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THE CLINICAL EFFECTIVENESS OF PROBIOTICS AND AUTOPROBIOTICS IN TREATMENT OF *HELICOBACTER PYLORI*-ASSOCIATED DYSPEPSIA

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Abstract. The aim of our study was to evaluate the clinical performance of a monotherapy by *Enterococcus faecium*-based probiotics and indigenous autoprobiotics against *H. pylori* associated dyspepsia. *Materials and methods.* There were examined 95 patients with dyspepsia. The entire patient cohort underwent clinical evaluation including filling out the questionnaire to assess dyspepsia symptoms before and after treatment, gastric endoscopy as well as gastric multifocal biopsy (gastric body and gastric antrum) and verification of *H. pylori* infection with the three clinical laboratory methods (biochemical, bacteriological and molecular detection). An antagonistic *in vitro* activity of probiotics against *H. pylori* was detected by drop plate method for probiotic strains *Enterococcus faecium* SF68 and *Bifidobacterium bifidum* (Bifiform), *Enterococcus faecium* L3 (Laminolact), and autoprobiotic strains combined with indigenous *Enterococcus faecium*. To examine an antagonistic activity of probiotics and autoprobiotics in clinical trials, we used a starter culture based on the *Enterococcus faecium* L3 strain and an autoprobiotic based on indigenous *Enterococcus faecium*. The probiotic or autoprobiotic were administered orally to patients with gastritis twice a day at dose of 50 ml (8.0 lgCFU/ml) for 20 days. *H. pylori* eradication was assessed by stool antigen test 1.5–2 months after the end of treatment. *Results.* Initially the *H. pylori* infection was confirmed with 49.4% of patients. The sensitivity of *H. pylori* to the probiotics was detected in 81% of individuals for indigenous Enterococci (the autoprobiotic), 76% — for Laminolact, and in 62% — for Bifiform. 22 patients with previous history of allergic reactions to antibiotics used in routine *H. pylori* eradication regimens were divided in two cohorts. One cohort (10 patients) received the autoprobiotic only, another cohort (12 patients) received only probiotic. Monotherapy with autoprobiotic resulted in 100% *H. pylori* eradication, single-agent therapy with probiotic led to 60% eradication of *H. pylori*. Dyspepsia symptoms were completely resolved in both groups of patients. *Conclusion*. Our research demonstrated the sensitivity of examined *H. pylori* strains to be similar for traditional eradication treatment agents (antibiotics) and the proposed intervention agents (probiotics and autoprobiotics). An autoprobiotic monotherapy

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with indigenous enterococci led to higher levels of *H. pylori* eradication than with *E. faecium* L3-based probiotic agent. Our work demonstrated advantage for application of probiotics in patients with antibiotic allergies or other obstacles for the standard eradication therapy. Nonetheless, further investigation to better understand underlying mechanisms of action, as well as larger observational and randomized studies, are necessary to determine the scope of therapeutic application for probiotics and autoprobitics to eradicate *H. pylori* infection.

Key words: *Helicobacter pylori, eradication, probiotics, autoprobiotics, enterococci, Enterococcus faecium.*

