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Research Article

Polymethylsiloxane Polyhydrate (Enterosgel®) in the Complex Treatment of Diarrhea Syndrome in Children with Diseases of the Digestive System

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Abstract

Objective: To evaluate the clinical efficiency of polymethylsiloxane polyhydrate (Enterosgel®) in the complex treatment of diarrhea syndrome in children.

Patients and Methods: We carried out a retrospective analysis of the clinical results of 64 patients with gastroenterocolitis of non-infectious etiology (mean age 6.4 ± 0.7 years), i.e. a complete study of patients with complex treatment by Enterosgel®. The comparison group with no treatment by Enterosgel® consisted of 31 children (mean age 6.5 ± 0.9 years) with diarrhea syndrome. We conducted a comparative assessment of intoxication symptoms, the nature of the stool, clinical blood tests, and the length of hospital stay.

Results: Normalization of the stool in patients whose complex treatment included Enterosgel® was faster, the length of hospital stay decreased by almost 2 times, and there were no negative changes in blood tests.

Conclusion: The complex treatment of children with the pathology of the digestive system accompanied by diarrhea syndrome is efficient with the enterosorbent effect of Enterosgel®.

Keywords: *Children; Diarrhea Syndrome; Diseases of the Digestive System; Polymethylsiloxane Polyhydrate (Enterosgel®)*

Introduction

Diarrhea is the body's response to intestinal pathogens. Intestinal epithelial cells signal the infection, producing chemokines, drawing immune cells to the affected area. They are also actively involved in the protection of humans, causing apoptosis and releasing endogenous antimicrobial peptides, which present nonspecific factors of the humoral innate immune system and provide protection against a wide range of bacteria, fungi and enveloped viruses [1-3]. In order to eliminate pathogenic factors, intestinal epithelial cells need the help of immune cells. A key role in controlling the earliest stages of the pathological process, acting as immunological sentinel and active effectors, is played by intestinal dendritic cells, well known for their ability to induce and control adaptive immunity. However, inflammatory monocytes, which quickly and massively collect on the infected mucosa, appear to be involved in the loss of the integrity of the intestinal epithelium, which is accompanied by the penetration of pathogenic factors into the body.

The research interest in drugs that can prevent the penetration of pathogens and toxins into the human body and, possibly, prevent the development of the disease, has existed for many years. Since ancient times, healers have prescribed various options for preparations of clay, coal, and wood for the treatment of poisoning, dysentery, jaundice, which was the beginning of sorption therapy. Sorbents - namely

pectin - are widely used to this day in the nutrition of people in many countries, in the form of desserts after meals. The rich history of the use of sorbents is reflected in the writings of the great healers Hippocrates and Avicenna. In "The Canon of Medicine", Avicenna placed methods of body cleaning in the third place on the list of seven tenets of the health preservation art [4].

At present, enterosorption has become an integral part of the treatment of a number of diseases, with a good evidence base, and with a decent place in high-quality clinical guidelines. Therefore, the popularity of sorption therapy is high among both doctors and patients.

Taking into account evidence from evidence-based medicine, sorption therapy is effective in the following clinical situations:

- Acute diarrhea in children and adults [5-10].
- Chronic diarrhea of various etiologies [11].
- Prevention of colorectal cancer [12,13].
- Prevention and treatment of constipation, diverticulitis and fecal incontinence [14,15].
- Hypercholesterolemia, prevention of cardiovascular diseases and metabolic syndrome [16-20].
- Cholestasis syndrome [21,22].
- Irritable bowel syndrome [23].

The group of drugs, enterosorbents, is very extensive and heterogeneous, combining many drugs of different composition and action - the ability to bind exogenous and endogenous compounds in the gastrointestinal tract, as well as supramolecular structures and cells. The therapeutic effect of enterosorbents is considered from the position of direct and indirect effects:

- **Direct action:** The ability to adsorb poisons and xenobiotics directly from the lumen of the digestive organs. Sorption begins in the stomach and continues in the small intestine, where food elements, mucosal secretion components, digestive enzymes, regulatory peptides, microbial cells and toxins are sorbed.
- **Indirect action:** Suppression or weakening of toxic-allergic reactions, inflammatory processes, reducing the load on the organs of detoxification and excretion, eliminating flatulence and improving the trophism of the intestinal wall.

