# EFFICIENCY AND SAFETY OF ENTEROSGEL (POLYMETHYLSILOXANE POLYHYDRATE) IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME

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# Efficiency and safety of Enterosgel (polymethylsiloxane polyhydrate) in the treatment of irritable bowel syndrome

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*Introduction.* **Irritable Bowel Syndrome (IBS) is a psychosocial functional gastrointestinal disorder significantly reducing the patient's quality of life. The study objective was to assess the efficiency of administration of silicon-containing enterosorbent (Enterosgel) in patients with diarrhea-predominant IBS.**

*Materials and methods.* **30 patients with diarrhea-predominant IBS (16 women and 14 men) were included in the study. All the patients were divided into two groups: the main group was treated by enterosorbent "Enterosgel" (dosage 22.5 g 3 times a day, 1 hour after meals for 21 day), the reference group was treated with bismuth tripotassium dicitrate 1 tablet 3 times a day 30 minutes before meals and 1 tablet at night for 21 days. To assess the treatment efficiency, patients' complaints were evaluated using GSRS questionnaire, stool frequency and form were assessed as well as myoelectric activity of the digestive tract (apparatus "Gastroenteromonitor-GEM-01").**

*Results.* **As a result of the treatment, patients of the main group have achieved a statistically significant reduction in the severity of abdominal pain, diarrhea syndrome, dyspepsia scales, and on the total GSRS scale. After therapy with the comparator, in patients of the reference group intensity of abdominal pain, reflux syndrome, diarrhea syndrome and dyspepsia have significantly decreased. The most clinically significant changes observed in patients of the main group included normalized stool frequency (slowing to 7 times a week), normalization of stool form (up to type 4 on the Bristol scale) and a decrease of pain severity.**

*Conclusion.* **There have been no significant differences between groups in assessment of digestive tract MEA, however, the aberrant GIT response of patients with diarrhea to food intake was revealed: a decrease instead of an expected increase of MEA was noted. Thus, the study has found that application of Enterosgel reduced the complaints of patients with diarrhea-predominant IBS and abdominal pain severity, thus contributing to the harmonization of quality of patient's life. The treatment schedule, which can be recommended for use in patients with diarrhea-predominant IBS is: per os for 3 consecutive weeks at a dose of 22.5 g 3 times a day 60 minutes before meals (a dose of paste diluted in 200 ml of cool boiled water or washed down with 200 ml of cool boiled water).**

**KEY WORDS:** Enterosorption - Enterosgel - Irritable bowel syndrome - Myoelectrical activity.

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Irritable bowel syndrome refers to psychosocial functional gastrointestinal disorders manifested by recurrent abdominal pain and impaired bowel evacuation frequency in the absence of its organic changes.[1] Deterioration of QOL of IBS patients influences the disability duration and, as a con-

sequence, deteriorates economic and social losses; it should be noted that the highest incidence is among young working people (at the age from 24 to 41).[2]

Nowadays, considering the absence of the unified diagnostic test (marker), it is a common practice to verify IBS diagnosis according to Rome criteria (version III), where the disease is defined as recurrent abdominal pain or discomfort for at least three days per month for three consecutive months that should be noted for at least six months. IBS is associated with the following two or more characteristics:

1) Improvement after defecation

2) Change in stool frequency during the disease

3) Change in stool form with the disease onset.[17] Considering Bristol stool form scale and Rome III criteria, it has been proposed to divide IBS patients into the following groups: constipation-predominant IBS, diarrhea- predominant IBS, mixed type of IBS. It is important to note that in a patient different IBS subtypes can vary throughout the illness.

Application of Roman criteria allows to adhere to a specific algorithm for IBS verification, which is caused by insufficient study of its pathophysiology. Most researchers tend to believe that in pathophysiology of IBS disorder of colonic motility, visceral hypersensitivity (nociception threshold or densification of pain impulses within the normal sensitivity threshold) and changes in the functioning of links along the brain-gut axis are crucial. In the recent years, it has been found that IBS pathogenesis is more complicated. Such factors as inflammation [4] (including development and maintenance of mild inflammation in the intestinal wall, for example in patients with IBS postinfection,[5]), immunological [6] and dietary factors,[7] colon microbiota disorders [8] as well as changes in enteroendocrine system and its cells [9] play an important role in the disease progression.[10]

To date, IBS treatment schedules are not standardized, and there is no single treatment algorithm of various IBS forms. It is believed that this is due to the problem of search and objective assessment of the drug efficiency and is associated with lack of knowledge, IBS pathophysiology complexity and a variety of clinical manifestations. On administration of treatment for IBS patients, a detailed study of the history of the disease and differentiation of complaints (abdominal, general, psychological, etc.) is of great importance, which will largely determine the therapy tactics. Normalization of lifestyle and diet regime, psychotherapy are important components in the treatment of this disease. For IBS treatment, various groups of drugs are used, including antispasmodics, laxatives, anti-diarrheal drugs, pro-and prebiotics, and antidepressants.