ЭФФЕКТИВНОСТЬ ПРОБИОТИКОВ И АУТОПРОБИОТИКОВ В МОНОТЕРАПИИ ДИСПЕПСИИ, АССОЦИИРОВАННОЙ С ИНФЕКЦИЕЙ *HELICOBACTER PYLORI*

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Резюме. Цель исследования: оценка эффективности пробиотиков на основе энтерококков и индигенных энтерококков (аутопробиотиков) в монотерапии диспепсии, ассоциированной с *Helicobacter pylori. Материалы и методы.* Мы провели обследование 95 пациентов, страдающих диспепсией. Обследование включало в себя опрос для оценки жалоб до и после лечения, фиброгастродуоденоскопию (ФГДС) с взятием биоптатов из тела и антрального отдела желудка для верификации инфекции *H. pylori* (биохимический, бактериологический и молекулярно-генетический метод). Для исследования антагонистической активности капельным методом в системе *in vitro* использовали пробиотики бифиформ (*Enterococcus faecium* SF68 и *Bifidobacterium bifidum*) и ламинолакт (*Enterococcus faecium* L3), аутопробиотик на основе индигенного *Enterococcus faecium*. Для исследования антагонистической активности *in vivo* использовали пробиотическую закваску на основе штамма *Enterococcus faecium* L3 и аутопробиотик на основе индигенного *Enterococcus faecium* (патент РФ № 2546253). Препараты назначали *per os* дважды в день по 50 мл (8,0 lgKOE/мл) на 20 дней. Контроль эрадикации проводился с использованием определения антигена микроорганизма в кале через 1.5–2 месяца после окончания лечения. *Результаты.* Инфекция *H. pylori* была выявлена у 49,4% пациентов. Определена чувствительность изолятов микроорганизма к индигенным энтерококкам (аутопробиотику) в 81%, ламинолакту — 76% и бифиформу — 62% случаев. Часть обследованных получала в качестве монотерапии пробиотик или аутопробиотик (пациенты с указанием в анамнезе на аллергические реакции на прием антибиотиков, используемых в схемах стандартной эрадикационной терапии). При использовании аутопробиотика элиминация возбудителя составила 100%, при использовании пробиотика — 60%. Купирование симптомов диспепсии было полным как при приеме пробиотика, так и аутопробиотика. *Заключение.* Чувствительность исследуемых штаммов *H. pylori* к аутопробиотику и пробиотикам сравнима с чувствительностью микроорганизма к часто используемым в схемах эрадикации антибиотикам. Монотерапия аутопробиотиком на основе индигенных энтерококков показала более высокий процент элиминации возбудителя, чем применение закваски на основе штамма *E. faecium* L3. В случае невозможности использования стандартной антихеликобактерной терапии назначение как пробиотиков, так и аутопробиотиков является обоснованным. Однако необходимы дальнейшие исследования для расширения доказательной базы оценки эффективности препаратов на основе энтерококков в эрадикации *H. pylori.*

Ключевые слова: *Helicobacter pylori, эрадикация, пробиотики, аутопробиотики, энтерококки, Enterococcus faecium.*

Introduction

Since the discovery of the role of *Helicobacter pylori* infection in the development of various diseases, particularly peptic ulcer and chronic gastritis, there has been a continuous search for improved methods of eradication of this microorganism. One potential way to improve anti-*H. pylori* treatment regimens is to include probiotics — medications (live microorganisms) that are used to improve the gut microbiota. An emerging need for new treatment agents for *H. pylori* eradication is growing in importance on the grounds of: 1) a decrease in the effectiveness of standard anti-*H. pylori* therapy due to an increase in *H. pylori* resistance to antibiotics, 2) side effects of proton pump inhibitors and antibacterial drugs, 3) reluctance of patients to take antibiotics [7]. Both international and Russian treatment guidelines allow for the use

of probiotics. Both the fourth and fifth editions of the Maastricht Consensus Report state that some probiotics and prebiotics may be an effective supplement to standard eradication therapy [16, 17]. The clinical guidelines of the Russian Gastroenterological Association on the treatment of *H. pylori* infection in adults state that including probiotics in anti-*H. pylori* therapy improves therapy success and reduces the incidence of adverse events, namely remove the risk of *C. difficile*-associated diarrhea [2]. The VI Moscow Consensus of the Gastroenterological Scientific Society of Russia on the management of patients infected with *H. pylori* also emphasized that anti-*H. pylori* treatment is most effective and safe when supplemented with prebiotics or probiotics [3].

A number of meta-analyses demonstrated that the use of probiotics in addition to standard anti-*H. pylori* therapy improves both the effectiveness of eradication and reduces the frequency of side effects [15, 18, 20, 22, 24].