Modern requirements for enterosorbents are defined as follow [2]:

- Sorbents should not have toxic properties,
- Preparations should not injure the mucous membranes of the digestive tract,
- Must be completely evacuated from the intestines, not being absorbed into the systemic circulation,
- Have a high sorption effect,
- Do not disturb the normal intestinal microbiota,
- Be suitable for use by different patient groups.

One of the main parameters that determines the quality and drug efficiency for sorption is sorption capacity. This indicator determines the amount of substance absorbed by the mass unit of the sorbent, which is determined "*in vitro*" (therefore, it may be somewhat different in a real patient). The rate of sorption capacity is indicated in the instructions for use.

Another important parameter to determine the drug efficiency is the ability of sorption of molecules of different sizes and masses. Also, of importance is the active surface of the enterosorbent, i.e. the total area of the adsorbing surface per unit mass of the drug, which is not the same with the above-mentioned sorption capacity [24].

One of the enterosorbenotes, which has been used for the treatment of diarrhea of various origins for more than 30 years, is Enterosgel - polymethylsiloxane polyhydrate - a drug with a high sorption capacity (150 m^2/g) and selective action only with respect to medium molecules. The indications for appointment are intoxication, renal failure, purulent-septic conditions, allergic diseases, radiation injuries, diarrhea, and liver damage. It has no age limit.

Enterosgel is of interest due to its high efficiency, which is based on the innovative structure of the silicone matrix, i.e. the "molecular sponge", which allows to differentially sorb the middle molecules of exogenous (toxins) and endogenous (metabolic products) origin.

Studies of this drug in Russia and abroad have shown a positive effect of the drug for many even complicated diseases. Thus, Enterosgel was efficient in an experiment with a burn disease sorbing toxins and improving the function of the small intestine to utilize the decay products, preventing endotoxemia [25]. Proven positive effects of polymethylsiloxane are shown in bacterial infections such as salmonellosis, Flexner shigellosis, clostridial diarrhea, and bacterial overgrowth syndrome [26-29].

Of interest is the study of Petukhov., *et al.* (2000) on the use of Enterosgel in patients with malabsorption, in which the effect of the drug was proven not only in relieving clinical symptoms in patients, but also in improving the condition of the small intestinal mucosa according to endoscopy [30].

The research on the positive role of mucoprotectors in the new pathology for gastroenterologists titles "leaky gut syndrome" [31] echoes these data.

In general, it should be noted that the preparation of a special form of organosilicon structure has good prospects for widespread clinical use.

Enterosorbents, despite their very ancient use in treatment, are still usable drugs. The use of this drug group has gone far beyond the limits of gastroenterology helping patients with various diseases, including such "civilization diseases" as cardiovascular pathology and disorders of lipid and carbohydrate metabolism. The natural and safe composition of drugs is useful for healthy people to prevent diseases of the digestive system and metabolic disorders, that allows achieving a higher quality of life, which is a priority task of the healthcare.

Objective of the Study

To evaluate the clinical efficiency and safety of polymethylsiloxane polyhydrate (Enterosgel®) in the complex treatment of diarrheal syndrome of non-infectious etiology in children.

Patients and Methods

We conducted a post-registration observational study evaluating the efficiency and safety of Enterosgel for children with pathology of the digestive system. The study was carried out from July to October 2018 on the base of the Gastroenterology Department of the

Veltischev Research and Clinical Institute for Pediatrics, Pirogov Russian National Research Medical University upon the request and financial support of TNK SILMA LLC, Russia, Agreement No.IT-10 dated June 15, 2018. A retrospective analysis of the efficiency and safety of Enterosgel® was carried out in 225 children aged from one month to 17 years (mean age 6.9 ± 3.1 years): 110 boys and 115 girls treated for the pathology of the digestive system. The study was solid.

Patients were treated according to the protocols adopted in the hospital, in accordance with the clinical standards and protocols (diet, vitamin therapy and eubiotic drugs depending on the test results), to which Enterosgel® was added orally 3 times a day between meals and medicines (1.5 - 2 hours a.c. and no less than 2 hours p.c.). One tablespoon with its maximum filling was carefully rubbed on the walls of the dishes in 30 ml of water (2 tablespoons) until a homogeneous suspension was obtained, after which the total volume was adjusted to 150 - 200 ml.

