**A Review of Fixed-Dose Four-Factor Prothrombin Complex Concentrate for Vitamin K Antagonist Reversal: Does One Dose Fit All?**

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Four-factor prothrombin complex concentrate (4F-PCC) has emerged as the preferred option for emergent reversal of vitamin K antagonists (VKA); however, the optimal dosing strategy is unknown. Although several studies have tried to determine the optimal dose of 4F-PCC using a variety of dosing regimens, no dosing strategy has been found to be superior. Many of these studies have evaluated a low fixed dose of 4F-PCC instead of an individualised dose as recommended in the product label. In this article, the authors aim to evaluate the efficacy and safety of various 4F-PCC fixed-dose strategies for emergent reversal of VKA and assess the limitations of the existing literature.
To achieve the objective, the authors conducted a search of the PubMed database from the earliest available date to 2018 to find relevant articles describing fixed-dose 4F-PCC for reversal of VKA. The reference lists of relevant articles were also manually checked. Most of the currently available studies are mainly observational and heterogeneous in design.
A very low fixed dose of 500 IU is probably inappropriate for the successful reversal of VKA,
but increasing fixed doses from 1000 to 1500 IU has had some degree of success and may be considered for VKA reversal. However, many of these studies identified a trend towards insufficient stabilisation of the international normalised reversal (INR) index in patients with high baseline INR values or intracranial bleeding, suggesting that higher doses of 4F-PCC are needed in these patients. The available studies are underpowered to determine whether there is a dose-dependent association with thrombotic risk. More randomised studies are needed to establish the optimal dosing strategy and determine the function of fixed-dose 4F-PCC.