In addition, reduction of the side effects incidence of standard eradication therapy, some probiotics may have an antagonistic effect on *H. pylori* by inhibiting the growth of the microorganism. The undelying mechanism of descibed inhibition might be driven by producing antimicrobial products (bacteriocins, lactic acid, hydrogen peroxide and other) or by competing for survival (through colonization resistance) [6]. This prompted studies to evaluate the effectiveness of probiotic monotherapy in the treatment of *H. pylori* infection. This kind of therapy can be recommended for people who have allergic reactions to antibiotics, who are non-compliant to antibiotic therapies, as well as for family members of patients infected with *H. pylori*.

There are many of both Russian and foreign studies confirming the promising positive results of using probiotics monotherapy to eradicate *H. pylori*, with efficacy varying from 6 to 48% [6, 9, 10, 11, 13, 14, 19]. Probiotics are an emerging promising solution not only due to their ability to inhibit the growth of pathogenic microorganisms, but also because they are effective in restoring the composition of the gastrointestinal tract microbiota, as well as have a positive effect on the human immune system, mucus formation, and motility of the gastrointestinal tract [6].

However, the use of probiotics monotherapy, despite their high safety, also has its disadvantages: a relatively low eradication rate and a long course of treatment (1 month or more). The use of probiotic strains may not have a sufficiently significant antagonistic effect on *H. pylori* and a pronounced positive effect on the gastrointestinal microbiota, because they transit through the small intestine and colon. Moreover, it remains unclear how to choose a suitable probiotic for each individual.

Autoprobiotics, strains of normal microbiota isolated from a particular individual and designed to correct human microecology, are an innovative way to increase the effectiveness of eradication without producing negative effects on the microbiota. Autoprobiotics stay in the colon longer, which allows to reduce the time of treatment. Autoprobiotics prepared from native (indigenous) lactobacilli, bifidobacteria, or enterococci may become the drugs of choice, since immunological tolerance to them is formed from the first years of life, and they do not come into conflict with other the resident microbiota of the human body [21]. There already are studies showing the effectiveness of autoprobiotics based on indigenous strains of *Lactobacillus* spp. in the restoration and stabilization of the content of the main representatives of the normal gut microbiota (*Bifidobacterium* spp., *Lactobacillus* spp. and autoprobiotics based on *E. coli*) in treating dysbiotic disorders caused by the use of antibacterial drugs [1, 8], as well as indigenous strains of *Enterococcus* spp. in the treatment of intestinal pathology and neurological diseases [12].

The aim of our study was to evaluate the clinical performance of a monotherapy by probiotics and autoprobiotic *Enterococcus faecium* for *H. pylori* associated dyspepsia. We also evaluated gastric microbiota characteristics in the absence and in the presence of this microorganism.

Materials and methods

We examined 95 patients suffering from dyspepsia. Prior to commencing the study, all patients signed an informed consent to a comprehensive medical examination. The following groups were not included in the study: people who had received a course of eradication therapy within the previous two years, people who had taken antibiotics, proton pump inhibitors (PPIs), antacids, or bismuth containing drugs within the previous two weeks, as well as people with severe physical illnesses (including oncologic ailments) and/or infectious pathologies, pregnant and breastfeeding women.

The comprehensive examination prior to treatment included: survey to evaluate complaints (epigastric pain and signs of dyspepsia), gastroendoscopy, which included biopsies from gastric antrum and body to confirm *H. pylori* infection, and gastric microbiota analysis. The closing examination following the full treatment included an survey to evaluate complaints and collection of fecal samples to perform immunochromatographic stool tests for the detection of *H. pylori*.

Confirmation of Helicobacter pylori infection. Biochemical, bacteriological, immunological and genetic methods were used to confirm the presence of a pathogenic microorganism in the gastric mucosa. The result was considered positive when the infection was detected by all methods or by any one ofest the methods. The effectiveness of eradication was evaluated by determining the *H. pylori* antigen in feces.