To assess the clinical efficiency of Enterosgel in the complex treatment of diarrhea syndrome, among the examined children, 64 patients with gastroenterocolitis of non-infectious etiology (average age 6.4 ± 0.7 years) were singled out for a study of patients whose complex treatment included Enterosgel®. The group did not include patients with an etiologically established intestinal infection who received treatment in the infectious diseases department.

The comparison group consisted of 31 children (mean age 6.5 ± 0.9 years) with diarrhea syndrome, in which the complex treatment did not include Enterosgel®.

A comparative assessment of the severity of clinical manifestations of intoxication, body temperature, the nature and frequency of stool, changes in the main indicators of clinical blood tests, and the length of stay in the hospital was carried out.

The statistical data processing was performed using Microsoft Excel 2010, SPSS Statistics data analysis package (version 20) and StatSoft Statistica (version 6.0). Quantitative variables were described with the number of patients (n). Nonparametric statistics methods were used. Data were presented as a median and interquartile range. When analyzing samples that do not obey the law of normal distribution, the non-parametric Mann-Whitney test was used. Differences between the values were considered statistically significant at $p < 0.05$.

Results

Upon admission to the hospital, the body temperature of children in the main group was 37.0 ± 0.1°C and ranged from 36.5 to 37.8°C, in the comparison group - 37.1 ± 0.1°C with a fluctuation range of 36.6 to 37.8°C. After three days of treatment, the body temperature in patients of the main group was 36.7 ± 0.1°C, in the comparison group - 36.7 ± 0.1°C (Figure 1).

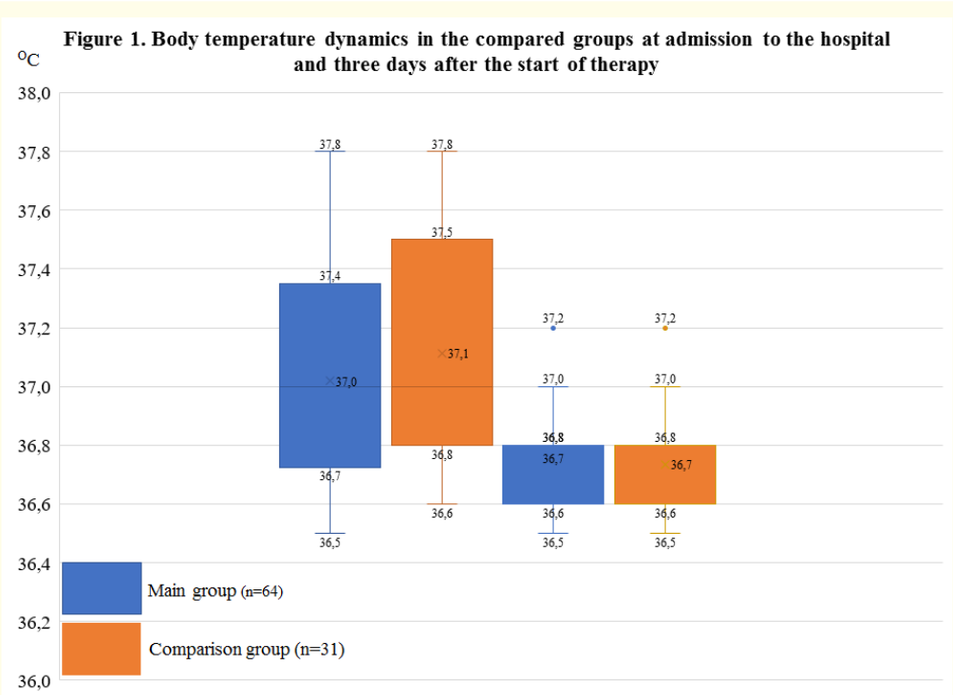

Figure 1: *Body temperature dynamics in the compared groups at admission to the hospital and three days after the start of therapy.*

