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**EFFICIENCY AND SAFETY OF SILICEOUS ENTEROSORBENTS IN  
THE THERAPY OF *HELICOBACTER PYLORI*-ASSOCIATED DISEASES  
OF THE UPPER GASTROINTESTINAL TRACT**

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ORIGINAL ARTICLE

# Efficiency and safety of siliceous enterosorbents in the therapy of *Helicobacter pylori*-associated diseases of the upper gastrointestinal tract

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## ABSTRACT

**BACKGROUND:** Due to prevalence of *Helicobacter pylori* (*H. pylori*) infection, treatment of patients with *H. pylori* - associated diseases of the upper gastrointestinal tract (GIT) is an important medical problem. However, eradication therapy carried out in such patients is not always effective, as on its background side effects often appear. In this regard, the development of alternative treatment regimens using drugs with antimicrobial activity and the ability to bind and excrete metabolites, toxins and other harmful substances is relevant.

**METHODS:** Thirty patients with a mean age 45.6±10.5 years were included in the study. Patients in the study group received enterosorbent (polymethylsiloxane polyhydrate) for three weeks, in the control group eradication therapy for seven days. In all the patients before and after treatment, standardized complaint questionnaire and GSRs questionnaire, fiberoptic gastroduodenoscopy and urease test were used to evaluate the therapy efficiency.

**RESULTS:** On administration of Enterosgel®, significant positive clinical dynamics was revealed regarding gastric and intestinal dyspepsia, similar to the observed dynamics in the group of patients treated with standard eradication therapy. When analyzing fiberoptic gastroduodenoscopy data after treatment, all the patients experienced improvement of endoscopic view of the upper GIT. Against the background of the therapy, in most patients contamination dissemination of the antrum with *H. pylori* decreased. The results showed promising use of Enterosgel® for the treatment of patients with *H. pylori* - associated gastroduodenitis.

**CONCLUSIONS:** We consider it promising to continue clinical trials of Enterosgel® as a part of standard eradication therapy of *H. pylori* - associated diseases of the upper GIT, in order to optimize the eradication schemes.

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**Key words:** Enterosorption - Polymethylsiloxane - *Helicobacter pylori* - Respiratory tract diseases.

In the late XX century, when Australian scientists B. Marshall and R. Warren described an isolated and cultured microorganism later called *Helicobacter pylori* (*H. pylori*), it was an earth shaker of view of the nature of upper

gastrointestinal tract (GIT) chronic inflammatory diseases.<sup>1</sup> Currently *H. pylori* is regarded as the leading causative agent of peptic ulcer, chronic gastritis, gastric cancer and gastric lymphoma.<sup>2</sup> The total world population con-

tamination is about 60%. Its level in Russia ranges from 40 to 90%. In connection with all the above said, treatment of patients with *H. pylori* - associated diseases of the upper GIT is an important medical problem. The introduction of *H. pylori* eradication therapy of gastroduodenal lesions into clinical practice, including a proton pump inhibitor (PPI) in combination with two or three antimicrobials, is common, reasonable and effective enough, and leads to an improvement in quality of life, reduction of exacerbations and disease relapses. However, in quite a large number of patients treated, it was of low efficiency or it caused side effects such as diarrhea, flatulence, nausea, bitter or metallic taste in the mouth, which reduce compliance and compel the specialists to refuse the conventional therapy. Moreover, there are certain patient categories in which conventional helicobacter therapy is contraindicated. Inefficiency of *H. pylori* therapy is associated with both individual features of the patient and the type of infection agent.<sup>3, 4</sup> An important point in unsuccessful eradication is the development of resistance to antibiotics used in treatment regimens.<sup>5</sup> Resistance to clarithromycin, the key antibacterial drugs therapy of *H. pylori*, continues increasing: in some regions it is 20%. Resistance of *H. pylori* to metronidazole in certain countries<sup>6</sup> varies from 60 to 80%. A certain decrease in sensitivity of the microorganisms to fluoroquinolone drugs has been also noted.<sup>7</sup> In this regard, the development of alternative treatments is interesting, including drugs with antimicrobial activity and the ability to bind and excrete metabolites, toxins and other harmful substances, without being absorbed in the GIT.<sup>8, 9</sup> One of these drugs is a new-generation enterosorbent (Enterosgel®), which has a high selective sorption activity and selective spectrum of activity towards GIT microflora. Enterosgel® is an organosilicone adsorbent for removal of toxic substances from the body, correction of microbiocenosis and recovery of the mucous membranes in the GIT epithelium. Sorption and detoxification properties of Enterosgel® are provided by its porous globular structure, preferably with pores of average diameter. Enterosgel® bactericidal

properties are expressed through its binding and removing pathogenic microorganisms and their metabolic products from the GIT. The drug does not inhibit saprophytic GIT microflora of the digestive tract. By absorbing the mucosa irritating substances (exotoxins and endotoxins of pathogenic bacteria, toxic metabolites), Enterosgel®, with its regenerative action, helps to restore mucous membranes. It enhances immune defense of the epithelial barrier in the mucous membranes, increasing Ig A level. In connection with the above said, in the research clinical efficacy and safety of Enterosgel® (active ingredient polymethylsiloxane polyhydrate) has been investigated. The effect of the study drug on the dynamics of clinical symptoms, laboratory and morphological parameters, psycho-emotional indicators and quality of life were evaluated.

