An innovative approach in the treatment of H. pylori infection in children.

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The significant reduction in the effectiveness of *H. pylori* infection eradication therapy in recent years [10] [5] is due primarily to the increase in resistance of bacteria to antibiotics, indicating the need to develop an alternative method of treatment [1] [21]. The widespread use of antibiotics is rather paving the way to a modifying effect on the intestinal microbiota. In the Maastricht Consensus Report [3] it is reflected that one of the perspective directions of the treatment of *H. pylori* infection is the use of acid-probiotic strains (*S. boulardii*, *L. rhamnosus* GG, *L. reuteri*, *L. plantarum*, *L. acidophilus*, *L. gasseri*) [12] [15] as a means of adjuvant therapy of *H. pylori*.

The action of probiotics is multifaceted and can not be reduced to simple intestinal colonization [2]. Probiotics affect the structure and function of the commensal microbiota, modulate the response of epithelial cells and the immune system, restore the integrity of the intestinal barrier by reducing translocation of bacteria and macromolecules, reduce the severity of gastric mucosal inflammation [16], inhibit pathogenic bacterial activity by producing antimicrobial peptides, and short chain fatty acids, reduce the local pH in the intestinal lumen, creating unfavorable conditions for the development of pathogens and stimulate epithelial mucin production, leading to a reduced capacity for the attachment of pathogens to epithelial cells. They reduce the adhesion of *H. pylori* and inhibit growth of epithelial cells of the stomach due to lactate production [6] and bacteriocins [2], and inhibit H. pylori urease [9].

Several studies have demonstrated the high effectiveness of probiotics not only as an adjuvant [7] [8] [14] [17] [19] [20] [22] but also as monotherapy in *H. pylori* infection [13] [18]. In Russia in 2014 there was the HELINORM® product used containing in its composition the substance Pylopass ™ (*Lactobacillus reuteri* DSMZ17648) - a strain that specifically coaggregates and reduces the mobility of *H. pylori*, resulting in a bound pathogen which can not enter anymore the gastric mucosa and is excreted from the stomach [1].

The aim of our study was to determine the effectiveness of the product Helinorm containing the inactivated bacterium *Lactobacillus reuteri* in monotherapy of *H. pylori*

infection in children, as well as to evaluate its impact on the incidence of adverse drug reactions, and the percentage of eradication in combination with standard anti-*Helicobacter* scheme.

We observed 49 children (20 girls and 29 boys) aged 9 to 17 years with chronic HP-associated gastroduodenal diseases: 47 children (96%) with chronic gastroduodenitis, 2 children with duodenal ulcer (4%) not previously treated with eradication therapy. An esophago-gastro-duodenoscopy was performed in all children by standard technique with a biopsy of the mucous membrane of the antrum, gastric body, duodenum, followed by morphological study of biopsy specimens. The morphologic changes were assed using the visual-analogue scale (Aruin LI, 1996) according to which the degree (mild, moderate, severe) of mononuclear and neutrophil infiltration, atrophy of glands, intestinal metaplasia, was determined. In addition, we conducted a quantitative assessment of *Helicobacter* bacteria colonized in the mucous, the determination of its forms (spiral-form, coccal), their percentage and their preferential localization (in the pits on the surface) in the mucosa.

The division into groups was carried out in accordance with the selected treatment scheme. The 1st group consisted of 17 children, with a short history and a moderate severe character of the gastroenterological discomforts. The endoscopic picture predominated in this group displayed superficial gastritis of moderate severity (64.5%) in combination with a surface duodenitis (88.2%). All these children obtained for 4 weeks the monotherapy with HELINORM®, 1 capsule (200 mg) per day during the meal, washed down with a little water.

The comparison group consisted of 16 children treated with the classical scheme of eradication in accordance with the guidelines of NASPGHAN-ESPGHAN, advising optimal schemes, which are a combination of PPI with two antibiotics: amoxicillin + clarithromycin / amoxicillin + metranidazol / clarithromycin + metronidazole [9]. According to national clinical guidelines [3] the addition of bismuth tripotassium dicitratobismuthate to the standard triple therapy can increase its effectiveness.

We chose the eradication scheme omeprazole + amoxicillin + metronidazole + Denol. The drug is prescribed in a dose of age. The duration of therapy was 10 days. All the children in this group had a long history of gastrointestinal complaints of varying severity (moderate to intense). The endoscopic pictures provide predominant

common superficial gastritis of moderate severity (50%), focal antral gastritis (25%), erosive gastritis, antral (18, 8%) in combination with a surface duodenitis (81.2%).

The third group of 16 children received the above eradication scheme for 10 days in combination with HELINORM®. The duration of therapy was 4 weeks. This group included children with severe complaints and having a long gastroenterologic history, but they did not have previously receive any eradication therapy. The endoscopic picture was dominated by common superficial gastritis (68.8%), erosive gastritis, antral (25%) in combination with a surface duodenitis (100%). Two children (12.5%) were diagnosed with ulcer bulbs (12 sc) without signs of bleeding.

To assess the dynamics of complaints a questionnaire was used for the following symptoms: abdominal pain, belching, heartburn, nausea, vomiting, abnormal bowel movements, taste change, rash on the body. The intensity of the symptoms was recorded by the patient before, during the whole treatment (10 days) after completion of therapy and at follow-up examination.

Statistical significant differences we found in eradication schemes. In the patients treated with HELINORM® the gastrointestinal symptoms have been stopped faster, taste disorders were rarely developed, no increase in abdominal pain and changes in the nature of stool were observed.

In order to evaluate the effectiveness of therapy, not earlier than 6 weeks after completion, endoscopy was executed again with biopsy of the mucous membrane of the antrum, stomach and duodenum body. For the diagnosis of *H. pylori* a rapid urease test ("HELP" -test "AMA" OOO, Russia, St. Petersburg), a carbon 13C breath test (13C UBT HeliforceTM, Beijing Richen-force Science Technology Co., Ltd, China), "Helic“-test using the indicator "Helic" -tubes ("AMA" OOO, Russia, St. Petersburg), morphological study of biopsy specimens with assessment of morphological changes on the visual analogue scale Aruin were used.

After control examination the successful eradication of *H. pylori* was achieved in 68.75% of children of the control group treated with standard therapy. HELINORM® monotherapy was effective in 50% and in combination with the scheme of quadruple 60% of cases have been eradicated. In the groups with HELINORM a good tolerability was observed, adverse drug reactions were less frequently monitored and more symptoms of inflammatory changes of the gastric mucosa were greatly decreased in comparison with the control group.

Our research has confirmed, *L. reuteri* have a pronounced anti-helicobacter activity and its use as adjuvant therapy of *H. pylori* in children appears to be very promising, especially in the case of detection of infection with *H. Pylori* with no absolute indications for eradication. A superficial gastritis HELINORM® monotherapy is superior to standard therapy, because it is better in relieving clinical symptoms and morphological changes in the gastric mucosa, which is a favorable parameter in reducing the risk of atrophic gastritis in the long run.

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