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Features of diagnostics, clinical course and treatment of helicobacter pylori infection in children

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The article is devoted to study of endoscopic, morphologic and clinical features of the course of chronic diseases of the upper parts of digestive system associated with Helicobacter pylori infection in children. The age prevalence of gastrointestinal diseases among schoolchildren, features of their accommodation, nutrition, and education were studied using screening questionnaire. Comparative efficacy of several invasive and non-invasive Helicobacter pylori diagnostic techniques in children was tested. The diagnostic value of qualitative Helicobacter pylori stool antigen test employing and comparative efficacy of different methods of eradication therapy (triple- and quadro-) based on using bismuth containing drugs and the proton pump inhibitors were studied. The tolerance and frequency of side effects associated with the use of eradication therapy were investigated.

Key words: *gastritis, gastroduodenitis, stomach ulcer, Helicobacter pylori, diagnostics, treatment, eradication.*

Cechy diagnozy, przebiegu klinicznego oraz leczenia infekcji u dzieci wywołanych Helicobacter pylori

Artykuł poświęcony jest badaniom endoskopowych, morfologicznych i klinicznych cech przebiegu przewlekłych chorób górnych części układu trawiennego związanych z infekcją Helicobacter pylori u dzieci. Badania przeprowadzone przy pomocy kwestionariusza objęły częstotliwość występowania chorób żołądkowo-jelitowych wśród dzieci szkolnych, warunki ich zamieszkania, wyżywienie oraz poziom wykształcenia. Porównano też kilka inwazyjnych i nieinwazyjnych technik diagnozowania Helicobacter pylori u dzieci. Oceniono też wartość diagnostyczną testu antygenowego oraz skuteczności różnych metod terapii z zastosowaniem leków zawierających bizmut oraz inhibitorów pompy protonowej. Dodatkowo badano tolerancję oraz częstość występowania skutków ubocznych związanych z zastosowanym leczeniem.

INTRODUCTION

Helicobacter pylori (H.pylori) is one of the most common pathogens in humans which cause the diseases of the upper gastrointestinal tract (UGIT) [4, 7, 9, 12, 14, 20]. During the last years in Ukraine we have observed an increase in the prevalence of chronic gastroduodenal diseases both in adults and children. The frequency of these diseases has increased more than 1.5 times for the last 3 years and reached 160 per 1000 children's population. For this reason they account for the large part of the diseases in children and teenagers [17–19].

The most common diseases among children are the gastroduodenal illnesses associated with H. pylori. The different clinical presentations, the influence of daily life conditions, and the family genetics are the reasons for why H. pylori is considered the infectious disease with characteristics of uncontrolled epidemic in our country. The role of H. pylori in the development of chronic gastroduodenal diseases is well known around the world; however there is a lack of information about the prevalence of H. pylori in children and teenagers in the countries like Ukraine [5, 19, 23]. There are no reports about the virulence and pa-

thogenicity of H. pylori strains, the modes of transmission in children, and the role of family and school environment in the transmission. The optimal protocols of eradication therapy are still vague, because of the regional patterns of antibiotic resistance of H. pylori. Asymptomatic chronic erosive gastritis, ulcer disease, stomach dyspepsia requires the development of new algorithms for diagnosis and treatment, planning surveillance in a regional scale, especially in countries with a considerable economic deficit [6, 10, 11, 20, 23].

In spite of considerable experience in studying of various aspects of H. pylori infection questions of epidemiology, the degree of pathogenicity of regional strains, routes of transmission in children, and the optimal treatment methods have not been clarified and still represent a matter of debates [2, 15, 18, 21].

The leading role of *H. pylori* in ulcer disease, gastritis, non-ulcer dyspepsia, and gastric cancer has been confirmed. The connection between *H. pylori* and the development of reflux-esophagitis and ulcers which are induced by using non-steroid anti-inflammatory medicines is less clear. However, it is proved that *H. pylori* could be found in 90–100 % of patients with duodenal ulcers and in 85–90 % with gastric ulcers [3, 5, 19].

