

CASE: 45 y/o male receiving warfarin therapy for h/o DVT and PE with INR goal of 2.5-3.5 admitted to the hospital for planned follow-up surgery secondary to hernia repair. Patient's normal drug regimen was comprised of non-interacting meds.

Warfarin therapy withheld x2 days for prior hernia surgery; INR was 1.43 @ time of procedure.

Warfarin therapy was again withheld, patient given vitamin K 10mg IV and 2U FFP pre-op. Therapeutic INR value was reached 11 days post-op with aggressive warfarin dose titration.

Use Of Phytonadione (Vitamin K) - The Correct Choice For Reversal Of The INR

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Options-SC, IV, PO

◆IV administration of vitamin K provides rapid correction of INR (seen within 6-8 hours) in circumstances where it may be warranted (INR>20, patient with bleeding, immediate surgery requirement) however the chance of overcorrection is greatly increased than with other methods

◆Oral vitamin K has been proven in some studies to be more effective than the SC route, and one may expect results within 24 hours, 48 hours if INR > 9

◆Low-dose IV (<0.5mg) and oral dosing (2.5-5mg) has shown to be an alternative to high-dose IV(1-10mg) and SC routes (1-10mg) and provides for less overcorrection of the INR

◆IV and oral administration is more rapid and effective than SC administration

Guidelines for Management of Nontherapeutic INR's

➤INR supratherapeutic but <5 w/o significant bleeding:

Omit dose or lower dose; resume therapy at lower maintenance dose when INR in therapeutic range

➤INR >5.0 and < 9.0 w/o significant bleeding or in patients requiring rapid reversal:

Omit warfarin dose

Vitamin K 1mg IV or Vitamin K 2.5mg SQ or PO; resume therapy when INR returns to therapeutic range or when appropriate

➤INR >9 and <20 and rapid reversal not necessary:

Omit warfarin dose

Vitamin K 2.5mg IV or 5mg SC or PO; resume warfarin once INR returns to therapeutic range or when appropriate

➤INR >20:

Omit warfarin dose.

Administer FFP (10ml/kg) with vitamin K 5-10mg IV or 5mg PO/SC

Resume warfarin once INR returns to therapeutic range

Points to consider:

1)Vitamin K doses of >5mg have been associated with warfarin resistance, the effect of which can last from 7-14 days

2)Due to risk of allergic reaction, Vitamin K IV must be administered at a rate of no greater than 1mg/minute

3)Vitamin K should not be administered IM due to significant risk of hematoma

4)Use clinical judgment in risk versus benefit (thrombosis vs. bleed) when considering reversal of anticoagulation

WARFARIN RESISTANCE

- ◆ Extensive literature is not available however studies indicate that genetic mechanisms are responsible for hypersensitivity and resistance
- ◆ One form of hereditary resistance involves increased clearance of warfarin, possibly due to gene duplication of cytochrome P450 enzymes which may result in an ultra-rapid metabolism phenotype
- ◆ Second form involves pharmacodynamic mechanisms -patients require high doses of warfarin, have normal kinetics, high blood concentrations of the drug, and normal half-lives of blood clotting proteins. These patients are also hyper-responsive to Vitamin K.

References:

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