Intestinal Dysbiosis in Systemic Inflammation and Possibilities of Its Correction with Probiotics

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Authors’ contributions

This work was carried out in collaboration between both authors. Author KG designed the study, managed the analyses of the study, performed the statistical analysis, managed the literature searches and wrote the protocol. Author AD designed the study, read and approved the final manuscript.

ABSTRACT

Aims: To estimate intestinal microbial changes and study the efficacy of probiotic preparations in systemic inflammation.

Study Design: Cohort design.

Place and Duration of Study: Sumy State University, Medical Institute. Department of Microbiology and Clinical Immunology, Kharkiv Medical Academy of Postgraduate Education.

Methodology: The study involved 162 patient with chronic infections various sites, including 58 (35.8%) patients with respiratory tract infections, 56 (34.6%) patients with infections of the genitourinary system, and 48 (29.6%) - with purulent inflammatory postoperative complications. We studied the quantitative and qualitative composition of intestinal microflora on the background correction of probiotic preparations.

Results: We have found quantitative and qualitative changes of intestinal microflora in all patients with chronic infections. Dysbiotic changes manifested in reducing the number of major orders symbionts (Lactobacillus spp., Bilidobacterium spp, Escherichia coli) with normal enzymatic properties) and increase the number of pathogenic microorganisms (Staphylococcus aureus).
Clostridium spp., Candida spp.). In all study groups after using probiotics, the number of pathogenic microorganisms (S. aureus, S. saprophyticus, S. epidermidis, C. albicans, and Cl. perfringens) were decreased and tended to restore normal range of microbial landscape.

**Conclusion:** So, dysbiotic disorders of the intestine in patients with chronic inflammation characterized by decrease in the number of basic gut symbionts and reducing its protective properties that accompanied the advent of pathogenic microorganisms. In our study probiotics demonstrated statistically significant improvements in the qualitative and quantitative composition of microflora.

**Keywords:** Microflora; dysbiotic changes; probiotics; systemic inflammation.

### 1. INTRODUCTION

Gastrointestinal (GI) tract is inhabited by more than 1,000 species of bacteria with total number of more than $10^{14}$ cells at a concentration of $10^7$ to $10^{12}$ cells / g of intestinal contents.

Microbial community, developing together with the host during his lifetime, establishes with him, as a rule, a symbiotic relationship that is favoured by the physiology [1,2]. Intestinal homeostasis can be interpreted as a set of interactions between the host and microbiota colonizing the gut. This set includes motility, secretion, absorption, cellular composition and mitotic activity, the length of villi and crypts depth. It is generally recognized that the intestinal microflora plays an important role in human health and life [1,2]. Commensal flora has important and specific functions in metabolism, nutrition and protection from pathogens. The intestine is the largest immune organ of the human body. Protective bowel functions include three basic components: the intestinal flora, intestinal epithelium and the intestinal immune system. In recent years, it managed to more clearly define the role of microbiota in the formation and regulation of the immune system. Thus, the segmented filament bacteria activate Th17-cells [3], while Clostridium induce regulatory T-cells [4,5]. So, the intestinal microflora helps to preserve the delicate balance between the immunoregulatory (Treg) and proinflammatory (Th17) cells and can modulate the immune status of the adaptive immune response, which ensures the preservation of homeostasis. Invading pathogens can disrupt homeostasis, which leads to an intense immune response, accompanied by an inflammatory response and impaired intestinal barrier. Studies have shown a very low incidence of bacterial translocation, while maintaining a standard amount of obligate anaerobes in the intestine, from which it can be concluded that anaerobic bacteria are the main inhibitors of bacterial overgrowth and translocation of E. coli and other potentially pathogenic bacteria. Disorders of intestinal homeostasis, measured in a changing the qualitative and quantitative composition of the normal flora and, above all, reducing the number of anaerobic bacteria, impaired of the interaction between the microbiome and the host qualifies as dysbiosis, which can reduce the resistance of the intestine to pathogens. Thus, the intestinal flora may be a cause or a consequence of various pathological conditions of humans. In particular, the intestinal microbiota is considered as a possible etiological factor of several metabolic disorders and, at the same time, as an important therapeutic target in several pathological conditions [6].

