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Research Article

Possibilities of Autoprobiotic Therapy in Patients with Postinfectious Irritable Bowel Syndrome

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Abstract

Interest in the functional pathology of the gastrointestinal tract increased during the late XX century, which was reflected in a number of consensus papers from 1989 to 2016, known as the Roman I, II, III and IV Criteria. According to the Rome IV Criteria, functional intestinal disorders include functional bloating, functional constipation, functional diarrhea, irritable bowel syndrome (IBS).

One of the most common, complex and etiopathologically multifactorial forms of functional intestinal diseases is certainly IBS.

Keywords: *Irritable Bowel Syndrome; Intestine Dysbiosis; Postinfection Irritable Bowel Syndrome; Autoprobiotic*

Introduction

The prevalence of irritable bowel syndrome ranges from 10 to 20% among adult population with a tendency to increase morbidity by 1% per year [3]. The disease most often affects the working age population - the average age of patients is 20 - 40 years, and only half of them seek medical help, apparently because of complaints' sensitive nature.

Particular attention was paid to the postinfection irritable bowel syndrome (PIIBS) due to the peculiarities of this form of the disease: presence of microscopic inflammation in the intestinal mucosa, intestine dysbiosis induced by pathogenic microflora, used antibiotics [4]. According to retrospective and prospective studies, PIIBS develops in 6 - 36% of cases after acute intestinal infection (AII) and represents 6 - 17% of all forms of AII [1]. Pathogenesis of this type of AII can be described as follows: patient's pathogenic microorganisms along with antibacterial therapy lead to changes in the qualitative-quantitative composition of intestinal microflora, which provokes the development of immune disorders and sluggish subclinical inflammation of mucosa. The consequence of such disorders are visceral hypersensitivity and hyperreactivity, non-endocrine dysregulation at intestinal level. At the process's final stage, a pathological functional system including the intestines and brain appears [2].

The idea of clinical application of autoprobiotic therapy was proposed by V.I. Simanenkov and A.N. Suvorov. Personalized symbiote therapy was first tested in the work of Z.R. Sundukova, in which she demonstrated the effectiveness of the method on the example of patients with AII.

In the Department of Therapy and Clinical Pharmacology of the North-Western State Medical University named after I.I. Mechnikov, under the supervision of V.I. Simanenkov, a study was conducted which goal was to study the risk factors of development and to develop a prevention method from post-infection irritable bowel syndrome.

Materials and Methods

The study was in two stages. The first stage's task was to evaluate the outcomes of acute intestinal infections in St. Petersburg. In order to solve this task, 937 patients with virologically and/or bacteriologically verified diagnosis of AII being examined and treated in I.I. Botkin Clinical Infectious Disease Hospital No. 30 in St. Petersburg were analyzed. Then all of them were surveyed over the phone to identify patients with PIIBS. The telephone survey was approved by 435 patients (46%). A total of 502 patients (54%) were not available for the survey due to the following reasons: 280 people (30%) refused to answer the questions due to lack of free time, 222 patients (24%) had unreliable phone numbers in their medical history. Statistical processing of the received data array from 435 patients allowed to determine the frequency of development and to identify PIIBS risk factors among patients who had undergone PIIBS in Saint-Petersburg.

At the study's second stage, efficacy and safety of autoprobiotic therapy in AII patients in terms of PIIBS prevention were determined. At this stage, on the basis of the Department of Acute Intestinal Infections of IAB No. 30 named after V.I. Lenin. At the present stage a group of 88 patients carrying OCT of bacterial etiology was formed in Botkin Clinical Infectious Disease Hospital No. 30 in St. Petersburg and agreed to participate in randomized blind translational study of efficacy of different prevention options. By randomization method, three groups of patients were singled out: the first group - 30 patients who were planned to receive standard therapy with autoprobiotic therapy; the second group - 28 patients who were planned to receive standard therapy with commercial probiotic strain; the third group - 30 patients who were planned to receive standard therapy with placebo.

The commercial strain of enterococci *E. faecium* L-3 was used as a probiotic in the dissertation research. Autoprobiotic represented a lactic acid ferment containing its own strain of *E. faecium* - the gastrointestinal inhabitant of a particular patient. The placebo contained autoclaved milk. The course of placebo/commercial probiotic/autoprobiotic treatment lasted 10 days. Feces were bacteriologically tested before the therapy and three months after it. Patients were surveyed for PIIBS detection 3 and 6 months after the therapy.

