Helicobacter pylori eradication as prevention against chronic peptic ulcer disease in children

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Abstract

The changes caused by Helicobacter pylori are a slow, progressing inflammatory process developing from several to dozen years. H. pylori infection leads to an inflammatory response in the gastric mucosa with granulocyte infiltrates in an acute form of the inflammation, and lymphocytes, plasmatic, macrophages and eosinophils in a chronic form inducing the development of gastric and duodenal ulcers and gastric cancer in some patients.

The frequency and the type of morphological changes in the gastric mucosa were analyzed in children with positive IgG against H. pylori and the incidence of gastric and duodenal ulcers in family members of children examined was evaluated in our study. Gastritis was reported in 68.8% of children with positive IgG against H. pylori. Gastric ulcer was confirmed in 37.1% of families of children included in the study. Duodenal ulcers were found in 22.9% of families. The results obtained, indicate the usefulness of long-term observation and clinical follow-up of children with chronic gastritis of H. pylori ethiology taking into consideration bacterium eradication as prophylaxis of peptic ulceration.

Key words: Helicobacter pylori, prevention, children.

Introduction

Many authors suggest that past H. pylori infection in children is a very common phenomenon in early childhood. It has not been explained whether it is closely connected with a socio-economic factor or others, as for example, a host's immune response to the infection, which differs greatly from an adult's immune response. At the beginning, the infection develops without symptoms or subclinically, regardless the role of H. pylori in the pathology of the stomach. After about 2-4 weeks of an acute phase, the infection retreats from the corpus and develops into chronic infection located in the region of the pylorus with a normal clinical picture or mild gastritis within the corpus. In other patients, multifocal and atrophic inflammation develops affecting the corpus and the region of the pylorus. Bacteria are spontaneously eliminated in few patients. The development of an acute phase into a chronic process may result from host's ineffective defense mechanisms or numerous enzymes and cytotoxins produced by H. pylori [1-5]. In the examinations carried out in adults, it was proved that some strains of H. pylori producing VacA and CagA might induce the development of peptic ulcers or stomach cancer. Though more than 50% of H. pylori strains are virulent, this serious condition affects only minority of adults infected with these strains. There are few data concerning the influence of these virulence factors in children. The studies of H. pylori infection performed in the North America have not confirmed the relation between probable virulence factors-VacA and CagA and the onset of peptic ulcer disease. The strains possessing CagA gene were found in 75% of children with ulceration and 60% of children with gastritis histologically confirmed. The assessment of IgG immunoglobulin in the serum of children seemed to correlate with the stage of gastritis [9]. Inflammatory changes in gastric mucosa caused by H. pylori may persist from several to dozen years giving neutrophil infiltrates in the acute phase of the inflammation, and infiltrates of lymphoplasmatic cells, macrophages and eosinophils in the chronic phase. The size of leukocytic infiltrate correlates with the degree of colonization and damage to the mucosa. A low number of B lymphocytes are observed in the inflammatory infiltrate. Fewer $CD8^+$ lymphocytes contribute to the development of the inflammatory process in comparison with $CD4^+$ supporting lymphocytes [10]. The purpose of the

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Figure 1. **Age characteristics of children depending on dwelling place**

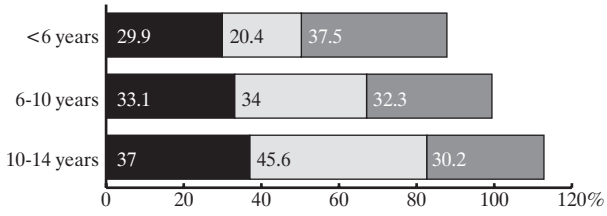


Figure 2. **Age characteristics of children with IgG titre evaluation against H. pylori**

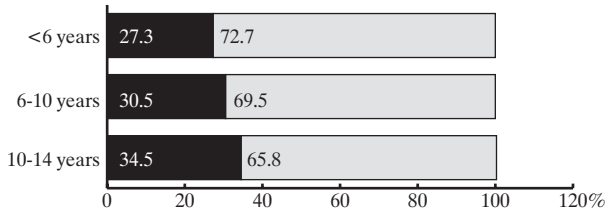
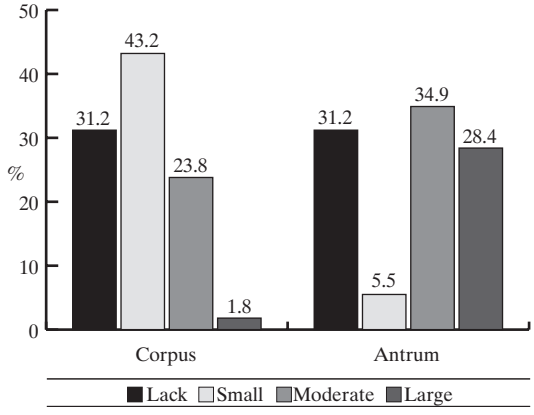


Figure 3. **Gastric corpus and antrum mucous membrane inflammation in children examined**



study was to assess the frequency and the type of morphological changes in gastric mucosa of children with positive IgG against Helicobacter pylori and the incidence of gastric and duodenal ulcer disease in family members of children examined.

