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Upper gastrointestinal mucosal lesions in children with juvenile idiopathic arthritis before the treatment

Patients suffering from collagen tissue diseases, including rheumatic arthritis, rather frequently present gastroduodenal disorders. This is mainly connected with the use of nonsteroidal antiinflammatory drugs (NSAID_s) and glucocorticoids or can be sometimes contributed to the concomitant *Helicobacter pylori* infection (1–5). The drug-induced mucosal injuries in both adults and children include a variety of alterations ranging from erythematous to ulcerative ones (6). So far, a few number of studies regarding the gastroduodenal endoscopic findings in children with juvenile idiopathic arthritis (JIA) have been performed. Moreover, these studies concerned the children being already treated with NSAID_s (3, 4, 6–9). To our knowledge, the studies on oesophago-gastroduodenal alterations in rheumatic children before the planned medication are lacking.

Bearing in mind that JIA as a representative of collagen tissue diseases can produce the damage of the small vessels inside the digestive tract and lead to the ischaemic alterations of them (10), we decided to investigate endoscopically the patients with JIA prior to treatment.

The aim of the study was to assess the prevalence, type and localization of mucosal lesions of the upper gastrointestinal tract visible at endoscopy. The other purpose was to evaluate the prevalence of possibly coexisting *Helicobacter pylori* infection in children with JIA.

MATERIAL AND METHODS

Fifty-two children (18 boys and 34 girls) aged 4–18 years were recruited for the study. In all of them, JIA was diagnosed on the basis of generally accepted criteria (11). Eighteen patients (34.6%) complained of mild epigastric pains prior to investigation. In 29 patients (55.8%) the onset of the disease was pauciarticular, in 19 (36.5%) – polyarticular and in 4 (17.3%) – a systemic one. No patient used NSAID_s or glucocorticoids prior to the investigation.

Oesophagogastroduodenoscopy was performed using the GIF-E or XP-20 gastroscope (Olympus). Biopsy specimens were taken from the gastric and duodenal mucosa for the histological study, antral biopsy specimens were used for the detection of *Helicobacter pylori* using both histological investigation and rapid urease test. Rheumatoid factor (RF) in serum was estimated according to the Waaler-Rose method and the titer of antinuclear antibodies (ANA) was determined by the

indirect immunofluorescence using the substrate HE p-2 (monkey liver). The routine histological investigations were performed in the Department of Pathomorphology (Lublin).

The investigations were accepted by the children's parents and approved by the Ethics Committee of the Medical University of Lublin. The statistical analysis was based on the u-test for the comparison of fractions (12).

RESULTS

The macroscopic mucosal lesions were observed in 48 out of 52 patients (92.8%). In all of them, they were hyperemic or oedematous changes of the oesophageal, gastric and duodenal mucosa or they were seen in one or two of the above mentioned segments. In 5 children (9.6%) these alterations were accompanied by petechiae and erosions, and in one patient (2, 8) a little bulbar ulceration in duodenal mucosa was detected. In 15 children (28.9%) a nodular granulation of the antral mucosa was visible.

The histological investigation revealed mild chronic superficial gastritis and/or duodenitis in all patients with visible changes. In 27 patients (51.9%) *Helicobacter pylori* infection was diagnosed basing on both the histology and rapid urease tests. In these patients the endoscopically visible lesions were found in all cases.

The seropositivity for RF was revealed in 15 children (28.8%) and the increased titers of ANA (above 1:40) – in 25 (48%) instances.

Bearing in mind that abdominal complaints and mucosal lesions could be caused by the coexisting *H. pylori* infection, a comparison of the results was made in two separated groups of patients: I. Group with *H. pylori* infection Hp (+) – 27 children; II. Group without *H. pylori* infection Hp (-) – 25 children. In both groups we evaluated the type of disease onset, type and localization of endoscopic findings, prevalence of abdominal pains and prevalence of the seropositivity for RF and for increased ANA titers.

Table 1 presents the data concerning the onset of JIA. The prevalence of the pauciarticular type of JIA was similar in both groups ($p > 0.05$). The polyarticular disease onset seems to be more often observed in Hp (+) group than in Hp (-) group (48.1% and 24% resp.) but this difference was not significant ($p > 0.05$). The systemic type of JIA was found in four (16%) patients in Hp (-) group and in no patient in Hp (+) group – the difference was statistically significant ($p < 0.01$).

