Management of Overanticoagulation for Patients on Warfarin or Phenindione

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Guideline Content

1.0 Introduction

Warfarin is an oral anticoagulation and is used in a variety of conditions. These include atrial fibrillation with a target INR 2.5 and range 2.0-3.0, the presence of thromboembolism with a target INR of 2.5 and range 2.0-3.0 or after the replacement of a heart value where target INR can be either 3.0 (range 2.5-3.5) or 3.5 (range 3.0-4.0). Phenindione is used as an alternative to warfarin when warfarin cannot be tolerated. Warfarin and phenindione slow down the blood clotting process and the risk of bleeding increases as INR increases. Direct Oral Anticoagulants (DOACs) including edoxaban, apixaban and rivaroxaban are also used in atrial fibrillation and in patients with VTE but do not alter the INR. Therefore these will not be considered in this guideline. Patients with an INR greater than target should be monitored for bleeding complications and should be managed appropriately according to the British Haematology Society guidelines. Patients with a high INR should be assessed for bleeding risk and patients at high risk of bleeding with an INR ≥ 8.0 should have their anticoagulation treatment reversed using phytomenadione (vitamin K).[1]

2.0 Purpose of the Guideline

To clarify the roles of Phytomenadione and Blood Products in the reversal of anticoagulation for overanticoagulation or bleeding in patients treated with Vitamin K Antagonists (warfarin or phenindione). To ensure that all patients that have a high INR are closely monitored and are assessed for bleeding risk. Patients with a high bleeding risk and an INR ≥ 8.0 should have their anticoagulation treatment reversed using phytomenadione. Direct Oral Anticoagulants (DOACs) do not alter the INR and therefore will not be considered in this guideline.

3.0 Scope of the Guideline

This document is applicable to all practitioners managing patients anticoagulated with warfarin or phenindione.

4.0 Definition of Terms

PCC – Prothrombin Complex Concentrate

This is a pooled fractionated plasma product containing a high concentration of the Vitamin K dependent coagulation factors (FII, FVII, FIX & FX). The current PCC available from the Ayr and Crosshouse laboratories is Beriplex but Octaplex is also used.

FFP – Fresh Frozen Plasma

This is a single donor plasma product containing all the coagulation factors at the normal concentrations found in the plasma. It takes 20-30 minutes to fully thaw a unit of FFP. Up to 4 units can be thawed at the same time.

INR – International Normalised Ratio.

A means of presenting a patient's prothrombin time in a manner that is easier to interpret for the monitoring of warfarin and other coumarin anticoagulant drugs.

5.0 Policy Content

5.1 Guidance for Inpatients

Major Bleeding

Where there is evidence of major bleeding, in particular bleeding from the gastro-intestinal tract (GIT) or central nervous system (CNS), warfarin/phenindione should be stopped and reversal should be with a combination of PCC and phytomenadione. Phytomenadione should be given intravenously at a dose of 5mg. This should be administered slowly over 30 seconds. Treatment in the presence of major bleeding is irrespective of the INR.

Reversal of anticoagulation in life threatening haemorrhage is discussed in a separate guideline (Major Haemorrhage Protocol).

PCC versus FFP

PCC contains a higher concentration of the necessary coagulation factors than FFP and can therefore provide a greater degree of reversal. PCC does not require to be thawed prior to use and is therefore available without delay. The volume of factor replacement is much less with PCC compared to FFP thus reducing any concerns regarding fluid overload.

It is recommended that PCC be used in this setting however notwithstanding the above comments FFP remains a useful agent and is effective in the management of bleeding associated with overanticoagulation.

Minor bleeding or No bleeding

Where there is no major bleeding anticoagulant reversal is guided by the degree of over-anticoagulation as described by the INR. Patients with a heart valve replacement and target INR 3.5 should receive a lower dose of phytomenadione.

INR ≥ 8.0

Phytomenadione should be given (2mg or 1mg orally or 1mg IV see note below on phytomenadione preparations). When administered intravenously phytomenadione should be given slowly over 30 seconds. Warfarin/phenindione should be omitted and INR checked daily. When restarted the dose of warfarin/phenindione should be reduced slightly.