A search of new effective ways of complex IBS therapy, in particular the use of enterosorbents, seems promising. Sorbents are substances possessing high adsorption capacity, which are not degraded in the GIT and are capable of binding exogenous and endogenous toxic substances (microorganisms and their toxins, poisons, excessive metabolites and other harmful substances) by adsorption and absorption, ion exchange or complexation. The story of enterosorbents goes back to antiquity: healers of the Ancient Egypt, India and Greece already used charcoal, clay, pounded tuffs and dead-burnt horn for the treatment of poisoning, dysentery, jaundice and other diseases. With this purpose, birch or bone charcoal was used by the healers of ancient Russia.[11]

The term "enterosorption" was proposed by Nikolaev V.G. et al. in 1983 [12, 13] to describe a new method of sorption therapy including daily oral administration of large (20-50 g) doses of highly active synthetic coal with spherical granulation obtained by pyrolytic processing of various polymer resins. It is also important that the authors have identified classical property of enterosorbents – non-invasion of the gastrointestinal mucosa, i.e. absence of systemic pharmacokinetics.[13]

Within the considered drug class, siliceous sorbents are especially noteworthy, Enterosgel being the most widespread among them and well-known for its selective properties.

TABLE I.—*Dynamics of expression of complaints in the study and control groups according to GSRS questionnaire.*

| Scale | Time of observation (beginning / end of treatment) | Number of patients. abs. (% of ) | | | | Number of patients. abs. (% of ) |
|---|---|---|---|---|---|---|
| | | Main group. n=15 | | Control group. n=15 | | |
| | | Me (Q$_1$; Q$_3$) | Difference of significance within a group. p | Me (Q$_1$; Q$_3$) | Difference of significance within a group. p | |
| Abdominal pain | Beginning | 5 (5; 7.5) | 0.003 | 6 (5.5; 8) | 0.004 | 0.175 |
| | End | 4 (2; 5) | | 5 (4; 6) | | |
| Reflux syndrome | Beginning | 6 (4.5; 6) | 0.343 | 5 (5; 7) | 0.003 | 0.442 |
| | End | 5 (3; 6) | | 4 (4; 5) | | |
| Diarrhea syndrome | Beginning | 12 (9.5; 15) | 0.003 | 11 (9.5; 15) | 0.021 | 0.102 |
| | End | 7 (3.5; 10) | | 10 (6; 11.5) | | |
| Dyspepsy | Beginning | 15 (10.5; 17) | 0.003 | 11 (8.5; 17) | 0.002 | 0.835 |
| | End | 8 (6; 10.5) | | 7 (6.5; 9) | | |
| Constipation syndrome | Beginning | 5 (4; 6) | 0.591 | 5 (4; 8.5) | 0.021 | 0.237 |
| | End | 5 (3; 7) | | 4 (3; 6) | | |
| Total score | Beginning | 46 (35; 50.5) | 0.004 | 44 (37; 48) | 0.001 | 0.835 |
| | End | 29 (23; 40) | | 33 (27; 35) | | |

## *Study objectives*

The objective of this study is to determine the efficiency and safety of application of Enterosgel, indicated for treatment of patients with diarrhea-predominant irritable bowel syndrome.

## **Materials and methods**

The study was conducted in the gastroenterology clinic of Northwest State Medical University named after I.I. Mechnikov. Thirty patients with diarrhea-predominant IBS (D-IBS) confirmed according to Rome III criteria were included in the study. The average age of the patients was 38.0 ± 10.2 years. Gender distribution of patients: men

- 14, women - 16. The patients were divided into 2 groups: 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; control group: treatment - bismuth tripotassium dicitrate. The drug was administered at a dose one tablet three times a day 30 minutes before meals and one tablet in the evening for 21 days.

Manifestation dynamics of gastrointestinal complaints was assessed using the standard questionnaire and GSRS questionnaire. GSRS questionnaire (Gastrointestinal Symptom Rating Scale) has been developed by department of studies on life quality (QOL), AS-TRA Hassle (I.Wiklund, 1998) and 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.

In all the patients, stool form and consistency was evaluated as well (Bristol scale) before and after treatment.

In all the patients, study of the GIT motor-evacuation function was performed by electrogastroenterography method (EGG) using the apparatus «Gastroenteromonitor GEM-01». Calculation of peripheral EGG is an evaluation method of electric activity of various GIT segments. Considering the data obtained in EGG, the following values were assessed: total level of GIT electrical activity; level of electrical activity for each one of the GIT segments studied. A standard study of GIT electrical activity consists of two stages: the first is a study on an empty stomach during 40 minutes, the second stage is a study during 40 minutes after the standard breakfast. After the treatment course the study was repeated, and the dynamics of basal values of GIT electrical activity was assessed. To evaluate the GIT motor activity, a special coefficient was calculated after the food load, equal to the ratio of total postprandial MEA to total fasting GIT MEA (postprandial coefficient – PPC).

