

The second question posed in their letter to the editor is why we used EBL greater than 50 ml in our algorithm to indicate the need for type and screen, whereas their study used EBL less than 50 to indicate no need for type and screen. This question is really about what to do with cases where EBL is 50 ml. We recognized that EBL is almost always reported as rounded values, and we made the decision to put cases with EBL of 50 ml in the “no type and screen” category, as long as the percentage of patients transfused was less than 5% and the transfusion index (average units/patient) was less than 0.3. This decision was based on the observation that many anesthesia providers enter “50” when EBL is minimal, because the electronic anesthesia records do not allow a text entry for EBL. In Dexter and Epstein’s proposed algorithm, the cases with EBL of 50 would be more likely to have a type and screen ordered, because they used EBL less than 50 as a criterion not to order a type and screen.

In summary, it is difficult to compare our maximum surgical blood order schedule with Dexter and Epstein’s study because our algorithms have more differences than similarities. In addition, our publication included the actual maximum surgical blood order schedule as an appendix, whereas theirs did not, making the comparison even more difficult. I can report, however, that our type and crossmatch to transfusion ratio has decreased by 29% since the release of the maximum surgical blood order schedule at our institution. This is the evidence that we have effectively reduced unnecessary blood orders, which will decrease cost, and perhaps improve patient safety, because the blood bank personnel can now focus on completing the blood orders for patients who may actually need transfusion.

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Factor Eight Inhibitor Bypass Activity for Novel Oral Anticoagulant Reversal

To the Editor:

In their excellent review on novel oral anticoagulants, Levy *et al.*¹ seemed to have deliberately ignored the potential of factor eight inhibitor bypass activity (FEIBA; Baxter AG,

Vienna, Austria) as a quick reversal agent in emergency situations. Levy *et al.* cited the study by Marlu *et al.*² but made no mention of the results on FEIBA as a reversal agent reported in that study and chose only to discuss the results on prothrombin complex concentrate and recombinant factor VIIa, while acknowledging that there is an activated form of 4-factor prothrombin complex concentrate.

Factor eight inhibitor bypass activity consists of nonactivated factors II, IX, X, and activated VII, which means that it is similar to 3-factor prothrombin complex concentrate and recombinant factor VIIa combined. It is inexpensive and has been used extensively and successfully in the management of patients with hemophilia A with inhibitors for several decades in many countries, including the United States,^{3,4} although FEIBA appears not to have been approved by the Food and Drug Administration yet. In the *ex vivo* study in healthy white males by Marlu *et al.*,² rivaroxaban reduced total and peak thrombin generation, as well as time to initiation of thrombin generation. Prothrombin complex concentrate normalized total thrombin generation but not the peak thrombin value or thrombin generation starting time. Recombinant factor VIIa corrected thrombin generation starting time but not total quantity or peak. Interestingly, FEIBA corrected all parameters at lower doses and overcorrected at higher doses. These authors also demonstrated a dose-dependent correction by FEIBA of the thrombin generation starting time prolonged by dabigatran. Their conclusion was that FEIBA at lower doses seems to be the most reasonable approach to novel oral anticoagulant reversal.²

Published a month before Levy *et al.*’s review was a case report from Davis, California, of a middle-aged man on dabigatran 150 mg two times per day who sustained a trans-septal perforation during atrial ablation.⁵ Within 60 min, approximately 4.5 l of blood was removed *via* pericardiocentesis. Intravenous low-dose FEIBA (3,159 units, 26 U/kg) over 15 min was administered. Hemostasis was noted within minutes of initiating the infusion with cessation of bleeding occurring soon after.

Several abstracts have also been published documenting improvement in bleeding parameters by FEIBA in novel oral anticoagulant-treated animals.⁶

Competing Interests

The author declares no competing interests.

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In Reply:

I appreciate your comments; however, the review did not deliberately ignore the potential of Factor VIII Inhibitor Bypassing Activity (FEIBA; Baxter AG, Deerfield, IL) as you suggest, and FEIBA is mentioned but details were not provided. However, if you check table 2, there is further discussion on the use of activated prothrombin complex concentrates.¹ The table legend specifically states that in patients receiving dabigatran, the use of an activated prothrombin complex concentrate such as FEIBA may be more effective, and there are no studies reporting the use of prothrombin complex concentrates on actual bleeding in patients. Further studies including the development of specific reversal agents are underway currently.¹ Of note is the study by Marlu *et al.*² that you describe is an *in vitro* study, and caution should be considered for extrapolating *in vitro* data to clinical application. You also reference a case report. Please note that case reports are interesting, but an n = 1 or 2 is not a case series. The authors also suggest that FEIBA appears not to be approved by the Food and Drug Administration, but this is not the case. Although using an activated prothrombin complex concentrate such as FEIBA appears to make sense, additional human data are needed before we can make definitive conclusions.

The studies described in more detail in the review article on prothrombin complex concentrates were actually performed in volunteers receiving therapeutic doses of the new oral anticoagulation agents including rivaroxaban and dabigatran.³ I am also a part of additional studies further

investigating the role of prothrombin complex concentrates for reversal of rivaroxaban in volunteers.* Of note is a specific reversal agent has also been developed for dabigatran, using an immunospecific Fab fragment (BI 655075).⁴ This novel therapeutic approach is entering into clinical trials.†

Clinicians when faced with life-threatening hemorrhage do indeed need to know all of the information and data available to manage these complex and critically ill patients.⁵ Further clinical studies are needed to best determine the optimal therapy for bleeding when it occurs in patients related to the novel oral anticoagulation agents.

Competing Interests

Dr. Levy has served or serves on research steering committees or advisory boards for CSL Behring, King of Prussia, Pennsylvania; Boehringer-Ingelheim, Ingelheim, Germany; Grifols, Research Triangle Park, North Carolina; and Janssen Research & Development, Raritan, New Jersey.

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Acute Kidney Injury, Surgery, and Angiotensin Axis Blockade

To the Editor:

We read with interest the Case Scenario: Hemodynamic Management of Postoperative Acute Kidney Injury.¹ The authors present a 59-yr-old patient with the only preoperative medication an angiotensin-converting enzyme inhibitor for hypertension, who suffers acute kidney injury

* Available at: <http://clinicaltrials.gov/ct2/show/NCT01656330>. Accessed October 9, 2013.

† Available at: <http://clinicaltrials.gov/ct2/show/NCT01688830?term=BI+655075&rank=1>. Accessed October 9, 2013.