Rapid urease test. We used the AMA RUT Expert test system to evaluate the urease activity of bacteria in the biopsy specimen and the AMA RUT Reader (AMA, Russia) for detection and record keeping. The AMA RUT Expert indicator is a test-slide with a well containing a reactive element sealed with a film. The slide has special marking on it, ensuring that the test results can be processed automatically.

Bacteriological method. Pure culture of the pathogen was isolated from biopsy specimens of gastric mucosa for each participant individually. Incubation protocol for *H. pylori* isolation microaerophilic conditions at 37°C for 5 days on the surface of a special culture medium (Columbia agar with 10% horse serum and 1% IsoVitalex, bioMerieux, France). The number of viable bacteria (CFU/g) was determined by plating corresponding 10-fold serial dilutions of biopsy specimens. Antimicrobial susceptibility testing performed with the disc-diffusion method, sensitivity to probiotics was determined by the drop plate method and the two-layer agar method. The bacteriological method is the gold standard in the diagnosis of helicobacteriosis, as it does not give false positive results, is specific and informative. Application of bacteriological method allowed our team to confirm that *H. pylori* was present in the sample, as well as to determine its sensitivity to antibiotics, probiotics, and autoprobiotics.

In addition to detecting *H. pylori* infection, we also performed a comparative analysis of gastric microbiota in the presence and in the absence of *H. pylori*. The viable bacteria count (CFU/g) in gastric biopsy specimens was determined by plating corresponding tenfold serial dilutions of suspensions on a number of selective dense culture media in Petri dishes and counting the bacterial colonies after incubation (24 hours) at 37°C. To determine the count of several genera of microorganisms such as *E. coli*, *Enterococcus* spp., *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp. at the same time, we used the following chromogenic selective media: Pronadisa 1424 (Spain), HiCrome Coliform Agar (India). The lactobacilli count was determined by plating the culture on the Pronadisa 1043 Agar MRS medium (Spain) and culturing in anaerobic jars with gas generating sachets (Thermo Scientific AN0025A (USA)) at 37°C for 48 hours.

Polymerase chain reaction. PCR was used to detect the *cagA* and the *vacA* genes and thereby detect *H. pylori* in the biopsy specimens. This method was chosen because it is highly precise and informative. Moreover, features of the gastric microbiota were determined by molecular genetic study (real-time PCR) using the Colonoflor test system and 16S rRNA metagenomic analysis.

Quantitative polymerase chain reaction. Quantitative polymerase chain reaction (qPCR) was performed using the kit Colonoflor 16 ("AlphaLab", Russia) corresponding to the set of marker colonic bacteria on the qPCR unit Mini-Opticon, BioRad. qPCR data on certain bacterial species were confirmed by classical bacteriology study.

Immune chromatographic test. The effect of probiotics and autoprobiotics used alone against *H. pylori* was evaluated by a non-invasive stool antigen test 1.5–2 months after treatment completion. Antigen determination in feces was carried out using the H&R *H. pylori* Vegal Farmaceutica S.L. test system, Spain.

Probiotic medication used for intervention. We used the probiotic autoprobiotic strains: *Enterococcus faecium* SF68 and *Bifidobacterium bifidum* (Bifiform, Ferrosan, Denmark) and (*Enterococcus faecium* L3 (Laminolact, "Avena", Russia) to study antagonistic activity *in vitro*. Antagonistic activity was determined using the drop plate method. The investigated probiotics were diluted in distilled water at a ratio of 1:100 and then added to a dish with agar on which the *H. pylori* strain was plated. Growth was assessed on day 6–7.

We used a starter culture based on the *Enterococcus faecium* L3 strain to study the antagonistic activity *in vivo*. This strain was isolated from fermented milk, deposited in GenBank (No SUB167269, 2 629 318 base pairs, contains 2717 genes) and in the collection of the All-Russia Research Institute for Agricultural Microbiology, ND-79, patent in Russia No 2220199. Genes encoding the synthesis of several bacteriocins (including enterocins A, B, Enx α, and Enx β) were found in the genome of this strain. The probiotics were administered for 20 days. The probiotic was administered *per os* twice a day at doses of 50 ml (8.0 lgCFU/ml).

