

Case Report

Should Treatment of *Helicobacter pylori* in Children Change?

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Abstract

Purpose: We aimed to evaluate complaints, laboratory findings, treatment response based on age group and density of HP and follow up outcomes of patients who were detected to have *Helicobacter pylori* (HP).

Patients and methods: Patients who underwent endoscopy from June 2013 to June 2014 and detected to be HP (+) were included in this study.

Results: The study included 107 cases. Mean age was 10.5 ± 4.84 years (median: 9.5 years). Most frequent presenting complaint was abdominal pain (68.2%). In histopathological examination, 57.9% of cases had mild, 31.7% had moderate and 10.3% had severe active chronic gastritis. Severity of HP positivity was mild in 33.6%, moderate in 35.5% and severe in 30.8% of cases. Administered treatment was 14 day classical therapy in 57.9%, quadruple therapy in 31.8% and tetradox protocol in 10.3% of cases. 60.7% of cases were found responsive at the end of the treatment. Regarding the patients who showed response to treatment, 40% received classical therapy, 43.1% received quadruple therapy and 16.9% received tetradox protocol. After treatment 17 of the patients treated with classical therapy and 7 of the patients treated with triple therapy were found to be HP positive, and none of the patients treated with tetradox protocol was positive for HP. There was significant difference in terms of eradication rate after treatment ($p < 0.001$).

Conclusion: *H.pylori* in childhood age is most frequently observed in cases having abdominal pain complaint. We believe it is most appropriate to evaluate the patient for HP density and the severity of gastritis during planning of the treatment.

ABBREVIATIONS

Hp: *Helicobacter pylori*; HPSA: HP Stool Antigen Test; UBT: Urea Breath Tests

INTRODUCTION

Helicobacter pylori (HP) is a Gram-negative, spiral-shaped and motile bacterium. It is the most important cause of chronic gastritis, duodenal and gastric ulcer, atrophic gastritis and intestinal metaplasia. Its incidence is increased with age throughout the world [1,2].

While non-specific symptoms like abdominal pain, nausea and vomiting are seen in acute HP infections, recurrent abdominal pain, dyspeptic complaints, pyrosis and edema are encountered mostly in chronic infections [3,4]. Endoscopy, bacterial culture, histological examination and urease test are interventional and urea breath test, HP stool antigen test and serological tests are the non-interventional diagnostic methods

[5]. In children, the HP infection did usually not cause any other finding except peptic ulcer [6]. While authors agreed that patients with peptic ulcer disease should be treated, some authors suggested that the patients with clinical symptoms should also be treated [6,7]. Regarding our study, patients, who were examined endoscopically in the pediatric gastroenterology outpatient clinic because of dyspeptic complaints and were diagnosed as HP-positive, are included and their demographical characteristics, complaints, laboratory findings, age groups, therapeutic responses, which were planned according to the HP-density and follow-up results, were investigated. Standard triple therapy is considered as the first-line treatment in the HP therapy. However, in the epidemiological studies, it was reported that the success rate of this therapy declined as a result of the increase in antibiotic resistance.

MATERIALS AND METHODS

The cases, which were examined endoscopically due to the

dyspeptic complaints and were HP-positive in the MoH Bakırköy Sadi Konuk Training and Research Hospital between June 2013 and June 2014, were included in the study. The therapies of the patients were planned in respect of their age and HP-density. We administered a quadruple therapy containing tetracycline to patients between ages 15 and 18 years. In the age group below 15 years, quadruple therapy consisting of lansoprazole, amoxicillin, clarithromycin and metronidazole was administered if the HP-density was high in the histopathological examination and a conventional triple therapy was administered if the HP-density was low. The HP eradication rate at the end of the therapy was evaluated with the HP stool antigen test (HPSA), urea breath test (UBT) in the 4th week.

RESULTS AND DISCUSSION

The total number of the enrolled patients was 107 (58.9% females; 41.1% males). Mean age was 10.5 ± 4.84 years (median: 9.5 years). The most common complaints were abdominal pain (68.2%; n=73) and nausea (17.8%; n=19). Other complaints encountered were vomiting (16.8%; n=18), heartburn, sour fluid in the mouth (13.1%; n=14), loss of appetite (23.6%; n=25), growth retardation (22.3%; n=24) and constipation (20.6%; n=22). At the admission, the height and weight percentiles in the 3.7% (n=4) of the cases were below 3, in 10.2% (n=11) were between 3 and 10. Only 42% (n=45) of the cases had a percentile above 50. Regarding the laboratory findings, 43.9% (n=47) of the patients had iron deficiency anemia. The mean hemoglobin value was 12.26 ± 1.44 gr/dl and platelet count was 320000 ± 85000 (in one patient the platelet count was 52000).