INR 6.0-7.9

For asymptomatic patients with INR in this range it is advised to omit warfarin/phenindione for 3 days then recheck INR. When restarted the dose of warfarin/phenindione should be reduced slightly.

INR 4.0-5.9

Generally dose modification is the only action required in these circumstances.

- INR 4.0-4.9
    - If target INR is 2.5 omit one dose and reduce the dose of warfarin/ phenindione. The INR should be rechecked in 3-5 days.

    - If target INR is 3.5 reduce the dose of warfarin/ phenindione. The INR should be rechecked in 3-5 days.

- INR 5.0-5.9
    - If target INR is 2.5 omit two doses and reduce the dose of warfarin/phenindione. The INR should be rechecked in 3-5 days.

    - If target INR is 3.5 omit one dose and reduce the dose of warfarin/phenindione. The INR should be rechecked in 3-5 days.

This advice is summarised in appendix 1

Phytomenadione Preparations
Phytomenadione (Konakion® MM, Konakion® MM Paediatric)
Two preparations of Vitamin K are available; both contain the same drug at the same dose/ml but with different excipient formulations such that **Konakion® MM** is suitable only for IV administration while **Konakion® MM Paediatric** can be used IV, IM or orally. It should be noted that the use of **Konakion® MM Paediatric** for Warfarin reversal in adults is an off label indication. Please refer to the NHS Ayrshire & Arran Code of Practice for Medicines Governance Section 9(a) – unlicensed medicines for further information:
http://athena/adtc/DTC%20%20Code%20of%20Practice/ADTCMG09(b).pdf

Notification of Anticoagulant Monitoring Team

It is the responsibility of the team treating the patient to ensure that the patient's usual anticoagulant monitoring team is notified and all relevant information passed on including inpatient anticoagulation chart. A copy of appendix 2 should also be sent to the relevant anticoagulant monitoring team.

Elective reversal of anticoagulation in the peri-operative setting is discussed in a separate guideline (ADTC 117).

5.2 Guidance for Anticoagulant Clinics

- When a patient attends an anticoagulant clinic with an INR ≥ 8 they should be assessed by the anticoagulant practitioner for any signs of bleeding or any complications that require intervention by the Consultant Haematologist. The Consultant Haematologist should be contacted if the patient has any signs of bleeding and should be admitted to hospital for further intervention if necessary.

- All patients with an INR≥8 should be treated with phytomenadione to reverse anticoagulation.
- Phytomenadione 2mg/0.2ml injection should be administered orally. The preparation used is Konakion MM Paediatric. The oral route of administration of this preparation is unlicensed and the patient should be made aware of this.
- The reasons for elevated INR and treatment should be clearly documented in the patient's anticoagulant notes and it should be noted that the oral route of administration is unlicensed for this product.
- The patient's INR should be recorded in the dosing record section of the anticoagulant notes along with the dose and route of administration of phytomenadione.
- Phytomenadione 2mg (0.2ml) should be administered to all patients with INR≥8 except patients with a heart valve replacement with a target INR 3.5. These patients should receive phytomenadione 1mg (0.1ml).
- Phytomenadione should be prescribed in the 'medicines to be given once only' section of the medicine prescription sheet and should be signed by the practitioner prescribing and administering it. An addressograph label should be attached to the prescription sheet and it should be filed in the patient's anticoagulant notes.
- The patient should be given an information leaflet entitled "treatment of overanticoagulation" (reference XHW05-066-GD) explaining why phytomenadione has been administered and what happens next. They should be advised to show this leaflet to relatives or carers to ensure that they are aware of treatment given.
- The INR should also be recorded in the patient's handheld Anticoagulant Therapy Record or "yellow book" along with written instructions to omit warfarin/phenindione. The patient should be advised not to take any warfarin/phenindione until advised otherwise. The dose and route of administration of phytomenadione should also be recorded in the Oral Anticoagulant Therapy Record Book.
- The date of the next two follow up appointments should be recorded in the handheld Oral Anticoagulant Therapy Record Book. One of these appointments should be for the following day at either an anticoagulant clinic or one of the designated hospital wards (ward 3A at University Hospital Crosshouse (haematology) or the Ambulatory Care Unit at University Hospital Ayr) and the other should be for the next routine clinic appointment.
- If the patient has to attend one of the designated hospital wards the practitioner should contact the ward to arrange a suitable appointment time for the patient to attend. A copy of Appendix 2 should be completed with details of treatment given and should be attached to the front of the patient's anticoagulant notes. This should be sent to the appropriate clinic/ward for their appointment the following day.
- A letter should be sent to the patient's GP surgery to inform them that phytomenadione was administered and of the INR recorded. This letter can be found on the DAWN AC computer database.

