Developed for Scotland by the National Plasma Product Expert Advisory Group (NPPEAG)

Protocol for the Reversal of Over-Anticoagulation with Warfarin
Title: Protocol for the reversal of over-anticoagulation with warfarin

Replaces: NPPEAG 2010 Guideline

Lead Author/Co-ordinator: Consultant Haematologist

Subject (as per document registration categories): Clinical Policy/Protocol

Keyword(s): Bleeding, warfarin, anticoagulants

Policy, Protocol, Procedure or Process Document: Protocol

Document application: Acute Sector

Purpose/description: To provide best management for patients who are over-anticoagulated on warfarin in order to reduce the risk of bleeding and to treat active bleeding in those in whom it has occurred.

Review: Review 2 yearly. Any significant changes in evidence will result in earlier alteration

Responsibilities for review of this document:

Lead Author/Co-ordinator: Consultant Haematologist

Review date: June 2018
Contents

Introduction 1

Protocol Application 1

Aims 1

Development 1

Guide to Reversal of Oral Anticoagulation on Warfarin 2-3

Bibliography 4

Distribution List 4

Appendix 1 – List of Abbreviations 5
Introduction
Around 1 to 1.5% of the population take warfarin to prevent thrombosis. The main complication of warfarin is bleeding. Major or life-threatening bleeding is seen in 2% of patients on warfarin each year. Fatal haemorrhage complicates warfarin use in 0.25% of patients annually.

Anticoagulation may result in excessive prolongation of clotting times without bleeding or with bleeding.

Protocol Application
This protocol based on the available evidence is to be used for all patients on warfarin. The protocol does not deal with the peri-operative management of patients on warfarin – this should be discussed with a consultant haematologist.

Aims
The main aims of this protocol are to prevent bleeding in patients who are over-anticoagulated and to treat bleeding in those in whom it has occurred. While there are randomised controlled studies to inform on the use of vitamin K, the recommendations on the use of the prothrombin complex concentrates which contain coagulation factors II, VII, IX and X (e.g. Beriplex) are based on observational data and expert opinion. The guidance is in fitting with the recommendations of the British Committee for Standards in Haematology (Keeling et al 2011). The recommendations for partial reversal of anticoagulation in asymptomatic patients with INR values between 4.5 and 10 have been left in place despite the publication of a randomised controlled study which indicated little benefit in reversal for these patients in terms of the number of bleeding events which were prevented in comparison with a group who received placebo (Crowther et al 2009) – this remains under review.

Development
This protocol was devised by the author, reviewed by the medicines committee and by an international expert in the field and approved by the Chair of the Acute Sector Clinical Practice Committee.

The protocol was then submitted to the Acute Sector Clinical Practice Committee for final review.
GUIDE TO REVERSAL OF ORAL ANTICOAGULATION ON WARFARIN
CLASSIFICATION OF BLEEDING COMPLICATIONS

BLEEDING

♥MAJOR

Vitamin K 5 mg IV and Beriplex P/N IV
Withhold warfarin

INR ≥ 8

♥Vitamin K 2.5mg orally/IV
Withhold warfarin

Check INR at 24 hours or earlier if deterioration in clinical condition

♥Vitamin K 1mg orally
Withhold warfarin

Reduce warfarin dose or withhold one dose

NO BLEEDING

INR 5 – 7.9

♥High Risk

Low Risk

MINOR

♥Vitamin K 2.5mg orally/IV
Withhold warfarin

Check INR at 24 hours

Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Low Risk

INR 5 – 7.9

♥High Risk

Low Risk

INR ≥ 8

♥Vitamin K 2.5mg orally/IV
Withhold warfarin

Check INR at 24 hours

Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Low Risk

INR 5 – 7.9

♥High Risk

Low Risk

INITIAL INR | BERIPLEX DOSE
---|---
2.0-3.9 | 1 ml/kg (approx 25 iu/kg)
4.0-6.0 | 1.4 ml/kg (approx 35 iu/kg)
>6.0 | 2 ml/kg (approx 50 iu/kg)

Immediate check PT and APTT

Adequate correction

Repeat PT and APTT in 4-6 hours

Adequate correction

Consider other factors contributing to prolonged coagulation tests
- DIC
- Congenital coagulation factor deficiency
- Liver disease
- Lupus inhibitor
- Inadequate replacement

SEEK HAEMATOLOGICAL ADVICE
**Classification of Haemorrhage**

**Fatal**
- Death due to haemorrhage (Demonstrated at autopsy, radiologically or clinically obvious)

**Major♥**
- Intracranial (CT or MRI documented)
- Retroperitoneal (CT or MRI documented)
- Intra-ocular (excludes conjunctival)
- Spontaneous muscle haematoma associated with compartment syndrome
- Pericardial
- Non-traumatic intra-articular
- Any invasive procedure to stop bleeding
- Active bleeding from any orifice plus BP ≤90mmHg systolic, or oliguria or ≥20g/l fall in haemoglobin

**Minor**
- Any other bleeding that would not influence your decision to anticoagulate a patient

---

**Cautions**

- Beriplex P/N contains heparin and is contraindicated in patients with heparin induced thrombocytopenia (present or previous)
- Beriplex P/N is also relatively contraindicated in patients with:
  1. An increased risk of thrombosis
  2. Angina pectoris and after recent myocardial infarction

- Maximum single dose of Beriplex is 5000iu
- In all clinical situations an assessment of the likely risks and benefits of administration needs to be made.

- In disseminated intravascular coagulation, prothrombin complex-preparations (e.g. Beriplex) may only be administered after termination of the consumptive state.

- Intravenous vitamin K may rarely cause anaphylaxis. Administration should be:
  - By slow IV bolus
  - Withheld in patients with a history of previous severe allergic reaction to vitamin K

- Oral Vitamin K – preparation used is the preparation for injection (10mg/ml) Konakion (Roche). Dilute dose in small amount of juice/water after drawing up in an oral syringe

- Standard risk patients do not require INR reversal at INR 5 – 7.9 but correction should be considered in “high risk” patients whose risk of bleeding is approximately 15 fold higher.

**Patients at high risk of warfarin associated bleeding:**
- Elderly
- Previous GI bleed
- Previous CVA (haemorrhagic or ischaemic)
- Anaemia
- Renal failure
Bibliography


DeZee KJ, Shimeall WT, Douglas K,M, Shumway NM, O’Malley PG. Treatment of excessive anticoagulation with phytonadione (vitamin K). Archives Internal Medicine 2006;166:391-397

Appendix 1

List of abbreviations

IV – intravenous
INR – international normalised ratio
PT- prothrombin time
APTT- activated partial thromboplastin time
CT- computerised tomography
MRI – Magnetic reasonance imaging