Pallor of the skin in the main group of patients was observed in 60 cases (93.8%), in the comparison group - in 30 cases (96.8%); p = 1.00000. Dryness of the skin in patients of the main group was observed in 59 children (92.2%); in the comparison group, in 30 children (96.8%); p = 0.66005. After 3 days of treatment, pallor of the skin in patients of the main group was observed in 33 cases (51.6%), in patients of the comparison group - in 23 cases (74.2%); p = 0.04584; skin dryness persisted in 19 children (29.7%) of the main group, and in 16 children (51.6%) of the comparison group (p = 0.04418). Gray skin color in patients of the main group was observed in 44 cases (68.8%), in patients of the comparison group - in 23 cases (74.2%); p = 0.63882. After 3 days of treatment, the gray tint of the skin was not observed in either group.

Nausea in children of the main group was observed in 20 cases (31.3%), in the comparison group - in 10 cases (32.3%); p = 1.00000. Vomiting in the main group was observed in 13 patients (20.3%), in the comparison group - in six children (19.4%); p = 1.00000. After 3 days of treatment in children of the main group, nausea persisted in three cases (4.7%), vomiting in one patient (1.6%); in the comparison group, nausea persisted in three children (9.7%); p = 0.38810, vomiting - in one patient (3.2%); p = 0.54849.

Gummy stools in patients of the main group were in 31 cases (48.4%), and in 39 cases (60.9%) the stool was also watery. In the comparison group, pasty stools were observed in 14 patients (45.2%); p = 0.82849; watery - in 21 patients (67.7%); p = 0.65101. Pathological impurities - mucus and greens - in feces were observed in 56 patients (87.5%) of the main group and in 26 patients (83.9%) of the comparison group (p = 0.75168). After 3 days of treatment in the main group, a pasty stool retained in 31 patients (48.4%), and there was no wateriness in the stool in any case. In the comparison group, the pasty stool retained in 22 cases (71.0%); p = 0.04829, there was no wateriness in any case. Impurity of mucus in the faeces of the patients of the main group after 3 days of treatment retained in eight children (12.5%), no admixture of green was observed in any case; in the comparison group, mucus in the faeces was observed in 10 cases (32.2%); p = 0.02768.

The main indicators of the clinical analysis of blood (hemoglobin level, absolute number of erythrocytes, leukocytes, neutrophils, lymphocytes, erythrocyte sedimentation rate) did not have significant differences in patients of the compared groups. After 3 days of treatment, there were no negative changes in clinical blood tests in patients from both the main group and the comparison group (Figure 2 and 3).

