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Letter to the Editor

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Efficacy of reduced-dose regimen of a capsule containing bismuth subcitrate, metronidazole, and tetracycline given with amoxicillin and esomeprazole in the treatment of *Helicobacter Pylori* infection

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Abstract

It is well known that triple therapy for *Helicobacter pylori* is losing efficacy worldwide. A regimen containing proton pump inhibitor and multiple-dose capsules of bismuth, metronidazole, and tetracycline has proven efficacy. In addition, a literature review on dosage of previous regimens shows that half-dose clarithromycin-based regimens are equally effective to full-dose regimens. However, the applicability of dose reduction to bismuth-based therapy is unknown. This communication shows that a reduced-dose bismuth-based regimen fails to achieve acceptable eradication rates.

Keywords

Helicobacter pylori, eradication, adverse events

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Dear Editor

Although some reports indicate a recent decrease in the prevalence of *Helicobacter pylori*,[1] infection with this organism remains a leading cause of peptic ulcer disease, gastric adenocarcinomas and MALT lymphomas. The American College of Gastroenterology guidelines and the Maastricht III consensus continue to recommend triple therapy as first-line treatment,[2] despite staggering evidence indicating a decrease in efficacy worldwide.[3] Bismuth-based quadruple therapy has consequently reemerged and is currently considered the preferred regimen in areas where clarithromycin resistance is high. Recently, in a large multi-centered trial across Europe,[4] a 10-day therapy consisting of proton pump inhibitor (PPI) and a multiple-dose capsule containing bismuth, metronidazole and tetracycline (Pylera®, Aptalis Pharma, Bridgewater, NJ, USA) showed an eradication rate of 80% on intent-to-treat (ITT) with an acceptable safety profile. The relative success of this combination therapy was somewhat offset by the large number of pills (14 tablets daily × 10 days) and four-daily dosing. A number of randomized studies have validated the equal efficacy of half-dose clarithromycin-based regimens compared with their full-dose counterparts.[5] Appealing as it may be, the applicability of this concept of dose reduction to bismuth-based therapy is unknown. This study was conducted to evaluate the efficacy of a capsule containing bismuth (B), tetracycline (T), and metronidazole (M) given with amoxicillin (A) and esomeprazole (E), all in reduced-doses, in *H. pylori* therapy. Secondary outcomes included tolerability, adverse events (AE), and cost.

Consecutive patients with documented *H. pylori* infection (positive rapid urease test, urea breath test (UBT), or histology) were prospectively enrolled in an open-labeled fashion after informed consent. The demographic characteristics of the enrolled subjects

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Table 1. Patient characteristics

Patient Characteristics	
Age	47.7 ± 14.4
BMI	27.3 ± 5.7
Males	53%
Smoking	54%
Current PPI Use	34%

Values are mean $\pm$ SD
PPI: proton pump inhibitor.

Table 2. Study results

ADE	Phase I (n = 34)	Phase II (n = 27)
Dosing Schedule	$2x(B_{140}M_{125}T_{125}) + A_{500} + E_{20}$ bid x10d	$3x(B_{140}M_{125}T_{125}) + A_{500} + E_{20}$ bid x10d
Eradication success (ITT)	20/34 (59%)	17/27 (63%)
Eradication success (PP)	20/30 (67%)	17/26 (65%)
Any ADE	10 (29%)	9 (33%)

ADE: adverse drug events.

are summarized in Table 1. Patients received detailed verbal and written instructions on the use of medications. All drugs were provided free of charge. Pill count was used to monitor compliance. Termination of the study was predetermined and set at less than 70% eradication after the first 20 patients using Simon's optimal two-stage design calculations. The study was approved by the Institutional Review Board at the American University of Beirut and registered at clinicaltrials.gov (ID:NCT02045251).

In phase I of the study, patients received two combination capsules each containing bismuth 140 mg, metronidazole 125 mg, and tetracycline 125 mg, plus amoxicillin 500 mg and esomeprazole 20 mg, all taken twice daily for a total of 8 tablets/d for 10 days (Table 2). In phase II patients received three combination capsules instead of two for a total of 10 tablets/d for 10 days (Table 2). Eradication was assessed using ^{14}C-UBT after >4 weeks of therapy. Patients were off acid suppressive therapy for >2 weeks prior to testing. Eradication rates were calculated on both ITT and per-protocol (PP) analyses. Compliance and AE were monitored during therapy. The study was limited by being a single-center study and the absence of a comparator arm. A total of 61 treatment-naïve patients participated in this study; 34 patients participated in phase I, with eradication documented in 20/34 patients (59% ITT; 68% PP); four patients were lost to follow-up while two failed to take the medication as instructed. After protocol adjustment, 27 patients participated in phase II, with eradication achieved in 17/27 patients (63% ITT; 65% PP; one patient failed to take the medications as instructed). The study was terminated early due to failure to achieve first-stage eradication endpoint. Tolerability was excellent in both phases, with mild AEs reported by 29% and 33% of patients in phases I and II, respectively. In conclusion, despite a favorable safety profile, this reduced-dose bismuth-based twice-daily regimen fails to achieve acceptable eradication rates.

Conflict of interest

None declared.

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References

1. Tonkic A, Tonkic M, Lehours P, et al. Epidemiology and diagnosis of *Helicobacter pylori* infection. *Helicobacter* 2012; 17(Suppl 1): 1–8.
2. Chey WD, Wong BC and Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. *Am J Gastroenterol* 2007; 102: 1808–1825.
3. Tursi A, Elisei W, Giorgetti G, et al. Decreasing efficacy of the standard seven-day triple therapy containing amoxycillin and clarithromycin in curing *Helicobacter pylori* infection in clinical setting in Italy: A 10-year follow-up study. *Panminerva Med* 2014; 56: 57–61.
4. Malfertheiner P, Bazzoli F, Delchier JC, et al. *Helicobacter pylori* eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: A randomised, open-label, non-inferiority, phase 3 trial. *Lancet* 2011; 377: 905–913.
5. Harb A, Abou Mrad R and Sharara AI. Full versus reduced dose antimicrobials in clarithromycin-based regimens for Helicobacter pylori eradication: A systematic review and meta-analysis. *Am J Gastroenterol* 2014; 109(Suppl 2s): S50:167.