In the endoscopic examination, all patients had hyperemia and nodular appearance in the antrum. Additionally, 18.7% (n=20) of the patients had stage A oesophagitis, 10.2% (n=11) stage B oesophagitis, 3.7% (n=4) erosive gastritis, 1.9% (n=2) ulcer in the antrum, 1.9% (n=2) duodenal ulcer and 1.9% (n=2) nodular appearance in the bulb as endoscopic findings. Histopathological evaluation showed that 57.9% (n=62) of the patients had mildly active chronic gastritis, 31.7% (n=34) moderately activated chronic gastritis and 10.3% (n=11) severely active chronic gastritis. In addition to gastritis, 20.5% (n=22) of the patients had findings of oesophagitis, 1.9% (n=2) antral ulcer, 1.9% (n=2) duodenal ulcer, 3.7% (n=4) partial villous atrophy and giardiasis, 4.7% (n=5) chronic duodenitis, 1.9% (n=2) total villous atrophy and coeliac disease. 33.6% of the cases (n=36) were mildly, 35.5% (n=38) moderately and 30.8% (n=33) severely HP-positive. During the follow-up, HPSA was carried out in 62 patients and UBT was carried out in 45 patients.

57.9% (n=62) of the patients had conventional treatment for 14 days, 31.8% (n=34) had triple therapy and 10.3% (n=11) had the protocol containing tetradox. 60.7% (n=65) of the patients responded to the therapy. Regarding the responders, 40% (n=26) had conventional treatment, 43.1% (n=28) had quadruple therapy and 16.9% (n=11) had the protocol containing tetradox. Evaluation of the groups in themselves showed that 41.9% of the patients, who had conventional therapy; 82.4% of the patients, who had quadruple therapy and 100% of the patients, who had protocol with tetradox were responders. The respond rates were statistically significant. Considering the evaluation of the UBT and HPSA performed in the 4th week; among the 45 patients, who had

Table 1: Presenting Symptoms of Patients.

	Number of Patients	%
Abdominal pain	72	68.2
Nausea	19	17.8
Vomiting	18	16.8
Heartburn and sour fluid in the mouth	14	13.1
Loss of appetite	25	23.6
Growth retardation	24	22.3
Constipation	22	20.6

Table 2: Treatment Protocols and eradication ratios.

Treatment Protocols	Number of Patients	Number of Patients respond of Treatment	Eradication ratios
Amoxicillin+Clarithromycin	62	26	41.9%
Amoxicillin+Clarithromycin+Metronidazole	34	28	82.3%
Amoxicillin+Clarithromycin+Metronidazole+Doxycycline	11	11	100%
Total	107	65	60.7%

UBT, 17 with conventional treatment, 7 with triple therapy were HP-positive, but none of the patients with the protocol containing tetradox were HP-positive.

Regarding the HPSA, 56% of the patients with the conventional treatment and 9.5% of the patients with quadruple therapy were positive. Eradication rates in this group at the end of the therapy displayed statistically significant difference. *Helicobacter pylori* are a widespread and commonly encountered infectious agent. Its incidence increases with age. In some areas, it is seen in children with age below 10 years [8,9]. The average age in our study was 9.5 years. In the studies, which were conducted in our country, the average age was below 10 years [10,11].

Although the HP infection in children did usually not present any finding except peptic ulcer findings, the patient might complain of recurrent abdominal pain, nausea, vomiting, growth retardation, loss of appetite, heartburn and sour fluid in the mouth as a result of chronic gastritis, gastric ulcer, atrophic gastritis and intestinal metaplasia. Although in the studies, the most common complaint encountered in HP-positive patients was recurrent abdominal pain, the correlation between the abdominal pain and the incidence of HP was not confirmed [6,12]. In their study, Erkan *et al.*, determined 16 HP positivity in 22 patients with the diagnosis of peptic ulcer [13]. In the study conducted by Doğan *et al.*, the common complaint was abdominal pain (82.4% of the cases) [14]. In our study, abdominal pain with an incidence of 68.2% (n=73) was the most common complaint during the admission. Other recorded complaints were nausea (17.8%; n=19), vomiting (16.8%; n=18), heartburn and sour fluid in the mouth (13.1%; n=14), loss of appetite (23.6%; n=25), growth retardation (22.3%; n=24) and constipation (20.6%; n=17). The developmental status of the patients was evaluated at the admission and the height and weight percentiles in the 3.7% of the cases (n=4) were below 3, in 10.2% (n=11) were between

3 and 10. Only 42% of the cases (n=45) had a percentile above 50. Regarding the laboratory findings, the mean hemoglobin value was 12, 26± 1.44 gr/dl and 43.9% of the cases (n=47) had iron deficiency anemia. Iron deficiency anemia is the most important extraintestinal finding of HP and investigation of HP infection was recommended in cases with treatment-resistant iron deficiency anemia [15].

