

**ENDOSCOPIC, HISTOLOGIC AND MICROBIOLOGIC
EVALUATION OF UPPER ABDOMINAL PAIN WITH SPECIAL
REFERENCE TO *HELICOBACTER PYLORI* INFECTION**

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Objective: To study children with significant upper abdominal pain of unidentifiable etiology and evaluate: (a) the relationship of pain to inflammatory esophago-gastro-duodenal lesions and *Helicobacter pylori* (HP) infection, and (b) the response to specific therapy. **Design:** Prospective study. **Setting:** Pediatric section of a tertiary referral gastroenterology center. **Subjects:** Thirty three consecutive children with significant upper abdominal pain [mean age 9.9 ± 2.7 , range 4-15 years; 20 males] were subjected to upper gastrointestinal tract endoscopy and antral mucosal biopsies obtained for rapid urease test (RUT), Gram's staining of impression/crush smears and culture for HP and histologic examination. Patients with HP gastritis were treated with triple therapy, colloidal bismuth subcitrate, amoxicillin and metronidazole, for two weeks. At 8 weeks from the initiation of therapy, patients were re-evaluated for symptoms and HP eradication by repeat endoscopy and antral biopsies. Patients with esophagitis, gastritis and duodenitis without HP infection were treated with ranitidine for 6 weeks. All the patients were followed up for 6 months. **Results:** Histology revealed antral gastritis in 28/33 (85%) patients. HP infection was present in 12/28 (43%) patients with antral gastritis. Symptomatic improvement with triple therapy was observed in 10/12 (83%) patients with HP gastritis and eradication of HP in 5/7. Improvement on ranitidine therapy was observed in 12/16 (75%) patients with HP negative gastritis. On follow-up, no patient with initial improvement with therapy had relapse of symptoms. **Conclusion:** Symptomatic children with HP related gastritis should be treated with triple therapy and HP negative gastritis with H₂-receptor antagonist.

Key words: *Helicobacter pylori*, Gastritis, Abdominal pain.

INFLAMMATORY mucosal lesions of the upper gastrointestinal (GI) tract, namely, esophagitis, chronic gastritis and duodenitis have been implicated in the pathogenesis of upper abdominal pain in children(1). *Helicobacter pylori* (HP) has emerged as an important pathogen in inflammatory gastroduodenal diseases

In adults(2). Recently, in children, HP related gastritis has been suggested as a cause of upper abdominal symptoms(3). There is paucity of data on endoscopic, histologic and microbiologic evaluation of children with upper abdominal pain, particularly from our country. We, therefore, undertook this prospective study

on children presenting with upper abdominal pain to evaluate: (a) the relationship of this symptom-complex to inflammatory esophago-gastroduodenal lesions and HP infection and (b) the response to specific therapy.

Subjects and Methods

Children with significant upper abdominal pain (affecting child's day to day activity \pm requiring medication for relief of pain) for more than one month with or without vomiting attending the Pediatric Gastroenterology Outpatient services were enrolled in the study. A thorough clinical evaluation, stool and urine examinations, blood counts, liver function tests, serum urea, creatinine and serum amylase were done in each case. Liver, biliary tract, pancreas, kidneys, ureters and urinary bladder were evaluated by ultrasonography. Patients with biliary, pancreatic or renal disease or any systemic illness, large bowel symptoms, history of ingestion of non-steroidal anti-inflammatory drugs, antibiotics, antacids, H₂-receptor antagonists or proton pump inhibitors in previous four weeks or history of previous abdominal surgery were excluded.

Endoscopy, Histology and Processing for H. pylori

All children were subjected to upper GI endoscopy and the findings recorded independently by two observers. Endoscopic mucosal biopsy specimens for rapid urease test (RUT), Gram's staining, HP culture (one piece each) and histologic examination (two pieces) were obtained from the antrum. The piece for RUT was immediately inoculated into the rapid urease medium(4) and observed periodically for 60 minutes for change of color from yellow to pink. Two pieces were transported to the laboratory in 0.2 ml of Columbia broth (Difco Laboratories, USA) for smear examination and culture. Impression and crushed

smears were prepared from one of these pieces, stained with modified Gram's method using dilute carbol fuchsin as counterstain. The other biopsy piece was homogenized and inoculated on sheep chocolate agar (Columbia agar base with 10% sheep blood; Difco) containing the following antibiotics: amphotericin B (2 mg/ 1), vancomycin (6 mg/1) and polymyxin B (2500 units/1)(5). The plates were incubated under microaerophilic conditions at 37°C using candle jar technique, and were examined after 3, 5 and 7 days of inoculation. Characteristic colonies were identified by Gram staining, motility and biochemical tests including catalase, oxidase and urease positivity. Biopsy specimens for histology were processed in the routine way and stained with Hematoxylin and Eosin (H & E), Giemsa and Warthin-Starry technique. The histopathologist was not aware of clinical or endoscopic findings. The criteria for HP positivity were culture positive and/or RUT and smear positive.

