In Response to Epistaxis in the Setting of Antithrombotic Therapy: A Comparison Between Factor Xa Inhibitors, Warfarin, and Antiplatelet Agents

In Reply:

We thank Dr. Wang et al. for their important remarks. Our retrospective study described the characteristics and severity of epistaxis in patients taking factor Xa inhibitors novel anticoagulants in comparison with patients taking warfarin or antiplatelet therapy.¹

In our practice, we do not routinely monitor factor Xa inhibitor drug levels in cases of epistaxis. Direct drug level measurements were obtained in two rivaroxaban patients (one had supratherapeutic levels) and one apixaban patient with normal levels. Patients were treated with apixaban or rivaroxaban in a variety of dosages. Also, most of the patients treated with apixaban or rivaroxaban have not experienced episodes of bleeding (of any type) prior to the index admission, despite having been treated with these agents for several months.

Factor Xa inhibitors have a shorter half-life, wider therapeutic index, and predictable pharmacokinetics/pharmacodynamics compared to warfarin.²–⁵ Therefore, although supratherapeutic drug levels should be taken into consideration, apparently, there is no reason to assume that there are more cases of high drug levels in the factor Xa inhibitors groups. Furthermore, in cases where there were higher supratherapeutic drug levels in these groups, one would expect worse outcomes compared to the warfarin group; this was not found. Still, we do recommend consulting a hematologist and obtaining factor Xa inhibitor levels in selected cases of refractory/recurrent epistaxis.

No antidotes were used in the factor Xa inhibitor groups. Currently, factor Xa inhibitor antidotes (andexanet alfa) are being investigated and are not available for routine clinical use. Other anticoagulation reversal drugs can be used such as fresh frozen plasma (FFP) or recombinant coagulation factors. In our study, two patients from the rivaroxaban group and one patient from the apixaban group received FFP already in the emergency room. Naturally, we agree that administration of reversal agents may improve outcomes in carefully chosen patients.

In the warfarin group, eight patients presented with supratherapeutic drug levels measured by international normalized ratio. Of these patients, six were treated with vitamin K and one patient received FFP in the emergency room. In our cohort, only 4/24 patients and 2/11 in the in the rivaroxaban and apixaban groups, respectively, were also treated with aspirin or clopidogrel. These relatively low rates do not account for the lack of observed difference between the groups.

In conclusion, despite the limitations of our cohort, according to our results, epistaxis can be effectively controlled with no worse and perhaps even better outcome in patients under factor Xa inhibitors in comparison with patients under other anticoagulation medications. We join Dr. Wang et al. in recommending that factor Xa inhibitor levels should be obtained in selected cases if possible, and that current and future anticoagulation reversal drugs are part of the treatment options.

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BIBLIOGRAPHY