Endoscopic evaluation is an interventional diagnostic method, which enables the observation of the gastroduodenal disorders and the biopsy necessary for the diagnosis of HP [5,16]. It is believed that the antral nodules detected during the endoscopic examination were related to HP gastritis. In the study of Sabbi et al., micronodular appearance was determined in 52% of the cases [17]. In studies conducted in our country, Özçay et al., [18] found out antral nodules in the 64.7% of patients, antral hyperemia in 5.9% and duodenal ulcer in 1.96%; Doğan et al., [14] detected 73.6% antral nodules, 10% antral hyperemia, 13% gastric ulcer and 1.2% duodenal ulcer. Endoscopic evaluation in our study revealed that all patients had hyperemia and nodular appearance in the antrum and additionally 18.7% (n=20) had stage A oesophagitis, 10.2% (n=11) had stage B oesophagitis, 3.7% (n=4) had erosive gastritis, 1.9% (n=2) had antral ulcer, 1.9% (n=2) had duodenal ulcer and 1.9% (n=2) had nodular appearance in the bulb. Histopathological examination showed 57.6% (n=62) mildly active chronic gastritis, 31.7% (n= 34) moderately activated chronic gastritis, 10.3% (n=11) severely active chronic gastritis. In addition to gastritis, 20.5% of the patients (n=22) had findings of oesophagitis, 1.9% (n=2) antral ulcer, 1.9% (n=2) duodenal ulcer, 3.7% (n=4) partial villous atrophy and giardiasis, 4.7% (n=5) chronic duodenitis, 1.9% (n=2) total villous atrophy and coeliac disease. 33.6% of the cases (n=36) were mildly, 35.5% (n=38) moderately and 30.8% (n=33) highly HP-positive.

Although there is a consensus that it is necessary to treat the patients with peptic ulcer disease related with HP [15], it is also suggested that patients with clinical symptoms should be treated [6,7]. As the monotherapy with an antibiotic in the *Helicobacter pylori* infections is not effective, a combination of the antibiotics is required. The most common treatment regimen is the double antibiotics treatment consisting of amoxicillin and clarithromycin with the addition of a proton pump inhibitor. In a study conducted in our country, an eradication rate of 87.5% was achieved with lansoprazole + amoxicillin + clarithromycin [14]. However, the HP eradication rates declined due to the antibiotic resistance, which developed as a result of the frequent use of antibiotic in the population [19]. Therefore, different combinations were tested in the treatment. While the resistance to metronidazole in Europe and US was between 20% and 50%, the same rate increased up to 70% in the developing countries [20-22]. As the eradication could not be fully achieved because of the antibiotic resistance, tetracycline was added to the treatment in children over 8 years of age [19]. In our study, the treatment was laid out according to the HP-density and age groups. In all patients, lansoprazole was the chosen proton pump inhibitor. 57.9% of the patients (n=62) had the conventional therapy for 14 days, which consisted of amoxicillin and clarithromycin, 31.8% (n=34) had the therapy consisted of amoxicillin + clarithromycin and metronidazole and 10.3% (n=11) had the protocol with tetradox, consisting

of amoxicillin + clarithromycin + metronidazole + tetracycline. At the end of the therapy they respond rate was 60.7% (n=65). Evaluation of the responders showed that 40% (n=26) had conventional treatment, 43.1% (n=28) had quadruple therapy and 16.9% (n=11) had the protocol with tetradox. The evaluation of the groups in themselves revealed that 41.9% of the patients with the conventional treatment, 82.4% of the patients with the quadruple therapy and 100% of the patients with the protocol containing tetradox were responders and this result was statistically significant (p<0.001). During the follow-up, 62 patients had HPSA and 45 patients had UBT. Regarding the evaluation of the patients with UBT and HPSA in the 4th week of the treatment; among the 45 patients, who had UBT, 17 with conventional treatment, 7 with triple therapy were HP-positive, but none of the patients with the protocol containing tetradox were HP-positive. Regarding the HPSA, 56% of the patients with the conventional treatment and 9.5% of the patients with quadruple therapy were positive. Eradication rates at the end of the therapy displayed statistically significant difference (p<0.001).

CONCLUSION

In the childhood, *H. pylori* infection is mostly encountered in the cases with the complaint of abdominal pain. Iron deficiency might come along with this clinical picture. The therapeutically success in HP infection was declined because of antibiotic resistance, which developed as a result of the uncontrolled usage of the antibiotics in the childhood. Therefore, we conclude that it would be more favorable to consider the HP-density and the severity of the gastritis observed in the histopathological examination in the planning of the therapy regimen.

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