Reviewer's report

Title: Efficacy of Rifabutin-based Triple Therapy as Second-line to Eradicate Helicobacter Pylori Infection

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Reviewer: TJ Borody

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General
Re-treatment of H. pylori infection after failure of first-line treatment is often problematic in clinical practice. This is because of the development of secondary resistance to key antibiotics used in the first-line treatment. Quadruple therapy may overcome therapeutic difficulties when first-line standard triple therapy fails. Even then, about 30% of patients will fail one or more eradication treatments of the infection and will remain H. pylori positive. The poor results are due to the emergence of double-resistant strains especially those resistant to clarithromycin and metronidazole which are difficult to eradicate. Thus, drugs without cross-resistance to nitroimidazoles or macrolides have been evaluated for use in re-treatment combination therapies. In this respect, rifabutin-based ‘rescue’ therapies represent a promising strategy for eradication failure. In this paper, the authors described a study comparing a rifabutin-based triple regimen (QAR) comprising of omeprazole 20 mg, amoxyxillin 1 gm and rifabutin 150 mg given per 12 hr and quadruple therapy (QT) (omeprazole 20 mg/12 hr, Bismuth citrate 120 mg/6hr, tetracycline 500 mg/6hr and metronidazole 500 mg/8 hr). The authors concluded that QAR is inferior to QT. Patients treated for 7 days with QT were predominantly DU and those treated with QAR were chronic gastritis. This probably explained in part the higher eradication rate of 70.4%, ITT with QT compared with 44.4% in the QAR group. The higher rate in the QT group may also reflect infection with a low prevalence of double resistant bacteria (although the study did not evaluate antibiotic susceptibility). However, this is not a problem with rifabutin-based combinations which have been shown to be highly effective for H. pylori strains with double resistance. Thus the difference in eradication rates detected between the two treatment regimens may not be real. In addition, a major reason for the poor outcome of the rifabutin-based therapy may stem from the relatively low dose of amoxicillin and proton pump inhibitor.

Indeed an eradication rate of 44.4% with QAR regimen in this study constitutes a highly ineffective treatment when compared with substantially higher rates achieved by other investigators using marginally different dosing. The authors failed to cite a study (Borody et al. 2005; 23:481-488) which showed that low dose rifabutin is ineffective unless combined with increased dose amoxicillin and pantoprazole which achieved eradication rate of 96.6% ITT and was highly effective against double resistant bacteria. In the light of this study and others, no new information is presented and the low eradication rate of QAR is disappointing. With rising clarithromycin resistance in the community and PPI-based triple therapy slowly losing efficacy, an effective back-up ‘rescue’ regimen is needed but QAR cannot be one due to reasons described above.

The manuscript is too long and should be substantially trimmed.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)