Low- & fixed-dose prothrombin complex concentrate: therapeutic, pharmacoeconomic, & operational outcomes

Objective:
Evaluate the clinical and operational outcomes resulting from a conservative dosing strategy for four-factor prothrombin complex concentrate (4F-PCC) for anticoagulation reversal.

Methods:
Anticoagulation reversal protocols were updated to reflect a multi-tiered approach (Fig. 1). Patients on warfarin were reversed with a fixed dose of 4F-PCC, patients on direct oral anticoagulants (DOACs)—specifically apixaban & rivaroxaban—were given a 25 unit/kg dose, andandexanet alfa was excluded from the Salina Regional Health Center (SRHC) formulary [1]. Order sets were updated to include an entry to consult pharmacy to dose when searching for 4F-PCC. This study was approved by the SRHC Institutional Review Committee & all data was obtained via retrospective chart review for calendar year 2020.

Results:
Using the updated 4F-PCC dosing strategies, SRHC used 98 fewer vials over the course of calendar year 2020 when compared to traditional dosing (Fig. 2). There was no clinically meaningful change in therapeutic efficacy as 90-91% of patients for whom data was available achieved hemostasis with an INR of 1.7 or less after treatment. Only 1 patient in each anticoagulation group required a repeat dose of 4F-PCC per protocol. No patient experienced a documented thrombotic event. Overall, drug cost avoidance from the multi-tiered strategy totals $1,113,030 when including drug expenditures related to andandexanet alfa. When pharmacists were consulted, average time to drug administration was 45 minutes compared to 67 minutes without pharmacist consult.

Conclusions:
A conservative dosing approach to anticoagulant reversal seems to be effective from a therapeutic, pharmacoeconomic, & operational standpoint.

In this data set, two patients did not achieve adequate INR reversal and one patient did but nonetheless was given a repeat dose of 4F-PCC with no explanation noted. The following baseline characteristics were compared amongst these three patients:
- Anticoagulant agent
- Baseline & post-treatment INR
- Comorbid malignancy
- Location of bleed (Fig. 3)
- Platelet count/concomitant anti-platelet therapy
- Serum creatinine (Scr)
- Time to administration
- Weight and body mass index (BMI)

Patients had no discernible similarities, sometimes dramatically so (e.g. INRs ranging from 3 to 20, Scr ranging from 0.66 to 5.12). No single measure alone (INR, anti-Xa, clinical correlation) is known to be sufficient to predict hemostasis [2]. This absence of a clinically meaningful pattern may lend support to use of more sophisticated assessment techniques, such as viscoelastic testing (eg thromboelastogram) [3].

References