severity is detected, and its severity can decrease as a result of using intestinal lavage or the "Pectovit" agent [9, 10]. We have found no evidence in literature about an impaired intestinal microflora composition in other types of poisoning.

The study objective was to evaluate the possibility of correcting intestinal microbiocenosis disorders by using IL in PPPD and in poisoning with cauterizing agents (PCA).

MATERIAL AND METHODS

The study included 50 male (76.4%) and female (23.6%) patients aged from 37 to 85 years (mean age was 42 [36; 52]) with PPPD and PCA, who were examined for the feces microflora composition. All patients were divided into four groups: group 1 including 12 patients with PCA who underwent IL; group 2 of 10 patients with PCA who underwent no IL; group 3 of 18 patients with PPPD who underwent IL; and group 4 of 10 patients with PPPD who did not undergo IL.

All patients on admission to the intensive care unit were in severe condition. In psychopharmacological drug poisoning, the patient consciousness depression scored from 3-5 (as assessed by Glasgow Coma Scale) was the leading manifestation of intoxication. In patients with PCA, the severity of their condition was predetermined by the area and depth of the gastrointestinal mucosa chemical burn. In both groups of patients of this cohort, the endoscopic examination revealed the severe 2nd-3rd degree burn of the oral mucosa, pharynx, esophagus and stomach and the 2nd-4th degree burn of the stomach.

All patients received the standard treatment in the Department of Acute Poisoning and Somatopsychiatric Disorders of N. V. Sklifosovsky Research Institute for Emergency Medicine, Moscow, in the period from 2016 to 2019.

The fecal microbial composition was determined by a bacteriological method [11]. A sample for the study was taken from the first portion of stool during IL, being labeled as "baseline", and then during self-defecation on the 5th day. In patients of the comparison groups, the feces sample labeled as "baseline" was the one taken on the first day. The second sample for the study was taken in the same way as in the patients of the study groups on the 5th day. The time from the moment of taking the material to its delivery to the bacteriological laboratory and inclusion in the workflow did not exceed 1.5–2 hours. In all patients, each biosample was studied for 10 microorganisms(species) A total of 100 bacteriology tests were performed.

To grade the severity of the impaired colon lumen microflora composition, we used the Dysbacteriosis Classification given in the Branch Standard "Patient Management Protocol. Bowel dysbacteriosis", according to which: Grade I Dysbacteriosis is characterized by a decreased content of bifidobacteria to 108-6 and/or of lactobacilli to 107-6 CFU/g of feces (depending on age), of typical E. coli to 106-5, or by an increased number of E. coli over 108 CFU/g of feces; Grade II Dysbacteriosis is defined as the decreased contents of bifidobacteria and lactobacilli, the presence of pathogenic flora in a concentration of 105 or more CFU/g of feces or the association of opportunistic microorganisms 103-104 CFU/g of feces; Grade III is characterized by the present associations of opportunistic microorganisms in high titers against the background of reduced amounts of bifidobacteria and lactobacilli [12].

The results were evaluated by comparing the number of patients who had deviations in the composition of certain microorganisms in each of the groups (their specific weight) before the treatment start and on day 5 The results were evaluated by comparing the percentage of the patients having certain deviations in stool flora composition (i.e. their specific weight) in each of the groups before the treatment start and on day 5.)

Patients of the study groups (1 and 3) were admitted at the hospital and, in addition to the standard therapy, underwent IL with using saline enteral solution (SES) [13].

To perform IL in patients with PPPD who were unconscious, after tracheal intubation, a nasogastric two-lumen tube of 3KS-21M type was placed, which perfusion lumen was connected to a gravitation system with a capacity of 1.5–2 liters filled with SES. The patient was positioned on his/her back with an elevated upper half of the body. The solution heated to 37-38° C was administered in portions of 150-200 mL every 5 minutes. After the administration of 1.5–2.5 liters of the solution, loose stools, and then watery discharge without intestinal contents (intestinate) appeared. In no stool after the administration of 2.5 L of the solution, the stimulation of the propulsive function of the intestine was started. The aspiration lumen of the tube was used to decompress the stomach and remove excess volume of solution from it.

