Bleeding – Management in patients taking oral anticoagulants

Oral anticoagulants include vitamin K antagonists (warfarin acenocoumarol, phenindione) direct thrombin inhibitors (dabigatran) and Factor Xa inhibitors (rivaroxaban and apixaban). For patients who are bleeding and taking one these oral anticoagulants:

STOP ORAL ANTICOAGULANT THERAPY. Follow the general steps below and the flow-chart on page 2.

- Initiate standard resuscitation measures.
- Bleeding should be controlled and support provided to balance the haemodynamic state.
- Attempt to reverse the anticoagulant effect where there is life-threatening bleeding.
- Dabigatran, rivaroxaban and apixaban do not have a specific reversal agent and their anticoagulant effect cannot be reversed by administration of vitamin K or plasma infusion.
- Check coagulation screen including activated partial thrombin time (aPTT), thrombin time (TT) and fibrinogen assay.
- Indicate time of last dose of dabigatran, rivaroxaban and apixaban when requesting tests.
  NB – half lives are – warfarin (40 hours), acenocoumarol (8-11 hours), phenindione (5.5 hours), dabigatran (12-18 hours), rivaroxaban (5-9 hours), apixaban (12 hours)
- Check full blood count (FBC), renal function and electrolytes (including calcium).

Notes:

1. Minor bleeding: defined as NOT moderate or major.

2. **Moderate to severe bleeding:** Reduction in Hb≥ 2g/dL, transfusion of ≥ 2 units of red blood cells or symptomatic bleeding in critical area or organ (e.g. intraocular, intracranial, intraspinal, intramuscular with compartment syndrome, retroperitoneal, intra-articular or pericardial bleeding

3. **Life threatening bleeding:** Symptomatic intracranial bleed, reduction in Hb ≥ 5g/dL, transfusion of ≥ 4 units of red cells, hypotension requiring inotropic agents or bleeding requiring surgical intervention

4. Dabigatran half life is increased to 27 hours in renal impairment

5 WUTH Clinical Guidance: Administration of Octaplex® is available on the intranet.

6. This is an off-label use of NovoSeven ®.

7. Risk factors for bleeding: Include – Age > 65, hypertension, diabetes mellitus, renal failure, liver failure, previous gastrointestinal bleed, previous cerebral bleed, concomitant antiplatelet therapy.

References:

Makris M, Van Veen J, Tait C.R., Mumford A.D. and Laffan M on behalf of the British Committee for Standards in Haematology (2012). Guideline on the management of bleeding in patients on antithrombotic agents. *British Journal of Haematology*, 2012, 160, 35-46

Management of Bleeding in Patients Taking a Newer Oral Anticoagulant (NOAC) Cheshire and Merseyside Clinical Networks available at http://www.cmcsn.nhs.uk//fileuploads/CMCN_Dabigatran_and_Rivaroxaban_Bleeding_Protocols.pdf

Bleeding – Management in patients taking oral anticoagulants

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Vitamin K antagonists: Warfarin Acenocoumarol Phenindione

Minor bleeding

1. Check INR.
2. If INR < 8 then omit dose and restart when INR < 5.
3. If INR > 8 **AND** risk factors[7] for bleeding then manage as above **AND** give 1 to 5mg vitamin K by mouth (Konakion MM® 2mg in 0.2ml ampoules). Repeat dose if INR still high after 24 hours.

Moderate to Severe Bleeding

Contact consultant haematologist on call:

1. Check INR.
2. Give phytomenadione 5 to 10mg vitamin K by slow intravenous injection.
3. If major bleeding then also give Octaplex® (prothrombin complex concentrate factors II, VII, IX and X) [2]. The dose will vary depending on the INR result and the product is issued by the Blood Transfusion Laboratory after authorisation by a Haematologist.

Direct thrombin inhibitors: Dabigatran

Minor bleeding

1. Consider activated charcoal if dabigatran ingested < 2 hours previously.
2. Local haemostatic measures.
3. Mechanical compression.
4. Tranexamic acid orally 15 to 25 mg/kg two to three times a day.
5. Delay next dose of dabigatran or discontinue treatment as appropriate.

Moderate to Severe Bleeding

Contact consultant haematologist on call:

1. Give oral charcoal application if dabigatran ingestion <2 hours previously.
2. Local measures.
   - Mechanical compression
   - Consider surgical intervention or wound packing
3. Fluid replacement.
   - Maintain good urine output as dabigatran renally excreted
4. Blood product transfusion.
   - Consider platelets if levels less than 70 to 80 x 109/L or patient on antiplatelet drug
5. Tranexamic acid 1g by slow IV injection over 10 minutes followed by 1g three times daily by slow IV infusion over 8 hours.
6. If rapidly deployable, haemofiltration offers the possibility of enhanced clearance (discuss with haematologist).

Ongoing life- threatening bleeding[4]:

Implement measures as above and consider

7. Octaplex®, activated prothrombin complex concentrate APCC and rFVIIa (NovoSeven®)[5] after discussion with haematologist.

Factor Xa inhibitors: Rivaroxaban Apixaban

Minor bleeding

1 Local haemostatic measures.
2. Mechanical compression.
3. Tranexamic acid orally 15 to 25 mg/kg two to three times a day.
4. Delay next dose of rivaroxaban or apixaban or discontinue treatment.

Moderate to Severe Bleeding

Contact consultant haematologist on call:

1.Local measures.
   - Mechanical compression
   - Consider surgical intervention or wound packing
2. Fluid replacement.
   - Maintain good urine output
3. Blood product transfusion.
   - Consider platelets if levels less than 70 to 80 x 109/L or patient on antiplatelet drug
   - Give tranexamic acid 1g by slow IV injection over 10 minutes followed by 1g three times daily by slow iv infusion over 8 hours
   - Octaplex®, APCC and rFVIIa (NovoSeven®)[5] should be considered after discussion with haematologist

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