

Suggestive Parameters for Eradication Therapy in Children with *Helicobacter pylori* Gastritis

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The relationship between *Helicobacter pylori* (*H. pylori*) infection and recurrent abdominal pain in children is still controversial. *H. pylori*-infected children with recurrent abdominal pain generally do not require treatment. However, benefit of treatment has been known to produce dramatic improvements in some patients. Furthermore, *H. pylori*-infected is associated with growth retardation, iron deficiency anemia and thrombocytopenia. The objective of this study was to find suggestive parameters for eradication of *H. pylori* gastritis. From 1992 to 2004, medical records of 42 children diagnosed as having *H. pylori* infection by endoscopy were retrospectively reviewed. Of those 42 patients, there were 36 patients with *H. pylori* gastritis without gastric or duodenal ulcer (85.7%), and 6 patients with ulcers (14.3%). Children with *H. pylori* gastritis were divided into 2 groups: responsive and unresponsive. Data including the duration of abdominal pain, endoscopic finding, histology, treatment, outcome and final diagnosis were collected. Additional data were obtained by telephone and letters. Of 36 patients, there were 24 and 12 patients in responsive and unresponsive groups, respectively. Three patients with anemia were all presented in the responsive group. Those experiencing abdominal pain less than 3 months more commonly belonged to the responsive group ($P=0.21$). Marked erythema of gastric mucosa was only seen in the responsive group ($P=0.136$). All cases of chronic moderate-active gastritis appeared in the responsive group ($p=0.03$). In conclusion, iron deficiency anemia and chronic moderate-active gastritis should be the suggestive parameters for eradication therapy in children with *H. pylori* gastritis.

Keywords: *H. pylori* gastritis, Abdominal pain, Anemia, Children

J Med Assoc Thai 2005; 88(Suppl 8): S21-6

Full text. e-Journal: <http://www.medassocthai.org/journal>

Helicobacter pylori is a Gram-negative bacteria that colonizes gastric mucosa causing chronic gastritis, duodenal and gastric ulcers, atrophic gastritis and intestinal metaplasia⁽¹⁾. Furthermore, it is also associated with growth retardation⁽²⁾, iron-deficiency anemia^(3,4) and thrombocytopenia⁽⁵⁾. Prevalence of *H. pylori* infection related to recurrent abdominal pain (RAP) longer than 3 months among Thai children is 15.2%-17.7%^(6,7). At present, eradication therapy is only recommended for children who have peptic ulcer, mucosa-associated lymphoid tissue lymphoma or atrophic gastritis⁽⁸⁾. The relationship between *H. pylori* infection and recurrent abdominal pain in children is

still controversial. In addition, conflicting data exist on the relationship between *H. pylori* infection and childhood RAP^(4,8-11). The recommendation from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition is that *H. pylori*-infected children with nonulcer dyspepsia or recurrent abdominal pain, or both, do not require treatment⁽⁸⁾. In general, patients who have acute severe or intractable recurrent abdominal pain, vomiting, hematemesis or unknown causes of iron deficiency anemia always undergo gastrointestinal endoscopy. When gastric or duodenal ulcer related to *H. pylori* is found, eradication therapy is prescribed. With regard to *H. pylori* gastritis without ulcer, physicians will make a decision on an individual basis on whether or not to treat the patients. Some patients with abdominal pain experience dramatic improvements after treatment and may be categorized in the subtype group. Parameters which

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suggest the need for eradication therapy in this subtype group are not available^(8,12,13).

The objective of this study was to determine parameters which would suggest eradication treatment of *H. pylori* gastritis in children.

Material and Method

From 1992 to 2004, medical records of forty two patients with problems of abdominal pain, hematemesis or anemia, with diagnosis of *H. pylori* infection made by gastrointestinal endoscopies in the Department of Pediatrics, Siriraj Hospital, Bangkok, Thailand were retrospectively reviewed. Endoscopic findings were presented as normal, nodular, mild erythema, marked erythema, erosion and ulcer of mucosa. Biopsies of mucosa were obtained from the first part of the duodenum, antrum, gastric body and esophagus. Specimens from the antrum and body of the stomach were used for rapid urease test and histology. Specimens were stained with hematoxylin and eosin to demonstrate spiral shaped Gram-negative bacilli. The diagnosis of gastritis was based on the histological criteria of the Sydney system classification. Patients were considered to be infected by *H. pylori* if urease test was positive and presence of *H. pylori*-like organisms in their histology.