Patients of the study group with PCA admitted at the hospital after the administration of pain relieving agents, antispasmodics, and glucocorticoids underwent the IL up to the scheme, for which they were given 200 mL of SES to drink every 5 minutes. In patients with swallowing disorders, a nasogastric tube was used to administer SES. The solution temperature was 18-22°C. After 1.5–2 hours, diarrhea occurred. The total volume of SES was 4.2 liters. The patients tolerated the IL procedure satisfactorily. Patients with PCA in the comparison group received the standard therapy.

STATISTICAL PROCESSING OF RESULTS

Statistical data processing was performed using the Microsoft Office Excel and StatSoft STATISTICA 10 software package. When the distribution differed from the normal distribution, intra-group differences were evaluated using the x2 test and Fisher exact test. The differences were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

The results of the study showed that the detected deviations in the fecal microbial composition of the patients' baseline samples were of the similar type. In each of the four groups, some patients showed decreased baseline titers of bifidobacteria and lactobacilli by 1-2 orders of magnitude, and an increased titer of opportunistic pathogenic flora to 105 CFU and higher and the detected S. aureus in samples. A comparative analysis of the incidence and nature of microbial composition impairments in the baseline samples in patients of the compared groups showed that the abnormalities in some parameters were comparable, those in others were quantitatively different, but these differences were not statistically significant.

Table 1 shows the intestinal microflora composition in patients of Groups 1 and 2 with PCA.

Table 1

Results of bacteriological examination of stool in patients of groups 1 and 2 with poisoning with cauterizing agents

No.	Microorganisms and their quantitative characteristics	Groups of patients, study stages, and the specific weight of cases					
		Group 1, (n=12), Abs. number (%)			Group 2 (n=10), Abs. number (%)		
		Baseline	Day 5	−Δ,%	Baseline	Day 5	−Δ,%
1	Bifidobacterium spp. ↓	7 (58.3)	2 (16.7)	71.4	6 (60)	4 (40)	33.3
2	Lactobacillus spp. ↓	4 (33.3)	2 (16.7)	50.0	6 (60)	5 (50)	16.7
3	Klebsiella spp. ↑	4 (33.3)	2 (16.7)	50.0	5 (50)	3 (30)	40
4	S. aureus**	1 (8.3)	—		2 (20)	1 (10)	50
5	Enterococcus spp.	-	-		-	-	
6	K. pneumoniae ↑	1 (8.3)	-2		(20)	1 (10)	50
7	E. coli with low physical activity* ↓	5 (41.7)	2 (16.7)	60.0	4 (40)	4 (40)	0
8	E. coli lactose-negative↑	2 (16.7)	-2		(20)	2 (20)	0
9	Proteus sp. ↑	1 (8.3)	-1		(10)	-10	
10	Candida spp. ↑	4 (33.3)	-3		(30)	2 (20)	33.3

Notes: "—" – normal; ↓ – the titer is reduced in relation to the normal; ↑ – the titer is increased in relation to the norm; * – E. coli with normal enzymatic activity; ** – regarded as abnormal

The data obtained showed that at baseline the patients in group 1 had qualitative and quantitative abnormalities in the microbiota composition. On the first day, the specific weight of patients with a reduced bifidobacteria titer by 1-2 orders of magnitude was 58.3%, and a decreased lactobacilli content was recorded in four cases (33.3%). In group 2, the specific weight of patients with similar values in those parameters was 60%, respectively. At the following stage of the study, the bifidobacteria and lactobacilli titers were reduced only in 16.7% of patients in group 1, and in 40% and 50% in group 2, respectively.