Table 1. Type of juvenile idiopathic arthritis in children non-infected and infected with *Helicobacter pylori*

Onset of the disease	Group				p
	<i>H. pylori</i> (-)		<i>H. pylori</i> (+)		
	n	%	n	%	
Pauciarticular	15	60	14	51.8	>0.05
Polyarticular	6	24	13	48.1	>0.05
Systemic	4	16	0	0	<0.01
Together	25	48.1	27	51.9	>0.05

Table 2 and 3 summarize the types of localization of the endoscopic findings. The presence of mucosal hyperaemia and/or oedema as well as petechiae and erosions was similarly often observed in the two analyzed groups of patients ($p>0.05$). The antral nodularity was statistically significantly more often seen in Hp (+) group than in Hp (-) patients ($p<0.001$). The mucosal lesions were localized mainly in all the investigated segments of the gastrointestinal tract and more rarely in two or one of them (Table 3). The completely normal mucosa was seen only in four patients in Hp (-) group. Epigastric pains were observed on seven out of 28 non-infected patients (28%) and in 11 out of 27 infected patients (40.7%). The difference was statistically significant ($p<0.01$).

Eighteen out of 52 patients (34.6%) with JIA complained of abdominal (epigastric) pains prior to the investigation. This symptom was present in seven (28%) patients in Hp (-) group and in 11 (40.7%) children in Hp (+) group – the difference was statistically significant ($p<0.01$).

As can be seen in Table 4, the prevalence of the seropositivity for RF and the percentage of increased serum ANA titers were similar in both analyzed groups of patients ($p>0.05$).

Table 2. Endoscopic findings in the upper gastro-intestinal tract and abdominal pains in children with juvenile idiopathic arthritis non-infected and infected with *Helicobacter pylori*

Endoscopic findings	Group				p
	<i>H. pylori</i> (-)		<i>H. pylori</i> (+)		
	n	%	n	%	
Erythema and oedema	21	84	27	100	>0.05
Erosions and petechiae	2	8	3	11.1	>0.05
Ulceration	1	4	0	0	>0.05
Antral nodularity	1	4	14	51.8	<0.001
No changes	4	16	0	0	<0.01

Table 3. Localization of upper endoscopic findings in children with juvenile idiopathic arthritis non-infected and infected with *Helicobacter pylori*

Localization	n (total)	Group				p
		<i>H. pylori</i> (-)		<i>H. pylori</i> (+)		
		n	%	n	%	
Oesophagus	1	1	4.0	0	0	>0.05
Stomach	2	2	8.0	0	0	>0.05
Oesophagus and stomach	2	1	4.0	1	3.7	>0.05
Stomach and duodenum	17	6	24.0	11	40.7	>0.05
Oesophagus, stomach and duodenum	26	11	44.0	15	55.5	>0.05
No changes	4	4	16.0	0	0	<0.05

Table 4. Prevalence of seropositivity for RF and increased titers of ANA in children with juvenile idiopathic arthritis non-infected and infected with *Helicobacter pylori*

Group	n	RF (+)		↑ANA	
		n	%	n	%
<i>H. pylori</i> (-)	25	9	36.0	13	52.0
<i>H. pylori</i> (+)	27	7	25.9	12	44.4
p		>0.05		>0.05	

DISCUSSION

Abdominal pains and abnormal endoscopic findings in the upper gastrointestinal tract observed in patients suffering from rheumatic arthritis are generally contributed to the side effects of antirheumatic drugs or to the coexistent *Helicobacter pylori* infection (5). It is not known yet, whether these two factors exert synergistic influence on the gastrointestinal mucosa, or they act independently (8, 13, 14). In our material the drug-dependent pathogenetic effect was excluded, for the investigations were performed prior to the treatment. It is possible but not certain that in the Hp (+) group the concomitant infection plays at least partially causative role in the development of gastroduodenal changes. However, the presence of the mucosal injuries in patients from the Hp (-) group implies that JIA may be *per se* a causative factor for these alterations. It could be most probably connected with vascular changes within the digestive tract and their consecutive ischaemic consequences (6, 10).

Fuller et al. (21) observed gastroduodenal mucosal alterations in 54.6% of their patients with osteoarthritis before any pharmacological treatment.

Collagen tissue disease including JIA produces not only general immunological reactions but also a local response of such origin within the gastroduodenal mucosa (4, 15, 16). This could be responsible for the inflammatory changes observed in our Hp (-) group of patients. It is noteworthy that only in four children with JIA non-infected with *H. pylori*, no endoscopic and histological abnormalities were stated. Therefore, in the majority of such cases, JIA was accompanied by the mucosal injuries in the upper gastrointestinal tract.

Helicobacter pylori is not only the main causative factor for gastroduodenitis but also – as a widespread microorganism it can complicate other diseases including rheumatic ones. In our material the prevalence of *H. pylori* infection in patients with JIA was similar to other reports (1, 4, 7, 17, 18). It is not established whether *H. pylori* being a potent stimulator of immunological reactions might play a role in the development of JIA, acting, for example, as a superantigen (19). It did not influence the type of JIA in our patients. The onset of the disease was similar in both Hp (+) and Hp (-) groups with the exception of the systemic one observed only in non-infected children.