5.3 Guidance for Ward/Clinic Follow-up (Next Day)

- If the patient attends one of the designated hospital wards for follow-up the next day a venous sample should be taken for INR and sent to the laboratory for analysis. When the INR result becomes available the ward doctor should be informed and he/she should decide if warfarin/phenindione has to be restarted and should advise on an appropriate dose. The patient should be contacted by telephone to inform them of whether to restart warfarin/phenindione and of what dose to take. It is therefore important to ensure that the patient will be contactable by telephone later in the day.
- The patient or their relative/carer should be asked to write the dosing instructions in their Anticoagulant Therapy Record "yellow book" and should be advised to show this to the Practitioner at the next anticoagulant clinic appointment.
- The designated hospital ward must make arrangements for the anticoagulant notes to be sent to medical records to ensure that they are available for the next anticoagulant clinic appointment.
- If the patient attends one of the anticoagulant clinics for follow-up, a venous sample should be taken and analysed as normal using a portable analyser. The Practitioner at the clinic should advise the patient on what dose to take until their next routine appointment.

6.0 Related NHS Ayrshire & Arran Documents

Perioperative Management of the Patient on Oral Anticoagulant and Antiplatelet Agents (ADTC 117)

Major Haemorrhage Protocol

7.0 References

1. Guidelines on oral anticoagulation with warfarin: fourth edition. British Journal of Haematology 2011; 154: 311-324
2. Phytomenadione (Konakion MM). Summary of Product Characteristics. Available from: http://medicines.org.uk (Accessed 19/02/2013. Last updated on eMC 17/08/2012)

8.0 Appendices

Appendix 1

Guideline for the reversal of warfarin/phenindione in bleeding and over-anticoagulation – Summary[1]

Clinical Situation	Action
Major Bleeding	
Any INR level	- Admit patient to hospital - Stop warfarin/phenindione - Give phytomenadione 5 mg IV - Give Prothrombin Complex Concentrate (Beriplex/*Octaplex*) Contact Haematologist to discuss dose of PCC or alternative factor replacement options
No bleeding or minor bleeding	
INR≥8.0	-Give phytomenadione 2mg orally or 1mg IV. Give 1mg orally to patients with a heart valve replacement and a target INR 3.5
INR 6.0 to 7.9	- Omit warfarin/phenindione for 3 days - Recheck INR in 3 days - Restart warfarin/phenindione when INR <5.0 but reduce dose of warfarin/phenindione
INR 4.0 to 5.9	- If target INR 2.5 and INR is 4.0-4.9 omit 1 dose and reduce dose of warfarin/phenindione - If target INR 2.5 and INR is 5.0-5.9 omit 2 doses and reduce dose of warfarin/phenindione - If target INR 3.5 and INR is 4.0-4.9 reduce dose of warfarin/phenindione - If target INR 3.5 and INR is 5.0-5.9 omit 1 dose and reduce dose of warfarin/phenindione - Recheck INR in 3-5 days

Appendix 2

Reversal of Over-anticoagulation Notification

Addressograph

Usual anticoagulant clinic:

- Hospital anticoagulant clinic

  …….

- GP surgery - name and address

  ……

  ……

INR recorded:
Target range for patient:
Indication for anticoagulation:

Reason for elevated INR (if any):
If drug related please specify drug if known:

Any bleeding or complications? ❑Yes ❑No
If yes state what they are:

Phytomenadione (vitamin K) …….. mg given Route of administration IV/oral

PCC (Beriplex/Octaplex) given? Yes/No Dose……..

Please check the patient's INR on ……., and ensure that the patient is given a dose of warfarin/phenindione, if appropriate according to their INR.

Review arranged at Anti-coagulant clinic/GP surgery On (Date) …… at ……

Name of Clinician/Practitioner: Signed

Designation: Date