Helicobacter pylori: Novel therapies

Eric Drouin MD FRCPC

E Drouin. *Helicobacter pylori*: Novel therapies. Can J Gastroenterol 1999;13(7):581-583. The ideal therapy for *Helicobacter pylori* would cure the infection without resulting in the development of antibiotic resistance. Current therapies have variable cure rates; the reasons for treatment failure include bacterial resistance and poor compliance. Some antibiotics, such as furazolidone, may be affordable agents to treat this infection worldwide. New proton pump inhibitors, such as rabeprazole, can potentiate antibiotics. Nutraceuticals and probiotics demonstrate interesting *in vitro* activity against *H. pylori*. Children rarely have symptoms to this infection and, therefore, are a suitable group in which to assess different nonaggressive therapies.

Key Words: *Helicobacter pylori*; Pediatrics; Probiotics; Nutraceuticals

Helicobacter pylori : nouvelles thérapeutiques

RÉSUMÉ : Le traitement idéal contre *Helicobacter pylori* guérirait l'infection sans entraîner de résistance aux antibiotiques. Les traitements actuels s'accompagnent de taux de guérison variables. Les raisons de l'échec thérapeutique sont notamment la résistance bactérienne et la piètre fidélité au traitement. Certains antibiotiques, comme la furazolidone sont des agents abordables en traitement de cette infection à l'échelle mondiale. Les nouveaux inhibiteurs de la pompe à protons, comme le rabeprazole, peuvent potentialiser l'action des antibiotiques. Les nutraceutiques et les probiotiques manifestent une activité *in vitro* intéressante contre *H. pylori*. Les enfants manifestent rarement de symptômes de cette infection et constituent par conséquent un groupe à qui conviendrait l'évaluation de diverses thérapeutiques non vulnérantes.

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* antihelicobacter activity have recently been found in Japan. These may prove to be more effective than ciprofloxacin, which in

Division of Gastroenterology, Hôpital Ste-Justine, University of Montreal, Montreal, Quebec

Correspondence: Dr Eric Drouin, Division of Gastroenterology, Hôpital Ste-Justine, 3175 Côte Ste-Catherine Road, Montreal, Quebec H3T 1C5. Telephone 514-345-4626, fax 514-345-4999, e-mail edrouin@ibm.net

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 sulcrafate 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. Sulcrafate 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 comprise 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.

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