Drugs. 2008;68(6):725-36.

Therapy for Helicobacter pylori infection can be improved: sequential therapy and beyond.

Graham DY, Lu H, Yamaoka Y.

Source：Department of Medicine, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas 77030, USA. dgraham@bcm.tmc.edu

Abstract

As with other bacterial infections, successful treatment of Helicobacter pylori infections depends on the use of antibacterial agents to which the organism is susceptible. In this article, we use the proposed report card grading scheme (i.e. grade A, B, C, D, F) for the outcome of clinical trials, where intention-to-treat cure rates >95% = A, 90-95% = B, 85-89% = C, 81-84% = D and <81% = F. The goal of therapy is to consistently cure >95% of patients (e.g. provide grade A results). Like tuberculosis, H. pylori infections are difficult to cure and successful treatment generally requires the administration of several antibacterial agents simultaneously. Duration of therapy is also important and depends upon whether resistance is present; 14 days is often best. With few exceptions, worldwide increasing macrolide resistance now undermines the effectiveness of the legacy triple therapy (e.g. a proton pump inhibitor [PPI], clarithromycin and amoxicillin) and, in most areas, cure rates have declined to unacceptable levels (e.g. grade F). The development of sequential therapy was one response to this problem. Sequential therapy has repeatedly been shown in head-to-head studies to be superior to legacy triple therapy. Sequential therapy, as originally described, is the sequential administration of a dual therapy (a PPI plus amoxicillin) followed by a Bazzoli-type triple therapy (a PPI plus clarithromycin and tinidazole) and has been shown to be especially useful where there is clarithromycin resistance. However, the cure rates of the original sequential treatment are grade B and can probably be further improved by changes in dose, duration or administration, such as by continuing the amoxicillin into the triple therapy arm. The sequential approach may also be more complicated than necessary, based on the fact that the same four drugs have also been given concomitantly (at least nine publications with >700 patients) as a quadruple therapy with excellent success. This article discusses the approach to therapy in the modern era where antimicrobial resistance is an increasing problem and legacy triple therapy is no longer an acceptable initial choice. Methods to achieve acceptable eradication rates (e.g. grade A or B results) are discussed and, specifically, sequential therapy is considered both conceptually and practically. Suggestions are provided regarding how sequential therapy might be improved to become a grade A therapy as well as how to identify situations where it can be expected to yield unacceptable results. New uses for current drugs are discussed and suggestions for subsequent randomized comparisons to overcome phenotypic and genotypic resistance are given. We propose a change in focus from comparative studies (designed to prove that a new therapy is superior to a known inferior therapy) to demanding that efficacious therapies meet or exceed a pre-specified level of success (i.e. grade A or B result). To do so, coupled with less concern about the effect of recommendations on the pharmaceutical industry, should provide clinicians with much higher quality information, and improve the quality of medical care and recommendations regarding treatment. Ultimately, there is little or no justification for comparative testing that includes an arm with known unacceptably low results. H. pylori gastritis is an infectious disease and should be approached and treated as such.

PMID: 18416582 [PubMed - indexed for MEDLINE]