The investigations reported from different countries proved the high prevalence of *H. pylori* infection in both adults and children. According to the data of the last year the prevalence of *H. pylori* colonization in the adult population of Ukraine is about 80–85 % but in children's population this value has not been established yet. However there are reasons to predict that it could be high enough around 40–70 % depending on child's age. The frequency of *H. pylori* infections increases with the age of the child. According to the data of Russian researchers *H. pylori* infection of 5–6 years old children in Russia is about 40–45 %, and in 14–15 years old children it reaches the level of adults – 65–70 %. The figures are substantially different in other countries. According to the literature *H. pylori* colonization of schoolchildren is around 4,2 % in Belgium, 28,9 % in Italy, 63 % in Czech Republic, 70 % in Russia, 80,6 % in Benin, 84 % in India, and 96 % in Albania. In developed countries, such as the USA, Germany, Sweden, Japan, the prevalence of *H. pylori* in child's age is lower, although with age it increases. The high prevalence of *H. pylori* in Ukraine can be explained by low socio-economic status of the population, unsatisfactory living conditions, peculiarities of feeding, insufficient hygienic skills, low level of sanitary education, and poor organization of medical care [5, 12, 20].

A systematic control of *H. pylori* infection in the leading countries of the world (such as the USA, Japan, countries of Western Europe) reduced its prevalence in children's population that in turn caused the decrease of frequency of stomach cancer, ulcer disease and gastroduodenitis. In Ukraine we can see steady increase in incidence of these diseases. The problem is that the treatment of children begins too late, in 1–3 years after the appearance of the first symptoms of the diseases. No less important is underestimation by the children's parents of the gastrointestinal child's complaints, insufficient information of pediatricians and family doctors about the role of *H. pylori* in the development of chronic gastrointestinal diseases in children. The situation is complicated due to use of outdated equipment, lack of possibilities for modern diagnostics, absence of clear national recommendations and standards of treatment, lack of prevention and control measures for these pathologies [4, 5, 16].

The inadequate plans of treatment and reduction of doses and duration of taking medications very often result in insufficient efficiency of eradication treatment in children. The situation is complicated by the high cost of noninvasive methods to control efficiency of eradication [8, 22, 23].

According to our data children from socially unfavorable families the number of which is rather considerably high in Ukraine are the most vulnerable to infecting and further development of the disease. In such families we can find low local immunity in children, lack of hygienic skills, overcrowding of flats and high frequency of parents infections. Taking all this into account one of the most important task is to conduct educational work in those families which has to be based on the results of our own local research. Thus, in spite of the high prevalence *H. pylori* in Ukraine and substantial increase of the incidence of *H. pylori* associated diseases we do not have the real possibilities for its timely diagnosis, treatment and prevention [5, 19, 23].

The way to improve treatment outcomes is the optimal combination of medicines for eradication therapy. According to generally accepted recommendations the treatment must be simple, have a good tolerance, accessible on costs and eradication effect has to exceed 80 %. However treatment patterns suggested for adults have being con-

stantly modified and not always can be used in pediatric patients. In 2000 the special European commission worked out the main principles of consensus of *H. pylori* diagnostics and eradication in children which were practically changed in various countries. The first Ukrainian recommendations for diagnosis and therapy of chronic stomach and duodenal diseases in children were proposed in Kyiv in 1999. They have being permanently modified because of the local peculiarities of *H. pylori* sensitivity to antibiotics and insufficient possibilities for laboratory evaluations. That is why the regional standards of investigation of patients with chronic UGIT diseases and *H. pylori* eradication are needed. They should take into account both the availability of laboratory and instrumental facilities and regional peculiarities of *H. pylori* sensitivity to antibacterial medicines [6, 8, 11, 13, 18, 22, 24]. We elaborated our first regional guidelines in 2000.

In spite of that our data suggest that almost the half of children visit qualified pediatric gastroenterologist only in 1.5–2 years after disease onset. Also fiber gastroduodenoscopy (FGDS) is performed only in 10–15% of the patients. Biopsy material is undertaken morphological study very rarely and only in isolated cases tests are performed to elicit the presence of *H.pylori*. Often it leads to ineffective treatment and development of recurrences within a year after the treatment has been employed. Even among pediatric gastroenterologists a widespread opinion exists that only diffuse gastroduodenitis and ulcerous lesions require complete triple- or quadrotherapy while mild gastroduodenitis limited to few areas of the stomach or duodenum and associated with *H.pylori* require monotherapy or therapy with 2 drugs.

