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Warfarin Side Effects

Warfarin (also known under the brand name Coumadin), a blood thinner that has been around for decades, can trigger a range of side effects. Some of the side effects include nausea, vomiting, diarrhea and abdominal pain. The most common side effect — bleeding — can be life-threatening. Rare side effects include stroke, gangrene and death.

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While warfarin can be a lifesaver for patients suffering from atrial fibrillation and other conditions that may cause a fatal blood clot, the drug also has its drawbacks.

Bleeding is the most common side effect and is described in a black-box warning on the drug's label. The side effect can be avoided through frequent blood tests and dose adjustments.

Vitamin K injections are used in bleeding emergencies to reverse the drug's blood-thinning action.

Common Side Effects

The drug may cause side effects ranging from inflammation of the skin (dermatitis) to nausea, vomiting, diarrhea, bloating and abdominal pain.

Other complications include:

- **Hypersensitivity or allergic reaction**
  can result in hives as well as anaphylaxis. When anaphylaxis occurs, the condition can become deadly and requires immediate emergency medical attention.
- **Hepatitis (inflammation of the liver)**
  cholestatic hepatitis has been found to occur in patients taking both warfarin and ticlopidine (a drug that also helps to prevent blood clots), at the same time.
- **Vasculitis (an extreme reaction to a drug)**
  leads to inflammation and damage to blood vessels, primarily in the skin.

Less Common Side Effects

Less common complications include bleeding in the brain, known as a hemorrhagic stroke.

Patients taking warfarin are required to undergo regular blood tests to monitor the drug's effectiveness. Avoiding monitoring can result in incorrect dosages and an increased risk for excessive, potentially life-threatening bleeding of the gastrointestinal tract and other regions of the body.

Warfarin is associated with these rare but serious side effects: tissue death, or gangrene, and calcifylaxis, which involves the calcification of a patient's blood vessels. The painful condition often leads to sepsis and organ failure and is fatal 60 to 80 percent of the time.

Other serious side effects can include acute injury to the kidneys and cholesterol embolisms (or clots) that travel through the bloodstream and become lodged in various blood vessels.

Bleeding Risks

Normally, when a person bleeds, clots form to stop the flow. But, bleeding can last much longer in individuals taking blood thinners, and may require emergency medical attention. Wounds and bruises may take longer to heal.

The oldest anticoagulant is warfarin, also known as Coumadin or Jantoven.

Major and sometimes deadly bleeding usually occurs within the first month of a patient using warfarin, according to the drug's label. Patients are more likely to experience this side effect if they have an elevated International Normalized Ratio (INR), a measure of how long it takes a person's blood to clot.

While an INR of 1.1 or less is normal in a healthy person, individuals using warfarin usually need to keep their INR in a therapeutic range of 2.0 to 3.0. Every single point increase in a person's INR doubles the bleeding risk. An INR over 4.0 can be a sign of thinning the blood too much, which increases a patient's risk for major bleeding.

Bleeding Risk Factors for Patients Taking Warfarin Include:

- Being 65 or older
- Having a history of a highly variable INR measure
- History of gastrointestinal bleeding
- High blood pressure
- History of stroke
- History of heart disease
- Kidney problems
- Certain genetic factors
- Using certain medicines together with warfarin, for example, aspirin
- Using warfarin for a long time period
- Anemia (a condition in which the number of healthy red blood cells is too low)
- Diabetes
- Cancer
- Trauma

Internal bleeding can include gastrointestinal bleeding as well as bleeding in the brain. Both conditions can be fatal.

A 2005 study in the Journal of General Internal Medicine examined bleeding risk among more than 1,200 patients taking warfarin at an outpatient Veterans Administration (VA) anticoagulation clinic. The patients were divided into three groups based upon the presence or absence of various risk factors: low, intermediate, or high-risk groups.

The study found that the patients in the high-risk group had a 10.6 percent chance of a major bleeding episode. Patients in the moderate- and low-risk groups had a 2.5 percent and 0.8 percent risk, respectively.

Tissue Necrosis

The drug can cause tissue necrosis, or the death of body tissue because of low blood supply to them. Gangrene is a tissue necrosis that affects a large area of tissue, causing the tissue to breakdown and die.

