Warfarin

Warfarin is a medication used in patients requiring chronic anticoagulation, such as those with a history of DVT or PE, or with atrial fibrillation or artificial heart valves. It works by inhibiting epoxide reductase, leading to interference in the synthesis of vitamin K-dependent clotting factors (II, VII, IX, X, C and S).Side effects of warfarin include bleeding, which necessitates the monitoring of a patient's INR, as well as necrosis, which is more common in protein C-deficient patients. Warfarin necrosis is caused by an initial prothrombotic state caused by the rapid decline in proteins C and S, and manifests as gangrene and massive skin necrosis. This drug is metabolized through the P-450 pathway, and thus providers should be cautioned of other medications effecting this pathway. Warfarin is a teratogen and can cause serious pregnancy complications.Reversal of warfarin's effects can be achieved rapidly with administration of vitamin K and fresh frozen plasma.



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Mechanism of Action

Interferes with Vitamin K-dependent Clotting Factors
Interfering with Viking (K) King making Clogs
This medication inhibits epoxide reductase. Due to this, vitamin K is unable to be reduced to its active form--hydroquinone (vitamin KH2). This prevents gamma-carboxylation of glutamic acid on the clotting factors II, VII, IX, X and proteins C and S. These factors are then incapable of binding to blood vessel endothelium, and become biologically inactive.

Extrinsic Pathway
X-triscuit Pathway
The effect of warfarin takes several days to develop because of the half-lives of already activated factors. This medication acts on the extrinsic pathway by preventing the activation of vitamin K, warfarin reduces the production of factors II, VII, IX and X (also Protein C and S).

Bridge with Heparin
Bridge with Hippie-heron
Heparin is usually administered with warfarin to prevent thrombosis. This is because for the first 4-5 days, though warfarin is preventing active factors from being formed, the previously formed factors must degrade. Due to their shorter half- lifes, Protein C and Protein S get degraded before the pro-coagulant factors. Hence , for a short period of time, the patient becomes pro-thrombotic.

Indications

Chronic Anticoagulation
Crone with Ant-tie-clogs
This medication is used to decrease the tendency to form or to prevent clots in patients at risk for their formation. Common ailments requiring chronic anticoagulation include atrial fibrillation, artificial heart valves, previous pulmonary embolism and previous deep vein thrombosis.

Side Effects

Bleeding
Bleeding
Hemorrhage is the most common side effect of warfarin administration. For this reason, physicians monitor patient PT and INR to make sure that it is only 2-4 times the normal range.

Necrosis
Necrosis-crow
Though rare, warfarin necrosis is a very serious side effect seen in patients taking this medication and leads to massive thrombus formation, causing skin necrosis and gangrene. This side effect stems from the initial inhibition of proteins C and S, leading to a prothrombotic state when starting this medication. Patients who are protein C deficient are more susceptible to this effect.

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Cytochrome P450

Side-toe-chrome P450-rocket

Warfarin is metabolized through the cytochrome P-450 pathway, and medications which induce or inhibit this pathway may lead to adverse effects. P-450 inhibitors would decrease the metabolization of warfarin, and can lead to increased bleeding risk. P-450 inducers could cause decreased bioavailability of warfarin and decreased anticoagulation.

Contraindications

Pregnancy

Pregnant-woman with Caution-tape

This drug has several effects on the fetus. It passes through the placenta, and may cause fetal bleeding. It is also a known teratogen, and can lead to skeletal abnormalities. Administration in the third trimester may give rise to CNS disorders.

Antidote

FFP + Vitamin K

FFP Frozen Plasma-tv and Viking (K) King

If reversal of warfarin action is necessary, or if there is a case of severe bleeding, vitamin K + fresh frozen plasma are administered. These can lead to rapid reversal of warfarin's effects.

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