Material and methods

The study included 595 children up to the age of 14 years, who underwent questionnaire examination in the national epidemiological program of Helicobacter pylori infection of The Ministry of Health and The Committee of Scientific Research N° 1-43016. A number of 176 children up to 6 years constituted 29.5% of the group; 197 children aged from 6 to 10 years – 33.2%; 222 children aged from 10 to 14 years – 37.3%. *Fig. 1* presents the structure of the group examined with regard to the place of living. Taking into consideration the gender, the group consisted of 295 boys (49.6%) and 300 girls (50.4%). The questionnaire examination performed in children up to 14 years and the assay of IgG level against H. pylori (blood samples, 2 ml each, were taken twice for clot) were aimed at evaluating the prevalence of this bacteria infection in the population randomly chosen in the region of North-Eastern Poland at the level of local district, country and provincial city. The questionnaire study, apart from the diseases of the gastrointestinal tract in children examined, referred to the incidence of gastric and duodenal ulcer disease in their family members and was to find a relation between the diseases mentioned above and H. pylori infection in the families examined. IgG antibodies against H. pylori were identified in the blood serum or plasma with a kit of "recom Well helicobacter IgG" of Mikrogen GmbH firm. The concentration of antibodies >24 U/ml was considered as positive. All children with a positive titre of IgG against H. pylori and accompanying peptic symptoms underwent gastroscopy after obtaining parents' written consent. Gastroscopic and histopathological evaluation of the antral and corpus mucosa was carried out according to The Sydney System assessing the infection severity, the stage and activity of gastritis. All children were given a quick urease test to detect H. pylori in the stomach bioptates using the kits produced and distributed by The Institute of Food and Nutrition in Warsaw. The correlation between non-measurable features was assessed by a independence test χ^2. The correlation was regarded statistically significant at $p<0.05$, whereas the correlation at the border of significance at $0.05 \leq p < 0.1$. Arithmetic means and standard deviations were used to present the mean IgG level.

Results

A positive result of serum IgG against H. pylori was found in 184 children aged up to 14 years (30.9%). In children up to 6 years, a positive result was determined in 48 children examined; in the group of 6-10 years – 60 children; in the age of 10-14 years – 76 children, which in particular groups constituted 27.3%, 30.5% and 34.5%, respectively, of all children included in the study *Fig. 2*. In children with a positive titre of IgG and clinical symptoms (109 children), gastroscopy showed that 34 children (31.2%) had no H. pylori infection in the corpus and antral mucosa. In other children, gastritis was differentiated in the antrum and corpus. Mild gastritis predominated in the corpus mucosa and was observed in 47 children (43.2%). In the antrum, moderate gastritis was found in 38 examined (34.9%) and severe in 31 children (28.4%). Mild gastritis was diagnosed in the antrum of 6 children (5.5%) (*Fig. 3*). The activity of gastritis measured by the amount of infiltrating granulocytes was higher in the antral than corpus mucosa. Chronic peptic ulcer disease was reported in 221 families of children included in the questionnaire study, which constituted 37.1% of the population examined. The lowest percentage of peptic ulcer disease was found in families of up to 6-year-old children (61 children – 34.6% and the highest

Table 1. **Gastric ulcer family history of examined children considering children's age**

Gastric ulcer in family history	Age of children							
	< 6 years		6-10 years		10-14 years		Total	
	N	%	N	%	N	%	N	%
Yes	61	34.6	74	37.6	86	38.7	221	37.1
No	115	65.4	123	62.4	136	61.3	374	62.9
Total	176	100.0	197	100.0	222	100.0	595	100.0

Significance evaluation p=0.6969; NS

Table 2. **Duodenal ulcer in family history of children considering children's age**

Duodenal ulcer in family history	Age of children							
	< 6 years		6-10 years		10-14 years		Total	
	N	%	N	%	N	%	N	%
Yes	39	22.1	46	23.4	51	23.0	136	22.9
No	137	77.9	151	76.6	171	77.0	459	77.1
Total	176	100.0	197	100.0	222	100.0	595	100.0

Significance evaluation: p=0.9662; NS

– in the families of 10-14-year-old children (86 children – 38.7%) – *Tab. 1*. Duodenal ulcer disease was reported in 136 families of children examined. Its percentage was lower when compared to gastric ulcer and equaled 22.9%. The highest percentage of duodenal ulcer was found in families of 10-14 year-old children and referred to 51 children (23%) – *Tab. 2*.