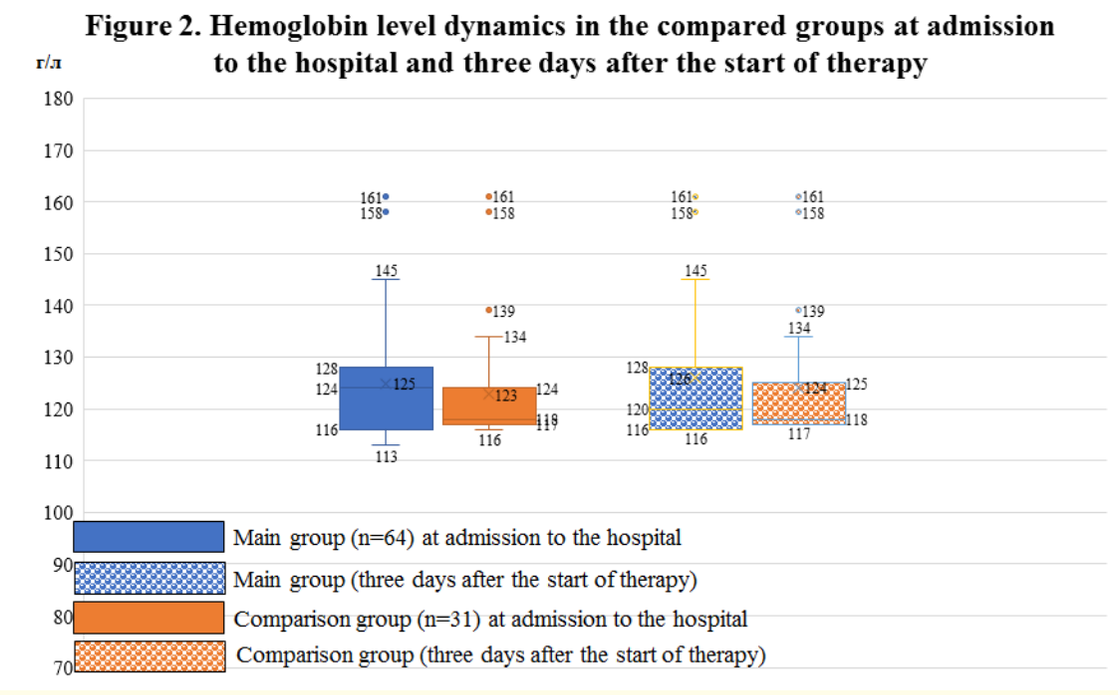

Figure 2: *Hemoglobin level dynamics in the compared groups at admission to the hospital and three days after the start of therapy.*

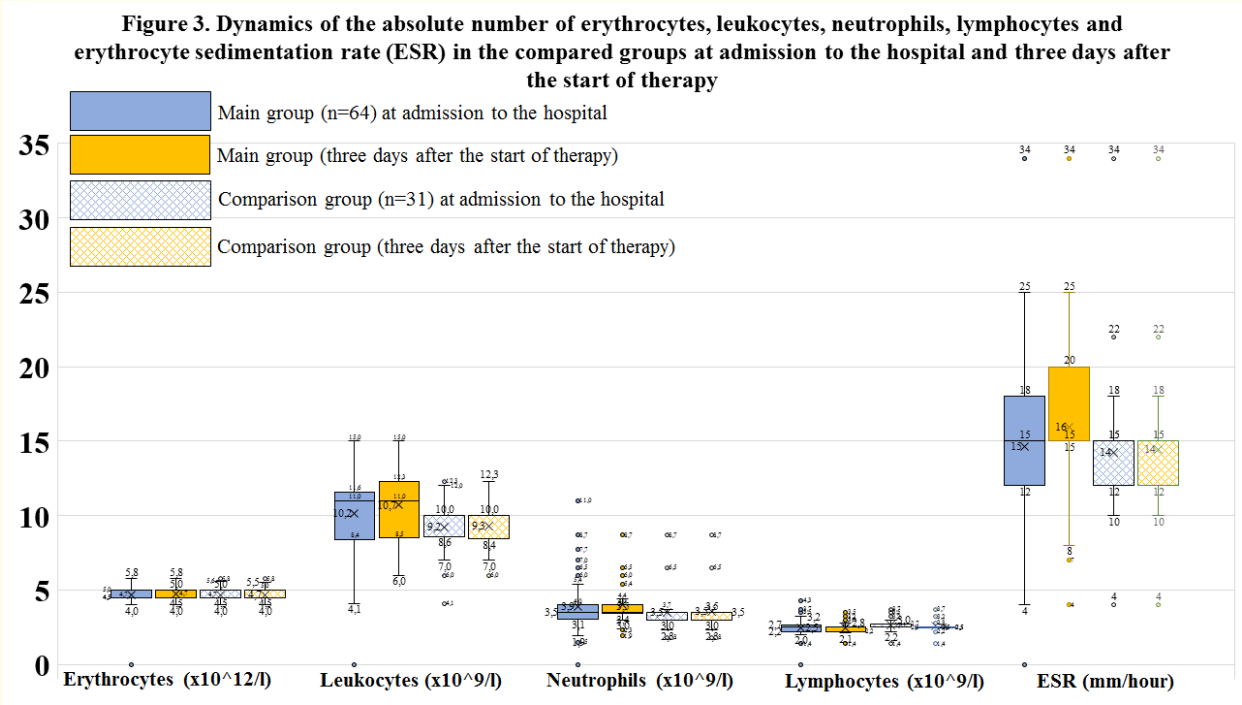

Figure 3: *Dynamics of the absolute number of erythrocytes, leukocytes, neutrophils, lymphocytes and erythrocyte sedimentation rate (ESR) in the compared groups at admission to the hospital and three days after the start of therapy.*

The average duration of inpatient treatment of children with diarrhea syndrome, which included Enterosgel® in the complex treatment, was 4.0 ± 0.4 days; whereas in the comparison group, the duration of hospital stay was 7.0 ± 0.5 ($p < 0.01$).