From 1992 to 1999, patients received triple therapy regimen (DMA treatment) including 120 mg of colloid bismuth subcitrate twice a day for 4 weeks, 250 mg of amoxicillin for 3 times a day and 20 mg/kg/day of metronidazole for 2 weeks. From 1999 to 2004, triple

therapy regimen was changed to OMC treatment including omeprazole 1 mg/kg/day up to 20 mg BID, clarithromycin 15 mg/kg/day and metronidazole 20 mg/kg/day for 2 weeks⁽⁸⁾.

Patients did not undergo repeated endoscopy except in some cases with recurrent episodes of pain, with unresolved symptom or for specific follow-ups. All patients were assessed for at least 6 months at the Pediatric Gastroenterology Clinic. The overall response from the treatment was evaluated 6 months after its initiation as (1) responsive group (resolution or near resolution) and (2) unresponsive group (deterioration of symptom or slight improvement). Further information after discharged from clinic and current symptoms was obtained from patients by telephone or letters.

Statistic

Data were presented in mean \pm SD or N (%) as appropriate. Chi-Square test was used for nominal data. Mann-Whitney test was used for analysis continuous data. P value of less than 0.05 was considered statistically significant.

Results

Of 42 patients with *H. pylori* infection, there were 36 patients with *H. pylori* without gastric or duodenal ulcer (85.7%), 3 patients with duodenal ulcer (7.1%) and 3 *H. pylori* patients with gastric erosion and duodenal ulcer (7.1%). A comparison of parameters for the responsive group of children with gastritis and the

Table 1. A comparison of parameters for the responsive group and the unresponsive groups

Parameters	Responsive	Unresponsive	P value
Number of cases	24	12	
Male	9	6	
Female	15	6	
Age (year)	9.5 \pm 2.4	9.2 \pm 1.7	
Duration of symptoms(month)	7 \pm 8.8	12 \pm 8.4	
Abdominal pain	22	12	
Duration of abdominal pain(month)	7.6 \pm 8.9	12 \pm 8.4	0.083*
Duration of abdominal pain (median,month)	3.5	12	
Anemia	3	0	0.53**
Vomiting	8	4	1.00**
Hematemesis	2	1	1.00**
OMC treatment	14	5	0.483**
DMA treatment	10	7	
Re-endoscopy	3	4	
Duration of follow-up (year)	2.6 \pm 2.5	3.1 \pm 3.7	

* Mann-Whitney test, ** Chi-Square test

Table 2. A comparison of abdominal pain, endoscopic finding and histology for the responsive and unresponsive groups

Parameters	Responsive	Unresponsive	p
Abdominal pain			0.21**
Abdominal pain less than 2 weeks	4 (100%)	0(0%)	
Abdominal pain 2weeks - 3 months	6(75%)	2(25%)	
Abdominal pain more than 3 months	12 (54.4%)	10(45.5%)	
Endoscopic finding			0.136**
Normal stomach	7(70%)	3(30%)	
Mild erythema stomach	8(55%)	7(45%)	
Marked erythema stomach	6(100%)	0(0%)	
Nodular stomach	6(60%)	4(40%)	0.7**
Histology			0.03**
Chronic mild-active gastritis	16(76.2%)	5(23.8%)	
Chronic moderate-active gastritis	6(100%)	0(0%)	
Chronic non-active gastritis	2(22.2%)	7(77.8%)	

** Chi-Square test

unresponsive groups were presented in Table 1 and 2. In *H. pylori* gastritis patients, there were 24 patients (66.7%) in the responsive group (mean age: 9.5±2.4 years; 15 females and 9 males) and 12 patients (33.3%) in the unresponsive group (mean age 9.2±1.7 years; 6 females and 6 males). Thirty-four patients had abdominal pain with the median duration of pain of 3.5 months in the responsive group and 12 months in the unresponsive group. The difference was not statistically significant ($p = 0.83$). There were 4 and 6 patients in the responsive group which experienced duration of pain for less than 2 weeks and between 2 weeks and 3 months respectively, whereas there were only 2 patients had pain between 2 weeks and 3 months in the other group. Anemia was only found in 3 patients of the responsive group.