Autoprobiotics maiking. Autoprobiotics were obtained as described in Russian patent No. 2546253 [5]: at least 1 ml fecal samples were collected from patients who had not taken antibiotics and/or probiotics for at least 10 days prior to collection; clones of indigenous strains of *Enterococcus faecium* were isolated from the samples using a culture medium containing sodium azide and crystal violet dye; then, colonies were selected based on the coloring; pure cultures were obtained by plating three pink-colored colonies with a burgundy center onto three sectors of Petri dishes with the same medium and incubated in a thermostat under aerobic conditions at t = 37°C, and tested by PCR for absence of genes of pathogenicity; then, non-pathogenic clones were selected and cultured in a soy hydrolysate at no less than 10 ml per liter.

The 5% culture medium was prepared by diluting a lactose-free dry protein-vitamin mixture "Super LF" (SLF) in a small amount of distilled water heated to 40° C in a ratio of 1:1 until a homogeneous suspension was obtained. The resulting suspension was filtered through 4 layers of medical gauze and diluted with the remaining amount of distilled water (DW). The ratio of components by weight in the final suspension should be: DW:SLF = 95.5. The resulting suspension was dispensed into 1–2 L plastic bottles and autoclaved at 120° C and 1.2 atm for 15–30 minutes, then cooled to a temperature of 40°C.

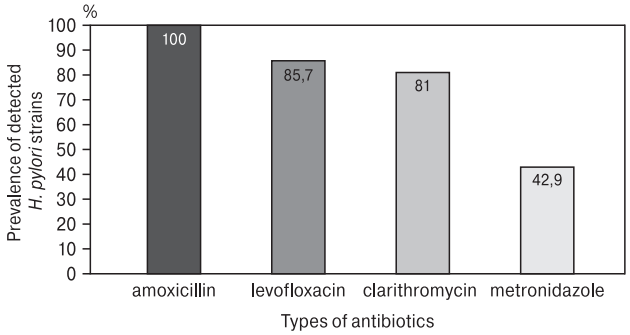

Figure 1. Prevalence of detected of *H. pylori* strains sensitive to antibacterial drugs

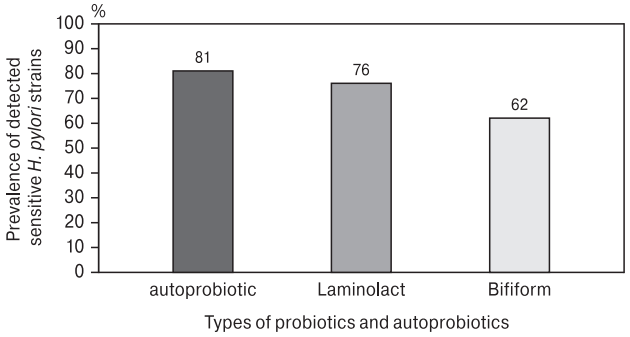

Figure 2. Prevalence of detected *H. pylori* strains sensitive to probiotics and autoprobiotics

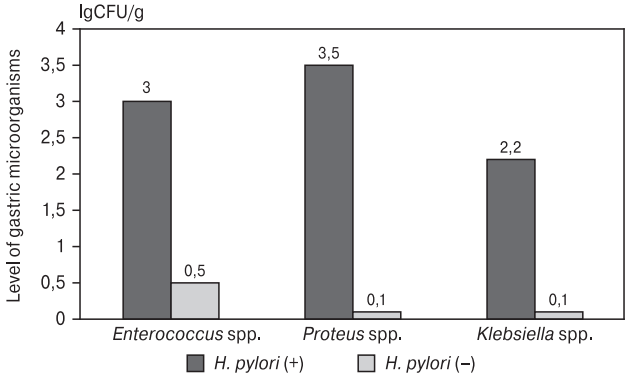

Figure 3. Quantitative level of various opportunistic bacteria in gastric biopsy specimens from patients with positive and negative *H. pylori*-status

