Meta-analysis: sequential therapy for Helicobacter pylori eradication in children

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CRD summary
This review found that sequential therapy could be considered as an alternative to triple therapy for the eradication of Helicobacter pylori infection in children. The poor quality of most of the trials means that the the primary data was unlikely to be reliable. However, as the review was well conducted and thorough, its overall conclusions may be reliable.

Authors' objectives
To compare sequential therapy to triple therapy for the eradication of Helicobacter pylori (H. pylori) infection in children.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched without language restrictions to May 2012. Search terms were reported. Reference list of identified trials and reviews were also searched. Unpublished material was sought by searching online trial registries and relevant conference abstracts.

Study selection
Only randomised controlled trials that compared sequential therapy to standard triple therapy for H. pylori eradication were eligible for inclusion. Participants had to be children (under 18) with H. pylori infection assessed using accepted methods. The primary outcome was the rate of H. pylori eradication, measured using an accepted method at least four weeks after treatment. Secondary outcomes were adverse events, treatment compliance and discontinuation of therapy.

In almost all trials the standard triple therapy was a proton pump inhibitor (omeprazole or lansoprazole) combined with two or three antibiotics. Duration of triple therapy was typically seven days, ranging from five to 14 days. The sequential therapy generally consisted of a proton pump inhibitor with amoxicillin for five or seven days followed by a proton pump inhibitor with two antibiotics for five or seven days. Most trials were conducted in Europe.

Two reviewers independently performed the study selection.

Assessment of study quality
Risk of bias was assessed using the Cochrane Collaboration’s tool which assesses sequence generation, allocation concealment, blinding and loss to follow-up. Two reviewers independently performed the risk of bias assessment.

Data extraction
The numbers of successful eradication and adverse events were extracted from all trials to calculate relative risks with 95% confidence intervals. Two reviewers independently performed the data extraction.

Methods of synthesis
Heterogeneity was assessed using $I^2$. Pooled relative risks were calculated, apparently using a fixed-effect meta-analysis, or using a random-effects analysis where $I^2$ exceeded 50%. Subgroup analyses were performed to determine the effect of duration of triple therapy and to compare trials available as full-text publications to those only available as abstracts. Further sensitivity analyses were planned but not performed due to low heterogeneity. Publication bias was assessed using a funnel plot.

Results of the review
There were ten eligible trials, five published as full text and five as abstracts, with 857 participants in total (range 30 to 165). Only two trials were considered to be at low risk of bias and only one study was described as being blinded.

Sequential therapy increased the rate of eradication compared to triple therapy (RR 1.14, 95% CI 1.06 to 1.23; $I^2=47\%$). When therapy duration was considered, sequential therapy was only significantly better than seven-day triple therapy (RR 1.17, 95% CI 1.07 to 1.27; five trials; $I^2=0\%$). Whether differences in effect according to triple therapy duration were statistically significant was not reported.
Adverse events were more common on sequential therapy (RR 1.27, 95% CI 0.94 to 1.70; six trials; I²=0), but the results were not statistically significant. There were no statistically significant differences when specific types of adverse event were investigated. Treatment discontinuation and compliance were found to be similar in both study groups, but full results were not reported. There was no evidence of publication bias.

**Authors' conclusions**

Ten day sequential therapy, rather than standard triple therapy, could be considered as an option for increasing eradication rates of *H. pylori* infection in children.

**CRD commentary**

This review was well conducted and addressed a well-defined research question with appropriate inclusion criteria. A thorough search was performed which identified some trials not published in full. Effort was taken to minimise reviewer error and bias throughout the review process. Trial quality was assessed and most trials were found to be of potentially poor quality, with only half the trials having been published in full. Trials were pooled in a meta-analysis.

The care taken to identify all relevant evidence in this review means that the results may be reliable, but, as the authors noted, the poor quality of the trials means these results should be interpreted with some caution.

**Implications of the review for practice and research**

**Practice:** The authors recommended that ten-day sequential therapy could be an option for increasing *H. pylori* eradication rates in children.

**Research:** The authors suggested that more trials were needed in this area, focusing on comparing therapies that achieve at least 90% success.

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