When ischemia is caused by occlusion of an artery or vein due to a clot (thromboembolism), it is necessary to convert the clotting cascade mechanism as soon as possible to re-establish circulation and prevent death (necrosis) of the tissues distal to the obstructed artery or vein (Kee, Hayes, & McCuiston, 2012). The body’s natural fibrinolytic mechanisms, wherein plasminogen is converted to plasmin that actively destroys fibrins in blood clots, takes approximately 1 to 2 weeks to occur (Swedberg & Harris, 2012). Thrombolytic therapy promotes rapid disintegration of the thrombus or embolus in many conditions, such as myocardial infarction (MI) (Kunadian & Gibson, 2012), acute stroke (Feske, 2012), pulmonary embolism (Stein & Matta, 2012), deep vein thrombosis (DVT) (Dasari, Pappi, & Hennebry, 2012), venous thromboembolism (Findlay, Keogh, & Cooper, 2010), frostbite injury (Gross & Moore, 2012), and central venous catheter occlusion (Baskin et al., 2012).

Discovery and First Use

The first thrombolytic medication, streptokinase, was discovered by accident by Dr. William Tillett in 1933. He noted streptococci bound together with plasma, but not serum. This led him to conclude fibrinogen to the enzyme, plasmin (Vallerand, Sanoski, & Deglin, 2012). Plasmin “digests the fibrin matrix” found in clots (Kee et al., 2012, p. 669).

The more commonly administered thrombolytic agents fall under the classification of fibrin-specific thrombolytic agents, which include tissue plasminogen activators (t-PA), alteplase (Activase®), reteplase (Retavase®), and tenecteplase (TNKase®) (Vaishnavi et al., 2011). Compared to streptokinase, fibrin-specific thrombolytic agents mimic the human tissue plasminogen activator and directly activate the conversion of plasminogen to plasmin, rapidly initiating fibrinolysis (Adams & Holland, 2011; Kee et al., 2012; Vallerand et al., 2012). Aside from digesting fibrin, newer thrombolytic agents also disintegrate fibrin, fibrinogen, and clotting factors V, VIII, and XII (Kee et al., 2012). In this article, detailed information regarding prototypes for each thrombolytic classification (streptokinase for nonfibrin specific and alteplase for fibrin-specific thrombolytic agents), current evidence related to their therapeutic use, and nursing care of patients administered with thrombolytic agents will be presented.

Nonfibrin-Specific Thrombolytics: Streptokinase

Streptokinase is the lone nonfibrin-specific thrombolytic agent available in the pharmaceutical market (Vaishnavi et al., 2011). It is administered to patients who have been diagnosed with acute MI, acute massive pulmonary emboli, DVT, and occluded venous catheters (Vallerand et al., 2012). Patients with active internal bleeding, diagnosed with stroke for the past 2 months, have undergone intracranial or intraspinal surgery, an intracranial tumor, or severe uncontrolled hypertension should not receive streptokinase therapy (Drugs.com, 2013a). Streptokinase may cross the placenta, increasing the risk of bleeding within the fetus. This medication falls under pregnancy category C (animal studies show harm to fetus, but there are no adequate studies in humans) (Vallerand et al., 2012).

Streptokinase is available in powder form for parenteral administration with 250,000, 750,000, or 1.5
Among patients (Kumar et al., 2010), the reaction is commonly reported in the bacteria, the bacteria inhibited due to antibody reactions, thus reducing therapeutic effects in plasminogen activation may also be inhibited due to antibody reactions, thus reducing therapeutic effects. Alteplase is the most cost-effective thrombolytic drug available (Ghosh, Pulicherla, Rekha, Rao, & Rao, 2012); however, it lacks the other characteristics to make it the ideal thrombolytic medication. Newer thrombolytic agents have been developed for use therapeutically to reduce medication allergies, improve on the half-life of the earlier forms of streptokinase, and prevent severe adverse effects. Alteplase is the most common thrombolytic medication available in the market as it replaced urokinase as the drug of choice for clearing occluded central venous catheters (Adams & Holland, 2011).