Discussion

Gastritis is a response to the infection. The severity of an inflammatory state and its consequences depend on the virulence of the strains, colonization density and an immune response. In children with a positive IgG, gastritis was observed in 68.8% of the examined and was differentiated in the antrum and corpus. Mild gastritis predominated in the corpus mucosa and developed in 47 children (43.2%). Moderate gastritis was prevalent in 38 children (34.95) and severe gastritis in 31 children (28.4%). All phenomena mentioned above, such as a damage to the protective mucous layer and epithelial cells caused by toxic agents and an inflammatory state persisting for years as well as the enhanced level of hydrochloric acid may lead to peptic ulcer disease. The discovery of H. pylori has contributed immensely to the understanding of the pathology of gastric and duodenal mucosa diseases. Gastric and duodenal ulcers in children are considered as primary in their development without any other systemic diseases. A positive family history of peptic ulcers is common in a clinical picture in this group of patients. The results of numerous examinations prove that gastritis is caused by H. pylori [11,12]. The next proof of the familiar character of gastritis and peptic ulcers in children is the grouping of H. pylori cases among the family members [13]. El-Omar et al. provided further molecular proofs of stomach cancer running in the family connected with H. pylori infection. The authors proved that the grouping of a gene coding the production of interleukin-1 was found in family cohorts with an increased risk of gastric mucosa atrophy, intestinal metaplasia induced by H. pylori and gastric cancer [8]. The group of children infected with H. pylori with atrophic gastritis and intestinal metaplasia described by Guarner enabled to connect H. pylori infection with their incidence in families and similar hereditary patterns of disease determinants [14]. The incidence of gastric ulcers equaled 37.1% and duodenal ulcer – 22.9% of the families questioned. The highest percentage of gastric and duodenal ulceration was observed in the group of 10-14 year-old children and was 38.7% and 23.0%, respectively. No statistically significant difference between gastric and duodenal incidence was found in the families of age groups. The indices of peptic ulcer incidence in childhood are low. Pediatric centers of endoscopic examinations occasionally report about the morbidity of 5-7 children with gastric and duodenal ulcers per year. Gold et al. proved that ulcers were present in 0.4% of all patients hospitalized. Male black and Latino teenage patients predominated in this group. Though the risk of peptic ulcer and gastric ulcer is connected with H. pylori-related gastritis, there are no randomized clinical control trials, which would prove that H. pylori eradication prevents ulcer development [15]. In children, H. pylori-related duodenal ulceration and gastritis and gastric metaplasia in the stomach are closely related to each other. It has been suggested that after the initial infection, gastritis develops followed by the gastric metaplasia of the mucosa in the duodenum and then the colonization of gastric metaplastic tissue foci with H. pylori and duodenal ulceration [12]. The results of Drumm's et al. studies showed that H. pylori-dependent gastritis was found in 90% of children with duodenal ulcer. An acute inflammatory state of the pyloric mucosa is closely related to the increased incidence of duodenal ulceration in all age groups. Similarly to adults, the development of duodenal ulceration rarely occurs in children without H. pylori infection. However, ulcers are more and more reported in children without H. pylori infection. These observations may result from many factors, among the others, a false negative histopathologic test due to the accidental missing of microorganisms while taking the sample with the low density of colonization, or the colonization of the proximal regions of the gastric mucosa caused by proton pump inhibitors or antibacterial medications. It has been proved that there is no recurrence of duodenal disease in children after H. pylori eradication. Yeung et al. presented 23 children with H. pylori-related gastritis with duodenal ulcers treated with Cymetydyn or combination of Cymetydyn and Amoxycycline [16]. In 6 children with H. pylori eradicated, no recurrence of duodenal ulcer was observed during 6 months after treatment. In contrast, in 50% of patients with cured ulceration, but with H. pylori infection (treated exclusively with Cymetydyn), ulcer disease recurred within 6 months. It was proved that after eradication healing duodenal ulcers were more frequently covered with gastric than intestinal epithelium. In our study, the percentage of the incidence of gastric and duodenal ulcers in the families of children examined

is high and suggests further monitoring of the infection as well as the examination of H. pylori infection in the family, taking into consideration genotype studies and an immuno-morphological response of the gastric mucosa.

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