In recent years, numerous evidence of the relationship of intestinal biocenosis with digestive tract diseases, cardiovascular system, obesity, diabetes, and malignant neoplasms of the stomach, colon, breast cancer, allergic, autoimmune diseases, and others has been received [7,8]. Moreover, the most frequent cause of dysbiotic changes is nutrition and eating habits in the diet. For example, the rich in fats and carbohydrates "western diet", that is usable, ready meals, mitigates host’s immune responses that enhanced of pathogenic and conditionally pathogenic bacteria survival and facilitates the colonization of mucosa [9,10].

The role of intestinal microbiota in the development of diseases has aroused interest to therapeutic use as probiotic agents.

The use of probiotics has been very effective in treating various diseases. For example, probiotics containing bifidobacteria and lactobacilli have proven effectiveness in the treatment of respiratory infections, gastrointestinal diseases and diseases of urogenital system [11]. Probiotics, which include certain strains of lactic acid bacteria cannot only reduce nasal colonization of pathogens
(Staphylococcus aureus, Streptococcus pneumoniae, beta-hemolytic Streptococcus), but also modulate the immune system in the diseases of the upper respiratory tract [12].

Except obligate anaerobes, an important place among the probiotic species occupies facultative anaerobic spore-forming bacteria Bacillus subtilis and licheniformis. These bacteria have a synergistic antagonistic effect of pathogenic organisms, without suppressing the resident one. Probiotics based on them proved to be effective in the treatment of dysbiosis of different degrees of severity and origin, including dysbiosis of infants, yersiniosis, ulcerative colitis, acute intestinal infections in children [2] and others.

Probiotics are useful not only for treatment but also for prevention of various infections [13]. In general, probiotics proved to be quite effective and, most importantly, safe means of restoring lost as a result of the pathological process of intestinal homeostasis [14,15]. At the same time a number of outstanding issues remain. Therefore, in most cases, commercial preparations of probiotics were administered without regard to the quantitative and qualitative changes in the microbial landscape, although it is logical and justified to apply, especially those probiotics that are able to modulate and replace lost or impaired types of normality. The purpose of this study was to analyze changes of the intestinal microbiota in systemic inflammation and the efficacy and safety of combination therapy, including the use of probiotics for the correction of dysbiotic disorders.

2. MATERIALS AND METHODS

2.1 Patients

The study was conducted on an outpatient basis of the Department of Microbiology and Clinical Immunology in Kharkiv Medical Academy of Postgraduate Education (KhMAPE). We examined 162 patients with chronic infections of different localization, not amenable to standard therapy, which were divided into 3 groups:

I (n=58) – Respiratory tract infections (obstructive bronchitis, bronchial asthma, glossitis, chronic tonsillitis, pneumonia) - 58 people;

II (n=56) – Infections of the genitourinary system (cystitis, pyelonephritis, prostatitis) - 56 people;

III (n=48) – Pyoinflammatory postoperative complications - 48 people;

Inclusion criteria were the presence of clinical and laboratory signs of intestinal dysbiosis.

The main symptoms and conditions attributed to intestinal dysbiosis include abdominal pain, bloating, flatulence, diarrhea, constipation, nausea and loss of appetite.

Laboratory analysis of stool has been investigated as marker of dysbiosis. The evaluation of dysbiosis may include comprehensive testing of various aspects of digestion, absorption, microbiology, and metabolic markers.

Microbial fecal analysis of the following components is considered investigational as a diagnostic test form the evaluation of intestinal dysbiosis:

- Levels of Lactobacilli, bifidobacteria, and Escherichia coli and other “potential pathogens,” including Bacillus cereus, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus aureus, Vibrio;
- Identification and quantitation of fecal yeast (including Candida albicans, Candida tropicalis).

Exclusion criteria included a data anamnesis of antibiotics and probiotics for the previous month. All patients were informed about the purpose and research plan and gave a written agreement to participate in the study.

