A Guideline for the Management of Warfarin-induced bleeding

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Warfarin is widely used as the oral anticoagulant therapy of choice in developed countries. For example, 1.5 million patients are treated with Warfarin in the USA alone. Moreover, with the increasing median age of the population, the number of patients receiving Warfarin worldwide continues to increase at an estimated 9% per annum. The most common and feared complication of Warfarin therapy is bleeding. The reported incidence of major and minor bleeding varies widely between different studies. However major bleeding requiring hospital admission is observed in 2-4% of Warfarin treated patients per annum. In addition, intracranial haemorrhage develops in 0.1-0.5% per annum. Intra-cerebral haemorrhages constitute the majority of these, and have an estimated mortality of 50-68%. Although the risk of bleeding increases exponentially with INR>5, it is important to recognised that many bleeding episodes develop despite the patients having an INR within the therapeutic range.

In view of the incidence of major bleeding complications associated with the use of Warfarin, together with the significant associated morbidity and mortality, it is clear that effective strategies need to be widely available to enable rapid Warfarin reversal. Recent studies have shown that complete and rapid reversal of over-anticoagulation is more readily achieved with the prothrombin complex concentrates (PCC) than with FFP. Consequently current BCSH consensus guidelines specifically recommend administration of PCC in preference to FFP, for the reversal of anticoagulation in patients with major bleeding. In Ireland, the only PCC product licensed for reversal of anticoagulation is Octaplex® (Octapharma). This product is solvent/detergent treated and nanofiltered PCC, which contains all four vitamin K dependant coagulation factors (FII, FVII, FIX and FX respectively) that are reduced in patients on Warfarin therapy. Although patients receiving Warfarin have underlying hypercoagulable states, recent studies suggest that the thrombotic risk associated with the administration of PCCs in this setting is low. Nevertheless, the relative risks of bleeding and thrombosis must be assessed on an individual basis for each patient who may require Warfarin reversal. In an effort to disseminate information regarding current best practice for Warfarin reversal, the National Centre for Hereditary Coagulation Disorders has produced this guideline.

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WARFARIN REVERSAL

NO BLEEDING OR MINOR BLEED

PATIENT'S INR	ACTION
3.0 < INR < 6.0 (target INR 2.5) 4.0 < INR < 6.0 (target INR 3.5)	1. Reduce warfarin dose or stop 2. Restart warfarin when INR < 5.0
6.0 <INR < 8.0, no bleeding or minor bleeding	1. Stop warfarin 2. Restart when INR < 5.0 3. If other risk factors for bleeding consider 1mg of Vitamin K(Oral)
INR > 8.0, no bleeding or minor bleeding	1. Stop warfarin 2. Restart when INR < 5.0 3. Give 1 – 2mg of Vitamin K(Oral) 4. Recheck INR between 12 & 24hrs

MAJOR OR LIFE-THREATENING BLEEDS

Life Threatening/ Major Haemorrhage

- Intracranial bleed
- Retroperitoneal bleed
- Intraocular bleed
- Muscle bleed with compartment syndrome
- Pericardial bleed
- Active bleed with hypotension or 2g fall in Hb

1 Stop warfarin
2 Consult Haematologist immediately
3 Vitamin K 10mg IV slowly
4 Give **PCC** (e.g. **Octaplex®)**

Patient's INR	Dose of PCC
INR 2.0 – 3.9	**25 IU/Kg**
INR 4.0 – 6.0	**35 IU/Kg**
INR > 6.0	**50 IU/Kg**

Post Infusion - Repeat INR immediately and every 4 hrs until Vitamin K effect is evident. Further doses of Vitamin K may be required and daily INR monitoring is always recommended.

References:

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