Helicobacter pylori: Novel therapies

Eric Drouin MD FRCP

A combination of different agents is generally used to eradicate Helicobacter pylori. Nevertheless, recently accepted treatment regimens still demonstrate failure rates as high as 20% (1). Furthermore, these regimens are relatively complex, with poor tolerability and reduced compliance in some patients, particularly children and adolescents. Antibiotic resistance is already a major problem in some countries and is likely to become increasingly prevalent (2).

Antibiotics and acid suppression are used together to eradicate H pylori. However, numerous difficulties exist with these regimens. Antibiotics are widely prescribed in the pediatric age group; therefore, antibiotic resistance is an ongoing problem, especially in young children. Current treatments are not affordable in many countries where H pylori infection is highly prevalent. The purpose of this review is to examine critically different agents (antibiotics, acid-suppressive drugs, mucosal protective agents and probiotics) that are potentially beneficial for H pylori eradication or prevention, in the light of cost, efficacy and tolerability.

ANTIBIOTICS

Because H pylori is a bacterium, antibiotics certainly will continue to be used as a therapeutic agent. Some progress has been made in the search for agents with enhanced efficacy (eg, furazolidone) (3). Two recent studies have used furazolidone in populations with high rates of metronidazole resistance.

In a Colombian population, Segura et al (4) used furazolidone, in combination with bismuth subcitrate and amoxicillin, for two weeks. The eradication rate was 86%, with good compliance and no significant adverse side effects. When this drug is used as dual therapy in combination with omeprazole, as expected, a lower eradication rate is observed (5). This antibiotic may offer an interesting alternative in developing countries for use in the management of resistant H pylori. However, no pediatric experience has been reported with this agent in the eradication of gastric H pylori infection.

Azithromycin is another macrolide with a theoretical advantage over clarithromycin in terms of a long elimination half-life and higher concentrations achieved in gastric tissues. However, contradictory results have been observed in the few clinical studies reported to date. This drug may play a therapeutic role in settings where poor compliance is expected and a short term course of treatment is needed (6,7).

New quinolone compounds with potent in vitro antibacterial activity have recently been found in Japan. These may prove to be more effective than ciprofloxacin, which in...
a French study, when used in combination with omeprazole and amoxicillin, achieved only a 25% eradication rate (8). However, quinolones are not recommended for young children because of the potential for cartilage injury, as shown experimentally in growing animals.

ANTISECRETORY DRUGS
Proton pump inhibitors and H2 blockers are widely used to potentiate the effect of antibiotics in the lumen of the stomach. Rabeprazole is a new proton pump inhibitor that inhibits the activity of urease, and has a lower in vitro minimal inhibitory concentration (MIC) than does omeprazole and lansoprazole. In one study, this new agent, combined with a variety of different antibiotics, eradicated H pylori up to 90% of the time (9).

Ebrotidine is a new H2 receptor antagonist that enhances the activity of many antibiotics and has a lower MIC than does ranitidine (10). This agent seems to be a cytoprotective agent that inhibits H pylori urease and proteases, and increases gastric mucus production. One small study compared ranitidine with ebrotidine, each combined with amoxicillin and metronidazole, and showed an H pylori eradication rate of more than 90% for both groups (11). Larger studies are needed to determine the role of this agent in H pylori eradication.

MUCOSAL PROTECTIVE AGENTS
Planotol is an oily ulcer-healing agent that increases the membrane permeability of H pylori. This agent was employed in a few small trials combined with antibiotics for three to four weeks, and showed eradication rates between 69% and 86% (2). Other agents, such as sulcralfate and ecabet, which can bind to H pylori and its surface-associated urease enzyme, as well as specific urease inhibitors, have been assessed for their efficacy in terms of active therapy toward H pylori eradication. Sulcralfate can potentiate the effect of antibiotics in vitro, but has yet to be evaluated critically as part of a quadruple therapy for resistant organisms.

NUTRICEUTICALS
Nutriceutical agents are another potentially interesting alternative to eradicate or prevent this infection in children. Honey has been used to treat dyspepsia in different countries for many years. In 1994, al Somal et al (12) reported the antibacterial activity of manuka honey. A 5% strength was able to inhibit completely H pylori growth after 72 h. Very recently, osmotic effect was shown to be the most important parameter for killing H pylori by different types of honey (13).

Capsaicin, the active ingredient in chili peppers, is known to improve experimentally induced gastric lesions using both acetylsalicylic acid and ethanol in rats. Jones et al (14) examined the in vitro activity of capsaicin on H pylori growth and showed a dose-dependent inhibition of growth. Further animal and human studies using this agent are required to assess its potential gastroprotective effects in vivo.

Aqueous garlic extract was also shown to inhibit H pylori growth in vitro (15). Stern bark extract from Mali, used as a decoction to treat dyspepsia for many generations, was also shown to inhibit H pylori growth in vitro (16).

PROBIOTIC AGENTS
A group from Spain studied the effect of lactobacilli in a gnotobiotic mouse model (17). Lactobacillus salivarius-infected gnotobiotic BALB/C mice and control germ-free mice were inoculated orally with H pylori to examine whether the probiotic would inhibit helicobacter colonization. H pylori did not colonize the stomach of L. salivarius-treated gnotobiotic BALB/C mice, whereas the organism colonized and caused gastritis in germ-free mice. Furthermore, L. salivarius given to infected mice resulted in the eradication of H pylori colonization (17). This interesting work raises the possibility that Lactobacillus species may be useful as a probiotic agent in the gastric mucosa.

Very recently, Opekun et al (18) reported healthy H pylori-infected volunteers treated either with hyperimmune bovine colostrum immune globulins or an oligosaccharide containing an H pylori adhesion target or recombinant human lactoferrin. Unfortunately, none of these adults had their H pylori eradicated.

CONCLUSIONS
Several interesting modalities for treating H pylori may be on the horizon. However, all of these novel therapies still need to be validated in vivo in large groups of patients. These agents are unlikely to replace standard antibiotic therapy but may offer an option as adjuncts to therapy, particularly for resistant infection. Current treatment regimens are generally effective but are relatively expensive and not affordable worldwide. Thus, there is a need for more inexpensive methods to prevent or treat this infection, particularly in underprivileged settings. Probiotics and nutriceuticals are theoretically attractive options. Children constitute a population in whom the infection is rarely symptomatic and, therefore, may benefit from well controlled, randomized trials using these novel antibacterial agents to eradicate H pylori colonization of the gastric antrum.

REFERENCES

Can J Gastroenterol Vol 13 No 7 September 1999

582