Comparison of the PIIBS frequency and the presence of side effects allowed to establish the autoprobiotic therapy's efficacy and safety.

Results and Discussion

The first stage

937 case histories of AII patients were analyzed in total, 489 of them were women and 448 men. The average age of patients was 34.2 ± 2.9 years. According to the results of the survey of 435 patients who could be contacted by phone, 92 (21.1%) patients were identified as having complaints after discharge from hospital. The timing of their occurrence is shown in figure 1. 70 (76,1%) patients had diarrhea, 18 (19,6%) - constipation, 4 (4,3%) - both. 48 (52,2%) out of 92 patients had a periodical abdominal pain. Therefore, based on the data from the survey of patients after hospitalization with infectious gastrointestinal diseases, the diagnosis of PIIBS according to Rome IV Criteria was established in 48 (11%) patients.

By using Mann-Whitney Criterion, the following data was obtained: normalization of body temperature in patients with PIIBS occurs later than in other patients: 6 days vs. 4, $p < 0,001$ (Figure 2). The tendency to more frequent prescription of combined antibacterial therapy to patients with PIIBS was found: the median value of antibiotics quantity in the group with PIIBS was 2, whereas among patients without PIIBS - 1, $p < 0,075$. The duration of hospitalization of patients, who subsequently developed PIIBS, was 12 days, while among other patients the same indicator was 7 days ($p < 0,001$, Figure 3).

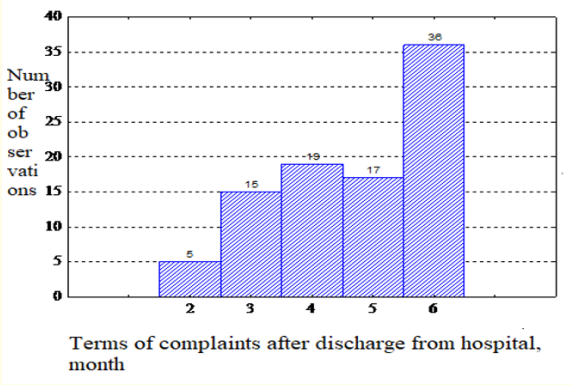

Figure 1: *Distribution of complaints after discharge from hospital by the survey results.*

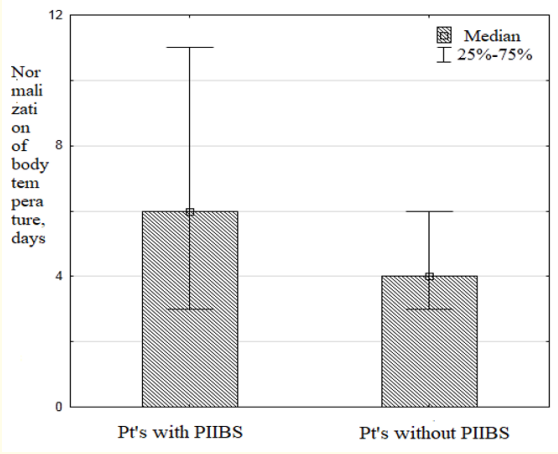

Figure 2: *Terms of body temperature normalization among patients as a function of postinfection irritable bowel syndrome.*

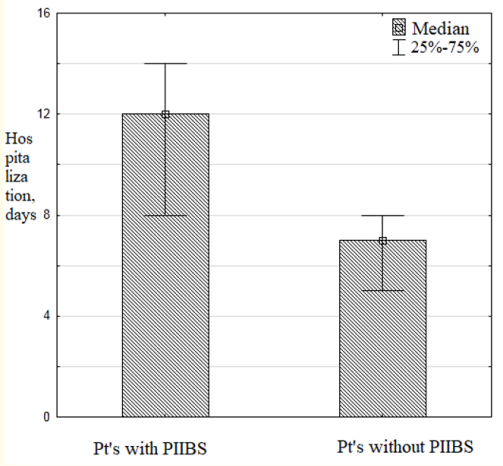

Figure 3: *Term of patients hospitalization, depending on the presence of post-infection irritable bowel syndrome.*

It should be noted that antibiotic treatment of patients with PIIBS started statistically significantly later in comparison with other patients: 3 days after the disease symptoms appeared vs. 2 days, p = 0,031. Late start of therapy may have contributed to the disease aggravation.