Statistical data processing was performed using program SPSS 17.0 (SPSS Inc., USA) with the help of Wilcoxon test (for paired observations) and Mann-Whitney test (for non-paired observations).

The dynamics of GIT complaints in patients of the main and control group on the scales of GSRS questionnaire are presented in Table I.

No differences were determined between the groups in relation to the dynamics of GSRS questionnaire scale values (p> 0.05).

In patients of the main group after treatment with the study medication, a statistically significant reduction was achieved in the severity of complaints on the scales of abdominal pain, diarrhea syndrome, dyspeptic syndrome, and on the scale of the total score. after therapy with the reference medication Patients in the control group the intensity of complaints significantly decreased for all the scales: abdominal pain, reflux syndrome, diarrhea syndrome, constipation and on the total score scale.

The most clinically significant changes observed in patients of the main group were normalization of stool frequency (decrease up to 7 times a week), normalization of stool form (up to stool type 4 on the Bristol scale) and a decrease in bodily pain. Unlike reference drug (bismuthate tripotassium dicitrate), in the treatment of patients with Enterosgel® beneficial effect was detected not only on subjective clinical IBS manifestations, but also in normalization of stool frequency and form.

In the patients of the main group value of the total fasting GIT myoelectric activity before treatment was Me = 21.4 mV (Q1 = 16.0; Q3 = 42.5), postprandial - Me = 32.4 mV (Q1 = 16.7; Q3 = 59.6). During the treatment with Enterosgel® total fasting value of GIT myoelectric activity was Me = 23.9 mV (Q1 = 11.2; Q3 = 46.9), postprandial - Me = 21.3 mV (Q1 = 14.4; Q3 = 40.9). Values before and after treatment were not statistically different (p> 0.05).

In patients of the control group value of the total GIT myoelectric activity before treatment was as follows: fasting Me = 21.2 mV (Q1 = 8.5; Q3 = 51.5), postprandial Me = 18.2 mV (Q1 = 6.4; Q3 = 48.8). After a course of the comparator drug total fasting value of GIT myoelectric activity was Me = 39.4 mV (Q1 = 8.3; Q3 = 53.4), postprandial - Me = 11.8 mV (Q1 = 10.1; Q3 = 38.3) also the values before and after treatment were not statistically different (p> 0.05).

PPC in patients of the main and control group before and after treatment is shown in Figure 1.

In 12 patients (40%) a decrease in PPC was observed (<1.0), reaching values <0.6 in 7 patients (23%). After treatment in 16 patients (53%) a reduction in PPC was observed (<1.0), while PPC increase (> 1.5) was observed in 8 patients (27%), of which in 5 pa-
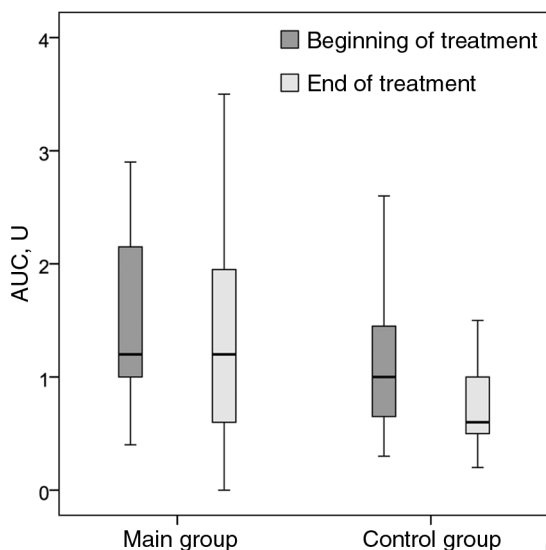
Figure 1.—The value of postprandial coefficient of GIT myoelectric activity in patients of the main and control group before and after treatment. Horizontal axis - observation group, vertical axis - the value of AUC, units. The dotted line is the postprandial factor equal to 1.0.

tients (17%) PPC was > 2.0. It is possible that after treatment on the background of clinical improvement, reduction of diarrhea and normalization of evacuation function a trend towards significant PPC decrease and postprandial power decrease is expected.

## Conclusion

The study of efficiency and safety of application of Enterosgel administered for treatment of patients with diarrhea-predominant irritable bowel syndrome had demonstrated safety and efficiency of the study medication.

Evaluation according to GSRS showed significant reduction on the scales of abdominal pain, diarrhea syndrome, dyspeptic syndrome as well as on the total measure scale. According to EGG, while studying MEA, a tendency towards normalization of GIT motor-evacuation function is evident.

## Summary

Enterosgel has a positive effect on the clinical performance, reducing abdominal pain severity and normalizing stool frequency in D-IBS patients, thus contributing to the harmonization of quality of life.

Treatment regimens that can be recommended for use in patients with D-IBS: 22.5 g of the paste with the active substance polymethylsiloxane polyhydrate three times a day one hour after meal orally for three consecutive weeks (the dose should be dissolved in 200 ml of drinking water or washed down with at least 200 ml of drinking water).

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