Four-factor prothrombin complex concentrate

Derived from Fresh frozen plasma, contains clotting factors II, VII, IX and X, with protein C & S to prevent thrombosis. Primary indication is to be given IV to reverse warfarin in emergency situations. However it is also used in other settings. Requires much lower volume than FFP to work. Also, when the INR gets down to about 1.4, PCC will continue to reduce the INR whereas FFP will have little or no benefit (the INR of FFP itself is ≈ 1.3–1.4). Optimal dosing is not known. Doses of 15–50 IU/kg have been given to hemophiliacs, but the clotting deficit differs in vitamin K depletion than in clotting factor absence. A reasonable dose that is often used is 25 IU/kg.

Indications

The administration of Prothrombin complex concentrate (PCC) facilitates emergency spinal surgery in anticoagulated patients who present with acute spinal pathology requiring urgent neurosurgical decompression.

Complications

The risk of PCC-associated thromboembolic events seems to be low and justifies the use of PCC in order to avoid permanent disablement resulting from delayed surgery or non-operation [1)].

A 4-factor prothrombin complex concentrate (4F-PCC), containing therapeutic doses of vitamin K-dependent coagulation factors, was recently licensed in the United States for reversal of vitamin K antagonist therapy. However, given the emergence of several oral anticoagulants for which there are no specific reversal agents, and the existence of many other complex bleeding disorders, it is likely that clinicians will seek to use 4F-PCCs for any number of off-label indications [2)].

Case series

There are no randomized trials comparing andexanet alfa and 4-factor prothrombin complex concentrate (4F-PCC) for the treatment of factor Xa inhibitor (FXa-I)-associated bleeds, and observational studies lack important patient characteristics. Singer et al. pursued this study to demonstrate the feasibility of acquiring relevant patient characteristics from electronic health records. Secondarily, they explored outcomes in patients with life-threatening FXa-I-associated bleeds after adjusting for these variables. They conducted a multicenter, chart review of 100 consecutive adult patients with FXa-I-associated intracerebral hemorrhage (50) or gastrointestinal bleeding (50) treated with andexanet alfa or 4F-PCC. We collected demographic, clinical, laboratory, and imaging data including time from last factor FXa-I dose and bleed onset. R The Mean (SD) age was 75 (12) years; 34% were female. Estimated time from last FXa-I dose to bleed onset was present in most cases (76%), and patients treated with andexanet alfa and 4F-PCC were similar in baseline characteristics. Hemostatic efficacy was excellent/good in 88% and 76% of patients treated with andexanet alfa and 4F-PCC, respectively (P = 0.29). Rates of thrombotic events within 90 days were

14% and 16% in andexanet alfa and 4F-PCC patients, respectively (P = 0.80). Survival to hospital discharge was 92% and 76% in andexanet alfa and 4F-PCC patients, respectively (P = 0.25). The inclusion of an exploratory propensity score and treatment in a logistic regression model resulted in an odds ratio in favor of andexanet alfa of 2.01 (95% confidence interval 0.67-6.06) for excellent/good hemostatic efficacy, although the difference was not statistically significant. Important patient characteristics are often documented supporting the feasibility of a large observational study comparing real-life outcomes in patients with FXa-I-associated bleeds treated with andexanet alfa or 4F-PCC. The small sample size in the current study precluded definitive conclusions regarding the safety and efficacy of andexanet alfa or 4F-PCC in FXa-I-associated bleeds [3].

Bobby L, Westlake E, Esplin N, Young S. Activated prothrombin complex concentrate for reversal of oral factor Xa inhibitors at a level 1 trauma center. Thromb Res. 2021 Aug 10;206:33-35. doi: 10.1016/j.thromres.2021.08.005. Epub ahead of print. PMID: 34399122.

A prospective, observational study of all patients undergoing coagulopathy reversal for intracranial hemorrhage from April 2013 to December 2013 at a single, tertiary care center was undertaken. Thirty three patients underwent emergent reversal of coagulopathy using either FFP or PCC at the discretion of the treating physician. Intracranial hemorrhage included subdural hematoma, intraparenchymal hematoma, and subarachnoid hemorrhage. FFP was used in 28 patients and PCC was used in five patients. International normalized ratio at presentation was similar between groups (FFP 2.9, PCC 3.1, p=0.89). The time to reversal was significantly shorter in the PCC group (FFP 256minutes, PCC 65minutes, p<0.05). When operations were performed, the time delay to perform operations was also significantly shorter in the PCC group (FFP 307minutes, PCC 159minutes, p<0.05). In this preliminary experience, PCC appears to provide a rapid reversal of coagulopathy. Normalization of coagulation parameters may prevent further intracranial hematoma expansion and facilitate rapid surgical evacuation, thereby improving neurological outcomes [4].

1)
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2)
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