There is growing evidence that turmeric can induce severe liver injury. Due to this and the analytical normalization after the suspension of immunosuppressive treatment we conclude that the most probable diagnosis for our patient is DI-AIH. However, the number of cases published so far is small, and more, it is needed to establish a definitive causal relationship.

Funding

There was no funding for this article.

Conflicts of interest

There were no conflicts of interest.

References

1. Björnsson E, Talwalkar J, Treeprasertsuk S, Kamath PS, Takahashi N, Sanderson S, et al. Drug-induced autoimmune hepatitis: clinical characteristics and prognosis. Hepatology. 2010;51:2040–8.
2. Czaja AJ, Carpenter HA, Moore SB. HLA DRB1*13 as a risk factor for type 1 autoimmune hepatitis in north American patients. Dig Dis Sci. 2008;53:522–8.
3. Luber RP, Rentsch C, Lontos S, Pope JD, Aung AK, Schneider HG, Kemp W, Roberts SK, Majeed A. Turmeric induced liver injury: a report of two cases. Case Reports Hepatol. 2019;2019:6741213, http://dx.doi.org/10.1155/2019/6741213 [PMID: 31214366; PMCID: PMC6535872].
4. Lee BS, Bhatia T, Chaya CT, Wen R, Taira MT, Lim BS. Autoimmune hepatitis associated with turmeric consumption. ACG Case Rep J. 2020;7:e00320, http://dx.doi.org/10.14309/crj.0000000000000320 [PMID: 32337301; PMCID: PMC7162126].
5. Lukefahr AL, McEvoy S, Alfafara C, Funk JL. Drug-induced autoimmune hepatitis associated with turmeric dietary supplement use. BMJ Case Rep. 2018;2018, http://dx.doi.org/10.1136/bcr-2018-224611, bcr2018224611 [PMID: 30206065; PMCID: PMC6144106].
6. Imam Z, Khasawneh M, Jomaa D, Iftikhar H, Sayedahmad Z. Drug induced liver injury attributed to a curcumin supplement. Case Rep Gastrointest Med. 2019;2019:6029403.
7. Halegoua-DeMarzio D, Navarro V, Ahmad J, Avula B, Barnhart H, Barritt AS, Bonkovsky HL, Fontana RJ, Ghabril MS, Hoofnagle JH, Khan IA, Kleiner DE, Phillips E, Stolz A, Vuppalanchi R. Liver injury associated with turmeric-a growing problem: ten cases from the drug-induced liver injury network [DILIN]. Am J Med. 2022, http://dx.doi.org/10.1016/j.amjmed.2022.09.026 [Epub ahead of print; PMID: 36252717; S0002-9343(22)00740-9].
8. Lombardi N, Crescioli G, Maggini V, Ippoliti I, Menniti-Ippolito F, Gallo E, Brilli V, Lanzi C, Mannaioni G, Firenzuoli F, Vannacci A. Acute liver injury following turmeric use in Tuscany: an analysis of the Italian Phytovigilance database and systematic review of case reports. Br J Clin Pharmacol. 2021;87:741–53, http://dx.doi.org/10.1111/bcp.14460 [Epub 20.07.20; PMID: 32656820].

Teresa Arzallus[a,*], Arantzazu Izagirre[a], Agustín Castiella[a], Silvia Torrente[a], Maddi Garmendia[b], Eva María Zapata[a]

[a] *Department of Gastroenterology and Hepatology, Donostia University Hospital, Spain*
[b] *Department of Pathology, Donostia University Hospital, Spain*

* Corresponding author.
E-mail address: teresa.arzallusmarco@osakidetza.eus (T. Arzallus).

