Evaluation of efficacy of fixed-dose four-factor prothrombin complex concentrate for the emergent reversal of vitamin k antagonists at two community hospitals

Authors: Shanelle Murray, PharmD; Saumil Vaghela, PharmD, BCPS; Frederick Villiard, PharmD, BCPS, BCCCP

Practice Site: Sentara RMH Medical Center, Harrisonburg, Virginia

Background: Hemorrhage remains a serious complication for patients who receive therapy with a vitamin K antagonist (VKA) such as warfarin. Bleeding secondary to warfarin use can be major and potentially life-threatening, requiring reversal of its anticoagulant effects to achieve rapid hemostasis. The use of four-factor prothrombin complex concentrate (4F-PCC) is an effective treatment modality that can be used for emergent warfarin reversal. The FDA-approved dose for the use of 4F-PCC is individualized based on patient body weight (up to and not to exceed 100 kilograms) and baseline international normalized ratio (INR) value. However, fixed dosing may provide comparable VKA reversal.

Objectives: The purpose of this study was to compare a post-implementation cohort who received a fixed-dose of 4F-PCC to a pre-implementation cohort who received a weight-based dose. The coprimary objectives of this study was achievement of a target INR ≤2.0 or ≤1.5 within 24 hours post 4F-PCC administration and the incidence of thrombotic events. Secondary objectives included reduction in time to administration of 4F-PCC and the difference in cost of fixed-dose versus variable weight-based dose.

Methods: This was a multicenter, observational, case-matched, two cohort study that compared the efficacy of 4F-PCC for the emergent reversal of warfarin using two different dosing strategies. The first dosing strategy was fixed-dose 4F-PCC where patients without an intracerebral hemorrhage and weighing less than 100 kilograms received 1500 units; patients with either an intracerebral hemorrhage or weighing 100 kilograms or greater received 2000 units. The second dosing strategy was weight-based. This study also evaluated the safety of using fixed dosing to avoid thrombotic events. It was conducted across two hospitals within the Sentara Healthcare System. Sentara RMH Medical Center (SRMH), a 238-bed community hospital, and Sentara Martha Jefferson Hospital (SMJH), a 176-bed community hospital were included. Patients presenting to the ED of these two hospitals between July 2021 and March 2022 were evaluated.

Preliminary Results: A total of 6 patients were included in the fixed-dose group and 6 patients in the weight-based group. Reduction in INR to 1.5 or less was achieved in 66.7% (n=4/6) of patients in the fixed-dose group and 50% (n=3/6) of patients in the weight-based group. Reduction in INR to 2.0 or less was achieved in 100% (n=6/6) of patients in the fixed-dose group and 83.3% (n=5/6) of patients in the weight-based group. There were no incidences of thrombotic events in any of the patients included in the study. The mean difference between the 4F-PCC order and administration time was reduced by 26.7% in the fixed-dose group as compared to the weight-based group (40.33 minutes versus 55 minutes). The mean cost of fixed-dose 4F-PCC in comparison to that of weight-based 4F-PCC was reduced by 46.4% ($15,314.66 versus $28,573.24).

Conclusion: Although the study was not powered, there were positive trends with the use of fixed-dose 4F-PCC such as achievement of INR reduction, improved time to administration, and cost-saving benefits. However, more studies with a larger patient population may be warranted to determine the broader applicability of these findings.