

A sequential 10-day regimen was better than standard triple therapy for eradicating *Helicobacter pylori* in older patients

Zullo A, Gatta L, De Francesco V, et al. High rate of *Helicobacter pylori* eradication with sequential therapy in elderly patients with peptic ulcer: a prospective controlled study. *Aliment Pharmacol Ther.* 2005;21:1419-24.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Gastroenterology ★★★★★☆☆

QUESTION

In older patients with peptic ulcer, is a sequential 10-day therapy regimen better than standard 7-day triple therapy for eradicating *Helicobacter pylori*?

METHODS

Design: Randomized controlled trial.

Allocation: {Not concealed}†.*

Blinding: Blinded {data collectors, outcome assessors, and data analysts}†.*

Follow-up period: 4 to 6 weeks.

Setting: 3 centers in Italy.

Patients: 179 patients > 65 years of age (mean age 69.5 y, 59% men) who were referred by their primary care physician for diagnostic upper endoscopy and had peptic ulcer (mucosal lesions \geq 5 mm) and *H. pylori* infection. Exclusion criteria were receipt of proton-pump inhibitors (PPIs), histamine-2-receptor antagonists, or antibiotics in the previous 4 weeks or taking nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin \geq once per week; known antibiotic allergy; liver cirrhosis; kidney failure; or intellectual impairment.

Intervention: Sequential regimen (10-d therapy with rabeprazole, 20 mg plus amoxicillin, 1 g twice daily for 5 d, followed by rabeprazole, 20 mg; clarithromycin, 500 mg; and

tinidazole, 500 mg twice daily for 5 d) ($n = 89$) or standard 7-day triple therapy (twice daily rabeprazole, 20 mg; clarithromycin, 500 mg; and amoxicillin, 1 g) ($n = 90$). Patients took PPIs before breakfast and dinner and antibiotics immediately after these meals.

Outcomes: *H. pylori* eradication (negative result on the rapid urease test and Giemsa staining and the absence of neutrophil infiltrate in gastric mucosa), ulcer healing, and side effects (diarrhea, abdominal pain, glossitis, vomiting, and urticaria).

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

154 patients (86%) had duodenal ulcer, and 25 patients (14%) had gastric ulcer. Patients

who received the 10-day sequential regimen had higher *H. pylori* eradication rates than did those who received standard 7-day triple therapy (Table). Ulcer healing did not differ between 10-day and 7-day groups (96% vs 92%). Groups did not differ for side effects.

CONCLUSION

In older patients with peptic ulcer, a sequential 10-day therapy regimen had higher *Helicobacter pylori* eradication rates than did standard 7-day triple therapy.

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*See Glossary.

†Information provided by author.

Sequential 10-day therapy regimen vs standard 7-day triple therapy for eradication of *Helicobacter pylori* in older patients at 4 to 6 weeks‡

Sequential 10-d regimen [§]	Standard 7-d triple therapy	RBI (95% CI)	NNT (CI)
94%	80%	18% (6 to 35)	7 (5 to 21)

‡Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

[§]Rabeprazole, 20 mg, plus amoxicillin, 1 g, twice daily for 5 days followed by rabeprazole, 20 mg; clarithromycin, 500 mg; and tinidazole, 500 mg, twice daily for 5 days.

||Twice-daily rabeprazole, 20 mg; clarithromycin, 500 mg; and amoxicillin, 1 g.

COMMENTARY

H. pylori remains an important cause of ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric adenocarcinoma. The effectiveness of the recommended first-line triple therapies (1) of PPI, clarithromycin, and amoxicillin or metronidazole may be declining; thus, new regimens are needed.

In the study by Zullo and colleagues, an impressive eradication rate of 94% was seen with the 10-day sequential therapy regimen compared with 80% with the gold-standard triple therapy regimen. The 14% therapeutic gain with a small NNT of 7 is clinically relevant. High rates of ulcer healing were seen with both regimens, as is expected with *H. pylori* eradication. Excellent compliance (> 95%) and minimal side effects (< 12%) were also observed. The study appropriately documented *H. pylori* status both before and after eradication treatment.

Some factors may affect the generalizability of this study. First, although it was randomized, patients were not blinded; however, since the primary endpoint was *H. pylori* eradication, lack of patient blinding should not influence eradication. Aspirin and NSAIDs were not allowed because taking these drugs would lower ulcer healing rates but would probably not reduce eradication. The study included older patients (> 65 y) in 3 Italian centers. Eradication rates in older patients

are unlikely to be reduced, but especially in older patients with gastric ulcer, cancer needs to be histologically excluded. An important factor is that these patients were treatment-naïve. As antibiotic resistance was not assessed in this study, the results cannot be applied to patients in whom treatment has failed. Finally, penicillin allergy is reported in up to 10% of patients (2), and the sequential regimen cannot be given to these patients.

A sequential 10-day therapy regimen is an effective *H. pylori* eradication regimen for treatment-naïve patients and represents a new first-line option to standard PPI-triple therapies.

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References

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