At baseline, in group 1, the titer of Klebsiella spp. was increased in 4 cases (33.3%). After 5 days, an increased concentration of Klebsiella was detected in 2 cases (16.7%). Staphylococcus aureus was detected in one patient during at baseline, but it was absent further, after the IL A similar situation was observed when assessing the K. pneumoniae.

A decrease in the number of Escherichia coli with a normal enzymatic activity (NEA) was detected at baseline in 41.7% of cases; the proportion of such patients after 5 days was only 16.7%, which was 2.5 times lower. In the remaining patients, these microorganism populations returned to normal quantities. An increased Candida spp. titer was noted in 33.3% of cases at baseline, but later, there were no patients identified with an excessive titer of these fungi.

Thus, the assessment of the quantitative and qualitative composition of intestinal microbiocenosis demonstrated that at baseline, in patients of group 1 with PCA there were dysbiotic impairments corresponding to grade II–III. On day 5 after IL, the content of bifidobacteria in stool reached normal values in 71.4%, and that of lactobacilli in 50% of patients who had a reduced titer at baseline. At the same time, the increased baseline content of opportunistic flora spp. returned to normal values. Such dynamics indicated a positive effect of IL on the gut flora lumen.

The assessment of the intestinal microbiocenosis state in the patients of group 2 showed that at baseline, they, as well as the patients of group 1, had dysbiotic impairments of varying severity. The specific weight of patients with reduced bifidobacteria and lactobacilli titers was 60%. A repeated study after 5 days showed a decrease in the concentration of bifidobacteria in 40%, and that of lactobacilli in 50% of patients. An increased titer of Klebsiella spp. was detected in 50% of cases at baseline, and in 30% of cases after 5 days. Staphylococcus aureus was isolated in 2 patients, and only in one after 5 days. K. pneumoniae was also detected at baseline in 2 cases, and only in one patient at the repeated study. A decreased content of Escherichia coli with normal enzymatic activity relative to the norm was detected in 5 patients; after 5 days, the situation practically did not change: a reduced titer of E. coli with NEA was found in 4 patients. An increased titer of lactose-negative escherichia was detected at baseline in 20% of cases; at the repeated study

after 5 days, the result remained the same. An increased Candida spp. titer was detected in 30% of cases, and in 20% of cases after 5 days.

Thus, the presented results showed that the standard therapy for PCA had a positive effect on the existing impairments in the intestinal microbiocenosis, but it is noticeably less pronounced than that of IL.

Table 2 shows the composition of the stool microflora in patients of groups 3 and 4 with PPPD.

Table 2

Results of bacteriological stool examination in patients of the 3rd and 4th groups with psychopharmacological drugs poisoning

No.	Microorganisms and their quantitative characteristics	Groups of patients, study stages, and the specific weight of cases					
		Group 3, n=18 Abs. number, (%)			Group 4, n=10 Abs. number, (%)		
		Baseline	Day 5	−Δ,%	Baseline	Day 5	−Δ,%
1	Bifidobacterium spp. ↓	9 (50)	3 (16.7)1	66.7	6 (60)	5 (50)	16.7
2	Lactobacillus spp. ↓	12 (66.7)	4 (22.2) 2	66.7	8 (80)	6 (60)	25
3	Klebsiella spp. ↑	3 (16.7)	1 (5.6)	66.7	5 (50)	3 (30)	40
4	S. aureus**	3 (16.7)	–		4 (40)	3 (30)	25
5	Enterococcus spp.	1 (5.6)	–		–	–	
6	K. pneumoniae ↑	1 (5.6)	–		5 (50)	2 (20)	60
7	E. coli with low physical activity* ↓	2 (11.1)	1 (5.6)	50.0	6 (60)	5 (50)	16.7
8	E. coli lactose-negative ↑	2 (11.1)	–		3 (30)	2 (20)	33.3
9	Proteus sp. ↑	1 (5.6)	1 (5.6)	0	1 (10)	–	
10	Candida spp. ↑	1 (5.6)	–		3 (30)	–	