Discussion

The body temperature was normalized after three days of treatment with the same frequency in both children treated by Enterosgel and those not treated by it. However, both compared groups did not include patients with an etiologically established intestinal infection, in which intoxication and temperature reactions are more pronounced. At the same time, such symptoms of intoxication as pallor and dryness of the skin, and in some cases, a gray tint of the skin cover, did occur. The pallor and dryness of the skin, which may indicate intoxication, disappeared significantly faster in patients, whose complex treatment included Enterosgel.

Nausea and vomiting, which indicated intoxication, were stopped in both compared groups approximately equally within three days from the start of treatment. However, the normalization of the stool, including the disappearance of pathological impurities in the feces in the form of mucus and greenery, in children with diarrhea syndrome occurred significantly faster when the complex treatment included Enterosgel.

There were no adverse effects on blood counts in patients treated by Enterosgel®, as evidenced by a comparative analysis with blood counts of patients who did not receive Enterosgel® and confirms the safety of its use in terms of an adverse effect on the blood test results.

Children with diarrhea syndrome stayed in hospital significantly less time when Enterosgel® was included in the complex treatment.

Conclusion

The complex treatment of children aged from one month (newborns) to 17 years with the pathology of the digestive system accompanied by diarrhea syndrome is efficient with the enterosorbent effect of Enterosgel®.

Ethics Approval and Consent to Participate

The study was approved by the Ethics committee of the Research and Clinical Institute of Pediatrics named after Yuri Veltischev of the Pirogov Russian National Research Medical University of the Ministry of Health of the Russian Federation. All participants gave their written informed consent to take part in the study. The study was done in accordance with the principles outlined in the Declaration of Helsinki (1964).

Consent for Publication

The written informed consent was obtained from the patients and their parents for the publication of this article. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Competing Interests

None of the authors has any competing interests in the manuscript.

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Authors' Contributions

GV collected the clinical material, interpreted data, organized discussion, designed the article, and wrote the first draft of the manuscript. VN analyzed all laboratory data obtained, provided the comparative analysis of all clinical data and laboratory results, and prepared the illustrative material for the manuscript. AI provided a critical revision of the article. All of the authors approved the final version of the article and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Bibliography

1. Kokryakov VN., *et al.* "Modern concept of antimicrobial peptides as molecular factors of immunity". *Medical Academic Journal* 4 (2010): 149-160.

2. Sidorenko SV and Tishkov VI. "Molecular basis of antibiotic resistance". *Advances of Biological Chemistry* 44.2 (2004): 263-306.

3. Simbirtsev AS. "Cytokines - a new system for regulating the body's defense reactions". *Cytokines and Inflammation* 1.1 (2002): 9-16.

4. Bondarev EV., *et al.* "The use of enterosorbents in medical practice". *Pharmacist Electron Resource* (2008): 13.

5. WGO practice guideline: acute diarrhea. World Gastroenterology Organisation (WGO). WGO practice guideline: acute diarrhea. Munich, Germany: World Gastroenterology Organisation (WGO) (2008): 28.

6. Mujawar QM., *et al.* "Efficacy of dioctahedral smectite in acute watery diarrhea in Indian children: a randomized clinical trial". *Journal of Tropical Pediatrics* 58.1 (2012): 63-67.

7. Kudlova E. "Home management of acute diarrhoea in Czech children". *Journal of Pediatric Gastroenterology and Nutrition* 50.5 (2010): 510-515.

8. Gutiérrez Castrellón P., *et al.* "An evidence based Iberic-Latin American guideline for acute gastroenteritis management in infants and prescholars". *Anales de Pediatría* 72.3 (2010): 220.e1-220.e20.

9. Wingate D., *et al.* "Guidelines for adults on self-medication for the treatment of acute diarrhoea". *Alimentary Pharmacology and Therapeutics* 15.6 (2001): 773-782.

10. Khediri F., *et al.* "Efficacy of diosmectite (smecta) in the treatment of acute watery diarrhoea in adults: a multicentre, randomized, double-blind, placebo-controlled, parallel group study". *Gastroenterology Research and Practice* (2011): 783196.

