FIBRINOLYTIC DRUGS

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In the last issue of Sutureline, we addressed antiplatelet and anticoagulant drugs in the Student Corner. In this article, we will finish investigating fibrinolytic drugs! Recall that antithrombotic drugs are commonly used for a host of medical conditions in which thrombi have or are likely to form including atrial fibrillation, coronary artery disease, deep vein thrombosis, and pulmonary embolism. We know that there are important categories of antithrombotic drugs that differ in their mechanism of action.

⇒ Antiplatelet: inhibit platelet activation or aggregation

⇒ Anticoagulant: affect fibrin formation

⇒ Fibrinolytic: degrade fibrin

The rest of this article will look at the fibrinolytic drugs and give you key points about the most common drugs and how they work.

Fibrinolysis
As their name implies, fibrinolytic drugs all break down fibrin, through enzymatic and biochemical reactions. Dissolution of a clot is the process called fibrinolysis, a process in which fibrin is degraded and the foundation of the clot is disrupted. Thus fibrinolytic drugs are used to dissolve an already formed clot. This is an important point. Fibrinolytic drugs are not intended to be used to prevent clots from forming!

Fibrinolytics are used to disrupt clots that have formed in situations such as acute myocardial infarction, acute ischemic stroke, and massive pulmonary embolism. In all of these cases, rapid clot dissolution is the main goal with the hope of restoring perfusion to the heart, preventing neuronal death in the brain, or restoring pulmonary artery function. These drugs can also be used for arterial and venous thrombi in the legs, by administration through a catheter to the occluded site.

FIBRINOLYTIC AGENTS

Fibrinolysis begins with activation of a proenzyme called plasminogen. Two other key players, thrombin and tissue plasminogen activator (t-PA), are released by cells from the lining of the injured blood vessel. t-PA converts plasminogen to an active form called plasmin, which then degrades fibrin.

The following are names of some fibrinolytic agents:

• Streptokinase

• Anistreplase

• Alteplase
• Reteplase
• Tenecteplase

Streptokinase and anistreplase both work with a plasminogen-streptokinase complex, basically meaning that they form a stable complex which activates additional plasminogen in the blood. They are not considered “fibrin specific,” but rather indirectly affect fibrin by increasing the formation of plasmin which breaks down fibrin and fibrinogen. Streptokinase comes from streptococcal bacteria. It is antigenic and can cause allergic reactions in patients, especially in patients with 

Alteplase, reteplase, and tenecteplase are “fibrin specific” drugs that selectively act on plasminogen which is fibrin bound. The drugs alteplase and reteplase are t-PA that has been produced by recombinant DNA technology. Tenecteplase is tissue-type t-PA that has been genetically engineered and is also used in the treatment of ischemic stroke, peripheral arterial occlusion, deep vein thrombosis, and pulmonary embolism.

ADVERSE EFFECTS

Since the purpose of fibrinolytics is to dissolve blood clots, this can cause excessive bleeding as a result of the alteration to the blood’s hemostatic abilities. Naturally occurring t-PA is produced at levels that does not cause systemic levels of plasmin generation. When fibrinolytics are used, there is the risk of causing a “systemic fibrinolytic state” resulting from high levels of unopposed plasmin in the blood. This systemic fibrinolytic state means that there is a reduction in the blood’s hemostatic abilities and therefore an increased risk of bleeding. This also means that you need to avoid using these medications in the following patients:

**General Contraindications for Fibrinolytics**

• Prior intracranial hemorrhage or hemorrhagic stroke
• Known structural cerebral vascular lesion, intracranial or intraspinal neoplasm
• Ischemic stroke within 3 months
• Suspected aortic dissection
• Active or recent bleeding (including bleeding diathesis, but excluding menses)
• Concurrent anticoagulant treatment
• Significant closed-head trauma or facial trauma within 3 months
• Platelet count <100,000/mm3
• Uncontrolled hypertension
• Suspected aortic dissection or pericarditis
There are other relative contraindications that exist. It is very important that each patient be assessed on a case-by-case basis to determine whether administration of fibrinolytics is safe and clinically indicated.

ADMINISTRATION AND MANAGEMENT

When used, streptokinase is given as an IV infusion over 30-60 minutes. Alteplase is given as an IV infusion over 60-90 minutes and may follow a bolus dose. Tenecteplase is given as a single IV dose. Reteplase is given in two IV doses, separated by 30 minutes.

In general, careful monitoring of the patient should include laboratory monitoring of coagulation factors, assessment of patient’s volume status, and any signs of significant bleeding. Avoidance of unnecessary needle sticks will help minimize the risk of bleeding from puncture sites. Allergic reactions to fibrinolytics can typically be treated with administration of an antihistamine (diphenhydramine) and a steroid.

If massive bleeding occurs, products such as cryoprecipitate, fresh frozen plasma, and platelets may be administered. Two antifibrinolytic agents that you should be aware of are tranexamic acid and aminocaproic acid. Both agents inhibit fibrinolysis and can be used in situations where excessive fibrinolysis has occurred. They both prevent and block plasminogen from binding to fibrin, thus inhibiting fibrinolysis. Tranexamic acid requires dosage adjustments for renal patients.

Disclaimer: Please note that all medications are to be taken as directed by a licensed healthcare provider. The preceding information is for educational purposes only and should always be used in conjunction with the most current recommendations and guidelines.

REFERENCES