During the last 8 years the Department of Faculty and Hospital Pediatrics at Lviv National Medical University together with the Departments of General Medicine and Microbiology was involved into the work for development of diagnostics and treatment of *H. pylori*-associated diseases in the Western region of Ukraine. From the very beginning our researchers proposed a family approach to diagnostics and treatment of this infection. At first, the results of our research were published in Polish Journal «Pediatria Wspolczesna Gastroenterologia, Hepatologia and Zywienie Dziecka» [15] and were reported in the USA (Georgetown Conference Centre, Washington DC, 2002) at the "Children's Environmental II: A Global Forum for Action" [16].

PURPOSE OF THE STUDY

To increase the efficiency of diagnostics and treatment of children with chronic diseases of UGIT associated with *H.pylori* by introducing the methods of early disease diagnosis, studying of clinical course features, and introduce the effective methods of noninvasive diagnostics and contemporary protocols of eradication therapy.

The study was carried out at several steps. First of all we have performed the primary screening of children (by the method of questionnaire) to identify the children with upper gastrointestinal complaints. The next stage was in-depth physical examination of these children at school setting to find out objective symptoms, which could confirm upper gastrointestinal diseases. Then we carried out the instrumental and laboratory investigation of the selected children to verify the diagnosis of upper gastrointestinal diseases and its etiology. After that the children with upper gastrointestinal diseases were arranged into two groups: colonized with *H. pylori* and those who were not. The last step was to investigate the efficiency of different methods of *H. pylori* diagnostics and protocols of eradication therapy in children with *H. pylori*-associated diseases based on clinical data and patterns of *H. pylori* antibiotic resistance.

At the first step of work the interviewing was conducted involving 17480 schoolchildren of 1–11 forms. The numbers of boys and girls were nearly equal.

According to the questionnaires it was found out that about 13% of schoolchildren live in incomplete families (with substantial increase in higher forms: from 9,9% to 14,7%, $p<0,001$), 8,6% – in hostels, 14,6 % children and parents considered their socioeconomic conditions as unsatisfactory. 55,4 % children did not have a separate room, 18,5 % – separate table for work, 14,2% – separate bed. One-third of schoolchildren have a dog or a cat at home which can be the potential source of *H.pylori* and helminthic infestation.

Analyzing the health condition of schoolchildren family members we found that most of them had chronic diseases of UGIT (32,6 %) comparing to morbidity due to diseases of respiratory system – 32 %, cardiovascular system – 28,7 % ($p<0,01$), and urinary system – 24,3 % ($p<0,001$). These data confirm the wide prevalence of gastroduodenal diseases in the population and indicate necessity of systematic measures directed against them to be taken for both children and their household.

The important risk factor in such diseases development was the violation of adequate chil-

dren's nutrition. From our questionnaire 13,3% of schoolchildren had irregular nutrition and 17,7% showed unsatisfactory diet by its quality. Almost 2,5% of schoolchildren ate only twice a day, and a general number of such kids grew threefold in senior forms. Practically, every fifth schoolchild ate nothing at school, where he or she stayed most of the day. Among first-class boys and girls only 25,5% used school dinners but among graduating pupils – 3,9%. The most popular kind of food was a sandwich which was brought by 2/3 children to school. Every second schoolchild had a harmful habit to eat just before sleep.

The main complaints of all age's schoolchildren were typical for gastroduodenal disorders. The most frequent complaint identified in 71% of children was abdominal pain. Almost a half of pupils complained on disturbance of appetite, periodic nausea, and regurgitation. The typical complaints were motility disorders of UGIT: epigastric burning, feeling that meal heavily swallows, bitter or sour taste in oral cavity. Prevalence of such complaints was substantially increased among the children of higher forms, which meant the increase of the pathology of digestive system prevalence with age.

Other complaints were headache, dizziness, fatigue, sweating, cold sensation in the limbs, changes of face colour at agitation. Prevalence of these symptoms was also increased in pupils of higher forms.

At the next step of the research, we selected children with probable pathology of the digestive system by specially developed computer analytic system.