11. Borghede MK., *et al.* "Bile acid malabsorption investigated by selenium-75-homocholic acid taurine ((75)SeHCAT) scans: causes and treatment responses to cholestyramine in 298 patients with chronic watery diarrhoea". *European Journal of Internal Medicine* 22.6 (2011): e137-e140.

12. Levi F., *et al.* "Dietary fibre and the risk of colorectal cancer". *European Journal of Cancer* 37.16 (2001): 2091-2096.

13. Bergman M., *et al.* "Effect of citrus pectin on malignant cell proliferation". *Biomedicine and Pharmacotherapy* 64.1 (2010): 44-47.

14. Marlett JA., *et al.* "American Dietetic Association. Position of the American Dietetic Association: health implications of dietary fiber". *Journal of the American Dietetic Association* 102.7 (2002): 993-1000.

15. Van der Hagen SJ., *et al.* "Conservative treatment of patients with faecal soiling". *Techniques in Coloproctology* 15.3 (2011): 291-295.

16. Brouns F., *et al.* "Cholesterol-lowering properties of different pectin types in mildly hyper-cholesterolemic men and women". *European Journal of Clinical Nutrition* 66.5 (2012): 591-599.

17. Bazzano LA. "Effects of soluble dietary fiber on low-density lipoprotein cholesterol and coronary heart disease risk". *Current Atherosclerosis Reports* 10.6 (2008): 473-477.

18. Murata Y., *et al.* "Adsorption of bile acid by chitosan-orotic acid salt and its application as an oral preparation". *Chemical and Pharmaceutical Bulletin (Tokyo)* 52.10 (2004): 1183-1185.

19. Out C., *et al.* "Bile acid sequestrants: more than simple resins". *Current Opinion in Lipidology* 23.1 (2012): 43-55.

20. Khediri F., *et al.* "Efficacy of diosmectite (smecta) in the treatment of acute watery diarrhoea in adults: a multicentre, randomized, double-blind, placebo-controlled, parallel group study". *Gastroenterology Research and Practice* (2011): 783196.

21. Kremer AE., *et al.* "Cholestatic pruritus: new insights into pathophysiology and current treatment". *Hautarzt* 63.7 (2012): 532-538.

22. Kremer AE., *et al.* "Pruritus in liver disease. Pathogenesis and treatment". *Nederlands Tijdschrift voor Geneeskunde* 155.52 (2011): A4045.

23. Hübner WD and Moser EH. "Charcoal tablets in the treatment of patients with irritable bowel syndrome". *Advances in Therapy* 19.5 (2002): 245-252.

24. Ursova NI and Gorelov AV. "Modern view on the problem of enterosorption. The optimal approach to the choice of drug". *Russian Medical Journal* 19 (2006): 1391-1396.

25. Pasechka NV. "The stabilizing effect of enterosgel on the structural bases of membrane digestion and absorption in the small intestine in severe thermal skin burns". *Fiziologichnyi Zhurnal* 42.5-6 (1996): 94-100.

26. Nikolaeva LG., *et al.* "An experimental study of the efficacy of enterosorbents in salmonellosis". *Zh Mikrobiol Epidemiol Immunobiol* 2 (1994): 7-11.

27. Nikolaeva LG. "The microbiological aspects of using enterosorbents in acute intestinal infections". *Lik Sprava* 8 (1993): 81-83.

28. Sturino JM., *et al.* "Effective Sequestration of Clostridium difficile Protein Toxins by Calcium Aluminosilicate". *Antimicrob Agents Chemother* 59.12 (2015): 7178-7183.

29. Parfenov AI., *et al.* "Postinfection irritable bowel syndrome". *Ter Arkh* 81.2 (2009): 39-45.

30. Petukhov AB., *et al.* "Results of use of Enterosgel for the treatment of diseases of the digestive system associated with impaired digestion and absorption. Clinical use of Enterosgel in patients with pathology of the digestive system: new approaches to therapy". Guidelines for doctors. Edited by Maev IA, Shevchenko YuN, Petukhova AB. Moscow (2000): 21-27.

31. Eutamene H., *et al.* "The role of mucoprotectants in the management of gastrointestinal disorders". *Expert Review of Gastroenterology and Hepatology* 12.1 (2018): 83-90.

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