2.2 Fecal Bacteriologic Culture

The study of qualitative and quantitative composition of microflora of the colon was carried out by plating ten-fold dilutions of faeces samples \((10^1 - 10^6)\) on a standard set of selective and differential diagnostic medium for the selection of intestinal microorganisms [16].

The contents of the colon in an amount of 2-3 g was taken to the laboratory and processed within 2 hours in a sterile vial without preservative. Collection of material was carried out before the use of antibiotics and bacterial preparations (probiotics, prebiotics et al.).

Primary inoculation of clinical material was performed quantitative method on nutrient media.
in accordance with the regulations. Ten-fold serial dilutions of each fecal sample were performed and plated on selective and non-selective media for enumeration of the members of the intestinal microflora. Stool samples were placed on solid media (Bismuth Sulphite Agar, EM agar (Levine), Endo Agar, Blood Agar, Baird-Parker Agar, Sabouraud Dextrose Agar, Clostridial Agar, Rogosa SL Agar, Bifidobacterium Agar, HiMedia Lab., India). The plates were incubated at 37 °C for 24 or for 48 h. The incubated microorganisms were then counted and identified with accordance to standard procedures. Summarized data of control group (10 healthy adult's) microflora contents served as a normal standard. During the survey, patients did not take medications with potentially possible effects on the gastrointestinal tract, including antibiotics.

Correction of dysbiotic disorders was carried out by taking into account the individual personified the intestinal flora changes. The structure included cocktail commercial preparations of Probiotic Complex (“Sanegra”, USA); Bifikol (“Biopharma Ukraine”); Laktiale (“Farmak”, Ukraine). All patients received probiotic drugs, depending on their microbial content. Thus, patients with a lack of lactobacilli, bifidobacteria and enterococci in feces samples received “Lactiale” according to the instructions. Due to the composition of preparations, “Probiotic Complex” was administered at reducing the number of bifidobacteria and lactobacilli; “Bifikol” was prescribed in cases with a deficit of E.coli. The scheme of correction was calculated for 1 month of taking probiotics. Clinical and microbiological changes were evaluated before and after correction by probiotics. All bacterial counts (colony-forming units (CFU)/g of wet feces) were transformed to logarithm (log_{10}CFU) for ease of statistical analysis.

2.3 Statistical Analysis

Statistical analysis was performed by using the statistical program «Statistika 10”. Numerical data are presented as “mean value ± standard SD”. Statistical analysis of results were considered significant when p <0.05.

3. RESULTS AND DISCUSSION

Demographic characteristics of the study groups are shown in Table 1. All patients on the basis of medical history and laboratory data were diagnosed with chronic functional or inflammatory bowel disease. Most of them showed signs of intestinal dysbiosis of various degree of severity. Dominated dyspeptic syndrome was also followed by pain and asthenovegetative syndrome.

Despite the clinical differences of presented forms of disease, all patients complained of recurrent pain in different parts of the abdomen, nausea, unstable stool, bloating of various severities. Thus, by the time of the study abdominal pain occurred in 70% of patients, disturbances of stool character presented in 91.9% of patients (diarrhea was predominant in 59.7%, stool retention - in 40.3%), nausea, lack of or reduced appetite in 58%, flatulence - in 85.8% of patients (Table 2). Patients were analyzed for intestinal parasitosis and it has been ruled out as a cause of intestinal symptoms.

Thus, based on the previous studies in institutions, in the group of patients with respiratory infections (Group I), the dominant pathogen of the disease was Staphylococcus aureus; in group with infections of the genitourinary system - E. faecalis and in group with pyoinflammatory postoperative complications - P. aeruginosa.