The patient's female gender was also associated with a high risk of PIIBS (OR = 2.83, p = 0.001).

By the method of calculating the odds ratio, it was found that the risk of PIIBS development was associated with the bacterial etiology of AII (group D salmonellosis (p = 0.032), bacterial-viral (developed among all patients, p = 0.001).

When analyzing other factors, such as a fever's intensity, presence of impurities in the stool, and age, the data on the indicators difference between patients with PIIBS and other patients was not obtained.

The second stage

In order to compare different methods of PIIBS prevention, 88 patients who had undergone AII were randomized into 3 groups. All patients received standard symptomatic treatment. Besides patients of the first group (30 patients) received autoprobiotic therapy, patients of the second group (28 patients) received probiotic strain *Enterococcus faecium* L-3, patients of the third group (30 patients) received placebo. The average age in all groups was comparable.

In the study's course (before randomization) all patients were proposed to evaluate the severity of a number of clinical symptoms: abdominal pain, flatulence, the nature of intestinal habit according to Bristol Stool Form, appetite and general well-being. The distribution of assessed clinical features was comparable across all clinical groups (Table 1).

Clinical sign	Group 1 (n = 30)	Group 2 (n = 28)	Group 3 (n = 30)	Confidence Ratio (p) when comparing indicators*
Abdominal pain	1 (1 - 2)	1 (1 - 2)	1 (1 - 2)	0,845
Flatulence	0 (0 - 1)	1 (0 - 1)	1 (0 - 1)	0,242
Intestinal habit	5 (4 - 5)	5 (4 - 6)	4 (4 - 5)	0,604
Appetite	1 (1 - 2)	1 (1 - 2)	1 (1 - 2)	0,945
General well-being	1 (1 - 2)	1 (1 - 2)	1 (1 - 2)	0,197

Table 1: *Expression of the disease clinical signs among the examined patients before randomization.*

**: Group comparisons were made using the single factor ANOVA Crucket - Wallis by rank.*

Feces of all patients were bacteriologically examined before randomization. Dysbiosis of the 2nd degree was diagnosed in 52 (59.1%) patients, the 3rd degree - in 36 (40.9%). The expression of the changes was comparable in all clinical groups.

The disease clinical course was repeatedly assessed 10 - 14 days after randomization and prescription of therapy.

In the indicators analysis, less abdominal pain was found in group 1 patients as compared to other patients 10 - 14 days after the randomization. In addition, group 1 patients had less severity of flatulence in comparison with other patients.

After 3 months, patients were again asked to assess the severity of clinical symptoms. 13 patients refused to take further part in the study or were unavailable by phone. The results of the remaining patients are presented in table 3.

Bacteria	Group 1 (n = 30)	Group 2 (n = 28)	Group 3 (n = 30)	Confidence Ratio (p) when comparing indicators*
Lactobacteria	7 (6 - 8)	7 (6 - 7)	7 (7 - 8)	0,107
Bifidobacteria	7 (6 - 8)	7 (6 - 8)	7 (6 - 7)	0,793
Enterococci	4,5 (4 - 5)	4 (4 - 5)	5 (4 - 5)	0,681
Escherichia coli	6 (5 - 7)	6 (5 - 6)	6 (5 - 7)	0,720
Other	1 (0 - 2)	0 (0 - 2)	0 (0 - 2)	0,163

Table 2: *Results of bacteriological study of feces in examined patients before randomization (data are presented as decimal).*

**: Group comparisons were made using the single factor ANOVA Crucket - Wallis by rank.*

Clinical sign	Group 1 (n = 28)	Group 2 (n = 24)	Group 3 (n = 23)	Confidence Ratio (p) when comparing indicators*
Abdominal pain	0 (0 - 0)	0 (0 - 1)	0 (0 - 1)	0,071
Flatulence	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0,071
Intestinal habit	3 (2,5 - 3)	3 (3 - 4)	4 (3 - 4)	0,004
Appetite	1 (1 - 1)	1 (1 - 1,5)	1 (1 - 2)	0,375
General well-being	1 (0 - 1)	1 (1 - 1)	1 (1 - 1)	< 0,001

Table 3: *Subjective severity of the disease clinical signs among the surveyed patients 3 months after randomization.*

**: Group comparisons were made using the single factor ANOVA Crucket - Wallis by rank.*

The presented results show that the majority of patients (in all groups) 3 months after the randomization did not report any abdominal pain or flatulence. However, the difference between the groups in intestinal habit assessment and general well-being remained: group 1 patients had better results in these parameters compared to the rest of the patients.