Among pupils selected for positive findings in screen-questionnaire and at examination, we could not confirm functional or organic disorders of UGIT in 38 % of pupils. In 23% of children there were clear clinical and/or instrumental signs of motility disorders such as duodenogastric and/or gastroesophageal refluxes. In 39% of selected schoolchildren we defined the organic changes of mucous membrane (GM) of UGIT which were typical for gastroduodenitis, gastritis or ulcer disease. 81% of them were associated with *H.pylori*.

To study endoscopic, morphologic and clinical features of the course of chronic diseases of UGIT associated with *H. pylori* comparing to similar diseases of other etiology we formed 2 groups of children. Into the main group we included 120 children (mean age – 12,52±1,83 years) with the inflammatory UGIT diseases associated with *H.pylori*. Into the group of comparison we included 20 children (mean age – 12,40 ±2,06 years) with the UGIT diseases which were not associated with *H. pylori*.

The spectrum of diseases in children from the main group was represented by chronic diffuse gastroduodenitis with increased acidity in relapse (65%) and chronic isolated gastroduodenitis (35%), 10,8% of children had duodenum ulcer and in 13,3% we diagnosed erosive gastroduodenitis. In the comparison group the spectrum of diseases based on main diagnoses was following: chronic diffuse gastroduodenitis with increased secretory function in relapse – 70% and chronic local spotty gastroduodenitis – 30%.

Having interviewed schoolchildren and elicited their social and domestic features we compared them to the similar outcomes in children of the main group and group of comparison. Analyzing the condition of residence we identified that children with helicobacteriosis more frequently lived in unsatisfactory conditions, in hostels or in incomplete families.

There was more chronic UGIT diseases (81,7%) in other family members in children from the main group and children from comparison group (30,5%, $p<0,001$) that confirms domestic origin of helicobacteriosis. Such a conclusion was supported by significant correlation between revealed colonization with *H.pylori* and presence of UGIT disease in family members ($r =+0,42$).

Our studies defined the necessity to improve organization of medical supervision of children with gastroduodenal pathology by pediatric gastroenterologist. In spite of the fact that most of the children had typical for chronic disorders of UGIT complaints only 13 children (10,8%) from the main group had underwent endoscopy and none of them had had target biopsy of gastric mucosa or *H.pylori* test. As a result children did not receive adequate treatment.

In the study we determined a similarity of clinical diseases manifestation in children of the both groups. At the same time, children with helicobacteriosis had rarely mild disease (respectively, 7,5% vs. 40%, $p<0,001$) and more frequently had recurrent abdominal pain (45,8% vs. 20,0%, $p<0,05$). Symptoms of UGIT motility disorders were very marked: sour reflection (87,5% vs. 65,0%, $p<0,01$), epigastric burning (43,3% vs. 15,0%, $p<0,05$), early satiation with food (53,3% vs. 25,0%, $p<0,05$), feeling of discomfort in epigastrium (respectively, 52,5% vs. 10,0, $p<0,001$). At physical examination children with helicobacteriosis substantially more frequently had an un-

pleasant smell from a mouth (77,5% vs. 30,0%, p<0,05), moderate dryness of skin (28,5% vs. 5,0%, p<0,05), muscular defense of the anterior abdominal wall at deep palpation (respectively, 55,8% vs. 30,0%, p<0,05). There was no difference in the frequency of the other symptoms between the 2 groups.

The all children in the both groups were investigated with EGDS supplemented with target biopsy of gastric mucosa in the antral and fundal parts of the stomach, and simultaneous gastric pH measurement. With EGDS we found a similar visual picture in the both groups of children which was characterized by motility disorders (change of retraction, presence of refluxes, functional insufficiency of cardiac part of the stomach, gastroesophageal prolapse, not fully closed pylorus), inflammatory changes (hyperemia of gastric mucosa, increase volume of secretory mucus). More secretions were found in the esophagus of children from the control group (respectively, 50,0% vs. 26,7%, p<0,05), while in the children from the main group there was significantly more gastric mucus (respectively, 94,2% vs. 65,0%, p<0,001). We observed destructive changes of gastric mucosa and duodenum (erosions, ulcers) only in children of the main group, but the number of these cases in our study was insufficient to reach statistically significant difference.