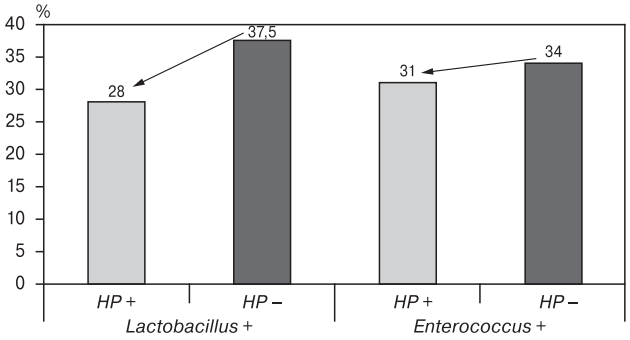

Figure 4. Prevalence of detected gastric *H. pylori* in patients with dyspepsia with isolated lactobacilli and enterococci

Seed doses were prepared by aseptically taking 50 mg of lyophilized starter culture and inoculating it with 2 ml of 5% culture medium cooled to 40°C. They were then cultivated in an aerobical condition for 14–16 hours at 37°C. The grown cell culture was transferred into 300 ml of sterile 5% culture medium cooled to 40°C and incubated in a dry-air thermostat for 14–16 hours at 37°C. The resulting biomass was used as a seeding dose for 1–2 L of culture medium. The starter culture which changed the structure of hydrolysate earlier than others was selected and used to prepare two liters of individual autoprobiotic product containing at least 108 CFU per 1 ml, which was administered to the patient orally at a dose of 50 ml 2 times a day for at least 20 days.

Methods of statistical analysis of study results. Statistical processing of the results was carried out using Statistica 10 for Windows (StatSoft, USA). Nonparametric pairwise multiple-comparison was used to evaluate the effectiveness of diagnostic methods and treatments. A p-value < 0.05 was considered statistically significant.

Results

Using various diagnostic methods, *H. pylori* infection was detected in 47 out of the 95 patients, or in 49.4% of the patients. The bacteriological method produced 21 positive results.

Evaluation of sensitivity of clinical isolates of Helicobacter pylori to antibiotics. We analyzed the sensitivity of the 21 isolated strains of *H. pylori* to the four antibacterial drugs most commonly used in the eradication therapy of *H. pylori*-associated diseases (Fig. 1).

The chart shows that the sensitivity to amoxicillin is the highest and reaches 100%, while sensitivity to metronidazole is half as high, with sensitivity to levofloxacin and clarithromycin falling between these two values. The data obtained are similar to the results of previous studies also conducted in St. Petersburg [4], which indicates a stable level of resistance of the pathogen to the antibacterial agents traditionally used in this region.

Evaluation of isolates of Helicobacter pylori isolates sensitivity to probiotics and autoprobiotics. The bacteriological (cultural) method also allowed to determine the sensitivity to probiotic and indigenous (autoprobiotic) strains of enterococci isolated from the fecal samples of patients prior to eradication therapy. According to the chart (Fig. 2), the highest number of clinical isolates were sensitive to indigenous enterococci (the autoprobiotic).

H. pylori sensitivity to antibiotics and probiotics allows for personalized treatment of *H. pylori*-associated dyspepsia. Such an individualized approach makes it possible to select the most effective means for both adjuvant therapy and monotherapy (if necessary).

Gastric microbiocenosis assessment in the presence or absence of Helicobacter pylori. We performed a comparative analysis of the gastric microbiota from 22 patients, 10 with positive *H. pylori*-status and 12 with negative *H. pylori*-status. The gastric microbiota of the patients from these two groups differed significantly (Fig. 3).

