Helicobacter pylori and duodenal ulcer: Guilty as charged

Although Bottcher first observed spiral bacteria in the human stomach in 1874 (1), the significance of bacterial infection of the stomach was largely ignored until the classic work of Warren and Marshall in 1982 (2). The organism they isolated, named Campylobacter pyloridis, is now known as Helicobacter pylori (3). In the intervening 12 years, there has been a virtual explosion of knowledge regarding the role of this bacterium in human disease and it is now accepted as a definite human pathogen for a number of upper gastrointestinal disorders.

**Epidemiology**

*H pylori* has been described worldwide, but higher infection rates are seen in developing than in developed countries (4). Furthermore, persons in developing countries acquire infection at earlier ages than do those in developed countries.

Although an environmental reservoir of infection has not been identified, there is considerable evidence implicating person to person transmission, including outbreaks from endoscopy equipment (5). As well, at least in some third-world countries, there is evidence of waterborne transmission (6). A zoonotic reservoir is suggested by higher seroprevalence rates in veterinarians (7) and abattoir workers (8) than in controls. Nevertheless, an animal reservoir has not been identified, and preliminary evidence suggests that the prevalence of *H pylori* infection is similar in vegetarians and non-vegetarians (4).

**Association with Specific Gastrointestinal Conditions**

*H pylori* is undeniably the cause of chronic ‘nonspecific’ gastritis (4,9), a condition located predominantly in the gastric antrum. There is to date no correlation between *H pylori* infection and nonulcer dyspepsia (4.8). There is clearly an increased risk of both adenocarcinoma and lymphoma of the stomach with *H pylori* infection (4,9), although the association does not appear to be causal.

There is strong evidence of causality for *H pylori* in peptic ulcer disease (4,9,10). The correlation between *H pylori* infection and duodenal ulcer (DU) is exceedingly strong, whereas the correlation with gastric ulcer (GU) is impressive, but not nearly as compelling.

Approximately 95% of DU that are not caused by a nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with *H pylori* infection. Furthermore, when DU is treated solely with H2 antagonist therapy, there is a greater than 70% probability of recurrence within 12 months (11), which is reduced only about 50% by continuing H2 antagonist therapy (12). In contrast, when DU treatment includes antimicrobial therapy to eradicate *H pylori* and where such antimicrobial therapy is effective, the one-year relapse rate is less than 10% (4,9,10,13).

The evidence linking *H pylori* to peptic ulcer disease is so compelling that even the staid United States National Institutes of Health (NIH) has acknowledged this association and recommends concomitant antimicrobial therapy for patients with DU in association with *H pylori* infection (10).

**What is the Best Regimen for Treating Duodenal Ulcer?**

Both the NIH consensus panel (10) and a recent Canadian report (14) recommend the addition of antimicrobial therapy for patients with DU who have *H pylori* infection. However, since at least 95% of patients with DU not precipitated by NSAID therapy will be infected with *H pylori*, we believe that it is unnecessary and needlessly expensive to test for the presence of *H pylori* infection in such individuals. Rather, all such individuals should be given antimicrobial therapy directed against *H pylori*.

At present, there are inadequate data to support treatment of DU with antimicrobial therapy alone in the absence of acid-suppressing therapy, although one study found combination antimicrobial therapy alone to be successful (15). As far as acid-suppressive therapy is concerned, superior efficacy has been demonstrated with omeprazole plus antimicrobial therapy compared with H2 antagonists plus antimicrobial therapy (16).

The specific antimicrobial regimen and the optimal duration of therapy also remain to be defined. The traditional approach has been to use ‘triple therapy’,

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using a combination of colloidal bismuth (which is not available in Canada) with metronidazole and either tetracycline (bwt) or amoxicillin (bam). These triple therapy regimens have traditionally been given with ranitidine or another H2 blocker, but more recently have also been given together with omeprazole.

The optimal duration of treatment has not been established, but a two-week course of omeprazole plus amoxicillin (500 mg qid) is highly effective (16). Of interest, the new macrolide clarithromycin, which has excellent in vitro activity against \textit{H pylori}, has demonstrated significant efficacy as a single agent for the treatment of \textit{H pylori} infection (17,18) and good results in combination with omeprazole in the treatment of DU (19). Further studies of clarithromycin for the treatment of DU are ongoing.

CONCLUSIONS

\textit{H pylori} is now firmly accepted as an important human pathogen and specifically the cause of the vast majority of cases of DU that are not due to NSAID therapy. It is now recognized that proper treatment of DU requires antimicrobial therapy to eradicate \textit{H pylori}, because eradication of \textit{H pylori} will markedly reduce the recurrence rate of DU and will obviate the need for long term antisecretory therapy in most individuals. Similar recommendations are probably prudent for GU, although the data are less definitive. The optimal drug regimen has not been defined, but a two-week course of omeprazole plus amoxicillin is one effective and simple regimen. There is inadequate evidence to recommend large population screening and treatment for asymptomatic \textit{H pylori} infection, although this is an important avenue of clinical research.

REFERENCES


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