Notes: "–" – normal; ↓– the titer is reduced in relation to normal; ↑ – the titer is increased in relation to normal; * – E. coli with normal enzymatic activity; ** – regarded as abnormal; the statistical significance of the difference compared to the baseline value (1 – $p < 0.05$ according to the $\chi 2$ test; 2 – according to Fisher exact probability test)

At baseline, in group 3, a decreased titer of bifidobacteria was noted in 50% of patients, and that of lactobacilli in 66.7%. On day 5, the proportion of patients with reduced bifidobacteria and lactobacilli titers were 16.7% and 22.2%, respectively, which was 3 times lower than the baseline value, the difference being statistically significant ($p<0.05$).

The baseline titer of Klebsiella spp. was increased in 16.7% of cases. On day 5, it remained elevated only in 5.6% of those patients. An elevated titer of K. pneumoniae before IL was identified in one patient. At 5 days after IL, it decreased to a normal value.

It should be noted that S. aureus, isolated at baseline in 16.7% of cases, was not seen after IL. Enterococcus spp. were detected before IL in one patient; at the next stage of the study, there was no increased growth of these microbes.

A decreased content of E. coli with normal enzymatic activity at admission to the hospital was observed in 2 patients. After IL, the amount of E. coli in one patient reached normal values, while in the other it remained reduced.

The content of lactose-negative E. coli was increased at baseline in 11.1% of patients, but no lactose-negative E. coli was detected on day 5. The content of Candida spp. was elevated in one patient at baseline; and on day 5 their titer was normal in all patients.

Thus, as a result of studying the state of intestinal microbiocenosis in patients with PPPD, the presence of grade II-II dysbacteriosis was identified. The obtained data showed that IL had a corrective effect on the quantitative and qualitative composition of the intestinal microbiocenosis. The proportion of patients with reduced baseline numbers of bifidobacteria and lactobacilli decreased by 3 times on day 5 after the IL and the specific weight of patients having the baseline high titer of pathogenic flora (105 CFU/g of feces and above) for some microorganisms (Klebsiella spp.) reduced by 3 times, and in other microorganism spp., except Proteus spp., the normalization of the quantitative and qualitative composition was observed.

Patients of group 4, similarly to those in group 3, showed the baseline impairments consistent with the presence of dysbacteriosis. When patients were admitted at the hospital, there was a decreased bifidobacteria titer compared to normal in 6 cases (60%), and a decreased lactobacilli titer in 8 cases (80%). In repeated investigation after 5 days, the proportion of patients with reduced concentrations of

bifidobacteria and lactobacilli practically did not change. Thus, the proportion of patients with a reduced bifidobacteria titer on day 5 was 50%; and 60% of patients showed a low content of lactobacilli. At baseline, 5 patients of group 4 showed an increased titer of Klebsiella spp.; at a repeated investigation, their concentration increased in 3 patients (30%). Staphylococcus aureus was detected in 40% of patients in this group. After 5 days, it was detected again in 30% of patients. A decrease from reference concentration of Escherichia coli with normal enzymatic activity was detected in 60% of cases at baseline, and in 50% of cases at the next stage of the study. Overgrowth of Candida spp. at the baseline investigation was observed in 3 patients; and subsequently, no elevated titers of yeast-like fungi were seen in them.

The results of the study showed that the patients of all groups, either with PCA or PPPD, showed the dysbacteriosis signs at baseline that were manifested by a decreased content of lactic acid flora and typical Escherichia coli by 1-2 orders of magnitude in stool samples and elevated titers of opportunistic species over 105 CFU/g. In addition, in 8%-40% of cases in different groups, S. aureus was detected, which should not normally be present. The revealed changes in the microbial composition of stool corresponded to grade II–III dysbacteriosis according to dysbacteriosis classification [12].