In the responsive group, endoscopic findings revealed 7 normal stomachs, 8 mild erythema stomachs, 6 marked erythema stomachs, and 6 nodular stomachs. In the unresponsive group, there were 3 normal stomachs, 7 mild erythema stomachs, and 4 nodular stomachs. Marked erythema of gastric mucosa was only found in the responsive group, but there was no statistical significance between groups ($p = 0.136$). Concerning histology of gastric mucosa, chronic moderate-active gastritis was more commonly found in the responsive group (6 patients) rather than the unresponsive group (no patients) ($p = 0.03$).

OMC treatments were used on 14 patients of the responsive group and 5 patients of the unrespon-

sive group. DMA treatments were used on 10 and 7 patients respectively. Repeated endoscopies were carried out on 3 and 4 patients of the responsive and unresponsive group respectively.

Regarding the long-term follow-up (longer than 1 year) for 18 patients, there were 4 patients with current occasional abdominal pain and 1 patient with a headache in the responsive group. In the unresponsive group, the final diagnoses included 6 psychosomatic disorders, 1 cyclic vomiting, 1 tumor of gall bladder and 4 unknown causes.

Discussion

Abdominal pain is the major symptom of symptomatic children with *H. pylori* infection. The relationship between eradication of *H. pylori* infection and recurrent abdominal pain in children is controversial⁽¹⁴⁻²²⁾. It is uncertain whether eradication of the infection leads to an improvement in children with RAP. Patients in this study had recurrent abdominal pain in 64.5% and abdominal pain with a duration of less than 3 months in 35.3%. Guidelines for the management of children with abdominal pain of less than 3 months relating to *H. pylori* infection is not available. In this study, there were more patients with abdominal pain of less than 3 months in the responsive group than in the unresponsive group. However this was of no statistical significance between the two groups. It has been reported that acute gastric mucosal lesion, characterized by severe erosion, hemorrhage or ulceration of gastric mucosa, is associ-

ated with post endoscopic transmission of acute *H. pylori* infection⁽²³⁾. Yang et al, reported that children with short term RAP (between 2 weeks and 3 months) had a higher anti *H. pylori* seropositive rate than those with RAP, but abdominal pain resolved without treatment in both groups⁽²⁴⁾. Duration of abdominal pain less than of 3 months may be associated with *H. pylori* infection, but it does not need eradication treatment.

In this study, there were 2 cases with iron-deficiency anemia, and one case with hematemesis, abdominal pain and iron deficiency anemia. All 3 patients received blood transfusion, *H. pylori* eradication and had their symptoms resolved without recurrence. Iron-deficiency anemia related to *H. pylori* infection is well documented in the literature and should be a suggestive parameter for decision-making to eradicate the infection.

Endoscopic finding from gastroduodenoscopy is an important parameter for decision making on management. Marked erythema, friability, erosion and ulcer of gastric and duodenal mucosa are indicated for eradication of the infection. In this study, normal mucosa, mild erythema, and nodular surface of gastric mucosa were not found differently in both groups. Marked erythema, which was only found in the responsive group, may be a suggestive parameter for treatment, but bias on the part of endoscopists could limit the use of such parameter.

H. pylori-associated gastritis is characterized by the presence of acute and chronic inflammation⁽²⁶⁾. The degree of mucosal inflammation varies in severity from minimal inflammatory to severe gastritis. Presence of atrophic gastritis and mucosa-associated lymphoid tissue lymphoma are indicators for treatment. In this study, chronic moderate-active gastritis was only found in the responsive group ($P = 0.03$). Severe or moderate-active gastritis are related to severe inflammation of mucosa, which is possibly associated with abdominal pain.

In this study, although the number of cases was only 36, all patients were assessed for at least 6 months and some patients were interviewed during the collection of data. A natural history of diseases in some patients was not available. In the responsive group, there were 4 patients with current occasional abdominal pain and 1 patient with a headache, so functional abdominal pain or organic diseases were unlikely. In unresponsive group, definite diagnosis were obtained in 2 patients (cyclic vomiting and tumor of gall bladder). Four patients underwent repeated endos-

copy showing normal endoscopic findings, negative rapid urease tests and normal histology. Failure of eradication of infection may be the other factor for unresponsive treatment. Generally, triple therapy led to a cure rate of between 80%-90%⁽²⁷⁾. Six psychosomatic disorders and 4 unknown causes in this group should be diagnosed as functional abdominal pain.

