Levofloxacin-based triple regimens were better than standard quadruple regimens for second-line eradication of *Helicobacter pylori*

Nista EC, Candelli M, Cremonini F, et al. **Levofloxacin-based triple therapy vs. quadruple therapy in second-line *Helicobacter pylori* treatment: a randomized trial.** Aliment Pharmacol Ther. 2003;18:627-33.

QUESTION

In patients with *Helicobacter pylori* infection that was not eradicated after initial triple therapy, are 10-day levofloxacin-based triple regimens more effective than standard 7- or 14-day quadruple regimens for second-line eradication?

DESIGN

Randomized (allocation concealed*), {unblinded}†,* controlled trial with 6-week follow-up.

SETTING

Gemelli Hospital, Rome, Italy.

PATIENTS

280 patients (mean age 48 y, 52% women) who had endoscopically confirmed nonulcer dyspepsia and a positive test result for *H. pylori* and in whom an eradication attempt with standard triple therapy had failed. Follow-up was 94%. All patients were included in the analysis.

INTERVENTION

70 patients each were allocated to 4 treatments: 1) a 10-day course of once-daily levofloxacin, 500 mg; twice-daily amoxicillin, 1 g; twice-daily rabeprazole, 20 mg (LAR); 2) a 10-day course of once-daily levofloxacin, 500 mg; twice-daily tinidazole, 500 mg; and twice-daily rabeprazole, 20 mg (LTR); 3) a 7-day course of 4 times daily tetracycline, 500 mg; 3 times daily metronidazole, 500 mg; 4 times daily bismuth salt, 120 mg; and twice-daily rebepraxole, 20 mg (7TMBR); or 4) a 14-day course of TMBR (14TMBR).

MAIN OUTCOME MEASURES

H. pylori eradication. Secondary outcomes included incidence of side effects.

MAIN RESULTS

Analysis was by intention to treat. Patients who received LAR or LTR regimens had higher rates of *H. pylori* eradiation than did those who received the 7TMBR or 14TMBR regimens (Table). The 14TMBR group had more overall side effects (Table), particularly taste impairment (vs LAR) and bloating (vs LTR). The LAR and LTR groups did not differ from the 7TMBR group for side effects (Table).

CONCLUSION

In patients with *Helicobacter pylori* infection in whom triple therapy had previously failed, 10-day levofloxacin-based triple regimens were more effective and had fewer side effects than standard 10- or 14-day quadruple regimens.

Source of funding: Fondazione Ricerca in Medicina.

For correspondence: Dr. A. Gasbarrini, Universita Cattolica del Sacro Cuore, Rome, Italy. E-mail angiologia@rm.unicatt.it.

*See Glossary.

†Information provided by author.

Levofloxacin, amoxicillin, and rabeprazole (LAR) or levofloxacin, tinidazole, and rabeprazole (LTR) vs tetracycline, metronidazole, bismuth salt, and rabeprazole for 7 days (7TMBR) or 14 days (14TMBR) for *Helicobacter pylori* infection at 6 weeks‡

Outcomes	LAR	LTR	7TMBR	14TMBR	RBI (95% CI)	NNT (CI)
H. pylori eradication	94%	—	63%	—	50% (26 to 85)	4 (3 to 6)
	94%	—	—	69%	37% (18 to 66)	4 (3 to 8)
	—	90%	63%	—	43% (19 to 78)	4 (3 to 8)
	—	90%	—	69%	31% (11 to 60)	5 (3 to 13)
					RRR (CI)	
Overall side effects	10%	—	21%	—	53% (–4 to 7)	Not significant
	10%	—	—	33%	70% (36 to 86)	5 (3 to 11)
	—	11%	21%	—	47% (–14 to 76)	Not significant
	—	11%	—	33%	65% (30 to 83)	5 (3 to 13)

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

COMMENTARY

Currently, the recommended second-line treatment for *H. pylori* infection is quadruple therapy consisting of a proton-pump inhibitor, bismuth salt, metronidazole, and tetracycline for a minimum of 7 days. Although the reported eradication rate varies from about 57% to 90% (1, 2), the complicated nature of this regimen limits its clinical usefulness.

Levofloxacin-based triple therapy has been investigated as an alternative second-line treatment. The reported eradication rate, which varies from 63% to > 90%, is similar to that of quadruple therapy. In the study by Nista and colleagues, levofloxacin-based triple therapy was more efficacious and better tolerated than quadruple therapy. In contrast, a recent study found that levofloxacin-based triple therapy was inferior to quadruple therapy (eradication rate 63% vs 83%) (3). In addition, previous studies did not report excessive adverse events with quadruple therapy. How could one account for such a discrepancy?

Documenting that a new therapy is superior to a standard therapy with good efficacy is difficult. The study by Nista and colleagues was designed with an assumption of a 70% success rate with quadruple therapy and an 80% success rate with levofloxacin-based triple therapy. With a power of 80%, a sample size of 313 rather than 70 patients per group would be needed to detect a 10% difference. Thus, to show a significant benefit with a newer therapy, a trial must be either extremely large, or have poor results with the standard quadruple therapy (eradication rate 63% to 69%) coupled with very good results for the new levofloxacin-based triple therapy (eradication rate 90% to 94%).

Overall, this study confirmed that levofloxacin-based triple therapy is efficacious and well-tolerated. Whether it is superior to quadruple therapy needs to be determined by meta-analysis. Finally, by emphasizing the importance of drug compliance with first-line therapy, which is a crucial factor in treatment success, the need for second-line treatments may be reduced.

Francis K.L. Chan, MD, FRCP
Prince of Wales Hospital, Chinese University of Hong Kong
Hong Kong, China

References

1. **Gisbert JP, Gisbert JL, Marcos S, et al.** Aliment Pharmacol Ther. 1999; 13:1311-6.
2. **Miehlke S, Kirsch C, Schneider-Brachert W, et al.** Helicobacter. 2003;8: 310-9.
3. **Perri F, Festa V, Merla A, et al.** Aliment Pharmacol Ther. 2003;18:815-20.