The chart demonstrates that bacteria from the genera Proteus, Klebsiella and Enterobacter were found only in samples collected from patients infected with *H. pylori*. We found no statistically significant correlation between the presence of *H. pylori* and *Fusobacterium* spp., *Faecalibacterium prausnitzii* and *Bacteroides fragilis, B. thetaiotaomicron, Bifidobacterium* spp.

It should be noted that when lactobacilli and enterococci were detected in the gastric samples at a concentration greater than 3 lgCFU/mL, the probability of detecting *H. pylori* was lower (Fig. 4).

Consequently, as demonstrated on Fig. 3 and Fig. 4, we observe an increased presence of opportunistic pathogen belonging to the *Enterobacteriaceae* family combined with concurrent regress in numbers of colonies of enterococci and lactobacilli (non-pathogenic microorganism) in *H. pylori*-positive patients. We suggest that observed imbalance in gastric microbiota can be attributed as an underlying cause for development of symptoms of dyspepsia and following *H. pylori*-associated diseases.

Gut microbiome study by qPCR. The study was performed by comparing the following microorgamnisms (the quantitative content of representatives of the intestinal microbiota): the total number of bacteria, *Acinetobacter* spp., *Citrobacter* spp., *Escherichia coli* and enteropathogenic *E. coli, Proteus* spp., *Lactobacillus* spp., *Bifidobacterium* spp., *Bacteroides thetaiotaomicron, Bacteroides fragilis group, Clostridium difficile, Clostridium perfringens, Enterococcus* spp., *Faecalibacterium prausnitzii, Fusobacterium nucleatum* and *Parvimonas micra*.

Changes in the microbiota before and after therapy had no significant differences in patients receiving probiotics and autoprobiotics. When considering the composition of the microbiota before and after therapy of all patients, it was shown that the quantitative content of *Ruminococcus, Metanobrevibacterium, Roseburia, Eubacterium, Blautia, Enterococcus* increased. The populations of *Prevotella, Streptococcus, Salmonella, Parvimonas Fusobacterium, Citrobacter, Klebsiella, Enterobacter, Bacteroides theiotaomicron* on the contrary decreased (Fig. 5).

Assessment of the clinical impact in treatment of H. pylori infection. Within the main group of patients, we distinguished a separate cohort of 11 patients who previously had recorded allergic reactions to antibiotics that are used in standard eradication treatment regimens. This cohort was divided into two subgroups: one received probiotic alone (5 patients) and the other received solely autoprobiotic therapy

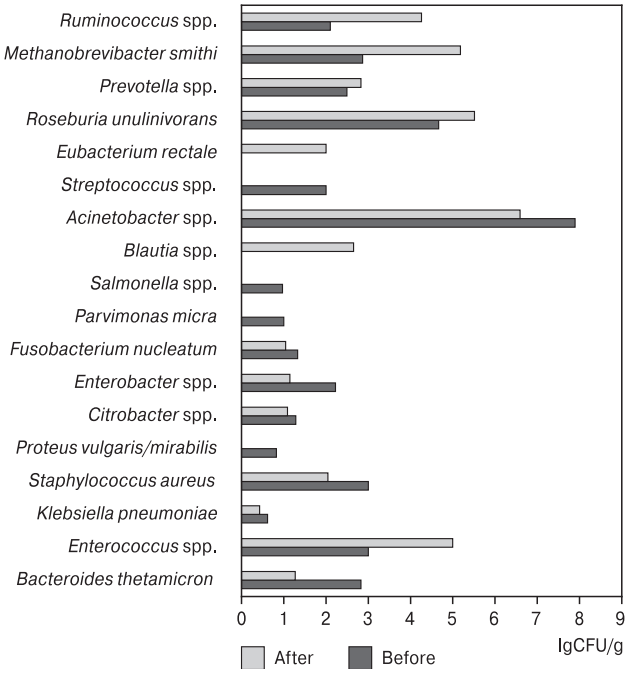

Figure 5. Gut microbiota profile before and after autoprobiotic- and probiotic-therapy of *H. pylori*+ gastritis

(6 patients). The summarized results for clinical efficacy in relieving the symptoms of dyspepsia and the anti-*Helicobacter* activity of these drugs is demonstrated in Tables 1 and 2.