At morphological study of biopsy materials of gastric mucosa taken from the antral part of the stomach, all children of the main group had certain inflammatory changes while in the group of comparison such changes were found only in 65% of children (p<0,001). Degree of inflammatory process was substantially higher in children with helicobacteriosis. In children from the main group there was considerable local infiltration by lymphocytes, neutrophiles, and cellular polymorphism. Some of them had a mixed local spotty character of gastric mucosa infiltration. In 4 children of the main group we observed lymph follicles with germenative centers typical for helicobacteriosis [12]. The other changes of antral gastric mucosa, local atrophy of glands, polyp like changes of GM, local intestinal metaplasia, and congestion were similar in the both group.

In biopsy samples taken from the fundus of the stomach of children from the main group there was greater activity of inflammatory process with more frequent lymphatic and neutrophil infiltration, local intestinal metaplasia of gastric epithelium. The other morphological changes of GM in the fundal part were not different in the both groups of children.

Thus, considerable degree of inflammation of GM, massive infiltration of mucus membrane with cellular elements, formation of follicular lymphoid hyperplasia, local intestinal metaplasia must alert physician to think about the disease of *H.pylori* etiology.

Nowadays diagnostics of *H.pylori* infections in children is based on the data obtained by various methods which differ each from other by the degree of invasiveness, additional equipment used, time required, specificity and sensitivity [1, 4, 7, 12, 16]. For the last time morphological investigation is the most important diagnostic method of *H.pylori* infection which is considered as a "gold standard" of this bacteria identification [12]. According to our data, the presence of *H.pylori* was determined in biopsy samples of antral part in 103 children (85,8%) and in biopsy materials from fundal part in 61 child (50,8%) that corresponds to the findings of other authors. Negative results of combined fundal and antral biopsy were documented in 5 (4,17%) children of the main group suggesting the high sensitivity of this method (~ 96%). It is useful to note that in some children of the main group *H.pylori* was identified only in biopsy materials of fundal part of GM that necessitates not only antral but fundal biopsy also.

Until now EGDS has been an important invasive method of diagnostics of UGIT chronic diseases associated with *H. pylori*. One third of our children from the main group did not have the clear endoscopic signs of helicobacteriosis despite the presence of infection proven by histological investigation and ELISA.

We used the print smears of GM taken from the areas of maximal hyperemia and edema. Positive diagnosis of helicobacteriosis was documented only in 67 children (55,8%) of the main group that questions the value of this method as a main diagnostic tool taking into account a high percent of errors and availability of more sensitive and specific assays for verification of the diagnosis.

CLO-test and bacteriological method also had low sensitivity (respectively 70,8% and 60%) that substantially limited their use in practice of pediatric gastroenterologist.

Enzyme linked immunosorbent analysis of RIDASCREEN® for Helicobacter by which we determined the presence of antibodies (IgG) against *H.pylori* in the blood serum showed positive result in 112 children (93,3%) with helicobacteriosis. Express method employing one-step strip-

test for assaying of anti-helicobacter antibodies in capillary blood showed positive result in 110 children (91,7%). Results of express method were insignificantly less accurate than the results obtained by ELISA but this method was more acceptable in routine practice of pediatric gastroenterologist, pediatrician or family physician. Sensitivity of 92% is considered enough for wide use of the method and its simplicity as well as a possibility to get prompt result make it very comfortable.

At the same time we noted that its use in children younger than 10 years brought the increase of negative results which is probably associated with features of immune system in this age. Last time we started to use the test systems for immunochromotographic detection of *H.pylori* antigens (Cito Test H. Pylori Ag) in excrements. The results were positive in 93% of infected children independently of age. It is simple and comfortable for use.

Comparing sensitivity and convenience of different methods for *H.pylori* determination one can make a conclusion that a very sensitive method of *H.pylori* infection diagnostics is a morphologic method which has some flaws because of its invasiveness. Modern non-invasive methods of diagnosis with use of ELISA and immunochromotographic reactions have a sensitivity which is close to the "gold standard" and may be used in clinical practice decreasing the need for EGDS. Method Cito-Test-H.pylori-Ag is very promising and convenient for diagnostics.