In the groups of patients who underwent IL, a significant decrease from the elevated increased baseline titer of opportunistic microorganisms was recorded on day 5, till their complete disappearance. Meanwhile, on day 5 after IL, the specific weight of patients with reduced lactoflora titer decreased by 50-71.4% in PCA group and by 66.7% in PPPD group. It follows that in this patients population, the content of normal microflora increased and reached normal values in the period of 5 days after IL. Thus, after IL, the titer of some species of opportunistic pathogenic flora significantly decreases or completely disappears and that of the lactic acid approaches the normal one. This effect of selective gastrointestinal decontamination is provided by two factors. During IL, the entire contents of the digestive tube are mechanically washed out, including the oral microflora, which includes the bulk of opportunistic pathogens. At the same time, mucosal normoflora, tightly lined to the mucosa and covered with a layer of mucus, insoluble in and indelible by water, remains intact during IL, which ultimately ensures the numerical predominance of normoflora over the remnants of opportunistic pathogenic one. Another positive factor is the prebiotic effect of SES, which acidic reaction (pH 5.5–5.8) can inhibit the growth of opportunistic (proteolytic) microflora and stimulate the development of lactoflora.

CONCLUSION

As a result of the study, we have found that severe poisoning with psychopharmacological drugs is associated with quantitative and qualitative impairments of intestinal microbiome, which confirms the results of our previously published research (V. A. Matkevich, 2006, 2012, 2013) [9, 14, 15], and the study by A.V. Badalyan et al. (2016) [10]. Along with this, in this work we have found out that in severe PCA, dysbacteriosis of grade II–III can also be detected. The identified changes in the microbiome fit into the modern concept of a single-type reaction occurrence under the impact of external stress factors: a decrease in the population of normoflora and an increase in the amount of opportunistic pathogenic flora. It is known from literature that an increase in the opportunistic flora amount to a certain value is accompanied by an increase in its virulence and invasiveness, and a decrease in the normoflora population leads to the decrease of its protective potential, which, in fact, is associated with intestinal translocation and systemic inflammatory response, being the predictors of infectious complications (pneumonia, sepsis) and multiple organ failure [3, 5, 6, 11]. Understanding this causal relationship implies the necessity and importance of therapeutic measures to suppress opportunistic flora and maintain the normoflora population. Studies of the recent 20-30 years have shown that antibiotics are not suitable for solving this problem, since they uncontrollably suppress the growth of both the pathogens, and also the normoflora components with known consequences. Probiotics, for a number of reasons, also failed to meet the expectations of investigators [7]. The use of bacteriophages, due to their strict species specificity, is limited due to difficulties in determining their targets.

The growing popularity of fecal microbiota transplantation as a means of correcting microbiome impairments is essentially a probiotic therapy with all its disadvantages, but unlike which, for safety reasons, it additionally requires a thorough examination of the donor.

As a result, meta- and prebiotics have remained the safest and most effective means of correcting microbiome impairments to date. However, their disadvantage is that it takes a long time (several days or weeks) to achieve the desired result. In urgent conditions, when the result is needed in the next few hours, their therapeutic effect simply does not have time to manifest itself.

The habitation of microbiota in two different zones (mucosal and cavitary) and its subdivision into two groups by morphological characteristics and functional properties provides a unique opportunity to remove opportunistic pathogenic flora as an integral part of the cavitary one by using the IL. At the same time, the mucosal part, mainly consisting of normoflora components, being tightly lined to the gastrointestinal mucosa, remains intact. Thus, the numerical ratio of microorganisms changes in favor of normoflora during the short time of the IL procedure (within 3 hours); meanwhile, the pharmacological correction of intestinal microbiocenosis impairments, including that with pectovit [10], requires much longer time. It is known that when the competition from antagonistic species is eliminated, microflora is able to quickly restore its population under favorable conditions. Thus, the cavitary lactic acid microflora is restored due to the growth of the mucosal population. After reaching more than a thousand-fold excess over the amount of opportunistic pathogenic flora, the normoflora becomes capable of controlling its growth due to the factors of interspecific antagonism. Under these conditions, as a result of reverse gene rearrangement, the opportunistic flora loses its virulence and invasiveness [3].

