

# Bovine lactoferrin added to triple therapy increased *Helicobacter pylori* eradication rate

Di Mario F, Aragona G, Dal Bó N, et al. Bovine lactoferrin for *Helicobacter pylori* eradication: an open, randomized, multicentre study. *Aliment Pharmacol Ther.* 2006;23:1235-40.

**Clinical impact ratings:** Gastroenterology ★★★★★☆

## QUESTION

In patients with *Helicobacter pylori* infection, is bovine lactoferrin added to triple therapy more effective than triple therapy alone for eradicating *H. pylori*?

## METHODS

**Design:** Randomized controlled trial.

**Allocation:** Unclear allocation concealment.\*

**Blinding:** Blinded (data analyst).\*

**Follow-up period:** 9 to 11 weeks.

**Setting:** 14 centers in Italy.

**Patients:** 402 *H. pylori*-positive patients (mean age 52 y, 52% men) with dyspeptic symptoms, gastritis, and peptic ulcer disease. Exclusion criteria were previous *H. pylori* eradication therapy, history of definitive acid-lowering surgery, reflux esophagitis > Los Angeles classification grade A, previous esophageal surgery, proton-pump inhibitors within the previous 2 weeks or any antibiotics within the previous 4 weeks, allergy to clarithromycin or benzimidazole, chronic renal and hepatic diseases, any neoplasm, or pregnancy or lactation.

**Intervention:** Esomeprazole, 20 mg; clarithromycin, 500 mg; and tinidazole, 500 mg

twice daily for 7 d (triple therapy) ( $n = 136$ ); bovine lactoferrin, 200 mg twice daily for 7 days, followed by triple therapy ( $n = 132$ ); or bovine lactoferrin, 200 mg twice daily, plus triple therapy ( $n = 134$ ).

**Outcomes:** *H. pylori* eradication (negative result on the C13 urea breath test or *H. pylori* stool antigen test) and side effects.

**Patient follow-up:** 97% (intention-to-treat analysis).

## MAIN RESULTS

Patients who received bovine lactoferrin plus triple therapy had a greater *H. pylori* eradication rate than did patients in the bovine lactoferrin followed by triple therapy or triple

therapy-alone groups (Table). Groups did not differ for side effects: Rates were 6.7%, 9.0%, and 9.5%, respectively.

## CONCLUSION

In patients with *Helicobacter pylori* infection, bovine lactoferrin added to triple therapy was more effective than triple therapy, alone or preceded by bovine lactoferrin, for eradicating *Helicobacter pylori*.

*Source of funding:* No external funding.

*For correspondence:* Professor F. Di Mario, University of Parma, Parma, Italy. E-mail francesco.dimario@unipr.it. ■

\*See Glossary.

### Bovine lactoferrin (BL) added to triple therapy (TT), BL followed by TT, and TT alone for *Helicobacter pylori* (*H. pylori*) infection at 9 to 11 weeks†

Outcome	BL + TT	BL followed by TT	TT alone	RBI (95% CI)	NNT (CI)
<i>H. pylori</i> eradication	90%	—	77%	16% (4.4 to 30)	9 (5 to 29)
	90%	73%	—	22% (8.8 to 38)	7 (4 to 15)
				RBR (CI)	NNH
	—	73%	77%	4.8% (−9.3 to 17)	Not significant

†RBR = relative benefit reduction. Other abbreviations defined in Glossary; RBI, RBR, NNT, NNH, and CI calculated from data in article.

## COMMENTARY

The award of the Nobel Prize to Marshall and Warren in 2005 marks the success of a 2-decade effort in the battle against *H. pylori*. *H. pylori* infection is a major cause of peptic ulcers and stomach cancer, and its eradication effectively cures and prevents ulcers (1).

The most commonly used regimen for *H. pylori* eradication comprises a proton-pump inhibitor plus 2 antibiotics (amoxicillin, clarithromycin, or metronidazole) orally for 1 week (2). Similar to other infections, *H. pylori* drug resistance has increased recently and treatment failure has become more common. The study by Di Mario and colleagues reported that adding bovine lactoferrin to triple therapy (esomeprazole, clarithromycin, and tinidazole) achieved an eradication rate up to 90%, compared with 77% in patients who received triple therapy alone.

Should we prescribe lactoferrin-based quadruple therapy to every patient with *H. pylori* infection? Before doing so, a few questions need to be answered. First, triple therapy frequently causes gastrointestinal upset. A larger trial is required to determine if the addition of lactoferrin would further increase or decrease side effects. Second, needing to take more tablets could prompt drug noncompliance. Whether a high eradication rate can be maintained outside the trial setting is unknown. Third, the study was done in Italy, where clarithromycin resistance is

uncommon. In patients with clarithromycin-resistant genotypes, eradication rates with clarithromycin-based regimens can be < 50% (3). Fourth, lactoferrin seems to potentiate the effect of tinidazole (4). In areas with high tinidazole or metronidazole resistance, lactoferrin may not have additional benefits. Therefore, the mechanism of action of lactoferrin should be elucidated and its effectiveness in different populations should be confirmed before more widespread use is recommended.

Francis K.L. Chan, MD, MBChB, FRCP, FACC  
Vincent W.S. Wong, MD, MBChB, MRCP  
Chinese University of Hong Kong  
Hong Kong, China

## References

- Chan FK, Chung SC, Suen BY, et al. Preventing recurrent upper gastrointestinal bleeding in patients with *Helicobacter pylori* infection who are taking low-dose aspirin or naproxen. *N Engl J Med.* 2001;344:967-73.
- Chan FK, Leung WK. Peptic-ulcer disease. *Lancet.* 2002;360:933-41.
- De Francesco V, Margiotta M, Zullo A, et al. Clarithromycin-resistant genotypes and eradication of *Helicobacter pylori*. *Ann Intern Med.* 2006;144:94-100.
- Di Mario F, Aragona G, Dal Bo N, et al. Use of bovine lactoferrin for *Helicobacter pylori* eradication. *Dig Liver Dis.* 2003;35:706-10.