Bovine lactoferrin added to triple therapy increased Helicobacter pylori eradication rate


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 follow 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.

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*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†

<table>
<thead>
<tr>
<th>Outcome</th>
<th>BL + TT (%)</th>
<th>BL followed by TT (%)</th>
<th>TT alone (%)</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. pylori eradication</td>
<td>90%</td>
<td>—</td>
<td>77%</td>
<td>16% (4.4 to 30)</td>
<td>9 (5 to 29)</td>
</tr>
<tr>
<td></td>
<td>90%</td>
<td>73%</td>
<td>—</td>
<td>22% (8.8 to 36)</td>
<td>7 (4 to 15)</td>
</tr>
</tbody>
</table>

|                       | RBR (CI)    | NNH                   |
|                       |            |                       |
| 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.

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References