

## **Four-factor prothrombin complex concentrate fixed dosing versus package insert for emergent warfarin reversal: a retrospective cohort study**

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**Objective:** Four-factor prothrombin complex concentrate (4F-PCC) is used for warfarin reversal in cases of life threatening bleeding and urgent surgical procedures. The package insert (PI) dosing is widely used, but studies suggest a lower weight-based fixed dosing has similar efficacy with lower risk for thromboembolism. This chart review aims to evaluate the RGH 4F-PCC fixed dosing protocol and compare outcomes to PI dosing for warfarin reversal.

**Methods:** This was a retrospective chart review evaluating adult patients who received 4F-PCC to reverse warfarin following either PI dosing (25-50 units/kg depending on INR), or RGH fixed dosing (1,500 units for INR less than or equal to 5 and weight less than or equal to 100 kg, and 2,000 units for INR more than 5 or weight more than 100 kg for non- intracranial hemorrhage (ICH) or need for urgent invasive procedure; and 25 units/kg for INR more than or equal to 1.5 for ICH). The time frame for enrolling patients was May 2017 to March 2018 for the PI group, and March 2019 to December 2020 for the fixed dosing group. All patients were co-administered vitamin K; dose and route were determined by the provider. The primary outcome of the study was achievement of INR less than or equal to 1.5 within 4 hours of 4F-PCC administration. Secondary outcomes include achievement of INR less than or equal to 2, the need to repeat the 4F-PCC dosing, thrombotic events within 30 days of 4F-PCC administration, all-cause mortality within 30 days and cost benefit.

**Results:** The chart review included 43 patients in the fixed dosing group and 51 patients in the PI group. The primary outcome of post-INR less than or equal to 1.5 was achieved by 34 patients (79%) in the fixed dosing group vs 48 patients (94%) in the PI group ( $P = 0.059$ ). The secondary outcome of post-INR less than or equal to 2 was achieved by 42 patients (98%) in the fixed dosing group vs 51 patients (100%) in the PI group ( $P = 0.45$ ). None of the patients received a second dose of 4F-PCC. In the fixed dosing group, three patients developed a thrombotic event within 30 days (7%), and 9 deaths due to any cause (21%) vs 5 thrombotic events (10%) and 12 deaths (23.5%) in the PI group ( $P = 0.722$  and  $P = 0.8$ ; respectively). Utilizing the fixed 4F-PCC dosing led to approximately \$20,000 cost savings per year.

**Conclusion:** The results of this retrospective chart review suggest similar efficacy and safety between the 4F-PCC RGH fixed dosing and PI dosing. The 4F-PCC RGH fixed dosing protocol may contribute to cost benefit. Given this is a single-center, small sample, retrospective chart review, a randomized controlled trial is needed for further validation.