

Treatment of Patients Overanticoagulated with Warfarin

Scope

This guideline applies to the management of possible hemorrhagic complications in patients overanticoagulated with warfarin. It applies only to adults 19 years of age and over. This is one of four related documents to be published concurrently. See also:

- *Initiation and Maintenance of Warfarin Therapy*
- *Management of Warfarin Therapy During Invasive Procedures and Surgery*
- *Warfarin: A Guide for Patients*

RECOMMENDATION 1: Establish the cause of elevated INR

The causes of elevated INR should always be investigated. In many cases, merely correcting the cause (e.g. dose, compliance, change in diet, liver disorder or other illnesses) will bring the INR back into the patient's target range.

RECOMMENDATION 2: Management of elevated INR with no or minor bleeding

a) INR < 5

- Omit 1 dose
- Increase the frequency of INR monitoring (2 to 3 times a week)
- Resume therapy at 10-20% lower dose

INR 5 – 9

- Omit 1 to 2 doses
- Increase the frequency of INR monitoring (daily)
- Resume therapy at 10-20% lower dose when INR reaches patient's target range
- If the patient is at high risk of serious bleeding, consider administering vitamin K₁* 2 to 3 mg orally

INR > 9

- Discontinue warfarin temporarily
- Consider administering vitamin K₁* 3 to 5 mg orally
- Increase the frequency of INR monitoring (daily) and give additional vitamin K₁ if INR is not substantially reduced by 24-48 hrs
- Resume therapy at 20% lower dose when INR reaches patient's target range and monitor INR closely until stable. Consider more frequent routine INR monitoring

* If Vitamin K₁ is not available in your local pharmacy, it can be obtained from your local ER.

RECOMMENDATION 3: Management of elevated INR with serious or life threatening bleeding†

- If patient's clinical status is compromised due to bleeding, admit to an acute care facility for assessment and management
- Discontinue warfarin temporarily
- Attempt local control of bleeding
- Give frozen plasma or other blood products such as recombinant factor VIIa or prothrombin complex concentrate
- Administer vitamin K₁, 5-10 mg by slow intravenous infusion (rate < 1 mg/min)
- Monitor INR 6 hourly and treat with repeat dosing of vitamin K₁ and/or frozen plasma as necessary.

† Serious or life threatening bleeding includes gastrointestinal, retroperitoneal, intracranial or intraocular hemorrhage, or bleeding from any orifice plus any of the following:

- BP < 90 mm Hg systolic
- oliguria or drop in hemoglobin > 20 g/L
- bleeding requiring transfusion or hospitalization
- an invasive procedure to stop the bleeding.

Rationale

The major challenge in warfarin therapy is its narrow therapeutic range. Even a mild degree of overanticoagulation may lead to hemorrhage. Bleeding is the most serious complication of warfarin therapy.¹⁻⁴ The average yearly bleeding complication rates are 0.1-1% for fatal bleeding, 0.5-6.5% for major bleeding, and 6.2-21.8% for minor bleeding.⁴

Risk factors for bleeding among patients with elevated INR include first year of warfarin therapy, age > 65 years, hypertension, alcoholism, liver disease, or previous history of gastrointestinal bleeding and/or stroke.⁴

The most common sites of serious bleeding are gastrointestinal tract, genitourinary tract, and soft tissues including wounds.¹ An underlying cause should always be considered.

Management of overanticoagulation includes investigation and correction of underlying cause, bringing the INR back into the patient's target range by changing warfarin dosage and administration of vitamin K₁ or blood products, and management of active bleeding.

Vitamin K: Oral vitamin K₁ therapy is safe, effective and convenient.^{6,7} Subcutaneous vitamin K₁ should be avoided as it may be absorbed unpredictably. Likewise, intramuscular vitamin K₁ should be avoided as it promotes intramuscular hemorrhage. Intravenous vitamin K₁ is the most predictable,⁶ but can cause facial flushing, diaphoresis, chest pain, hypotension, dyspnea, anaphylaxis and cerebral thrombosis, and should be given only in emergency situations and by slow infusion. Some effect of oral vitamin K₁ therapy on INR is usually observed within 24 hours and with intravenous vitamin K₁ in 6-8 hours.^{6,7} Patients who have received vitamin K₁, particularly parenteral doses above 5-10 mg, may be difficult to reanticoagulate. Accordingly, doses of vitamin K₁ should be kept as low as feasible. An oral formulation of vitamin K₁ is no longer available in Canada; most pharmacies administer oral doses of the parenteral preparation in juice. Oral vitamin K₁ therapy may not be appropriate for patients with disorders that may affect the absorption of vitamin K₁ such as sprue or other malabsorptive syndromes. If emergency reversal of warfarin is required for life and limb threatening hemorrhage, plasma or other blood products such as prothrombin complex concentrate or recombinant factor VIIa may be used⁴ in consultation with a specialist.

References

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Sponsors

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