ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Evaluating the Association of *Helicobacter pylori* to GERD

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G&H What is the prevalence of *Helicobacter pylori* infection in the general population?

GF The prevalence of *H. pylori* infection throughout the world has been decreasing steadily in recent years. It is more common in older individuals, those with lower socioeconomic status, and in the developing world. The overall prevalence in the Western world is estimated to be approximately 25%.

G&H Could you discuss the prevalence of *H. pylori* infection in terms of patients with gastroesophageal reflux disease, Barrett esophagus, or esophageal cancer?

GF The issue of *H. pylori* infection associated with gastroesophageal reflux disease (GERD), Barrett esophagus, and esophageal adenocarcinoma is complex. We know from a variety of systematic reviews that the prevalence of *H. pylori* infection is lower in patients with GERD, when compared to control patients. However, there is considerable regional variation, with the difference being more prominent in the Far East than in Europe and North America. There is a considerable amount of heterogeneity observed among studies. Similarly, Barrett esophagus patients are less likely to be infected with *H. pylori* than are population controls.

Because the prevalence of *H. pylori* infection has been falling in the Western world at the same time that the incidence of esophageal carcinoma has been increasing, it seems logical to investigate a relationship between these two opposing time trends. A number of epidemiologic studies have demonstrated a negative association between *H. pylori* infection and esophageal adenocarcinoma. This association has also been described with the *H. pylori* cytotoxin-associated gene A (*cagA*)-positive strain, which is felt to result in more intense inflammation and a greater tendency to gastric atrophy. A recent meta-analysis found the pooled odds ratio for the prevalence of *H. pylori* infection in esophageal adenocarcinoma to be 0.52 (95% CI 0.37–0.73) and for the *H. pylori cagA*-positive strain to be 0.51 (95% CI 0.31–0.82).

G&H Could you expand on the current understanding of the relationship between *H. pylori* and GERD?

GF The most likely mechanism of any potential protective effect of *H. pylori* stems from its influence on the potency of the gastric refluxate. It is hypothesized that the distribution and severity of *H. pylori*-related gastritis, rather than the presence or absence of *H. pylori* infection, may effect the potency of the gastric refluxate. Antral-predominant gastritis, as is typically seen in duodenal ulcer patients, is associated with increased acid secretion, whereas corpus-predominant gastritis, often accompanied by gastric atrophy, is associated with decreased acid secretion. Circumstantial evidence suggests that the distribution and severity of gastritis caused by *H. pylori* infection may be a factor in the development of GERD in some patients. With this under consideration, it now appears clear that eradication of *H. pylori* infection does not cause reflux.

It should be pointed out that many clinicians mistakenly think that *H. pylori* infection protects against GERD and its related complications; however, it is not protection as much as association. This is a controversial issue, and protection is too strong of a term for this relationship;

the above statements are observations based merely upon observational studies, which do not allow one to make clear-cut conclusions regarding cause and effect.

G&H Can you further discuss the current understanding of *H. pylori* infection as it relates to esophageal cancers?

GF The primary mechanism postulated for a protective effect of *H. pylori* infection, with regard to esophageal cancer, centers around decreased acid secretion caused by *H. pylori*-induced gastric atrophy, particularly with *cagA*-positive strains. A recent population-based case control study from Ireland found that severe gastric atrophy, as measured by pepsinogen I/II ratios, was associated with a clearly decreased risk of esophageal adenocarcinoma, giving support to this as a putative mechanism of protection from esophageal adenocarcinoma. However, that same study also found that the protective effect of *H. pylori* infection was also encountered in atrophy-negative subjects, suggesting that mechanisms other than gastric atrophy are involved in the potential protective effects of *H. pylori* infection for esophageal adenocarcinoma. These may include neutralization of acid by ammonia from *H. pylori*, pro-apoptotic effects of *H. pylori* on adenocarcinoma cell lines, and alterations in ghrelin secretion.

G&H In which strains of *H. pylori* infection and which types of GERD patients have these proposed associations been examined?

GF Research on this issue has been most heavily studied with the *cagA*-positive strain, which is thought to promote increased inflammation and progression to atrophic gastritis. As mentioned above, the results of the studies are mixed, but overall the bulk of the evidence suggests that the *cagA*-positive strain appears to be associated with a decreased risk of esophageal cancer.

G&H Does the presence of *H. pylori* infection affect the treatment of a patient with GERD?

GF In the past, there was quite a bit of controversy regarding this issue. However, it has become clear over recent years that the presence or absence of *H. pylori* infection should not influence treatment decisions for reflux disease. According to the Maastricht recommendations that were published last year and other consensus recommendations, *H. pylori* infection, when diagnosed, should be eradicated. Thus, *H. pylori* infection eradication should not affect the outcome of proton pump inhibitor therapy in GERD, at least in the Western population. Thus, routine testing for *H. pylori* infection is not recommended in GERD patients. Whether or not patients should be tested prior to long-term maintenance therapy with proton pump inhibitor therapy remains unclear at this time.

Suggested Reading

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