In order to determine the effectiveness of various protocols of eradication therapy, their tolerability and complications 120 children where divided into 4 groups depending on given particular protocol of treatment. The group 1 comprised of 30 children who took de-nol (colloid bismuth subcitrate) + flemoxin-solutab (amoxiciline) + clarytromicin (fromilid) (DFC); the group 2 – 30 children who took de-nol + flemoxin solutab + furazolidon (DFF); the group 3 – 30 children who took proton pump inhibitor (PPI) nexium + flemoxin-solutab+clarytromicin (NFC); the group 4 – 30 children who took de-nol + flemoxin-solutab + claritromicin + nexium (DFCN).

Duration of the treatment lasted 7 days and medication doses were as follows: de-nol – 8 mg/kg/24 hours – 2 intakes, flemoxin solutab – 50 mg/kg/24 hours – 2 intakes, clarytromicin (fromilid) – 7,5 mg/kg/24 hours – 2 intakes, furazolidon – 8 mg/kg/24 hours – 3 intakes, nexium – 0,5 mg/kg/24 hours – once in the evening.

Prescribing therapy we followed a «family approach» to diagnosis and treatment of helicobacter-associated children's illness which was implemented into the practice of gastroenterologists in our region for the first time. This approach gave us an opportunity to eliminate the bacteria in household and prevent possible re-infection in children after complete eradication being achieved.

Dyspepsia and abdominal pain were frequent and prevalent findings in helicobacteriosis together with signs of motility disorders of UGIT and weakness. Evolution of pain in the groups of children depended on the therapy received, localization of pain, and timing to meals. In group 1 feeling of pain decreased on 5,64±0,23 day and pain relived on 7,80±0,31 day from the beginning of treatment. In children of the group 2 the decrease and disappearance of pain occurred within the similar period of time. Children treated with nexium (group 3) had faster disappearance of pain in comparison to 2 groups above. In the group of children received quadrotherapy we documented similar to group 3 dynamics of pain. It was also faster than in groups 1 and 2.

The similar dynamics was observed for the group of clinical symptoms suggestive to motile disorders of UGIT such as heartburn and pain in the chest, belching and hoarseness of voice in the morning.

Summarizing the observation of disease clinical course we can make a conclusion that in each group there was a decrease in frequency of complaints and relief from symptoms of illness. In groups of patients where eradication therapy included bismuth based drug (1st and 2nd group) and antibiotics eradication of pathologic symptoms was slower and there was no considerable difference between these two groups. In sub-groups where eradication therapy included PPI timeframe for resolution of pathologic symptoms was faster.

An important component in the assessment of therapy efficacy is tolerability, frequency and severity of adverse events and complications resulting in finishing of the treatment.

In general the all medications mentioned above were well tolerated with no complications or adverse effects seen in any group. At the same time breakdown of adverse events differed. The lowest frequency of adverse events (33,3%) was

TABLE 1. Frequency of side effects in children on eradication therapy

Data	1st group n=30	2nd group n=30	3rd group n=30	4th group n=30
Total	10	14	14	16
Mild	9	12	13	12
Moderate	1	2	2	4
Severe	0	0	0	0
Nausea	3	9	4	3
Vomiting	0	1	0	0
Change of taste	1	1	1	1
Diarrhea	4	1	8	7
Dizziness	0	0	0	1
Eruption, itching	0	1	1	1
Dryness in mouth	0	0	0	1

TABLE 2. Effectiveness of eradication therapy

Groups	Schemes of medicines	Effectiveness (%)
1	De-nol+ Flemoxin + Clarithromicine	86,7%
2	De-nol+Flemoxin+Furazolidon	80%
3	Nexium+ Flemoxin + Clarithromicine	86,7%
4	De-nol+ Flemoxin + Clarithromicine+Nexium	93,3%

in the group 1 and highest – 53,3% was in the the group 4. In the 2nd and the 3rd groups side effects were documented in 14 cases (46,7%) (Table 1).

Grading adverse events we used the following criteria: mild – symptoms present but do not change behavior of a child; moderate – symptoms present and change behavior of a child, but do not require stopping the treatment; severe – symptoms present and are so severe that advocate finishing treatment.

Some purgative effect observed in the 1st, 3rd and 4th groups of children may be explained by prokinetic action of macrolides and reaction to PPI. The most frequent side effects in the 2nd group of children were mild nausea likely because of taking of furazolidon. There were no constipation or flatulence, increase in pain syndrome, or disturbance of sleeping.

