Implementation and Outcomes Assessment of a 4-factor prothrombin complex concentrate (4F-PCC) Tiered Fixed Dosing Protocol in a Health System.

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The aim of this study was to evaluate compliance to the newly implemented fixed dosing protocol while assessing the revised dose for 4F-PCC and the need for further invasive intervention to reverse the bleeding.

Patients presenting with an acute life-threatening bleed while taking warfarin or direct oral anticoagulants (DOACs) are often managed emergently. In the setting of acute bleeding, while 4F-PCC has been routinely used as a reversal agent, its optimal dosing regimen remains controversial. Currently manufacturer dosing is pretreatment, INR restricted, and weight based as listed below:

- Patient weight 50 kg-100 kg = 4F-PCC 2000 units +/- 10% (1800-2200 units)
- Patient weight <50 kg or >100 kg = 4F-PCC 2500 units +/- 10% (2250-2750 units)
- Revises with 4F-PCC 500 units +/- 10% as needed for continued bleeding

Additionally, 4F-PCC only has a Food and Drug Administration (FDA) indication for warfarin reversal despite its common use in reversal of DOAC-related bleeding. A fixed dose strategy can have many advantages including shorter preparation time and thereby shorter time to administration, and overall less cost. In addition, the operational advantage of using a fixed dose is another contributor to the cost reduction of weight-based restriction doses.

In 2020, Parkview Health system in Fort Wayne, IN implemented a protocol utilizing a fixed-dose weight-based 4F-PCC dosing schedule in patients with life threatening warfarin or DOAC-related bleeding.

**BACKGROUND**

**OBJECTIVE**

Implementation and Outcomes Assessment of a 4-factor prothrombin complex concentrate (4F-PCC) Tiered Fixed Dosing Protocol in a Health System.

**METHODS**

- Eligible for and treated with massive transfusion protocol
- 18 years or older
- Received at least one dose of 4F-PCC within the Parkview Health system between November 1, 2020, to June 15, 2021.

**Exclusion Criteria**

- Overall hemostasis, a commonly evaluated outcome, was not evaluated in our present study thereby preventing a proper assessment of measured outcomes.
- Further limitations include the off-indication use of 4F-PCC. Occasionally, 4F-PCC was used for type of anticoagulant prior to use, indication for acutaphylactic, 4F-PCC dose information, use of blood products/posttransfusion, and need for further invasive intervention.

**RESULTS**

- Nine encounters were excluded due to massive blood transfusion protocol
- Of the 119 administrations collected and analyzed, there was a single incidence of 4F-PCC dosing (post-operative surgical bleeding).

**RESULTS**

- Seventy-six percent of administrations (91 out of 119) complied with the health system dosing protocol
- Of the 119 administrations, 100 (84%) did not require invasive intervention within 48 hours of 4F-PCC administration. Seventeen of those administrations were in the pre-surgical setting of 4F-PCC use where this attribute is not applicable. (Tables 2 and 3).

**DISCUSSION & CONCLUSIONS**

- Doing a seven-month period, 4F-PCC was administered adherent to hospital dosing protocol with minimal need for readjustment. Although the assessed dosing regimen is clear, it can be difficult to accurately dose 4F-PCC when considering variability of the available products and the dosage vials manufactured.
- The most common reversal need for bleeding was in atrial fibrillation patients onwarfarin therapy. Least commonly, 4F-PCC was used in supraventricular arrhythmia in and dabigatran or fondaparinux anticoagulant use reversal which are not indicated treatments.
- Utilization of this dosing protocol for 4F-PCC is associated with considerable cost minimization.
- Both models comparing the two dosing regimens showed dose reductions and therefore cost reductions when using the fixed dose weight-restricted dosing schedule compared to the standard dose recommendations.
- The assessed dosing regimen was also associated with certain positive outcomes including limited need for readjusting and minimal requirements of invasive intervention for bleeding control.
- These results show that weight-restricted fixed dosing is an alternative for dosing 4F-PCC in both warfarin and DOAC-related bleeding reversal.

**NEED FOR FURTHER INVESTIGATION**

- May be advantageous especially in patients weighing over 100 kg particularly in cost reduction.
- This dosing strategy is useful in dosing 4F-PCC for DOAC-related bleeding reversal as there is no standard, package insert recommended dosing.
- The clinical features in this subset were found to be consistent with values prior to implementation of the fixed-dose protocol.
- Overall hemostasis, a commonly evaluated outcome, was not evaluated in our present study thereby preventing a proper assessment of measured outcomes.
- Further limitations include the off-indication use of 4F-PCC. Occasionally, 4F-PCC was used when there was bleed or for reversal in DOAC-related bleeds, which may impact cost analysis and stand-in outcomes.

**REFERENCES**