



Role of concomitant therapy for *Helicobacter pylori* eradication: A technical note

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Abstract

We read with interest the recent meta-analysis by Lin *et al* who evaluated the effectiveness of concomitant regimen for *Helicobacter pylori* (*H. pylori*) in Chinese regions. They found that 7-d concomitant regimen is undoubtedly superior to 7-d triple therapy (91.2% vs 77.9%, $P < 0.0001$). However, it is a common belief that a triple therapy lasting 7 d should be definitively removed from the clinical practice for its ineffectiveness. Only its prolongation to 14 d may give satisfactory success rate. Thus, the assessment of an old and outdated treatment versus a more recent and successful one does not seem to bring novel and useful information. Moreover, a 7-d duration has not been ascertained for concomitant regimen, as main guidelines recommend a 10-d schedule for this scheme. Therefore, only studies comparing 10-d concomitant versus 14-d triple seem to be appropriate according to current Guidelines and would clarify which regimen is the most suitable worldwide. Additionally, in this meta-analysis concomitant and sequential therapy showed similar performances, despite it is common opinion that sequential is more prone than concomitant therapy to fail when metronidazole resistance occurs, and China is characterized by high rate of resistance to this antibiotic. None of the included studies evaluated *a priori* antibiotic resistances, and the lack of this detail hampers the unveiling of this apparent contradiction. In conclusion, the lack of the evaluation of the quality of included trials as well as their high heterogeneity constitute a burdensome limit to draw solid conclusions in this meta-analysis. On the bases of these considerations and the low number of examined trials, we believe that further studies and the knowledge of antibiotic resistances will support with high quality evidence which is the best regimen and its optimal duration.

Key words: *Helicobacter pylori*; Eradication; Sequential; Concomitant; Triple therapy; Antibiotic resistances

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Core tip: Concomitant therapy is one of the most effective first line regimen for *Helicobacter pylori* eradication. The comparison with other regimens (sequential or triple) in a selected geographical region (China in this case) implies several issues. The low number of included studies, the lack of quality evaluation and the high heterogeneity may undermine the strength of a meta-analysis. Therefore, further studies are needed to prove which is the best first line eradication treatment in China, according to the geographical differences in antibiotic resistances.

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TO THE EDITOR

We read with interest the recent meta-analysis by Lin *et al*^[1], who evaluated the effectiveness of concomitant regimen for *Helicobacter pylori* (*H. pylori*) in Chinese regions in a first line context. The choice of deal with this eradication treatment in a selected geographical area is absolutely appropriate, since, as we have already demonstrated^[2], a single therapeutic approach is not fitting worldwide. Indeed, geographical variations in antibiotic resistance rates strongly influence the outcome, therefore the most proper regimen should be considered on the basis of the antibiotic resistance pattern in each area.

However, the results of this meta-analysis deserve special considerations. First, three studies compared 7-d concomitant versus 7-d conventional triple therapy, demonstrating that concomitant regimen is significantly superior to 7-d triple therapy (91.2% vs 77.9%, $P < 0.0001$). However, it is a common belief that a triple therapy lasting 7 d should be definitively abandoned, due to the disappointingly low success rate. Currently, only the prolongation of triple therapy to 14 d can be advised to overcome this limit^[3,4]. Moreover, the outcome of a meta-analysis should be the comparison of two regimens that may have a similar effectiveness; the assessment of an old and outdated treatment versus a more recent and successful one could not bring novel and useful information. The search strategy of this systematic review did not retrieve trials evaluating concomitant versus 14-d triple therapy in China, but only this

comparison could state whether concomitant is really more effective than triple therapy. Furthermore, the duration of 7 d for concomitant therapy is not considered optimal, since Guidelines recommend a 10-d regimen^[3,5]. Additionally, the comparison between 10-d concomitant and 10-d triple therapy showed a similar success, even if this analysis was based only on one study and this aspect could cause to judge the result questionable.

Another issue involves the comparison of concomitant versus sequential regimen. Herein, it has been demonstrated a similar eradication rate (86.9% and 86% respectively, $P = 0.69$). This finding is in agreement with other meta-analyses^[6,7] and previous experiences in Western countries^[8,9]. However, it is common opinion that sequential therapy is more prone to fail when metronidazole resistance occurs^[10]. Indeed, Georgopoulos *et al*^[11] showed that the success rate of sequential regimen decreased from 89.8% to 70%, while a reduction of only 2% occurred for concomitant regimen in the presence of metronidazole resistance. This observation does not seem to agree with the results of this meta-analysis, since China and Far East are considered as high metronidazole resistance areas^[2]. Therefore, concomitant therapy would be expected to achieve a higher success rate than sequential therapy. Furthermore, in order to support this consideration, a recent trial in Korea showed eradication rates of 77.8% for concomitant and 70.6% for sequential regimens at intention-to-treat analysis^[12]. This controversial aspect could be explained only by the analysis of metronidazole resistance in treated patients. On the other hand, Authors themselves observed that this issue was not investigated in included trials.

Finally, we believe that the lack of quality assessment and the high heterogeneity of included studies constitute a relevant limit to draw solid conclusions in this meta-analysis. Therefore, further studies and the knowledge of antibiotic resistance pattern will support with high quality evidence the assessment of the best regimen and its optimal duration^[13-17].

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