Title: Evaluation of 4-factor prothrombin complex concentrate dosing for factor Xa inhibitor reversal

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Introduction: Four-factor prothrombin complex concentrate (4F-PCC) has shown promise as an effective agent for reversing bleeding associated with Xa inhibitors. Although guidelines recommend a 4F-PCC dose of 50 units/kg, supporting literature regarding the safety of this dose is limited, and introduction of the Xa inhibitor antidote andexanet alfa has raised new challenges regarding 4F-PCC effectiveness. The objective of this study was to evaluate the safety and efficacy of 50 units/kg 4F-PCC for the reversal of factor Xa inhibitor-associated bleeding at an urban, academic medical center.

Methods: This was a retrospective, observational study conducted at a single center from April 2018 through August 2019. Patients who received 4F-PCC for reversal of Xa inhibitor-associated major bleeding were included in the study. Patients were excluded if they experienced an ischemic stroke or acute coronary syndrome in the 30 days prior to enrollment or were placed on comfort care measures within 48 hours. The efficacy endpoint was achievement of excellent or good hemostasis assessed using the modified Sarode criteria. The safety endpoint was occurrence of thromboembolic events at 30 days. Secondary outcomes included all-cause mortality, intensive care unit (ICU) length of stay, and hospital length of stay.

Results: Thirty patients received 4F-PCC for the reversal of major bleeding associated with apixaban (n=17) or rivaroxaban (n=13) use. The majority of patients presented with intracranial bleeding (73.3%), and median dose of 4F-PCC given was 49.0 units/kg. Reversal was assessed as excellent or good in 80% of patients. Only one patient (3.3%) experienced a thromboembolic event, and death occurred in 5 patients (16.7%). Median ICU and hospital length of stay were 2.9 and 7.1 days, respectively.

Conclusion: 4F-PCC administered at a dose of 50 units/kg was demonstrated to be safe and effective for the reversal of major bleeding associated with Xa inhibitors.