Feces of patients were bacteriologically examined before and 3 months after randomization and prescription of therapy. The results are presented in table 4 and figure 4.

Bacteria	Group 1 (n = 28)	Group 2 (n = 24)	Group 3 (n = 23)	Confidence Ratio (p) when comparing indicators*
Lactobacteria	7,5 (7 - 8)	7 (7 - 8)	7 (7 - 8)	0,564
Bifidobacteria	9 (9 - 10)	9 (8 - 9)	8 (8 - 9)	< 0,001
Enterococci	6 (6 - 7)	5 (5 - 5,5)	5 (5 - 5)	< 0,001
Escherichia coli	7 (6 - 7)	6 (5 - 6)	5 (5 - 6)	< 0,001
Other	3 (3 - 4)	3 (3 - 3)	2 (1 - 2)	< 0,001

Table 4: *Results of the bacteriological study of feces among the examined patients 3 months after randomization.*

**: Group comparisons were made using the single factor ANOVA Crucket - Wallis by rank.*

The content of *Bifidobacteria, Enterococcus, Escherichia coli* and other bacteria in the feces of patients in group 1 was higher 3 months after randomization than in other patients.

6 months after the randomization, the examined patients were surveyed over the phone on the studied clinical parameters. 7 patients were not available.

Differences between indicators in groups reached the level of statistical significance in assessing overall well-being and pain.

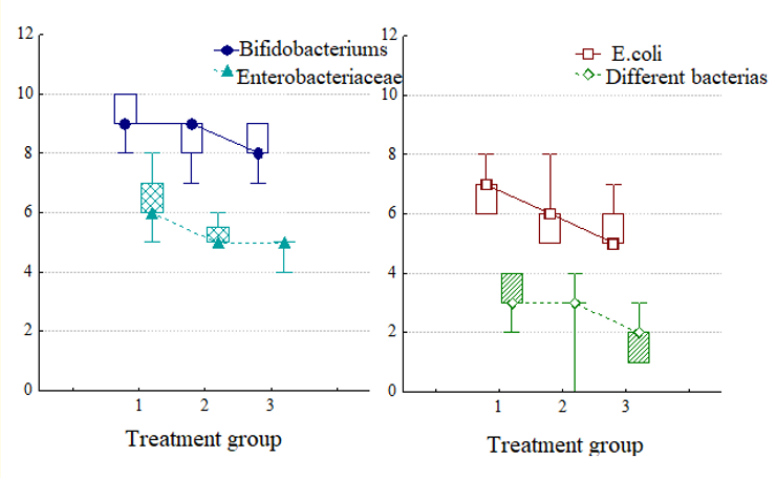

Figure 4: *Content of different bacteria in the feces of the examined patients 3 months after randomization.*

Among the analyzed clinical signs, there were significant differences in abdominal pain intensity (from 10-14 days after randomization) and general well-being (6 months after randomization) (Table 5).

Clinical sign		Patients with PIIBS (n = 15)	Patients without PIIBS (n = 53)	Confidence Ratio (p) when comparing indicators*
Abdominal pain	Before randomization	1 (1 - 1)	1 (1 - 2)	0,783
	After 10 - 14 days	1 (1 - 1)	1 (0 - 1)	0,038
	After 3 months	1 (1 - 1)	0 (0 - 0)	< 0,001
	After 6 months	1 (1 - 1)	0 (0 - 0)	< 0,001
Flatulence	Before randomization	1 (0 - 1)	1 (0 - 1)	0,625
	After 10 - 14 days	0 (0 - 1)	0 (0 - 0)	0,498
	After 3 months	0 (0 - 0)	0 (0 - 0)	0,318
	After 6 months	0 (0 - 0)	0 (0 - 0)	0,060
Intestine habit	Before randomization	5 (4 - 5)	4 (4 - 5)	0,441
	After 10 - 14 days	4 (3 - 5)	4 (3 - 4)	0,597
	After 3 months	3 (3 - 4)	3 (3 - 3)	0,151
	After 6 months	6 (6 - 6)	4 (4 - 4)	0,007
Appetite	Before randomization	1 (1 - 2)	1 (1 - 2)	0,770
	After 10 - 14 days	1 (1 - 2)	1 (1 - 1)	0,513
	After 3 months	1 (1 - 2)	1 (1 - 1)	0,513
	After 6 months	1 (1 - 1)	1 (1 - 1)	0,227
General well-being	Before randomization	1 (1 - 2)	1 (1 - 2)	0,906
	After 10 - 14 days	1 (1 - 1)	1 (1 - 1)	0,832
	After 3 months	1 (1 - 1)	1 (1 - 1)	0,644
	After 6 months	2 (2 - 2)	1 (1 - 1)	< 0,001