Effectiveness and safety of high-dose dual therapy PPI-amoxicillin dual therapy for first-line *Helicobacter pylori* in Chile: Experience from the retrospective study

Efectividad y seguridad de la terapia dual IBP-amoxicilina en dosis altas como terapia de primera línea en la erradicación de *Helicobacter pylori* en Chile: experiencia desde un estudio retrospectivo

In Chile, over 70% of adults are infected with *Helicobacter pylori*. This bacterium plays a key role in the development of a number of different diseases, gastric cancer in particular, so effective treatment is essential in clinical practice. It has been suggested that clarithromycin should not be used in any regimen when resistance to this antibiotic is >15%.[1] Recently, a Chilean study showed a resistance rate to clarithromycin of 26%. In this scenario, the effectiveness of triple therapy (proton pump inhibitor [PPI], clarithromycin and amoxicillin) was only 63.8%.[2] Despite that, a study in Chile involving 242 patients showed that 54.9% were treated with this therapy.[3] The Spanish Consensus Conference has suggested a non-bismuth-based quadruple (concomitant) regimen (PPI, clarithromycin, amoxicillin and metronidazole) or a quadruple combination with bismuth (PPI, bismuth, tetracycline and metronidazole) as first-line treatment.[1] Others have also recommended high-dose dual therapy as a first-line treatment for *H. pylori* eradication.[3,4]

We describe here the results on the effectiveness and safety of high-dose dual therapy from a retrospective, observational, descriptive study conducted at our centre from March to September 2022. The research protocol for the study was approved by the scientific ethics committee of the Universidad de los Andes [University of the Andes] with ID CEC2022071. We excluded all patients who had previously received any other *H. pylori* eradication regimen. All patients were treated with esomeprazole 40 mg three times a day (30 min before breakfast, lunch and evening meal) and amoxicillin 750 mg four times a day (with breakfast, lunch, afternoon tea and evening meal) for 14 days. The effectiveness of the dual therapy was evaluated with the *H. pylori* stool antigen test (Pylori-Strip test) which was performed six weeks after the end of eradication treatment and with at

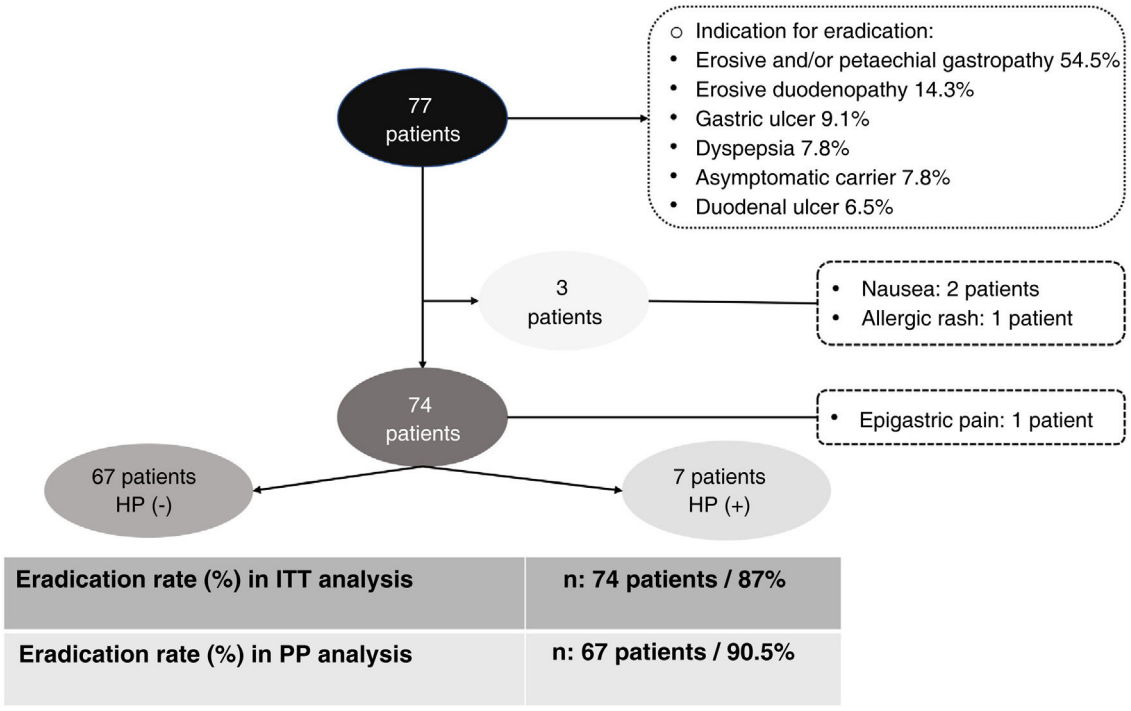

Figure 1 Flowchart of the patients included in the study.
HP: *Helicobacter pylori*; ITT: intention to treat; PP: per protocol.

least 14 days without PPI treatment, with a negative result confirming the effectiveness of the regimen.