Microbiological study of all the patients revealed decrease in the concentration of bifidobacteria in fecal samples 3-4 orders of magnitude 5.0 (log_{10}CFU/g) in 77.6% of patients with diseases of the respiratory system, 92.9% - with diseases of urogenital system as well as in 93.8% with postoperative complications. The number of lactobacilli in 80 - 83% of all patients groups also did not exceed 7.0 (log_{10}CFU/g). Assessing patient’s intestinal microbial landscape, it is noteworthy reduction the amount of E. coli with normal enzymatic activity. Thus, in group I in 45 patients (82.7%) its concentration in 1 g of feces did not exceed 5.0 (log_{10}CFU/g); in group II - 16 (29%), in group III - 24 (50%). E. coli with hemolytic activity was not found in all groups.

Additionally, it is worth noting a significant decrease in the concentration of the most important bacteria of the intestinal microflora - Enterococcus. Therefore, in all patients of group I and II the amount of E. faecalis and E. faecium in the colon was not in line with the reference values and became 5.0 (log_{10}CFU/g), but in group III the concentration of enterococci was normal in 36 patients (75%). In 14% of patients in group I and 58% - in group III Candida spp. in the
amount of 4.0-7.0 (log_{10}CFU/g) was detected in stool samples, at maximum permissible concentration of 2.0 ± 0.5 (log_{10}CFU/g).

Thus, changes in colon microflora were to reduce the number of indigenous microflora and its protective properties, which showed the emergence of pathogenic microflora of S. aureus, S. epidermidis, S. saprophyticus, Cl. perfringens, as well as Candida (Tables 3-5). Correction of dysbiotic changes within 1-2 weeks leads almost to the normalization of defecation and complete disappearance of other symptoms of intestinal dyspepsia such as flatulence and abdominal pain.). Repeated microbiological analysis carried out after receiving probiotics showed a statistically significant positive trend in the microbial composition in most patients (Tables 3-5).

So, in patients of all groups, indexes of the indigenous intestinal flora, lactobacilli and bifidobacteria, showed a general tendency to restore their normal amount and concentration of E. coli in 85-92% of patients returned to normal. In addition, all groups showed complete suppression of the number of conditionally pathogenic microflora (S. saprophyticus, S. epidermidis, C. albicans, Cl. perfringens), while the number of S. aureus in group II (7%) and III (6%) became 2.0 (log10CFU/g). None of the patients resulted in side effects of taking probiotics or allergic reactions.

Microbiological study of intestinal contents in patients of all groups showed significant changes in qualitative and quantitative composition of gut flora in patients with chronic inflammatory processes of different localization.

Chronic inflammation is accompanied by a sharp decline in the number of major symbionts of the colon (Bifidobacterium, Lactobacillus, Escherichia coli, and others.), as well as an increase in the number of conditionally pathogenic microflora (S. aureus, S. saprophyticus, S. epidermidis, C. albicans, Cl. perfringens).

The importance of the intestinal microbiome for a healthy body and in diseases is becoming increasingly clear as a result of study of the "body" and its changes in various diseases.

The major microbial community that lives in the gut provides host defense against pathogens, helps digestion and absorption of nutrients and trace elements, the production of vitamins, neutralization of toxins, and the formation of the immune system.

Changes in the composition or the function of the microbial ecosystem called dysbacteriosis have been shown at a plurality of diseases such as atherosclerosis, obesity, metabolic syndrome, allergy, diabetes and inflammatory bowel disease, infections and other diseases [17,18]. At the same time, the intestinal flora of critically ill patient changes considerably as a result of reduced number of obligate anaerobes, Bifidobacterium and Lactobacillus, while the number of Pseudomonas and Staphylococcus increases, and this coincides with our results [19]. According to the researchers, the mechanism of changes in the gut flora in case of serious inflammation is a violation of the intestinal mobility (peristalsis) [8,19]. The newly proposed model assumes that the composition and spatial distribution of intestinal microflora is regulated independently from the damaging inflammation trigger [20]. Inflammation results in a progressive reduction of microbial diversity, transition from >95% of Gram-positive bacteria (Firmicutes) to >95% of Gram-negative bacteria (Proteobacteria) and translocation through the mucosa of such invasive bacteria as adherent-invasive E. coli or Salmonella.