Table 5: *Subjective intensity of the disease clinical signs in the examined patients depending on presence of post - infection irritable bowel syndrome.*

**: Group comparisons were made using the single factor ANOVA Crucket - Wallis by rank.*

Patients who developed PIIBS 3 months after randomization had lower content of *Lactobacteria, Bifidobacteria*, *Enterococcus*, *Escherichia coli* and other bacteria in their feces compared to other patients. In addition, a low content of *Lactobacteria* before randomization ($p < 0.05$) was found in patients with developed PIIBS.

After 6 months of patient monitoring, the diagnosis of PIIBS according to the Rome IV Criteria was preserved in 15 out of 68 patients.

The distribution of patients with PIIBS by clinical groups is shown in figure 5.

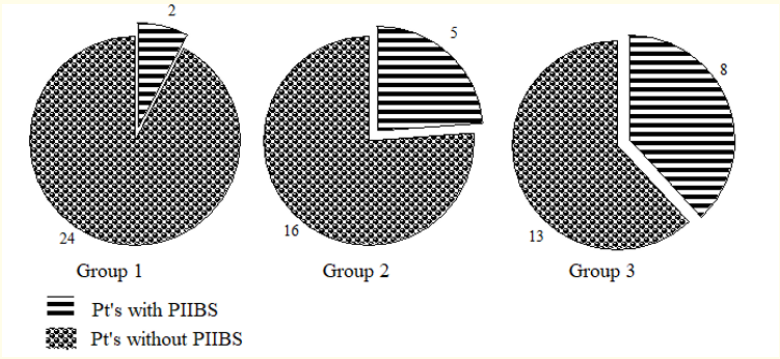

Figure 5: *Distribution of patients according to the presence of postinfection irritable bowel syndrome in different clinical groups.*

From the given data we can see that PIIBS remains less often in group 1. When comparing PIIBS frequency in groups 2 and 3, the changes did not reach the level of statistical significance ($p = 0,099$).

Conclusion

1. Postinfection irritable bowel syndrome develops in 11% of patients who have suffered from acute intestinal infection of medium and severe degree.
2. The most significant risk factors for postinfection irritable bowel syndrome are: a long period of fever, prolonged hospitalization, later initiation of antibacterial treatment, the use of a combination of antibiotics for acute intestinal infection, as well as female gender.
3. The risk of post-infection irritable bowel syndrome development is associated with low number of strains of normal intestinal microflora after acute intestinal infection and antibacterial therapy.
4. Autoprobiotic therapy facilitates faster reduction of acute intestinal infection symptoms and restoration of intestinal normal flora in comparison with therapy with commercial probiotic strain and placebo.
5. Autoprobiotic therapy against the background of symptomatic treatment of acute intestinal infection is associated with a reduced risk of post-infection irritable bowel syndrome in comparison with therapy with commercial probiotic strain and placebo.

Therefore, PIIBS, being one of AII development options, has its own development regularities, preconditions, special pathogenesis factors that should be taken into account when choosing tactics of PIIBS prevention.

Bibliography

1. Ivashkin VT and Sheptulin AA. "Abdominal pain". Moscow, Medpress-Inform (2012): 58.

2. Simanenkov VI and Lutaenko EA. "Diagnostics and therapy of post-infection irritable bowel syndrome". *Consilium Medicum (Gastroenterology)* 2 (2011): 42-48.

3. Mayev IV. "Irritable bowel syndrome". Doctor's handbook. Moscow: Forte-Print (2012): 52.

4. Marshall JK., *et al*. "Postinfectious irritable bowel syndrome after a food-borne outbreak of acute gastroenteritis attributed to a viral pathogen". *Clinical Gastroenterology and Hepatology* 5.4 (2007): 457-460.

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