

## Severe obscure gastrointestinal bleeding successfully treated with idarucizumab

Key words: Idarucizumab. Dabigatran. Gastrointestinal bleeding. Antidote.

Dear Editor,

Anticoagulation management is a real clinical challenge in the setting of gastrointestinal bleeding (1). One of the main disadvantages of direct oral anticoagulants (DOACS) has been their approval in the absence of an antidote. Idarucizumab is a monoclonal antibody designed for the immediate reversal of dabigatran anticoagulant activity (2).

### Case report

An 84-year-old man with a known atrial fibrillation, anticoagulated with dabigatran at 150 mg/12 h, type 2 diabetes and COPD, presented to the Emergency Room due to melena without hemodynamic derangement over a 48 hour period. In 2014, a 6 mm ileal angiodysplasia was identified as a possible cause of an episode of gastrointestinal bleeding after gastroscopy, colonoscopy and videocapsule. The first analytical exam identified hemoglobin levels at 10.1 g/dl, international normalized ratio (INR) of 1.3 and a cephalin time of 50.8 s; the rest of parameters were normal. His condition suddenly deteriorated in the Emergency Room, with hypotension, anemia and a massive melena; 5 g of i.v. idarucizumab were administered in ten minutes, a transfusion was performed and a gastroscopy and colonoscopy did not identify a source of the bleeding. His condition rapidly improved and there were no further signs of bleeding. Dabigatran was resumed on the sixth day. There has been no rebleeding or thromboembolic events after six months of follow-up.

**Table 1.** *Idarucizumab in gastrointestinal bleeding*

Author	Study	n	Bleeding source	Dose	Outcome
Pollack CV Jr. 2017 (3)	Open, multicenter non-controlled clinical trial (RE-VERSE AD)	301 (131 GIB)	52 UGIB 47 LGIB 42 not investigated/ occult	5 g	Hemostasis in 11.4 hours in the group with uncontrolled bleeding (no specific data for the subgroup with GIB) 30-day mortality: 11.1%
Simon A 2017	Clinical case	1	Non-investigated LGIB (rectal bleeding)	10 g	MOF and death
Gendron N 2017 (4)	Clinical case	3 (2 GIB)	Peptic ulcer Rectal adenocarcinoma	5 g	Undetectable levels of dabigatran within 1 hour. Bleeding controlled Undetectable levels of dabigatran within 12 hours. Bleeding controlled
Alhashem HM 2017 (5)	Clinical case	1	Duodenal ulcer	5 g	Normalization of INR and prothrombin time in 1 hour Embolization due to failure of previous endoscopic therapy

GIB: gastrointestinal bleeding; UGIB: upper gastrointestinal bleeding; LGIB: lower gastrointestinal bleeding; CRD: chronic renal disease; MOF: multiple organ failure; INR: international normalized ratio.

## Discussion

Idarucizumab is the first antidote available against DOAC. The most rigorous analysis that led to its approval is the RE-VERSE-AD study (3). In this study, 45.5% of hemorrhages were gastrointestinal bleeds with a median time to bleeding cessation of 2.5 hours. Recent data indicate that anticoagulation can be resumed within 24 hours once the bleeding is under control. Therefore, dabigatran was probably restarted later than necessary in the current case (1,3). Even though idarucizumab is already included in some clinical guidelines, it is important to highlight some points. Firstly, there are no studies with survival as primary outcome; most of the research in this area has focused on laboratory parameters. In addition, the largest published cohorts were funded by the pharmaceutical company that markets dabigatran and idarucizumab, which could have introduced bias in the results (2). Furthermore, post-marketing experience in gastrointestinal bleeding is scarce and only data from clinical cases and small case series are available (Table 1). Finally, idarucizumab is expensive and dabigatran clearance is rapid (half-life of 13 h) if renal function is normal. Therefore, its use should be restricted to severe cases or a recent intake of dabigatran. In our case, the severity of the bleeding justified the use of idarucizumab, which had excellent results.

*Enrique Rodríguez-de-Santiago, María Sierra-Morales  
and Javier Martínez-González*

*Gastroenterology and Hepatology Service. Hospital Universitario Ramón y Cajal.  
IRYCIS. University of Alcalá. Alcalá de Henares, Madrid. Spain*

**DOI: 10.17235/reed.2018.5298/2017**

## References

1. Alberca-de-Las-Parras F, Marín F, Roldán-Schilling V, et al. Management of antithrombotic drugs in association with endoscopic procedures. *Rev Esp Enferm Dig* 2015;107:289-306.
2. Gottlieb M, Khishfe B. Idarucizumab for the reversal of dabigatran. *Ann Emerg Med* 2017;69:554-8.
3. Pollack CV, Reilly PA, Van Ryn J, et al. Idarucizumab for dabigatran reversal - Full cohort analysis. *N Engl J Med* 2017;377:431-41.
4. Gendron N, Feral-Pierssens AL, Jurcisin I, et al. Real-world use of idarucizumab for dabigatran reversal in three cases of serious bleeding. *Clin Case Rep* 2017;5:346-50.
5. Alhashem HM, Avendano C, Hayes BD, et al. Persistent life-threatening hemorrhage after administration of idarucizumab. *Am J Emerg Med* 2017; 35:193.e3-193.e5. DOI: 10.1016/j.ajem.2016.06.096