Specific factors associated with inflammation, which cause intestinal dysbiosis, remain unclear. Perhaps the basis of dysbiosis are perturbations in the microenvironment, such as increased accessibility of the substrate for the growth of Gram-negative bacteria (for example, iron and serum, increased number of dead or dying cells) and loss of substrates for Gram-positive flora (for example, the mucus of goblet cells). Genetic susceptibility seems to affect the threshold of dysbiosis in response to an external trigger, as well as the ability to control the self-reinforcing cycle of dysbacteriosis/inflammation. Our studies have shown that probiotics proved to be safe and quite effective correction of dysbiotic disorders associated with chronic inflammation. The use of probiotics resulted in clinically significant results, but the bacteriological changes were not associated with all the important species of bacteria, and not all cases were statistically significant. Probiotics are generally defined as live microbes which, when taken in adequate amounts, confer a health benefit to the person taking them. The criteria for the use of commensal species as probiotics are human origin, acid resistance, and survival during the
transition through the gastrointestinal tract, the lack of pathogenicity, production of antimicrobial substances (bacteriocins), modulation of immune activity [21]. Lactic acid bacteria (lactobacilli and bifidobacteria) are most commonly used as probiotics that do not cause inflammatory reactions. However, other bacteria, including pathogenic E. coli, yeast, especially Saccharomyces boulardii, and multi-view cocktails are also used as probiotics. The number of components of such drinks may be more than 30 species, including Lactobacillus casei, L. plantarum, L. acidophilus, L. delbrueckii subspecies bulgaricus, Bifidobacterium infantis, B. breve, B. longum, and Streptococcus salivarius spp. thermophilus. Fermented dairy products enriched by probiotic bacteria are a good example of functionally oriented products. Annual sales of such beverages in Europe exceed 1.2 bln. euro [22]. The use of probiotics has a major beneficial effect not only on the accompanying dysbiosis, but also on the underlying disease, including critical conditions.

Thus, a 4–8 week course of taking probiotic strain of Lactobacillus GGAT 53103 in case of liver cirrhosis accompanied by hepatic encephalopathy resulted in reduced endotoxemia and normalization of intestinal microbial scenery without any side effects [23]. The use of two probiotic strains of Bifidobacterium breve BR03 and B. breve B632 inhibited production of proinflammatory cytokine TNF-α in children with celiac disease [24]. Probiotic preparation containing Lactobacillus paracasei CRL-431, Bifidobacterium BB-12 and Streptococcus thermophilus TH-4, decreased the number of Clostridium spp. and production of secretory IgA with simultaneous increased content of bifidobacteria and lactobacilli in children with recurrent respiratory tract infections [25].

However, probiotics may interact and have an impact on host gut flora, but it is not limited to the level of the intestine.

Recently, there had been data that intestinal microbiota improves the efficiency, has health-promotion, antifatigue effects on the host and plays an important role in maintaining the balance of energy [Monda obz]. Thus, it was shown that Lactobacillus plantarum TWK10 (LP10), depending on the dose, leads to increase in muscle mass and grip strength, enhanced energy harvesting and exercise performance.

Perhaps lactic acid, which is produced by lactobacilli, can be used by bacteria using lactate to produce butyrate. There was formation of adenosine triphosphate (ATP) along this pathway. Thus, during exercise, probiotics can play a particular role in energy production. In the study, it was shown that the LP10 supplementation by reducing the levels of ammonia, lactate and creatine kinase, had an antiphatique effect and greatly contributed to increasing the efficiency of exercises in mice [26].

Therefore, our research and the study of other authors give grounds to assert that the probiotic preparations are a powerful tool for the normalization of intestinal flora at dysbiosis of various origins and can be added to basic therapy.

