What is the best regimen for *Helicobacter pylori* eradication in Canadian Arctic Aboriginals?

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Canadian Aboriginal populations have a high prevalence of *Helicobacter pylori* infection and an increased risk for the development of gastric cancer (1). Thus, there is a need to identify effective *H pylori* eradication regimens in this at-risk population. In the current issue of the *Journal*, Morse et al (2) (pages 701-706) report results from a randomized controlled trial comparing sequential versus standard clarithromycin-containing triple therapy in *H pylori*-infected adults from the community of Aklavik (Northwest Territories) (2). The study was part of a participatory research project focusing on community-identified research goals investigating the burden of *H pylori* disease in Arctic Aboriginal communities.

In the study by Morse et al (2), *H pylori*-infected patients >15 years of age were randomly assigned to either a 10-day treatment of standard triple therapy consisting of a proton pump inhibitor (rabeprazole), amoxicillin and clarithromycin, or sequential therapy. Antibiotic resistance rates to clarithromycin and metronidazole were available for almost one-half of the subjects, allowing tailored treatment. If clarithromycin resistance was detected, patients were randomly assigned to sequential therapy or quadruple therapy.

Several important points are noteworthy in this study. First, as identified in other Canadian Aboriginal populations, the prevalence of *H pylori* infection remains high in this community despite a diminishing *H pylori* prevalence in most segments of the Canadian population. Second, the prevalence of precancerous lesions, gastric atrophy and intestinal metaplasia were high, supporting the increased risk for development of gastric cancer in this population and underscoring the need for effective *H pylori* eradication regimens.

When outcomes were assessed by the more stringent intention-to-treat analysis, the effectiveness of both therapies was disappointing, with only 55% efficacy with triple therapy and 57% with sequential therapy. With these poor outcomes, it is important to consider why the results were suboptimal. The success of treatment for *H pylori* is determined, in large part, by the presence of antibiotic resistance and patient adherence (3). In the study by Morse et al (2), of the 50 subjects who underwent sensitivity testing, the rates of clarithromycin and metronidazole resistance were 10% and 26%, respectively. Thus, it is likely that similar resistance rates were present in the remaining subjects who were randomly assigned to triple versus sequential therapy. The updated Maastricht guidelines (4) do not recommend clarithromycin therapy if the local clarithromycin resistance rate is >15%. Thus, one potential explanation for the poor efficacy is antibiotic resistance.

Poor adherence to therapy is an additional important determinant of efficacy (3). In the study by Morse et al, the overall adherence levels were suboptimal (60%). In fact, even in the group who underwent antibiotic sensitivity-directed therapy, the eradication rates were still low. However, in subjects with 100% compliance, treatment effectiveness increased in both the triple therapy and sequential therapy groups to 65% and 75%, respectively. Thus, the combination of antibiotic resistance and decreased adherence likely account for the poor efficacy of both triple therapy and sequential therapy.

Although sequential therapy was initially regarded as superior to triple therapy, follow-up studies indicate that the efficacy of sequential therapy is not as good as the original studies suggested. Sequential therapy loses efficacy in the presence of clarithromycin and metronidazole resistance (3). In the study by Morse et al, even when assessed by per-protocol analyses, efficacy of sequential therapy was well below the recommended cure rates of 80% to 90%, suggesting that this regimen is not an optimal choice in this particular community unless adherence can be improved.

Morse et al should be commended for providing key information concerning *H pylori* infection in a Canadian Aboriginal Arctic community. This study shows that, in this at-risk population, the efficacies of two currently recommended eradication regimens are suboptimal, likely due to both antibiotic resistance and poor compliance. These findings support further studies aimed at identifying effective therapies by focusing on both optimized regimens based on known antibiotic susceptibility rates in the community and promoting adherence.

REFERENCES