Tissue necrosis is a rare occurrence side effect that usually occurs within a few days after starting warfarin. According to published evidence, one in 10,000 patients taking warfarin will develop skin necrosis (2004 case report in the Annals of Dermatology). It affects men four times as frequently as women. Risk factors include: obesity, viral infection and liver disease, as well as several protein deficiencies (for example, deficiencies in proteins C and S).

The symptoms include a bluish or blackish discoloration of the skin along with pain and numbness in the region. The skin eventually breaks down into sores that have a foul-smelling discharge. Gangrene and necrosis can affect the skin and internal organs. It is a dangerous and potentially deadly condition that usually requires surgery, antibiotics and oxygen therapy. Severe cases can lead to amputation.

FACT

While warfarin-induced skin necrosis (WISN) usually develops within three to 10 days of starting the drug, it can occur months or years later.

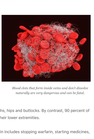
Source: International Journal of General Medicine

A blood clot can form together with tissue necrosis at the location where the tissue death has occurred. Blood clots can block blood flow in affected areas, break apart, and even move to more critical parts of the body, such as the brain or lungs.

Calcification of Blood Vessels

Calcification of blood vessels, also known as calcifylaxis or calcium uremic arteriolopathy, has been reported in patients taking warfarin with or without end-stage kidney disease, according to the drug's label.

Calcifylaxis is a serious, often fatal, condition in which the blood vessels become blocked by a build-up of calcium that prevents blood from flowing to the skin and internal organs. The lack of blood flow leads to tissue damage and necrosis (death of tissue).



A blood clot, pictured above, can block blood flow.

The first signs of calcifylaxis are usually ulcers that form in the skin and then become infected. The lage are most often affected. These ulcers may start as tender red areas that eventually develop a twisted pattern, or mottled, lace-like purplish discoloration of the skin. Eventually, the ulcerations become gangrenous, and a person may develop sepsis.

Unfortunately, the effects of calcifylaxis are often irreversible and many people die from infection within a few months.

According to a on "warfarin-induced calcifylaxis," the death rate is as high as 60 to 80 percent.

Distinguishing between warfarin-induced calcifylaxis (WIC) and warfarin-induced skin necrosis (WISN) may be difficult because the signs and symptoms are similar, as are many of the complications.

Blood clots that form inside veins and don't dissolve naturally are very dangerous and can be fatal.

Only a skin biopsy can definitively differentiate between the two conditions. But the location of lesions can also provide clues. WISN lesions usually appear in fatty regions, such as the breasts, thighs, hips and buttocks. By contrast, 90 percent of patients with WIC develop lesions on their lower extremities.

Treatment of calcifylaxis from warfarin includes stopping warfarin, starting medicines, wound care and pain management.

Kidney Injury, Emboli and Other Side Effects

Warfarin is linked to acute (sudden onset) kidney injury in patients who have a history of kidney disease. Kidney injury may be related to excessive blood thinning and blood being present in the urine. Drug labeling for warfarin recommends more frequent monitoring of blood-thinning effects in patients with kidney problems.

The drug may increase the risk of the release of atheromatous plaque emboli, or hardened cholesterol and fat particles, that can travel throughout the bloodstream, become lodged in small blood vessels and block blood flow.

This condition can result in various signs and symptoms depending on where the embolization (the passage of the clot and process of obstruction) occurs. The most common symptoms involve the skin, gangrene of the extremities and kidney failure.

Cholesterol emboli most commonly affect the kidneys, followed by the pancreas, spleen and liver. When intercontinental affect the feet, the condition is referred to as "purple toes syndrome." The symptoms of "purple toes syndrome" include pain and discoloration to the pads of toes.

Risk Factors for These Side Effects Include:

- Moderate to severe liver problems
- Infectious diseases or disturbances of intestinal bacteria
- Use of an indwelling catheter
- Moderate to severe high blood pressure
- Eye surgery
- Polycythemia vera (blood cancer that increases the number of red blood cells in the bloodstream)
- Diabetes (high blood sugar)
- Inflammation of blood vessels

Please seek the advice of a medical professional before making health care decisions.

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