The type and localization of endoscopically visible mucosal injuries were nearly the same in the above mentioned two groups except for the antral nodularity characteristic of *H. pylori* infection (2) found more often in Hp (+) than in Hp (-) group (51.8% and 4% resp.). Similar observations were made by Ishikawa et al. (20).

The analysis of the prevalence of seropositivity for RF and of the percentage of the increased ANA titers revealed no differences between the two selected groups of JIA patients. One can presume that these immunological events are not connected with *H. pylori* infection coexisting with the basic disease. It is in contradiction with opinion of Nakamura et al. (18), who observed the inverse correlation between the RF prevalence and *H. pylori* infection in patients suffering from rheumatic arthritis.

This paper suggests the purposefulness of further, more detailed studies on the histological and immunological properties of gastrointestinal disorders connected with JIA. However, its results let us share the opinion of Ashorn et al. (1) that endoscopy is needed in some patients suffering from rheumatic diseases prior to the planned medication, especially when they present gastrointestinal symptoms.

CONCLUSION

1. The majority of children with juvenile idiopathic arthritis present mucosal alterations within the upper gastrointestinal tract before the medication.

2. In nearly half of patients, the oesophago-gastro-duodenal mucosal changes exist despite the lack of coexisting *Helicobacter* infection, which implies the causative role of the basic disease in their development.

3. Juvenile idiopathic arthritis is rather often accompanied by *Helicobacter pylori* infection.

4. *Helicobacter pylori* infection seems not to influence the presence of rheumatoid factor and increased antinuclear antibody titers in children with juvenile idiopathic arthritis.

5. It seems reasonable to consider the purposefulness of endoscopical investigation before the planned treatment with anti-rheumatic drugs.

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SUMMARY

In 52 children suffering from juvenile idiopathic arthritis endoscopic investigation of the upper gastrointestinal tract was performed before the medication. 34.6% of patients complained of mild epigastric pains prior to the investigation. In 51.9% patients *Helicobacter pylori* infection was diagnosed. The mucosal injuries (oedema, erythema, petechiae, erosions) were visible in 48 out of 52 patients (92.8%). The type and localization of mucosal alterations were similar in *H. pylori* positive and *H. pylori* negative patients except for antral nodular granulations stated more often in the infected children. In 21 out of 25 non-infected with *H. pylori* patients (84%) the macroscopic and histologic signs of superficial gastroduodenitis were stated. No correlation between *H. pylori* infection and the presence of rheumatoid factor in serum or the increased titer of antinuclear antibodies was found. On the basis of own investigations one can state that the epigastric pains often belong to the clinical picture of juvenile idiopathic arthritis. It is postulated that both JIA and *Helicobacter pylori* may influence the development of gastrointestinal mucosal alterations. It is reasonable to consider the indication for endoscopy in some JIA patients prior to medication, especially when gastrointestinal symptoms are present.

Uszkodzenie śluzówki górnego odcinka przewodu pokarmowego u dzieci z młodzieńczym idiopatycznym zapaleniem stawów

U 52 dzieci z młodzieńczym idiopatycznym zapaleniem stawów wykonano badanie endoskopowe górnego odcinka przewodu pokarmowego przed rozpoczęciem leczenia. 34,6% pacjentów skarżyło się na bóle w nadbrzuszu w okresie przed badaniem. U 51,9% chorych stwierdzono zakażenie *Helicobacter pylori*. Uszkodzenia błony śluzowej w postaci zaczerwienienia, obrzęku, wybroczyn lub nadżerek wykazano u 48 pacjentów (92,8%). Rodzaj i umiejscowienie tych zmian były podobne u chorych zakażonych i niezakażonych *H. pylori* z wyjątkiem objawu „grudkowania” w obrębie wpustu, stwierdzanego istotnie częściej u dzieci zakażonych. U 21 spośród 25 chorych niezakażonych *H. pylori* istniały makroskopowe i histologiczne cechy zapalenia żołądka i dwunastnicy. Nie wykazano związku pomiędzy infekcją *H. pylori* i obecnością czynnika reumatoidalnego oraz wysokością miana przeciwciał przeciwjądrowych w surowicy. Na podstawie badań własnych stwierdzono, że bóle w nadbrzuszu są częstym objawem towarzyszącym młodzieńczemu idiopatycznemu zapaleniu stawów. Można przypuszczać, że zarówno samo zapalenie stawów, jak również infekcja *H. pylori* mogą przyczynić się do rozwoju zmian w śluzówce górnego odcinka przewodu pokarmowego. Należy rozważyć wskazanie do badania endoskopowego w niektórych przypadkach młodzieńczego idiopatycznego zapalenia stawów, zwłaszcza wówczas, gdy towarzyszą mu objawy żołądkowo-jelitowe.