Thus, the sanogenic effect of IL associated with the correction of microbiome impairments contributes to a decrease in intestinal translocation and enterogenic endotoxemia and, as a consequence, to a decrease in the incidence of infectious complications in acute poisoning, which we showed earlier [16, 17].

FINDING

1. Severe poisoning with cauterizing agents and psychopharmacological drugs is accompanied by intestinal dysbacteriosis of grade II-II. At the same time, a decreased titer of bifidobacteria in the studied groups is found in 58.3–60%, and that of lactobacilli is found in 33.3-60% of patients with poisoning with cauterizing substances; the corresponding variables for poisoning with psychopharmacological drugs, respectively, range from 50% to 60% and from 66% to 80%. The titer of some opportunistic pathogenic flora representatives exceeding 105 CFU/g is found in 8.3%-33.3% of cases in the studied groups in poisoning with cauterizing agents, and in 5.6%-16.7% of cases of poisoning with psychopharmacological drugs.

2. After intestinal lavage, the baseline titer of Klebsiella spp. decreases twice in cases of poisoning with cauterizing agents, and by 3 times in cases of poisoning with psychopharmacological drugs; other opportunistic pathogenic flora studied (except Proteus spp. in cases of poisoning with psychopharmacological drugs) has not been detected. Meantime, the specific weight of patients who have sustained poisoning with cauterizing agents and psychopharmacological drugs and have reduced titers of bifidobacteria and lactobacilli decreases by 3.5 and 3 times, respectively, the difference being statistically significant compared to the baseline values ($p<0.05$).

3. The standard therapy for poisoning with cauterizing agents and psychopharmacological drugs has a positive effect on the existing impairments of the intestinal microbiocenosis; in most respects its effect is less pronounced than intestinal lavage

REFERENCES

1. Ryabichenko EV, Bondarenko VM. Role of Gut Bacterial Autoflora and Its Endotoxins in Human Pathology. *Journal of Microbiology Epidemiology Immunobiology.* 2007;(3):103–111. (in Russ.)
2. Khristich TN. Kishechnaya mikroflora: rol' v klinicheskom techenii ryada zabolevaniy vnutrennikh organov. *News of Medicine and Pharmacy. Gastroenterology*. 2009; (304). (in Russ.) Available at: http://www.mif-ua.com/archive/article/11027 [Accessed 18 May 2021]
3. Shenderov BA. *Meditsinskaya mikrobnaya ekologiya i funktsional'noe pitanie: in 3 vol*. Vol. I: Mikroflora cheloveka i zhivotnykh i ee funktsii. Moscow: "GRANT" Publ.; 1998. (in Russ.)
4. Beloborodova NV. Integration of Metabolism in Man and His Microbiome in Critical Conditions. *General Reanimatology*. 2012;8(4):42. (In Russ.) https://doi.org/10.15360/1813-9779-2012-4-42
5. Tret'yakov EV, Varganov MV, Nifontova EE. Sovremennyy vzglyad na kishechnuyu translokatsiyu bakteriy kak osnovnuyu prichinu gnoyno-septicheskikh oslozhneniy pri destruktivnom pankreatite. *Advances in current natural sciences.* 2013;(9):78–80. (in Russ.)
6. Leyderman IN, Sentsov VG, Vorontsov SV. Fenomen povyshennoy kishechnoy pronitsaemosti kak proyavlenie sindroma kishechnoy nedostatochnosti (SKN) u bol'nykh s otravleniyami prizhigayushchimi zhidkostyami sredney i tyazheloy stepeni. *Intensivnaya terapiya*. 2008;(2). (in Russ.) Available at: https://icj.ru/journal/number-2-2008/158-fenomen-povyshennoy-kishechnoy-pronicaemosti-kak-proyavlenie-sindroma-kishechnoy-nedostatochnosti-skn-u-bolnyh-s-otravleniyami-prizhigayuschimi-zhidkostyami-sredney-i-tyazheloy-stepeni.html [Accessed 11 Mar 2020]
7. Ardatskaya MD, Chicherin IYu. *Disbakterioz kishechnika. Kakuyu mikrofloru budem zashchishchat' i vosstanavlivat' – svoyu ili chuzhuyu?* (in Russ.) Available at: http://www.disbak.ru/php/content.php?id=4367 [Accessed 11 Mar 2020]
8. Grigor'ev PYa, Yakovenko EP. Narushenie normal'nogo sostava kishechnogo biotsenoza i metody ego korrektsii. *RMJ Suppl Bolezni organov pishchevareniya*. 2004;(2):84–88. (in Russ.)
9. Matkevich VA. *Enteral'naya detoksikatsiya organizma pri ostrykh peroral'nykh otravleniyakh: Dr. med. sci. diss. synopsis.* Saint Petersburg; 2013. (in Russ.) Available at: https://dlib.rsl.ru/viewer/01005531576#?page=28 [Accessed 12 Dec 2020].

