Implementation and Evaluation of Fixed Dosing Prothrombin Complex Concentrate for Warfarin Reversal

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Purpose: Kcentra™ is a 4-factor prothrombin complex concentrate containing exogenous clotting factors II, VII, IX, and X, sourced from human plasma. Kcentra™ may be used for the reversal of warfarin in the setting of acute bleeding or emergent surgery. Currently, the Kcentra™ package insert recommends weight-based dosing (units/kg) for the reversal of warfarin; however, the 2020 American College of Cardiology Expert Consensus Decision Pathway recommends 1000 units for a major non-cranial bleed and 1500 units for all other major bleeds. In August 2020, The University of Kansas Health System implemented a fixed dosing protocol for Kcentra™ in the setting of warfarin reversal. Our protocol now recommends 1500 units for intracranial hemorrhage, and 1000 units for all other bleeds, in conjunction with vitamin K. Providers have the option to give an additional 500 units based on patient specific factors, such as pre-treatment INR, weight, presence of continued bleeding, and if the INR remains above goal post-treatment.

Methods: A single-center, retrospective chart-review was used to evaluate the efficacy and adherence to the fixed dose Kcentra™ protocol. Patients 18 years and older were included if they received Kcentra™ for reversal of warfarin after policy implementation. Patients were excluded if they were younger than 18 years old, had a pre-treatment INR of <2, received a dose lower than the recommended fixed dose 4f-PCC protocol dosing, or received Kcentra for direct oral anticoagulation (DOAC) reversal or factor deficiency. The primary outcome assessed was achievement of an INR less than 2 post fixed dose Kcentra™. Secondary outcomes included percentage of patients receiving supplemental doses in addition to the initial bolus, percentage of patients receiving concurrent vitamin K therapy, 30 day mortality, and predicted number of 4f-PCC units conserved.

Results: In the five months following implementation, 12 patients were included in the post-implementation analysis. Of the patients included, the majority required Kcentra for intracranial hemorrhage (41.7%, n=5), followed by reversal for emergent procedure (33.3%, n=4). Four of the twelve patients included failed to achieve an INR <2 after receiving fixed dose Kcentra; however, none of the 12 patients received a supplemental dose. All patients included in the analysis received concomitant vitamin K therapy, and one patient died within 30 days of receiving Kcentra. Overall, the predicted number of units conserved were estimated to be 22,900 units.

Conclusions: Overall, this retrospective chart review following the implementation of a fixed dose Kcentra protocol at a large academic medical center has proven to be effective in terms of INR reversal and clinical outcomes. Potential limitations include that analysis occurred immediately after implementation, and providers may not have been aware of the new changes to the KCentra policy and its related dosing recommendations. An additional limitation includes the lack of standardized INR draws after Kcentra administration. Additional data may be helpful to continue analyzing the trends of adequate INR reversal and need for supplemental doses.