Indications for alteplase administration include acute MI, acute ischemic or thrombotic stroke, pulmonary embolism, and occluded IV catheters (Wilson et al., 2012). It is available in sterile powder form in 2 million units per vial (Drugs.com, 2013a). When administered directly into the vein or intravenously (IV), the onset and peak of the fibrinolysis effect is immediate (Kee et al., 2011; Vallerand et al., 2012). The recommended dosage of streptokinase for patients with acute MI is 1.5 million units given direct IV continuously over 60 minutes. It can also be given directly into the coronary artery in adults with a recommended dosage of 20,000 units given bolus, followed by 2,000-4,000 units/min infusion for 30-90 minutes (Vallerand et al., 2012). A general rule of when to start thrombolytic therapy for patients with symptoms of acute MI is to administer medications within 4 to 6 hours after symptom onset (Kee et al., 2012). Initial dosage of 250,000 units of streptokinase is administered to patients diagnosed with DVT, pulmonary embolism, arterial emboli, or arterial thrombosis. Follow-up dosage of 100,000 units per hour after the initial dose differs in length of therapy according to the condition. For patients with pulmonary emboli, arterial emboli, and arterial thromboses, follow-up dosage administration should last for 24 hours, and 72 hours for patients with deep vein thrombosis (Vallerand et al., 2012).

When streptokinase is administered for the first time, the medication will go through an antibody clearance which shortens the half-life of the medication to 23 minutes (Drugs.com, 2013a; Vallerand et al., 2012). The half-life extends to 83 minutes with subsequent administrations (Vallerand et al., 2012). Plasminogen activation may also be inhibited due to antibody reactions, thus reducing therapeutic effects (Kumar et al., 2010). Due to its origin, the bacteria Streptococci, allergic reaction is commonly reported among patients (Kumar et al., 2010).
mg per vial for catheter administration, or 50 mg (29 million units) and 100 mg (58 million units) per vial for thromboembolism therapies (Drugs.com, 2013b). Alteplase has the same contraindications, side effects, and pregnancy category as streptokinase. Continuous monitoring for possible hemorrhage and hypersensitivity reactions should also be followed as with streptokinase.

Recommended dosage of alteplase for myocardial infarction using the accelerated or front-loading infusion is 15 mg given bolus, then 0.75 mg/kg (up to 50 mg) over 30 minutes, then 0.5 mg/kg (up to 35 mg) over the next 60 minutes. Front-loading infusion is often accompanied by heparin therapy. For the 3-hour infusion for MI, recommended dosage is 60 mg over the first hour with 6-10 mg given as bolus over the first 2 minutes, then 20 mg over the second hour, and another 20 mg over the 30 hours. Total dosage should equal 100 mg of alteplase (Vallerand et al., 2012). Alteplase, similar to streptokinase, should also be administered within 4 to 6 hours of onset of acute MI symptoms (Kee et al., 2012). In the case of pulmonary embolism, recommended dosage of alteplase is 100 mg over 2 hours, followed with heparin therapy (Vallerand et al., 2012). For patients diagnosed with acute ischemic or thrombotic stroke, alteplase should be administered within 3 hours of onset of symptoms (Kee et al., 2012). Recommended dosage is 0.9 mg/kg (not to exceed 90 mg) given as an infusion over 1 hour with 10% of the dose given as bolus over the first minute. Lastly, for occluded central venous catheters, 2 mg/2 mL should be instilled into the occluded catheter. This can be repeated after 2 hours if the catheter is still occluded (Vallerand et al., 2012).

Evidence through randomized controlled trials has repeatedly shown intravenous administration of alteplase within 3 hours after onset of stroke has significant favorable neurological outcomes compared to placebo (odds ratio 1.7, 95% CI, p=0.008). Furthermore, the European Cooperative Acute Stroke Study (ECASS), ECASS II, and Alteplase Thrombolysis for Acute Non-interventional Therapy in Ischemic Stroke (ATLANTIS) trials have shown alteplase could be administered to patients up to 6 hours upon onset of stroke symptoms, although this has not been endorsed in clinical guidelines, with a significant favorable result after 90 days of treatment versus placebo (52.4% vs 45.2%, odds ratio 1.34, 95% CI, p=0.04) (Wechsler, 2011). Due to the fact that 4 out of 10 patients arrive after the 3-hour window for administering alteplase for ischemic stroke, there has been a call to evaluate current evidence-based clinical guidelines regarding the therapy. Three multi-national studies have shown administration of alteplase up to 4.5 hours after the onset of symptoms still resulted in favorable neurological outcomes, though significance was not established (Powers, 2011).

For acute MI, the Thrombolysis in Myocardial Infarction (TIMI) Phase I trial showed re-establishment of circulation was twice as many in alteplase administration compared to streptokinase for patients with occluded coronary arteries (Kudian & Gibson, 2012). Patients with pulmonary embolism who received thrombolytic therapy had a lower case fatality rate attributable to the condition compared to those who did not receive thrombolytic therapy (15% vs. 47%; p<0.0001) (Stein & Matta, 2012). In cases of occluded central venous catheters, alteplase cleared 52% of occlusions within 30 minutes with a mean clearance of 86% after two doses. The researchers recommend other newly developed thrombolytic agents, such as reteplase, have higher clearance rates compared to alteplase (Baskin et al., 2012).