The objective of this study was to determine the efficacy and safety of Enterosgel® designated for treatment of *H. pylori*-associated diseases of the upper GIT.

### Materials and methods

The study was conducted in the gastroenterology clinic of Northwest State Medical University named after I.I. Mechnikov. The study was approved by the committee on research ethics at the institution in which the research was conducted and any informed consent from human subjects was obtained as required.

Thirty patients with *H. pylori*-associated diseases of the upper GIT were included in the study. The average age of the patients was 45.6±10.5 years, 14 men and 16 women. The patients were divided into two groups: 1) the main group (N.=15): treatment with Enterosgel® one dose of pasta 22.5 g (active substance polymethylsiloxane polyhydrate) three times a day after meal during three weeks; 2) control group: treatment - eradication therapy (omeprazole 20 mg twice a day, amoxicillin 1000 mg twice a day, clarithromycin 500 mg twice a day for 7 days). Manifestation dynamics of gastrointestinal complaints was assessed using the standard questionnaire and Gastrointestinal Symptom Rating Scale (GSRS)

questionnaire. GSRs questionnaire has been developed by the Department of studies on life quality (QOL), ASTRA Hassle (I. Wiklund, 1998) and it is used for QOL assessment of patients with gastrointestinal diseases. The questionnaire consists of 15 points organized in five scales: abdominal pain (questions 1, 4), reflux syndrome (questions 2, 3, 5), diarrheal syndrome (questions 11, 12, 14), dyspeptic syndrome (questions 6, 7, 8, 9), constipation syndrome (questions 10, 13, 15), total measurement scale (questions 1-15). The scale values range from 1 to 7; higher values correspond to more expressed symptoms and lower QOL.

Statistical data processing was performed using the program «SPSS Statistics 17.0» (SPSS Inc., CIIA).

## Results

Activity dynamics of gastrointestinal complaints in the studied patients of group 1 and 2 according to GSRs questionnaire scales before and after treatment course is shown in Table I.

On comparison of the groups studied, statistically significant differences were found by the scales of GSRs questionnaire between the groups regarding diarrhea syndrome ( $z=-3.164$ ,  $P=0.001$ ): after the eradication therapy course,

patients of Group 2 started experiencing diarrhea syndrome, while in patients of Group 1, expression of diarrhea syndrome decreased. It is noteworthy that of 9 patients of Group 1 in which stool frequency was higher than 7 times a week, 4 patients experienced a tendency towards normalization. Patients in Group 1 had a statistically significant decrease on the scale of dyspeptic complaints severity ( $z=-2.113$ ,  $P=0.035$ ) and reduction of the total score of measurements ( $z=-2.133$ ,  $P=0.033$ ). Patients in Group 2 showed increased complaints of diarrhea syndrome ( $z=-2.829$ ,  $P=0.005$ ), the number of scores for the rest of the scales did not significantly change after a course of eradication therapy.

It is interesting to note that as a result of the data evaluation of GSRs questionnaire, no expected positive dynamics on the scale of measurement of the total patients was found in Group 2 after a course of eradication therapy. Apparently, the observed lack of change on the scale measuring total score is due to the fact that, despite after a course of eradication therapy patients suffered less from gastric dyspepsia, they experienced more frequent stools, unformed stools and need to urgently void the bowel.

We enrolled patients with the most common GIT complaints: excessive passage of flatus

TABLE I.—Activity dynamics of gastrointestinal complaints in patients with *Helicobacter pylori*-associated gastro-duodenitis according to GSRs questionnaire.

Scale	Time of observation	Mean values				Significance of differences between the groups, (P)
		Group 1, N.=15,		Group 2, N.=15		
		M±s	Me	M±s	Me	
Abdominal pains	Beginning	4.9±1.8	5.0	4.9±2.1	5.0	0.486
	End	4.3±1.3	4.0	4.9±1.5	4.0	
Reflux syndrome	Beginning	6.1±3.1	6.0	6.5±3.3	6.0	0.653
	End	5.3±2.4	6.0	5.3±2.4	5.0	
Diarrhea syndrome	Beginning	5.9±4.3	4.0	3.6±1.4	3.0	0.001*
	End	4.9±2.5	3.0	6.2±3.1	6.0	
Dyspeptic syndrome	Beginning	11.6±5.5	12.0	11.0±5.6	11.0	0.744
	End	8.9±3.5	8.0	8.9±3.4	8.0	
Constipation syndrome	Beginning	4.4±1.4	5.0	3.3±0.5	3.0	0.838
	End	4.3±1.2	4.0	3.3±0.5	3.0	
Scale of total measurements	Beginning	32.9±11.7	29.0	29.3±9.4	28.0	0.202
	End	27.7±6.3	26.0	28.6±6.0	28.0	

$P<0.01$ .