Treatment Subgroups

Patients with gastritis due to HP infection were treated with triple therapy: colloidal bismuth subcitrate (240 mg BD in children >10 yr and 120 mg BD in children <10 yr), amoxicillin (50 mg/kg/24 h q 8 h) and metronidazole (30 mg/kg/24 h q 8 h) for two weeks. At 8 weeks from the initiation of therapy, patients were re-evaluated for Symptoms and HP eradication by repeat endoscopy and antral biopsies (processed as earlier). Patients with esophagitis, gastritis and duodenitis without HP infection were treated with ranitidine (4 mg/ kg/24 h q 12 h to maximum of 300 mg/d) for 6 weeks. All the patients were followed up for 6 months. Symptomatic improvement was defined as complete relief of pain at least for 3 months following therapy.

Statistical Analysis

Fisher's Z test for single sample with

mutually exclusive categorization was used for statistical analysis.

Results

Thirty three children [mean age 9.9 ± 2.7 , range 4-15 years; 20 males] were studied. The duration of symptoms was 23.3 ± 17.4 months (range 1 month to 5 years). The site of pain was epigastric in 15 children, peri-umbilical in 8 and without definite localization in the upper abdomen in 10 cases of the 33 symptomatic children, abdominal pain was the sole symptom in 26 subjects; associated vomiting was present in 6 and heartburn and regurgitation in 1 child. Histology revealed antral gastritis in 28/33 (85%; $p=0.0004$) patients (20 with antral gastritis on both endoscopy and histology and 8 with normal endoscopy and antral gastritis on histology); the other 5 cases had normal antral histology (Table I). HP infection was present in 12/28 (43%) patients with antral gastritis. Although there was no difference in the efficacy of various histological stains for detection of HP, Giemsa was most convenient. None of the patients with normal antral histology had HP infection. Symptomatic improvement with triple therapy was observed in 10/12 (83%; $p <$

0.0001) patients with gastritis due to HP infection. Repeat evaluation was done in 7 children with HP gastritis and of these, 5 cases showed eradication of the organism. Four of these latter five cases also showed complete resolution in severity of gastritis from moderate to mild. The other three cases did not consent for repeat endoscopy. The two patients in whom there was failure to eradicate HP infection with triple therapy did not show any improvement in symptoms. No adverse effects were observed in children receiving triple therapy. Improvement on ranitidine therapy was observed in 12/16 (75%; $p=0.04$) patients with HP negative gastritis. Three patients with esophagitis alone improved with ranitidine therapy and other anti-reflux measures. On follow-up, no patient with initial improvement with therapy had relapse of symptoms.

Discussion

Our data shows that in children with upper abdominal pain, gastritis, duodenitis and esophagitis occur frequently (94%, 31/33). Antral gastritis associated with HP was found in 43% (12/28) and the

TABLE I—Summary of Endoscopic, Histologic and Microbiologic Characteristics (n=33).

Histologic/ microbiologic attribute	Endoscopic findings			
	Antral gastritis (n=16)*	Antral gastritis and duodenitis (n=4)*	Esophagitis (n=3)*	Normal (n=10)
Antral gastritis	16	4	0	8
Esophagitis	5	0	3	0
<i>H. pylori</i> positive	9	2	0	1
Culture positive	3	1	0	0
RUT# and staining positive	9	2	0	1

* Indicate number of patients with endoscopic findings for each category.

RUT=Rapid urease test.

remaining were HP negative (57%). Kilbridge *et al.* found antral gastritis in 40% of symptomatic children and of these, 55% were associated with HP infection(6). Glassman *et al.* found HP positive gastritis in 44% and HP negative gastritis in 30% of symptomatic children(3). Although gastritis associated with HP infection is frequent in symptomatic children, its relationship with symptoms is controversial. HP infection has been documented in 30% of asymptomatic children(7). An increasing prevalence of HP infection with increasing age has been observed among asymptomatic population(8). It appears that HP related gastritis is present in both symptomatic as well as asymptomatic children. This implies that HP gastritis is either not associated with symptoms or only a subgroup of these children develop symptoms. Evidence supporting an association between HP related gastritis and upper abdominal symptoms is based on the studies which showed symptomatic improvement in affected children following anti-Helicobacter therapy (9, 11). In our study, we observed symptomatic improvement following triple therapy in 10/12 patients with HP related gastritis. This symptomatic improvement correlated with HP eradication in all our cases. In 2 of our children treated for HP gastritis neither improvement in symptoms nor eradication of the organism were observed. The failure to eradicate HP in these patients was probably due to resistant organisms; a high frequency (70%) of metronidazole-resistant HP has been observed by us. None of our children with HP related gastritis with initial response to treatment had recurrence of symptoms on follow-up. In our study there was symptomatic improvement with ranitidine therapy in 75% of children with HP negative gastritis. Among this group, there was no relapse of symptoms during the follow-up. We recommend that children with significant upper abdominal

pain with out any obvious cause should be endoscopically evaluated for inflammatory mucosal changes and HP infection. HP related gastritis should be treated with triple therapy and HP negative gastritis with H₂- receptor antagonists. Pending placebo controlled randomized studies, we believe our treatment protocol to be safe and effective in symptomatic children with chronic antral gastritis.

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