### Table 1. Characteristics of the study cohorts (n=162)

| Characteristic         | I group (n=58) | II group (n=56) | III group (n=48) |
|------------------------|---------------|----------------|-----------------|
| Age (year/SD*)        | 31.5±6.3      | 29±8.4         | 37±11.2         |
| Sex n/%                |               |                |                 |
| -Male                  | 26 (45%)      | 17 (30%)       | 22 (46%)        |
| -Female                | 32 (55%)      | 39 (70%)       | 26 (54%)        |

*Mean ± Standard deviation (SD)

### Table 2. Dynamics of clinical symptoms before and after correction of probiotics

| Symptoms               | Before correction (n/M±SD) | After correction (n/M±SD) |
|------------------------|---------------------------|--------------------------|
| Abdominal pain         | 98 (60.4±3.87)            | 41 (25.3±5.3)*           |
| Diarrhea               | 57 (35±4.9)               | 6 (3.7±6)*               |
| Stool retention        | 74 (45.6±4.9)             | 5 (3±7.6)*               |
| Nausea and loss of appetite | 47 (29±6.6)     | 19 (11.7±7.3)*           |
| Flatulence             | 94 (58±3.4)               | 38 (23.4±5.3)*           |

*P = 0.05
Table 3. Fecal flora in patients with respiratory system diseases before and after correction of probiotics (n=58)

| Covariates | Fecal flora before correction (log_{10}CFU) | Patients (n=58) | Fecal flora after correction | Patients | Normal |
|------------|---------------------------------------------|----------------|-----------------------------|----------|--------|
| Bifidobacterium spp. | 5.0 ± 0.6* | 45 | 5.0 ± 0.6 | 9 | 9.6 ± 0.7 |
| Lactobacillus spp. | 5.9 ± 0.8* | 13 | 7.7 ± 1.0 | 49 | |
| E. coli (lac-) | 7.0 ± 0.9 | 13 | 7.0 ± 0.9 | 33 | |
| E. faecalis | 5.0 ± 0.9* | 29 | 5.9 ± 0.8 | 5 | 8.0 ± 1.3 |
| E. faecium | 5.0 ± 0.9* | 29 | 8.0 ± 1.06 | 53 | |
| E. coli Hly | ND | 58 | ND | 58 | ND |
| S. aureus | 5.0 ± 1.9 | 7 | ND | 58 | 2.7 ± 0.8 |
| S. epidermidis | 5.9 ± 2.4 | 6 | 5.0 ± 1.02 | 7.0 ± 0.9 | 24 |
| S. saprophyticus | 4.0 ± 1.4 | 8 | ND | 58 | 4.0 ± 0.6 |
| Candida spp. | 4.0 ± 1.4 | 8 | ND | 58 | 4.0 ± 0.6 |
| E. coli Hly | ND | 50 | ND | 58 | 7.7 ± 1.2 |
| E. faecalis | 4.0 ± 1.4 | 8 | ND | 58 | 7.7 ± 1.2 |
| E. faecium | 4.0 ± 1.9 | 4 | ND | 58 | 7.7 ± 1.2 |
| E. faecium | 7.0 ± 1.9 | 4 | ND | 58 | 7.7 ± 1.2 |
| Cl. perfringens | 5.9 ± 1.9 | 58 | ND | 58 | 2.1 ± 0.7 |

ND- Not detected, SD - Standard deviation
Log_{10} counts/g feces, Data is given as mean ± SD
* P<0.05 versus normal

Table 4. Fecal flora in patients with diseases of urogenital system (n=56)

