

***Helicobacter pylori* Infections and Gastroduodenal Disease**

[Macarthur C, Saunders N, Feldman W. *Helicobacter pylori*, gastroduodenal disease, and recurrent abdominal pain in children. *JAMA* 1995, 273: 729-734],

Helicobacter pylori has been postulated as a causal agent of chronic antral gastritis and peptic ulcer disease, particularly duodenal ulcers, in adults. However, the relationship between *H. pylori* infection and gastroduodenal complaints in children is less clear. It is uncertain, whether the *H. pylori* associated gastritis in children, represents a clinical entity that should be treated. The objective of this review was to assess the strength of cause-and-effect association between *H. pylori* infection and antral gastritis, peptic ulcer disease, and recurrent abdominal pain in children.

Pertinent English language research publications in children up to 18 years age, from January 1983 to July 1994 were identified and analyzed. In total, 45 studies (case series, cross-sectional surveys, and treatment trials) were retrieved. Hill's criteria for causal inference were used to determine the strength of the evidence for a causal relationship.

Results of 27 cross-sectional surveys in children, with sample sizes ranging from 25-363, were analyzed for evidence of association between *H. pylori* infection and antral gastritis. The prevalence of gastric *H. pylori* colonization ranged from 8-13% (median 26%) in this population of children. The rate

ratio of antral gastritis for children with gastric *H. pylori* colonization compared with those not colonized ranged from 1.9-71.0 (median 4.6). Rate ratio for primary antral gastritis could be calculated from 4 studies and varied from 4.3-18.7 (median 13.4). Six one-arm treatment trials, with no control groups, reported symptomatic relief and improvement in antral gastritis with clearance of *H. pylori*, on anti-helicobacter therapy.

Results of 18 studies, with sample sizes varying from 5-27 were analyzed, for determining the prevalence of *H. pylori* infection in children with primary peptic ulcer disease. The prevalence of *H. pylori* infection was consistently higher in children with duodenal ulcer disease (range, 33-100%; median, 92%) compared with children with primary gastric ulcer (range, 11-75%; median, 25%). Of the 3 treatment trials which were analyzed, the only placebo controlled study revealed no difference in duodenal ulcer healing rate between the study and control groups, on completion of therapy.

In total, 8 studies with sample sizes varying from 14 to 82 estimated the prevalence of *H. pylori* infection in children with recurrent abdominal pain. The reported prevalence rates of *H. pylori* infection ranged from 0-81% (median 22%). Only 3 of the studies defined the study group using Apley's definition for recurrent abdominal pain. In these children, the prevalence of *H. pylori* infection was much lower, ranging from 0-9% (median, 6%). Out of the 2 studies which simultaneously estimated the prevalence of *H. pylori* infection in a control group of children attending the hospitals for unrelated complaints, the

retrospective report revealed an increased risk of recurrent abdominal pain in children with *H. pylori* infection (rate ratio, 2.7%), while the prospective study revealed no significant difference in risk (rate ratio, 1.2%). No treatment trial could be identified in the children with *H. pylori* associated recurrent abdominal pain.

After applying Hill's criteria for causal inference it was finally concluded that there is a strong evidence for an association between *H. pylori* infection and antral gastritis and duodenal ulcer disease in children, while only weak evidence exists for an association with gastric ulcer and weak or no association with recurrent abdominal pain.

Comments

Helicobacter pylori is currently the subject of active research and intense debate. It has been postulated as a causal agent for a variety of enteral and non-enteral conditions like peptic ulcer disease, gastritis, recurrent abdominal pain, duodenogastric reflux, esophagitis, chronic diarrhea, short stature and unexplained weight loss (1-4). However, till date there is no consensus opinion among various authors on its definitive causal role in any condition. The questions of when to suspect and investigate for *H. pylori* infection, significance of isolation of the organism from a given case and whether/when to treat the patient with anti-helicobacter drugs still remain unanswered. The present meta-analysis was aimed at determining the strength of association between *H. pylori* infection and antral gastritis, peptic ulcer disease, and recurrent abdominal pain in children by critical evaluation of methodology and results of the studies available on the subject.

The analysis of studies aimed at evaluation of prevalence of *H. pylori* infection in children with primary peptic ulcer disease

suggested a strong association between *H. pylori* infection and duodenal ulcer disease in children but only a weak association between gastric ulcer disease and infection. However, *H. pylori* infection is neither necessary nor sufficient for ulcer development. A causal inference would be enhanced by evidence from randomized, double blind, placebo controlled trials (with long term follow up) to determine the effect of eradication of gastric *H. pylori* on the natural history of peptic ulcer disease in children. Currently, therefore, anti-*H. pylori* drugs may be considered only in symptomatic children with proven duodenal ulcer disease and definitive evidence of *H. pylori* infection who do not respond to conventional therapy.

Although, it was concluded that there is strong and consistent evidence that *H. pylori* infection is associated with antral gastritis in children, the clinical significance of this condition is unclear. Again, causal inference would be strengthened by evidence from randomized double blind, placebo controlled trials of therapy using reliable and valid measures of clinical symptomatology. Therefore, evidence is, as yet, insufficient to support treatment of *H. pylori* associated gastritis in the absence of peptic ulcer disease.

The results of studies aimed at determination of prevalence of *H. pylori* infection in children with recurrent abdominal pain (RAP) were inconsistent, implying that there is no concrete evidence of a causal relationship between *H. pylori* infection and RAP. Therefore, routine screening for this organism in children presenting with abdominal pain and anti-helicobacter treatment in cases with *H. pylori* associated recurrent abdominal pain, are currently not justified. Further, since symptomatic relief in absence of eradication of the organism is well established the aim of the therapy may need to be

redefined as treatment of symptoms and not the culture or biopsy report.

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