According to questionnaire assessment symptoms of dyspepsia were completely eliminated after treatment with autoprobiotic and probiotic. The use of autoprobiotics based on indigenous enterococci alone is more effective in eradicating *H. pylori* than the use of a starter culture based on the *E. faecium* L3 strain.

Discussion

The prerequisite for this study were problems with the use of antibiotics, such as insufficient efficacy and side effects (diarrhea, nausea, bloating, allergic reactions etc.). In this study, for the first time,

Table 1. Evaluation of the clinical effectiveness for autoprobiotics and probiotics in reversing symptoms in patients with *Helicobacter pylori*-associated dyspepsia

Symptom, frequency in %	Autoprobiotic		Probiotic	
	Before treatment	After treatment	Before treatment	After treatment
Eructation	33	0	60	0
Heartburn	50	0	60	0
Epigastric pain	100	0	100	0
Bloating	67	0	80	0
Nausea	17	0	40	0

Table 2. Evaluation of the clinical effectiveness of autoprobiotics and probiotics in *Helicobacter pylori* eradication

Parameters	Autoprobiotic (n = 10)	Probiotic (n = 12)
Effectiveness of anti-*Helicobacter* action: number of *H. pylori*-negative samples based on stool antigen test (immunochromatographic method), % (n)	83 (5)	60 (2)

the possibility of using autoprobiotics in monotherapy of *H. pylori*-associated dyspepsia is considered.

The choice of the type of autoprobiotic was associated with the high efficiency of autoprobiotic enterococci in the correction of gut dysbiosis, therapy of irritable bowel syndrome and metabolic syndrome. In addition, this study has already revealed an inverse correlation between the presence of enterococci in stomach biopsies and enterococcus and lactobacilli.

It is not surprising that when correcting the microbiota of the gastrointestinal tract with the help of indigenous enterococci isolated from the patient's feces, the elimination of the pathogen and the disappearance of dyspeptic symptoms were observed. Previously, such effects were described with the introduction of several probiotics, among which some of the most effective were based on *Enterococcus faecium* [21].

In vitro studies have demonstrated a high sensitivity of *H. pylori* to probiotics based on enterococci, including autoprobiotic, comparable to sensitivity to antibiotics. As it was shown earlier, the effect of probiotics is associated with the production of enterocins [6].

The intake of the functional food product containing *E. faecium* L3 and the autoprobiotic starter culture containing *E. faecium* have many positive effects: the disappearance of pain syndrome, heartburn, belching, flatulence, apparently due to the normalization of the composition of the gut microbiota and *H. pylori* eradication.

The use of autoprobiotics did not reveal significant differences in the composition of the gut microbiota after administration of probiotic *E. faecium* L3. The advantage of autoprobiotic can be the duration of the effect of autoprobiotics, established earlier [12].

Conclusion

For the investigated *H. pylori* strains the sensitivity is similar to both antibiotics used in standard eradication protocols and probiotics. The sensitivity of *H. pylori* to autoprobiotics based on indigenous enterococci is slightly higher than to probiotics. Treatment regimen with an autoprobiotic based on indigenous enterococci alone showed a higher eradication rate compared to a starter culture based on the *E. faecium* L3 strain. It is reasonable to include both probiotics and autoprobiotics in comprehensive eradication regimens due to dysbiotic changes of gastric microbiota in patients with dyspepsia and persisting *H. pylori* infection. When standard anti-helicobacter therapy cannot be used, autoprobiotics should be used as the preferred treatment. Enterococci-based drugs are the most promising for further research into the anti-*Helicobacter* effect of probiotics and autoprobiotics.

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