Does *Helicobacter pylori* play a role in the pathogenesis of childhood chronic idiopathic thrombocytopenic purpura?

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Abstract

Idiopathic thrombocytopenic purpura (ITP) is an acute self-limited bleeding disorder that can progress to chronic form in 10-15% of the cases. *Helicobacter pylori* (*H. pylori*) infection is a possible cause of chronic ITP. We studied 30 children with resistant chronic ITP for *H. pylori* infection based on the detection of *H. pylori* fecal antigen. This retrospective study was based on data obtained from medical records of 30 children aged between five and 17 years (median age at ITP diagnosis was ten years). A specially-designed data sheet was used to record information on age, sex, duration of disease, family history of bleeding disorders, previous treatments and median platelet count. In patients with *H. pylori* infection, antimicrobial treatment consisted of amoxicillin, metronidazol and omeprazol. Response was assessed every month for one year and defined as complete (platelet count >150×10^9/L) or partial (platelet count between 50 and 150×10^9/L). We detected *H. pylori* infection in 5 patients. In 4 of them increased platelet count was seen during one year of follow-up and in one patient the platelet count was acceptable during six months. Although the pathological mechanism of *H. pylori*-induced thrombocytopenia was unclear in our patient sample, the assessment of *H. pylori* infection and use of eradication therapy should be attempted in chronic and resistant ITP patients.

Introduction

Helicobacter is a genus of gram-negative bacteria causing peptic ulcer, chronic gastritis and lymphoma.[1] There is a suggestion that *H. pylori* has a role in the pathogenesis of chronic idiopathic thrombocytopenic purpura (ITP).[2] However, the relationship between *H. pylori* infection and cITP is less clear. In children, eradication of the infection was reported to produce an increase in platelet count in one study,[3] whereas another report failed to demonstrate this beneficial effect.[4] In adults, the connection between *H. pylori* infection and ITP is also controversial.[5,6]

In the light of this controversy, we designed the present study to evaluate the role of *H. pylori* in patients with chronic and resistant forms of ITP and the effect of *H. pylori* eradication on platelet count in these patients.

Materials and Methods

This retrospective study involved 30 children with chronic ITP younger than 18 years of age referred consecutively to the Motahari Outpatient Pediatric Clinic of Shiraz University of Medical Science, during 2003 to 2006. The research itself lasted 14 months (from 2006 to 2007) and was approved by the Medical Ethics Committee of Shiraz University of Medical Sciences (Table 1).

The median age at ITP diagnosis was ten years (range, 5-17 years). The inclusion criteria were thrombocytopenia of more than six months' duration (chronic ITP), lack of response to multidrug treatment with corticosteroids, intravenous immunoglobulin, RhoGAM (anti-D immunoglobulin) and splenectomy (for resistant forms of ITP), and platelet count below 100×10^9/L (Table 1). We used a specially designed data sheet to record information on age, sex, duration of the disease, median platelet count, type of previous treatment, and family history of autoimmune disorder. Stool samples were tested for *H. pylori* antigen with an enzyme-linked immunosorbent assay (ELISA) kit (Meridian BioScience, Cincinnati, OH, USA). In patients with *H. pylori* antigen an eradication regimen was given as follows: 1) omeprazol 1 mg/kg/day for four weeks, 2) metronidazol 30 mg/kg/day for two weeks, and 3) amoxicillin 60 mg/kg/day for two weeks.

Platelet recovery occurred one month after *H. pylori* eradication, which was confirmed by the disappearance of *H. pylori* antigen from stool. Subsequently, platelet count was checked every month for one year and compared with the patient's median platelet count before *H. pylori* eradication.

During the follow-up period, patients did not receive any medication. Response was defined as complete (platelet count >150×10^9/L) or partial (platelet count between 100 and 150×10^9/L), and relapse was defined as a decrease in platelet count to pre-treatment values.

Two statistical methods (paired *t*-test and Wilcoxon's signed rank test) were used to analyze the results. *p* less than 0.05 were considered statistically significant.

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Results

We detected 5 *H. pylori*-positive cases according to the presence of the antigen in stool. None of the patients complained of gastrointestinal problems. The prevalence of *H. pylori* infection in patients with chronic ITP was 16.6%.

After *H. pylori* was eradicated in patients with the infection, platelet count was rechecked monthly for one year (Table 2).