(observed in all patients included in the study); borborygmus (60% of patients in group 1 and 53% patients in group 2); abdominal heaviness (73% of patients in group 1 and in 67% patients in group 2); heartburn (47% of patients in group 1 and in 53% patients in group 2) as well as nausea (40% of patients in group 1 and group 2).

After a course of treatment with Enterosgel® in patients with *H. pylori* - associated gastro-duodenitis, significant positive clinical dynamics were observed. On the background of administration of Enterosgel® such symptoms as heartburn, regurgitation and excessive passage of flatus decreased. Reduction dynamics was similar in the surveyed groups.

Statistical comparison of efficiency of Enterosgel® and eradication therapy showed statistically significant differences between the groups: in group 1 patients, the frequency of complaints of excessive flatus passage decreased to a greater extent than that of the patients in group 2 ( $\chi^2=7.500$ ,  $P=0.006$ ); in patients of group 1, the frequency of complaints about the rumbling in the stomach decreased, while it increased in patients of group 2, ( $\chi^2=5.490$ ,  $P=0.019$ ); in patients of group 1 the frequency of abdominal pain decreased, while in patients of group 2, it increased ( $\chi^2=7.340$ ,  $P=0.007$ ); in patients of group 1, the frequency of diarrhea decreased, while in group 2 it increased ( $\chi^2=10.769$ ,  $P=0.001$ ).

### Discussion

According to the performed endoscopic study, after the course of eradication therapy, patients of group 2 experienced a significant improvement of the endoscopic view, while patients of group 1 showed a tendency towards decrease of inflammation of the upper GIT segments; after the course of treatment with Enterosgel®, a tendency towards reduction of inflammation in the upper GIT segments has also been noted, though no statistically significant endoscopic difference has been determined.

In all patients included in the study, urease test for *H. pylori* was carried out immediately after the fibrogastroduodenoscopy. According to test results, the presence of *H. pylori* was

detected in 100% of patients included in the study. After the therapy the degree of *H. pylori* infection has decreased. A comparative assessment of *H. pylori* infection showed a greater decrease in patients in group 2 treated with eradication therapy, the differences between the groups being statistically significant ( $\chi^2=5.400$ ,  $P=0.020$ ). Thus, eradication therapy has proved to be a natural and more effective than the therapy with the study medication in reducing *H. pylori* infection. At the same time, eradication therapy (group 2) has shown complete eradication of *H. pylori* in only 34% of cases, and proportion of patients with a significant infection decreased from 80 to 13%.

At the same time, proportion of patients with significant *H. pylori* infection in group 1 decreased from 86% to 47% after enterosorbent monotherapy. This, of course, refers to the activity of Enterosgel® towards *H. pylori* that can be used to enhance efficiency and safety of traditional eradication schemes.

### Conclusions

Clinical trials have demonstrated the safety and efficacy of Enterosgel® administered as a monotherapy to treat patients with *H. pylori* - associated gastroduodenitis.

Analysis of clinical picture in patients taking Enterosgel® has revealed significant positive clinical dynamics in relation to gastric and intestinal dyspepsia, similar to the observed dynamics in the group of patients treated with standard eradication therapy. At the same time, if patients with standard eradication therapy observed increase in the frequency of detection of intestinal dyspepsia symptoms, in patients receiving Enterosgel® the frequency of these complaints has decreased. In addition, when evaluating GSRs questionnaire, it was found that after a course of standard eradication therapy patients had frequent complaints of loose stools, whilst in patients treated with enterosorbent Enterosgel® severity of diarrheal syndrome, on the contrary, decreased. In the group of patients after a course of standard eradication therapy, according to GSRs, the expected positive dynamics on the scale of the total measure-

ment was not achieved. Apparently, the lack of favorable changes in the data was due to the fact that while receiving antibacterial agents within eradication therapy, patients in the observed group showed an increased concern about the frequency of stools, unformed stool appearance, and urgent needs to have a stool.

Upon analysis of fibrogastroduodenoscopy, after treatment all patients have shown endoscopic improvement of the upper GIT. Patients treated with standard eradication therapy had more pronounced and statistically significant positive dynamics.

On the background of the therapy, most patients have had a decrease in the severity of antral contamination with *H. pylori* according to urease test performed during endoscopy. Eradication therapy has naturally shown better results in reducing infection. A proportion of patients with *H. pylori* has reduced significantly, from 86% to 47%.

The following treatment scheme can be recommended for patients with *H. pylori*-associated diseases of the upper GIT: one dose of Enterogel® (22.5 g) with the active substance polymethylsiloxane polyhydrate 3 times a day 60 minutes after the meal orally for 3 consecutive weeks (diluted in 200 mL of lukewarm water or washed down with at least 200 mL of lukewarm water).

Given the above results, we consider it promising to continue clinical trials of Enterogel® as a part of standard eradication therapy of *H. pylori* - associated diseases of the upper GIT, in order to optimize the eradication schemes.<sup>10-15</sup>

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*Conflicts of interest.*—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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