In conclusion, duration of abdominal pain less than 3 months and marked erythema of gastric mucosal are probable parameters for decision making to eradicate the infection. Iron-deficiency anemia and chronic moderate-active gastritis should also be the suggestive parameters for therapy.

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ตัวแปรในการตัดสินใจกำจัดเชื้อ *H. pylori* ในผู้ป่วยเด็กที่มี *H. pylori* gastritis

ประพันธ์ อ่านเปรื่อง

ความสัมพันธ์ระหว่าง *H. pylori* gastritis และปวดท้องเรื้อรังในเด็กยังไม่ชัดเจน ปัจจุบันยังไม่แนะนำให้ยาเพื่อกำจัดเชื้อ แต่มีผู้ป่วยบางรายที่ตอบสนองต่อการรักษาดังกล่าว ดังนั้น อาจเป็นไปได้ว่าผู้ป่วยกลุ่มนี้เป็นกลุ่มจำเพาะที่การรักษานั้นได้ประโยชน์ นอกจากนี้ *H. pylori* gastritis ยังมีความสัมพันธ์กับการหยุดการเจริญเติบโตและการขีดเนื่องจากขาดธาตุเหล็กและเกล็ดเลือดต่ำ การศึกษานี้จึงมีจุดประสงค์ที่จะหาตัวแปรที่ใช้ในการตัดสินใจในการกำจัดเชื้อดังกล่าว ผู้ศึกษาได้ทำการ ศึกษาย้อนหลังในผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่ามีการติดเชื้อ *H. pylori* จากการทำการส่องกล้อง ทางเดินอาหารส่วนต้น ผู้ป่วยได้รับการติดตามการรักษาอย่างน้อย 6 เดือน ในกลุ่มผู้ป่วยทั้งหมด 42 รายที่มีการติดเชื้อ *H. pylori* มีผู้ป่วยที่มี *H. pylori* gastritis โดยไม่มี gastric หรือ duodenal ulcer จำนวน 36 ราย ผู้ป่วยจำนวน 18 รายที่มีการติดตามนานกว่า 1 ปีส่วนหนึ่งได้รับการสอบถามอาการปัจจุบันทางโทรศัพท์หรือจดหมายระหว่างที่ทำการศึกษานี้ ผู้ป่วย *H. pylori* gastritis ถูกแบ่งออกเป็น 2 กลุ่ม ได้แก่ (1) กลุ่มที่ตอบสนองต่อการรักษา จำนวน 24 ราย และ (2) กลุ่มที่ไม่ตอบสนองต่อการรักษาจำนวน 12 ราย การศึกษาพบว่าอาการขีดเนื่องจากการขาด ธาตุเหล็ก (3 ราย) พบได้เฉพาะในกลุ่มที่ตอบสนองต่อการรักษา ผู้ป่วยมีอาการปวดท้องทั้งหมด 34 รายพบว่า ระยะเวลาเจ็บป่วยน้อยกว่า 3 เดือนพบได้บ่อยในกลุ่มที่ตอบสนองต่อการรักษา ($p = 0.21$) และภาพที่เห็นจากการส่อง กล้องทางเดินอาหารที่ลักษณะแดงมากพบได้ในกลุ่มที่ตอบสนองต่อการรักษาเท่านั้น ($p = 0.136$) แต่ไม่มีความสำคัญ ทางสถิติ การตรวจ histology ของกระเพาะอาหารพบว่า chronic moderate-active gastritis พบในกลุ่มที่ตอบสนองต่อการรักษา เท่านั้นและมีความสำคัญทางสถิติ ($p = 0.03$)

สรุป: ภาวะขีดเนื่องจากการขาดธาตุเหล็กและ chronic moderate-active gastritis เป็นตัวแปรบ่งชี้ในการกำจัด เชื้อในผู้ป่วยเด็กที่มี *H. pylori* gastritis