We determined effectiveness of eradication therapy in 1,5 month after finishing it by means of non-invasive highly informative method of diagnostic of antigens *H.pylori* in feces – „*H.pylori* Stool antigens test"

According to our data the most effective was quadrotherapy effectiveness of which reached 93,3%. We failed to achieve eradication in 2 of 30 children from the group 4 although there was clinical improvement in the both cases. The probable cause of that was longstanding disease or prior repeat courses of monotherapy with de-nol, metronidazol, and furazolidon.

In the group of children where triple therapy was employed with de-nol and two antibiotics we had got good results – 86,7% of successful eradication. The lowest eradication rate was achieved in the group 2 where we applied furazolidon (DFF) – 80%. Changing de-nol to nexium did not change the frequency of eradication in the group 3 where it was 86,7% (Table 2). Taking into account that effectiveness of eradication therapy must be more than 80% it is better to use protocols with DFC, NFC, DFNC. Protocols employed nexium were better but more expensive and with more side effects.

Children with successful eradication of *H.pylori* as tested in 1,5 month after finishing therapy repeated antigens *H.pylori* studies in 6 and 12 months. In six months we got negative results in all children who had negative results at their first check of eradication status but 6–10% of children showed recurrence of mild UGIT motility disorders with heartburn, eructation, bad appetite, fast stomach filling sensation. In 12 months situation changed. In each group we found children with positive reaction to *H.pylori*. From the first group – 2 children (7,7% of successful eradication cases), from the second group – 3 children (12,5%), from the third group – 2 children (7,7%), from the fourth group – 1 child (3,6%). One may think that reappearance of antigens of *H.pylori* in feces may be caused by re-infection. All those children were from the families where household refused treatment despite the fact that some family members had symptoms characteristic to chronic UGIT diseases.

It is interesting to note that effectiveness of eradication therapy in a subgroup of 14 children

with poor compliance (dose missing, incomplete course of therapy) was only 50%. The repeated eradication course of quadrotherapy was available for 7 children but only in 4 cases we gained eradication. These data emphasized the crucial importance of compliance (proper dosing, frequency and length of treatment) in preventing of antibiotic resistance and increasing of eradication rate.

According to significant prevalence of symptoms and signs suggestive to UGIT motility dysfunction (clinical data and results of endoscopy examination), possible disorders of gut friendly flora at the background of the disease, and antibacterial therapy, deficit of water-soluble vitamins in children with chronic pathology of UGIT, all children were prescribed to receive prokinetic motylium (domperidon), probiotics (Lactobacteria GG (LGG)+Bifidobacteria) and polivitamin-mineral medicine Multitabs for the period of three weeks. Prescribing of rehabilitation therapy contributed to fast normalization of children condition.

CONCLUSIONS

The study proved the necessity of making early diagnosis in children with chronic gastroduodenal pathology which is quite prevalent among schoolchildren. Typically, schoolchildren produce complaints with characteristic patterns for functional and organic disorders of UGIT. Such children do not apply for qualified medical care for a long time but if even they receive it, it is insufficient. All mentioned above influence the success of further treatment. Screen for those children using interviewing with questionnaires allows selecting the individuals with symptoms and signs suggesting probable pathology of UGIT. Use of ELISA and immunochromatographic methods allows diagnosing of helicobacteriosis with a high degree of reliability which makes invasive EGDS unjustified for routine use in children with gastroduodenal pathology. In the case of performing EGDS it is imperative to make target biopsy GM at fundal and antral areas of the stomach.

Management of children with helicobacteriosis of UGIT should consist of eradication therapy and rehabilitation treatment. Eradication therapy requires strict compliance to eradication protocol and "family approach" to diagnosis and treatment. Most effective protocol for eradication of H.pylori is quadrotherapy which is indicated to children with erosive gastroduodenitis or ulcer disease of the stomach or duodenum. The best protocol of triple therapy comprised of de-nol, flemoxine, clarythromicin and was optimal on cost/effect ration and frequency of adverse events.

Obligatory condition for success was examination of the household and their simultaneous treatment in the case of eliciting of *H.pylori* carrier state. In the high risk families which members were not treated the risk of re-infection is increased.

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