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## Meta-analysis: the effect of supplementation with lactoferrin on eradication rates and adverse events during helicobacter pylori eradication therapy

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Review published: 2009.

### CRD summary

This well-conducted review concluded that lactoferrin supplementation to *Helicobacter pylori* eradication regimens improved outcomes and was better tolerated. The author's conclusions are supported by the data presented.

### Authors' objectives

To assess the effect of lactoferrin supplementation on the eradication rates and side effects during *Helicobacter pylori* eradication therapy.

### Searching

EMBASE (1980 to October 2008), Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 3, 2008), PubMed (1966 to October 2008), Science Citation Index (1945 to October 2008) and Chinese Biomedical Database (1981 to October 2008) were searched without language restrictions. Reference lists and conference abstracts were handsearched and experts were contacted to identify unpublished data. Search terms were reported.

### Study selection

Randomised controlled trials (RCTs) that evaluated the effect of bovine lactoferrin (bLf) for the eradication of *H. pylori* were eligible for inclusion. Studies had to include two branches of treatment. One branch could be triple therapy (proton pump inhibitors and two antibiotics) or quadruple therapy (proton pump inhibitors, bismuth and two antibiotics or ranitidine bismuth citrate plus two antibiotics) and the other the bovine lactoferrin-involved regimen. Studies had to include patients who had been treated or re-treated. Data had to be available for successful eradication rates and/or side effects during *H. pylori* eradication. Animal studies were excluded.

Outcomes measured were: eradication rates; occurrence of diarrhoea; nausea; taste disturbance and abdominal pain.

All the included trials were from Italy. Where reported, patients presented with peptic ulcer or non-ulcer disease. Patients were diagnosed for *H. pylori* infection by one or a combination of methods: histology; rapid urease test; urea breath test; and *H. pylori* stool antigen. Patients received antibiotic treatment for seven to 14 days. The dose of bovine lactoferrin was the same across all the included studies (200mg twice daily).

Two reviewers independently selected studies. Disagreements were resolved by consulting a third reviewer.

### Assessment of study quality

Trial quality was assessed using the Jadad scale (randomisation, double-blinding and withdrawal/drop-out criteria). Low-quality trials were those with 3 points or less out of a maximum of 5 points.

It was unclear how many reviewers assessed quality.

### Data extraction

Data was extracted using standardised data abstraction sheet. Odds ratios (OR) and 95% confidence intervals were calculated for all the outcome measures.

The authors did not state how many reviewers performed the extraction.

### Methods of synthesis

Trials were combined in a meta-analysis using a Mantel-Haenszel fixed-effect model by intention-to-treat and by a per-protocol analysis. Statistical heterogeneity between studies was assessed using the  $X^2$  test. Publication bias was assessed using funnel plots and the Egger test. Subanalyses of *H. pylori* eradication were planned a priori. Sensitivity analyses were performed to evaluate the influence of low-quality studies by confirming the odds ratios in the presence or absence of one or more studies.

### Results of the review

Nine RCTs (n=1,343) were included in the review. Four studies had a quality score of 5, four studies had a score of 4 and one study scored 3.

**Eradication rates:** Using intention to treat analysis, lactoferrin supplementation had statistically significant improved eradication rates in comparison to no lactoferrin (OR 2.26, 95% CI 1.7 to 3.0, p=0.0001). There was no statistically significant heterogeneity between trials (p=0.15). Further analyses were reported.

**Side effects:** Based on eight studies, lactoferrin supplementation was associated with a statistically significant reduction in total side effects (OR 0.57, 95% CI 0.35 to 0.94, p=0.03). There was evidence of statistical heterogeneity between trials (p=0.06).

Results for individual symptoms were also presented.

Subgroup analysis for specific antibiotics, duration of treatments and whether or not treatment was first-time or rescue showed similar results for eradication rates. Sensitivity analysis of low-quality studies and combining with probiotics did not affect the results significantly. There was no statistical evidence for publication bias.

## Authors' conclusions

Bovine lactoferrin supplementation was more effective at increasing the eradication rate of *H. pylori* and, in particular, for use in patients with eradication failure. Lactoferrin was also better tolerated.

## CRD commentary

The review question and inclusion criteria were clear. The search was extensive and included searches for unpublished studies. There were no language restrictions, so it was unlikely that relevant studies were omitted. Methods were used to reduce error and bias in some parts of the review process. Study quality was assessed. Sensitivity analyses were used to check that weak studies did not influence the results. Heterogeneity was assessed. The authors correctly noted that the meta-analysis was heavily influenced by two trials and that all the studies were conducted in Italy. The authors' conclusions accurately reflect the results of the review and are likely to be reliable.

## Implications of the review for practice and research

The authors did not state any implications for practice or further research.

## Funding

Not stated.

## Bibliographic details

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## Original Paper URL

<http://onlinelibrary.wiley.com/journal/122251172/abstract>

## Other publications of related interest

Zou J, Dong J, Yu XF. Meta-analysis on the efficacy of lactoferrin supplementation combined with standard treatment during *Helicobacter pylori* eradication therapy. *World Chinese Journal of Digestology* 2009; 17(9): 918-926.

## Indexing Status

Subject indexing assigned by NLM

## MeSH

Anti-Bacterial Agents /administration & dosage; Dietary Supplements /analysis; Helicobacter Infections /complications /drug therapy; *Helicobacter pylori* /drug effects; Humans; Lactoferrin /administration & dosage; Randomized Controlled Trials as Topic

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## Record Status

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.

## THE UNIVERSITY of York Centre for Reviews and Dissemination

CRD has determined that this article meets the DARE scientific quality criteria for a systematic review.

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