Median platelet count in our patients during one year after treatment increased from 18.6×10^9/L to 79.2×10^9/L with a *p* of 0.043 (Wilcoxon's signed rank test) and 0.001 (paired *t*-test). According to the definition of partial response (platelet count between 50-150×10^9/L) our data showed an increase in platelet count in our patients in this category. In 4 patients, platelet count remained constant during one year of follow-up, and in one patient it remained stable for six months and then decreased to its pre-treatment value (Table 3). At this time this patient showed evidence of re-infection in the fecal antigen test.

By repeating *H. pylori* eradication, the patient's platelet count increased one month after treatment, and remained stable during follow-up. None of the other 4 patients showed evidence of *H. pylori* infection after one year of follow-up. In the *H. pylori*-negative group, platelet count was checked monthly for one year but did not increase spontaneously.

Discussion

In 1998, Gasbarrini *et al.*[2] first reported improvements in platelet count after *H. pylori* eradication in adults with chronic ITP. Several studies have shown that platelet count in patients with ITP returns to normal after eradication.[7,8] Although the investigation and eradication of *H. pylori* infection in children with chronic ITP is a matter of debate, there are few reports about children with this disease.[9-12]

Although the association between the pathogenesis of ITP and *H. pylori* is still not well defined, the search for *H. pylori* infection and attempts to eradicate the bacterium in positive cases seem appropriate in adult patients as well as children. Some authors reported that the pre-treatment factor most consistently associated with platelet response to *H. pylori* eradication was shorter ITP duration,[13,14] but our study did not confirm this. Others have also suggested that patients with very low platelet counts appear to have fewer chances of responding, but we obtained a better response in this group. Torres *et al.*[15] found that *H. pylori* positivity was higher in older children, but we found no significant differences in this parameter between children of different ages. This may be due to earlier *H. pylori* infection in our country.[16]

The rate of positivity for *H. pylori* infection was lower in our series (16.6%) compared to the Italian pediatric population, in which a prevalence of 22-28% was found.[17,18] Other characteristics such as age, sex, and previous therapies, including corticosteroids and splenectomy, were not useful in predicting platelet response. Our results indicate that eradication of *H. pylori* is accompanied by a platelet response in some ITP patients, with ample variations in the response rate among different series. Bacterial factors (i.e., the variability of *H. pylori* strains) may account for these findings. In this connection, Emilia *et al.*[8] reported a response rate of 50% whereas we obtained a response rate of 100%, which was consistent with the findings of Gasbarrini *et al.*[2] It seems that *H. pylori* eradication is greatly favorable to standard ITP therapy due to low cost, its non-invasive nature and much less toxicity. So *H. pylori* infection eradication should be considered in those patients with chronic and resistant ITP.[19]

Table 1. Clinical and demographic characteristics in the *H. pylori*-positive and negative group before eradication.

	H. pylori-positive group	H. pylori-negative group
Age at ITP diagnosis (median and range)	10 (5-17) years	11 (5-16) years
Age at *H. pylori* test (median and range)	12 (9-16) years	12.4 (9-15) years
Sex (female/male ratio)	2:1	1.8:1
Prior treatment	Corticosteroid, IV IG, splenectomy	Corticosteroid, IV IG, splenectomy
Duration of follow-up before *H. pylori* test	3.48 years,	3.20 years
Median platelet count immediately before *H. pylori* eradication	20×10^9/L (10-30×10^9/L)	50×10^9/L (40-70×10^9/L)

Table 2. Monthly platelet count during 12 months after eradication of *H. pylori* in patients with chronic infection.

	Age (yrs)	Median platelet count immediately before *H. pylori* eradication (×10^9/L)	Median platelet count one month after *H. pylori* eradication (×10^9/L)	2 m*	3 m	4 m	5 m	6 m	7 m	8 m	9 m	10 m	11 m	12 m
1	12	10	15	55	59	69	50	67	69	66	59	63	62	64
2	8	28	30	94	68	91	70	91	87	94	80	95	84	90
3	13	32	43	87	83	89	79	80	89	90	80	81	82	88
4	14	25	32	90	83	88	87	92	93	89	94	85	87	88
5	9	32	20	95	97	89	94	95	99	30	23	29	39	30

Table 3. Platelet count in *H. pylori*-positive and -negative patients eradication.

	H. pylori-positive group	*H. pylori*-negative group
Median platelet count immediately before *H. pylori* eradication	20×10^9/L (10-30×10^9/L)	50×10^9/L (40-70×10^9/L)
Median platelet count after one year of follow-up	81×10^9/L (69-89×10^9/L)	52×10^9/L (38-59×10^9/L)

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