10. Badalyan AV, Ilyashenko KK, Vasina TA, Goldfarb YS, Yelkov AN, Luzhnikov YA. Violation of Intestinal Microbiocenosis and its Management During Rehabilitation in Patients with Acute Psychopharmacological Agents Poisonings. *Russian Sklifosovsky Journal Emergency Medical Care*. 2016;(4):32–36. (In Russ.)

11. Bondarenko VM, Gracheva NM, Matsulevich TV. *Disbakteriozy kishechnika u vzroslykh*. Moscow: KmK Scientific Press; 2003. (in Russ.)

12. *Ob utverzhdenii otraslevogo standarta "Protokol vedeniya bol'nykh. Disbakterioz kishechnika": Prikaz Minzdrava RF No 231 ot 9 iyunya 2003 g*. Available at: http://www.disbak.ru/php/content.php?group=615 [Accessed 11 Mar 2020]

13. Matkevich VA, Kiselev VV, Syromyatnikova ED, Grishin AV, Ermolov AS, Luzhnikov EA, et al. *Sposob detoksikatsii organizma*. Patent RF 2190412. Decl. 03.02.2000. Publ. 10.10.2002. Bull. 28. (in Russ.)

14. Matkevich VA. Kishechnyy lavazh – effektivnoe sredstvo korrektsii mikrobiotsenoza kishechnika. In: *Tezisy VI s"ezda nauch. ob-va gastroenterologov Rossii, (Moskva, 1–3 fevr. 2006 g.)*. Moscow: Anakharsis Publ.; 2006. Abs.E.26. (in Russ.)

15. Matkevich VA. Kishechnyy lavazh. In: Luzhnikov E.A. (ed.) *Meditsinskaya toksikologiya*. Moscow: GEOTAR-Media Publ.; 2012.Ch 4: 162–186. (Natsional'nye rukovodstva) (in Russ.).

16. Matkevich VA, Luzhnikov YeA, Ilyashenko KK, Petrov SI, Rozhkov PG. Role of Enteral Detoxification in the Prophylaxis and Treatment of Pneumonia at Acute Poisonings by Psycho-Pharmacological Preparations. *Toxicological Review*. 2012;(3):25–27. (in Russ.)

17. Matkevich VA, Luzhnikov EA, Belova MV, Yevdokimova NV, Syromyatnikova ED, Kurilkin YuA. The Role of Intestinal Translocation in the Origin of Endotoxemia in Acute Poisoning and Detoxification Effect of Intestinal Lavage. *Russian Sklifosovsky Journal Emergency Medical Care.* 2015;(4):16–21. (in Russ.)

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