**Nursing Care of Patients Undergoing Thrombolytic Therapy**

Due to the emergency situations and limited time thrombolytic therapy needs to be initiated for the most favorable outcomes, nurse-led emergency management of acute MI or acute ischemic or thrombotic stroke may become a possibility in the near future. Research since 2003 has shown nurses, with the support of other health care professionals, can have a high level of accuracy and safety in diagnosing and treating acute MI, reducing drug-to-door treatment times, and improving reperfusion rates to an earlier time (Sloman & Williamson, 2009). However, clinical guidelines have not endorsed this evidence yet. Nurses still have the duty to ensure their patients who are undergoing therapy for thrombolytics receive high-quality and safe nursing care. The first thing nurses should understand would be the thrombolysis treatment pathway. A thrombolytic pathway for patients diagnosed with acute ischemic stroke was recently published by Catangui and Stark (2012).

As thrombolytic agents are recognized as high alert medications due to the possibility of death with overdose or underdose of medication, nurses must continuously monitor patients for adverse effects and complications of therapy. As mentioned earlier, hemorrhage is a possible severe adverse effect. Should local bleeding occur during therapy, apply pressure to the site for at least 30 minutes to stop the bleeding (Vallerand et al., 2012). If severe bleeding occurs or signs of bleeding are evident, the infusion should be stopped immediately and the health care provider notified (Kee et al., 2012). Hemorrhage is often controlled by infusion of whole blood, packed red blood cells, fresh frozen plasma, or cryoprecipitate. Prior to treatment, blood type and cross matching should have been done. Also, inform the patient and family blood products should be made available during the course of treatment (Vallerand et al., 2012). Aminocaproic acid (Amicar®), a hemostatic, may also be administered as an antidote to thrombolytic agents (Adams & Holland, 2011).

To monitor blood volume and coagulation activity, laboratory tests (e.g., hematocrit, hemoglobin, platelet count, fibrin/fibrin degradation product titer, fibrinogen concentration, prothrombin time, thrombin
time, and activated partial thromboplastin time) will need to be taken before, during, and after therapy (Vallerand et al., 2012). Patients are also encouraged to limit their activity during therapy to reduce the chance of incurring bruising, injury, and bleeding. Invasive procedures and intramuscular injections will need to be delayed up to 8 hours post-infusion (Adams & Holland, 2011).

If a patient is treated for acute MI, ECG changes must be monitored continuously as dysrhythmias may occur. Health care providers should be notified as soon as possible should arrhythmias occur. Cardiac enzymes should be monitored, as well as the intensity, location, and radiation of chest pain. It is important to notify the health care provider if chest pain is not relieved or has recurred. If the patient is experiencing signs and symptoms of heart failure, heart rate and breath sounds should be monitored frequently (Schilling McCann, 2012). For patients treated for pulmonary embolism, pulse rate, blood pressure, hemodynamics, and respiratory status should be monitored. Respiratory status includes rate, degree of dyspnea, and arterial blood gases (Vallerand et al., 2012). Patients treated for DVT should have their affected extremities inspected and palpated every hour. Radiographic visualization of the thrombus via computerized tomography and Doppler may be needed to determine re-establishment of circulation (Vallerand et al., 2012). Lastly, for occluded venous catheters, the easiest way to determine clearance is to aspirate blood from the catheter. To prevent air embolism, the patient should be asked to exhale and hold his or her breath when connecting and disconnecting the IV syringe (Adams & Holland, 2011).

Patients and family should be informed regarding the reason for administering thrombolytic therapy, desired therapeutic outcomes, and the need for frequent monitoring for possible adverse effects. Since conditions indicated for thrombolytic treatment are often emergency situations, nurses should also take time to provide nursing care and support to family members during the patient’s duration of therapy. Lastly, teach patients and family members regarding expectations for the post-infusion period, including follow-up, any post-infusion drug therapies (usually anticoagulants or anti-platelet drugs), and need for lifestyle changes, such as avoiding smoking as it increases platelet aggregation, promoting the development of thrombi (Adams & Holland, 2011; Kee et al., 2012; Vallerand et al., 2012).

Conclusion

Thrombolytic medications can help establish reperfusion after occlusion of arteries and veins have developed such as in MI, stroke, pulmonary embolism, and DVT. Due to its potential for severe adverse effects or death, should any error in medication administration occur, thrombolytic agents are categorized as high-alert medications. It is the role of nurses to act quick and be vigilant during their care for patients undergoing this therapy to ensure high-quality care and safe treatment administration.

REFERENCES


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