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Four-Factor Prothrombin Complex Concentrate (4F-PCC) for the Treatment of Oral Factor Xa Inhibitor-Associated Bleeding: A Meta-Analysis of Fixed Versus Variable Dosing

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HIGHLIGHTS

Study results showed similar effectiveness and safety between the fixed and variable 4F-PCC dosing strategies across most evaluated outcomes

Fixed-dosing group had a significantly longer mean hospital LOS of 7.4 days (95% CI, 3.6-11.1; *P*<0.001) compared to 5.9 days (95% CI, 5.5-6.3) in the variable-dosing group

4F-PCC fixed dosing strategy may be a safe and effective alternative to variable weight-based dosing and was associated with lower 4F-PCC consumption

INTRODUCTION

Life-threatening bleed management in patients receiving oral FXa inhibitors can be challenging

Both fixed and variable 4F-PCC dosing strategies are used for managing oral FXa inhibitor-associated bleeding as first or second-line treatment when direct reversal agents are unavailable

STUDY CHARACTERISTICS

Objective
To evaluate the effectiveness and safety of fixed versus variable 4F-PCC dosing for the management of FXa inhibitor-associated bleeding

Study design
Systematic literature review and meta-analysis of clinical studies

Patient population
Adults ≥18 years old with oral direct FXa inhibitor-associated major bleeding*

Outcomes

Primary outcomes
Hemostatic effectiveness, mortality, thromboembolic events

Secondary outcomes
Overall 4F-PCC usage, total length of stay (LOS) in hospital, LOS in intensive care unit, and time to 4F-PCC administration

*Oral direct FXa inhibitors included rivaroxaban, apixaban, edoxaban, or betrixaban.

RESULTS

Pooled rates of hemostatic effectiveness (all definitions/criteria)

For all patients

Fixed dosing: **74.2%** (95% CI, 52.3-91.3)
Variable dosing: **79.2%** (95% CI, 74.4-83.7)
P=0.65

For the ICH subgroup

Fixed dosing: **72.9%** (95% CI, 60.4-82.6
Variable dosing: **81.0%** (95% CI, 75.4-86.2)
P=0.24

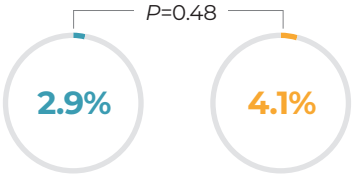
Mean initial 4F-PCC dose by weight was significantly higher with variable dosing compared to fixed dosing (*P*<0.001)

Fixed dosing
27 IU/kg
(95% CI, 26-28)

Variable dosing
38 IU/kg
(95% CI, 32-44)

Thromboembolic events

No significant difference in thromboembolic event rates

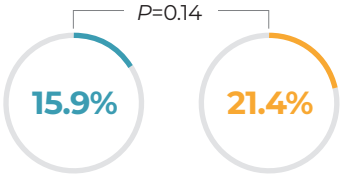


(95% CI, 0.0-8.7)
(95% CI, 2.2-6.3)

In the ICH subgroup, **the rate of thromboembolic events in variable-dosing studies was 4% (95% CI, 1.6-7.2); no fixed-dosing ICH studies reported thromboembolic events**

Mortality rates

No significant difference in mortality rates



(95% CI, 10.4-22.3)
(95% CI, 16.4-26.8)

Bleeding progression (i.e., index event) was reported as the most common cause of death, accounting for 85% of deaths

Hospital LOS was significantly longer in the fixed-dosing group, with a mean stay of 7.4 days (95% CI, 3.6-11.1; *P*<0.001) compared to a mean of 5.9 days (95% CI, 5.5-6.3) in the variable-dosing group

Abbreviations
4F-PCC: four-factor prothrombin complex concentrate; FXa: activated factor X; ICH: intracranial hemorrhage; IU: international unit; LOS: length of stay.

Reference
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