We included 77 patients with a median age of 52 (19–84), 54.5% male. Seventy-four patients completed the treatment. Effectiveness in the intention-to-treat group and in those who completed therapy was 87% and 90.5% respectively. Three patients discontinued treatment: two because of nausea and one because of urticaria. In the group that completed therapy, only one patient reported epigastric pain, this patient having a negative post-treatment eradication test. Fig. 1 shows a flow chart of the patients admitted to this study.

Our results show that high-dose dual therapy could be an alternative to quadruple (concomitant) therapy without bismuth or quadruple therapy with bismuth as a first-line treatment for *H. pylori* eradication. It is currently recommended that an eradication therapy be considered effective when it is capable of curing *H. pylori* infection in close to, or preferably more than, 90% of patients.[1] In our cohort of patients the effectiveness in the intention-to-treat group and in those who completed therapy falls within this target. A meta-analysis including six studies with a total of 1677 patients infected with this bacterium showed that high-dose dual therapy is equally as effective as the bismuth-containing quadruple therapy (intention-to-treat: 84.6% vs 83.7%, relative risk (RR) = 1.01, 95% CI: 0.97–1.06, $P = .49$; per protocol: 88.4% vs 89.0%, RR = 1.00, 95% CI: 0.97–1.04, $P = .99$), with fewer side effects and better patient adherence to treatment.[4] A Chilean study suggests that dual therapy, with an effectiveness of 88.6%, could be used as a first-line regimen in the eradication of *H. pylori*. However, only 35 patients (14.5% of the patients included in this study) were treated with the dual therapy regimen.[3] Effective inhibition of gastric acidity is a factor in the action of amoxicillin. This antibiotic is unstable in an acidic gastric environment and inhibition of gastric acid with PPI improves the stability and bioavailability of amoxicillin in the stomach.[4] When PPI are administered three to four times a day, a stable and sufficient gastric acidity suppression effect is obtained, which is independent of the CPY2C19 gene polymorphism. A recent meta-analysis including nine randomised controlled studies conducted in Asia shows that dual therapy with PPI and high-dose amoxicillin administered four times a day would have better efficacy and safety in eradicating *H. pylori* than other recommended guidelines.[4] The dosage and type of PPI used in different studies have been variable[4]; we decided to use esomeprazole 40 mg three times a day, as reported by other authors.[5] Prospective, randomised, controlled studies could define the best dose to use in high-dose dual therapy.

In conclusion, in this cohort of patients with *H. pylori* infection, high-dose dual therapy was shown to be effective and safe, raising the possibility that it could be used as first-line therapy here in Chile. Studies with larger numbers of patients should confirm these results.

Funding

No funding was received for this study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. Gisbert JP, Alcedo J, Amador J, Bujanda L, Calvet X, Castro-Fernández M, et al. V Spanish Consensus Conference on Helicobacter Pylori treatment. Gastroenterol Hepatol. 2022;45:392–417,
2. Arenas A, Serrano C, Quiñones L, Harris P, Sandoval M, Lavanderos M, etal. High prevalence of clarithromycin resistance and effect on Helicobacter pylori eradication in a population from Santiago, Chile: cohort study and meta-analysis. Sci Rep. 2019;9:20070, http://dx.doi.org/10.1038/s41598-019-56399-7.
3. Reyes D, Ortiz J, Fuentes-López E, Budnik S, Gándara V, Gallardo A, et al. Quadruple therapies are superior to standard triple therapy for Helicobacter pylori first-line eradication in Chile. Gastroenterol Hepatol. 2022;45:515–23, http://dx.doi.org/10.1016/j.gastrohep.2021.11.010.
4. Li C, Shi Y, Suo B, Tain X, Zhou L, Song Z. PPI-amoxicillin dual therapy four times daily is superior to guidelines recommended regimens in the Helicobacter pylori eradication therapy within Asia: A systematic review and meta-analysis. Helicobacter. 2021;26:e12816, http://dx.doi.org/10.1111/hel.12816.
5. Tai WC, Liang CM, Kuo CM, Huang PY, Wu CK, Yang SC, et al. A 14 day esomeprazole- And amoxicillin-containing high dose dual therapy regimen achieves a high eradication rate as first-line anti-Helicobacter pylori treatment in Taiwan: a prospective randomized trial. J Antimicrob Chemother. 2019;74:1718–24, http://dx.doi.org/10.1093/jac/dkz046.

