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Letter to the Editor

Lack of reversibility for NOACs

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Dear Editor,

I read with interest the recent discussion on the ENGAGE-AF trial written by Kaba et al.[1] The authors provide a comprehensive discussion of the novel oral anticoagulant (NOAC), Edoxaban. However, it is important to remind the readers that although NOACs are being promoted as first line for stroke prevention in atrial fibrillation, there is considerable risk of bleeding associated with their uses and no reliable reversible agent is available.

This increase in bleeding risk and the lack of reversal agent for the newer anticoagulants remain the main barrier for routine use of these new agents.[2] Using protamine, fresh frozen plasma, and cryoprecipitate has not been shown to reverse NOACs. Recombinant clotting factors are still under investigation. Recombinant activated factor VII has the potential to reverse NOACs, but its prothrombotic effects may prove problematic.[3]

Prothrombin complex concentrates (PCC) are concentrated clotting factors (II, IX, X with or without VII) have been showing promising results in reversing NOACs. Small randomized trials of PCC in healthy subjects receiving dabigatran showed that PCC restored thrombin potential to baseline.[2] Other agents like PER977 (antidote to factor Xa and IIa inhibitors),[4] and PRT064445 (inactive recombinant factor Xa) are being developed and investigated.[5] To date, no large studies have been reported for reversal of NOACs.

Given that most patients with atrial fibrillation are older with other comorbidities, risk of bleeding is very high in some patients. In our clinical practice, we have encountered many instances where patients on NOACs present with hemorrhage. The management of these patients becomes challenging for the practicing physician given the lack of reversibility agent. Thus, we emphasize the use of bleeding risk scores before starting these medications.

The clinical use of these anti-coagulants continues to grow, despite the uncertainty towards reversibility and other unreported side effects of these medications. The use of these NOACs should be evaluated in a case-by-case approach with stratification based on risk for bleeding and risk for embolism to achieve best outcomes. Until reversal agents are widely available and validated, caution should be exercised.

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