| Covariates | Fecal flora before correction (log_{10}CFU) | Patients (n=58) | Fecal flora after correction | Patients | Normal |
|------------|---------------------------------------------|----------------|-----------------------------|----------|--------|
| Bifidobacterium spp. | 5.0 ± 0.7 | 52 | 5.0 ± 1.02 | 24 | 9.6 ± 0.7 |
| Lactobacillus spp. | 5.9 ± 1.06 | 4 | 7.0 ± 0.9 | 32 | |
| E. coli (lac-) | 2.0 ± 0.3* | 32 | 2.0 ± 0.3 | 0 | 7.7 ± 1.2 |
| E. faecalis | 5.0 ± 0.7 | 8 | 7.0 ± 1.3 | 28 | |
| E. faecium | 7.0 ± 0.9* | 16 | 5.0 ± 0.9 | 28 | |
| E. coli Hly | ND | 46 | 5.9 ± 1.8 | 8 | 8.0 ± 1.3 |
| S. aureus | ND | 8 | 7.0 ± 1.7 | 16 | |
| S. epidermidis | 8.0 ± 1.4* | 32 | 8.0 ± 1.4 | 32 | |
| S. saprophyticus | 4.0 ± 0.5* | 46 | 5.9 ± 0.9 | 36 | 7.74 ± 1.2 |
| Candida spp. | 7.0 ± 2.2* | 10 | 7.0 ± 1.5 | 20 | |
| E. coli Hly | ND | 28 | 5.0 ± 0.9 | 28 | 7.7 ± 1.2 |
| S. aureus | ND | 20 | 5.9 ± 1.7 | 12 | |
| S. epidermidis | 5.9 ± 1.9* | 8 | 7.0 ± 1.8 | 16 | |
| S. saprophyticus | ND | 56 | ND | 56 | ND |
| Candida spp. | ND | 8 | 2.0 ± 1.9 | 4 | 2.7 ± 0.8 |
| Cl. perfringens | 5.9 ± 0.5 | 8 | ND | 52 | |
| ND- Not detected, SD - Standard deviation
Log_{10} counts/g feces, Data is given as mean ± SD
* P<0.05 versus normal
Table 5. Fecal flora in patients with pyoinflammatory postoperative complications (n=48)

| Covariates          | Fecal flora before correction (log_{10} CFU) | Patients (n=58) | Fecal flora after correction | Patients | Normal |
|---------------------|---------------------------------------------|-----------------|-----------------------------|----------|--------|
| Bifidobacterium     | 5.0 ± 0.7                                   | 45              | 5.0 ± 0.9                   | 24       | 9.6 ± 0.7 |
| spp.                | 7.0 ± 0.9                                   | 3               | 8.0 ± 1.6                   | 24       |
| Lactobacillus spp.  | 5.0 ± 0.7*                                  | 45              | 5.0 ± 0.8                   | 30       | 7.7 ± 1.2 |
| E. coli (lac+)      | 7.0 ± 0.9*                                  | 3               | 7.0 ± 1.7                   | 18       |
| E. faecalis         | 5.0 ± 0.8                                   | 42              | 5.0 ± 0.9                   | 27       | 7.7 ± 1.2 |
| E. faecium          | 7.0 ± 1.4                                   | 6               | 7.7 ± 1.6                   | 21       |
| E. coli Hly         | 7.0 ± 1.2                                   | 36              | 7.7 ± 1.3                   | 36       |
| S. aureus           | 7.0 ± 1.9*                                  | 3               | 2.0 ± 1.6                   | 3        | 2.7 ± 0.8 |
|                    | ND                                          | 45              | ND                          | 45       |
| S. epidermidis      | ND                                          | 48              | ND                          | 48       | 4.0 ± 0.6 |
| S. saprophyticus    | ND                                          | 48              | ND                          | 48       | 4.0 ± 0.6 |
| Candida spp.        | 4.0 ± 0.9                                   | 14              | 2.0 ± 0.4                   | 25       | 2.0 ± 0.5 |
|                    | 5.9 ± 1.6                                   | 14              | ND                          | 23       |
|                    | ND                                          | 20              | ND                          | 20       |
| Cl. perfringens     | 5.9 ± 1.8                                   | 3               | ND                          | 48       | 2.1 ± 0.7 |
|                    | ND                                          | 45              | ND                          | 45       |
| P. aeruginosa       | 5.9 ± 1.8                                   | 3               | ND                          | 48       | 2.8 ± 1.4 |
|                    | ND                                          | 45              | ND                          | 45       |

ND - Not detected, SD - Standard deviation
Log_{10} counts/g feces, Data is given as mean ± SD
* P<0.05 versus normal

4. CONCLUSION

Intestinal disorders in patients with chronic inflammation saw a decrease in the number of colon symbionts and reduction in their protective properties that accompanied the advent of pathogenic microorganisms. Probiotics demonstrated statistically significant improvements in the qualitative and quantitative composition of gut flora.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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