Role of prothrombin complex concentrates in reversing warfarin anticoagulation

Over the past year, several King County Hospitals have asked for our opinion on using prothrombin complex concentrates (PCCs) to reverse warfarin anticoagulation in patients with intracranial hemorrhage (ICH) and other life threatening bleeding episodes. The annual incidence of fatal bleeding in patients on warfarin is approximately 1%, with ICH accounting for the majority of cases. Warfarin interferes with production of the vitamin K dependent coagulation factors II, VII, IX, and X. Because reversal of warfarin anticoagulation by infusion of vitamin K can take more than 1-2 days, the standard of care has been to transfuse plasma into patients needing more rapid normalization of factor levels. PCCs also contain vitamin K dependent factors and are an alternative product that can be used to reverse warfarin anticoagulation. In most parts of the world there are PCC preparations that contain all 4 vitamin k dependent factors. The preparations available in the US lack factor VII requiring that 2 units of plasma be given in addition to the PCC. The main advantage of PCCs is that their small volume allows them to be infused quickly. Data generated with both 3-factor and 4-factor PCCs demonstrates rapid reversal of anticoagulation, based on in vitro coagulation assays. However, there are only a few underpowered randomized studies that looked at clinical outcomes so it is not possible to know if the more rapid reversal times associated with PCCs translate into better meaningful recoveries for patients. [1]

The small volume of fluid administered to patients receiving PCCs also has the potential to reduce the risk of circulatory overload associated with the rapid infusion of large volumes of plasma that are needed to reduce warfarin anticoagulation. Furthermore, PCC usage should minimize the incidence of other transfusion-associated adverse events. These products undergo virucidal treatment and theoretically should have almost no risk of inducing TRALI. The considerations against using PCCs are the potential thrombotic risk and the expense. With the current preparations of PCCs, thrombotic risk appears to be lower compared to older preparations. In a review article published in 2007, there were 7 thrombotic complications in 460 PCC treated patients, for an incidence of 1.5%.[2] The rate of thrombotic complications with the use of plasma has not been well established. As to cost in an off-label situation such as ICH, a

low dose (25U/kg) of PCC in a 70kg patient would cost approximately $1645.00, and a higher dose (40U/kg) would cost approximately $2632.00.
If you would like further consultation on developing a protocol for reversal of ICH in patients on Coumadin, feel free to contact us (neilj@psbc.org or theresan@psbc.org). If you choose to develop a protocol using PCCs, please be aware that the Blood Center does keep this concentrate in inventory. We also offer a return policy: as long as the product is kept at appropriate storage conditions and the boxes are intact and unmarked, any factor concentrate purchased from PSBC may be returned for credit with 4 months or more remaining prior to expiration. For more information, please contact the hemophilia department at 206-292-6507.
References:

1. Boulis NM, Bobek MP, Schmaier A, Hoff JT. Use of factor IX concentrate in warfarin-related ICH. Neurosurgery 1999; 45(5):1113-1118.

2. Leissinger CA et al. role of prothrombin complex concentrates in reversing warfarin anticoagulation: A review of the literature. Am J Hematol 2008;83:137-143.

3. Bershad EM and Suarez JI. Prothrombin Complex Concentrates for Oral Anticoagulant Therapy-Related ICH: A Review of the Literature. Neurocrit Care 2010;12:403-413.

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