Rodrigo Quera*, Andrea Córdova, Paulina Núñez, Christian von Muhlenbrock

Centro de Enfermedades Digestivas, Clínica Universidad de los Andes, Universidad de los Andes, Santiago, Chile

* Corresponding author.
E-mail address: rquera@clinicauandes.cl (R. Quera).

Barium enema: Compassionate therapy for refractory colonic diverticular bleeding?

Enema de bario: ¿terapia de uso compasivo para la hemorragia diverticular colónica refractaria?

A 67-year-old man with a history of arterial hypertension and religious orientation of Jehovah's Witness, and refusing to receive red cell concentrate (RCC) transfusions, was admitted for acute lower gastrointestinal haemorrhage (LGH). By performing an initial colonoscopy, the LGH was associated with a sigmoid diverticular origin, without locating any specific bleeding point for treatment. Because of exteriorization persistence, an abdominal angiography computed tomography (angioCT), an arteriography, and a second colonoscopy were performed, with no possibility of therapeutic application. Haemoglobin (Hb) levels progressively decreased to 4.2 g/dL. After compassionate administration of a barium enema, no new episodes of bleeding were reported, allowing discharge of the patient 12 days' post-enema, with an Hb level of 6.4 g/dL. At 88 months of follow-up, no new LGH episodes had been detected.

A 91-year-old woman with a history of hypertension, congestive heart failure, and atrial fibrillation on antiplatelet treatment was admitted for acute painless LGH, with initial haemodynamic instability. An angioCT was performed, visualizing multiple diverticula in the whole colonic tract, with an active bleeding point in the cecum. The patient did well and arterial blood pressure values returned to normal. Colonoscopy showed a cecal diverticulum with a visible vessel, treated with adrenaline and a haemostatic clip. Despite the endoscopic treatment, blood exteriorization persisted, with daily RCC transfusion requirements. During the following three weeks two more colonoscopies were carried out, along with a second angioCT with an arteriography, without revealing a specific bleeding spot to be treated. Finally, a barium enema was administered, leading to the cessation of the LGH. At 17 days' post-enema, the patient was discharged, with an Hb of 8.5 g/dL, after having received a total transfusion support of 17 RCC during the 5 weeks of admission. No new episodes of LGH were detected at 5 months of follow-up, when the patient was admitted for cardiac decompensation and acute pulmonary oedema with an end-of-live denouement.

LGH of diverticular origin is the main cause of bleeding below the angle of Treitz requiring hospital admission in patients over 50 years of age. The usual clinical course in this type of bleeding is self-limiting (80–90% of cases). However, there are patients who require aggressive management of the pathology, with the need for RCC transfusion support, as well as interventions such as colonoscopy, arteriography, or even surgery.[1] The patient's comorbidities and/or antecedents may lead to situations of contraindication of the usual management algorithms in this type of pathology, as in the two cases presented in this scientific letter. The use of barium enema as a therapeutic option in case of LGH of diverticular origin was first reported in 1970 by Adams et al.[2] Since then, a string of publications have appeared, most of them in the form of case-reports or short series of cases like our experience (Table 1).[3] Only one randomized clinical trial has been published, highlighting the usefulness of high-dose barium impaction therapy in the long-term prevention of recurrent bleeding (42.5% *vs.* 14.8%; log-rank test, $P = 0.04$).[2]

When performing a colonoscopy in case of colonic diverticular bleeding, it is difficult to locate the bleeding vessel and it is usually not possible to apply targeted therapy. Recently, non-directed endoscopic haemostatic techniques using haemostatic powder devices have appeared, with favourable results described (initial clinical success greater than 95%, with one-month rebleeding rate of 5.5–12.9%).[4,5] Although the use of the barium enema might hypothetically be compared to these devices for non-directed attempts at haemostasis, the published literature is limited and a