

Dabigatran

(OCTOBER 2011)

TO THE EDITOR: The article “Dabigatran: Will it change clinical practice”¹ has a dangerous error. In its Key Points, it says “dabigatran is a potent, reversible direct thrombin inhibitor.” In fact, it is *not* reversible.²

Shamefully poor editing.

VAN SMITH, MD, FACP

■ REFERENCES

1. Wartak SA, Bartholomew JR. Dabigatran: Will it change clinical practice? Cleve Clin J Med 2011; 78:657–664.
2. Antithrombotic drugs. Treat Guidel Met Lett 2011; 9:61–66.

doi:10.3949/ccjm.78c.12001

IN REPLY: This is not an error. When we¹ and others² said that dabigatran is a reversible direct thrombin inhibitor, we were referring to its effect at the molecular level, the appropriate description of its mechanism of action. However, we suspect that Dr. Smith means that there is no antidote to give in cases of bleeding or overdose. We share his concern and we discussed this in our article.

Unlike heparin, direct thrombin inhibitors act independently of antithrombin and inhibit thrombin bound to fibrin or fibrin degradation products. There are two types of direct thrombin inhibitors: bivalent (eg, hirudin) and univalent (eg, argatroban, ximelagatran, and dabigatran). The bivalent ones block thrombin at its active site and at an exosite and form an irreversible complex with it. The univalent ones interact with only the active site and *reversibly* inhibit thrombin, eventually dissociating from it and leaving a small amount of free, enzymatically active thrombin available for hemostatic interactions. Therefore, in contrast to the hirudins, they produce relatively transient thrombin inhibition.^{2–4}

As we pointed out in our article, the lack of an antidote for dabigatran and the lack of experience in treating bleeding complications are major concerns. Fortunately, the drug has a short half-life (12–14 hours) so that the

treatment is to withhold the next dose while maintaining adequate diuresis and giving transfusions as indicated. Activated charcoal, given orally to reduce absorption, is under evaluation but must be given within 1 or 2 hours after the dabigatran dose.¹ Dabigatran can be removed by dialysis (in part because it is a reversible inhibitor), a measure that may be necessary in life-threatening cases. Recombinant activated factor VII or prothrombin complex concentrates may be additional treatment options.^{1,4} With time will come experience and, we hope, evidence-based guidelines.

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■ REFERENCES

1. Wartak SA, Bartholomew JR. Dabigatran: Will it change clinical practice? Cleve Clin J Med 2011; 78:657–664.
2. van Ryn J, Stangier J, Haertter S, et al. Dabigatran etexilate—a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. Thromb Haemost 2010; 103:1116–1127.
3. Di Nisio M, Middeldorp S, Büller HR. Direct thrombin inhibitors. N Engl J Med 2005; 353:1028–1040.
4. Stangier J, Clemens A. Pharmacology, pharmacokinetics, and pharmacodynamics of dabigatran etexilate, an oral direct thrombin inhibitor. Clin Appl Thromb Hemost 2009; 15(suppl 1):95–165.

doi:10.3949/ccjm.78c.12002

CORRECTION

An error appeared in the article, “Managing cancer pain: Frequently asked questions,” in the July 2011 issue (Induru RR, Lagman RL. Managing cancer pain: Frequently asked questions. Cleve Clin J Med 2011; 78:449–464). On page 456, the fourth line of the right-hand column, “N-methyl-D-acetate” is incorrect. It should read “N-methyl-D-aspartate.” The error has been corrected in the online version of the article.

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