Alteplase Injection for Acute Ischemic Events

Alteplase (tissue plasminogen activator, recombinant; tPA) is approved by the U.S. FDA to treat acute ischemic stroke (AIS), acute myocardial infarction (AMI) to reduce mortality and incidence of heart failure, and acute massive pulmonary embolism (PE). Use the following drug information to increase your understanding of this agent and provide safe patient care.

Mechanism (Genentech, 2018)
Alteplase, given intravenously (IV), binds to fibrin in a thrombus and converts plasminogen to plasmin which initiates fibrinolysis. The initial half-life of alteplase is less than 5 minutes and it is cleared primarily through the liver.

Indications and Dosage (Genentech, 2018)
Available forms: 50-mg vial, 100-mg vial

- **Acute Ischemic Stroke (AIS)**
  - 0.9 mg/kg (not to exceed 90 mg dose) infused IV over 60 minutes with 10% of the total dose administered as an initial bolus over one minute.
  - Exclude intracranial hemorrhage as primary cause of stroke prior to treatment.
  - Initiate treatment as soon as possible after symptom onset.
    - Treatment recommended within 3 to 4.5 hours of stroke symptom onset.
    - Not recommended for patients who awoke with stroke symptoms or those with an unclear time of onset greater than 4.5 hours from last known well.
    - Patients with mild but disabling stroke symptoms are eligible however it is not recommended for those with NIHSS score between 0-5.

- **Acute Myocardial Infarction (AMI)**: based on patient weight; not to exceed 100 mg.
  - Administer as soon as possible after the onset of symptoms.
  - **Accelerated infusion**
    - Patient weight greater than 67 kg: 15 mg IV bolus, then 50 mg over first 30 minutes, then 35 mg over next 60 minutes.
    - Patient weight less than or equal to 67 kg: 15 mg IV bolus, then 0.75 mg/kg over first 30 minutes, then 0.50 mg/kg over next 60 minutes.
  - **3-hour Infusion**
    - Patient weight greater than 65 kg: 6-10 mg IV bolus, 50-54 mg over rest of first hour, then 20 mg over second hour, and 20 mg over third hour.
    - Patient weight less than or equal to 65 kg: 0.075 mg/kg IV bolus, 0.675 mg/kg over rest of first hour, 0.25 mg/kg over second hour, and 0.25 mg over third hour.
  - Review ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction for complete inclusion criteria.
Risk of stroke may outweigh the benefit in AMI patients at low risk for death or heart failure.

- **Acute Massive Pulmonary Embolism (PE):** 100 mg IV infusion over 2 hours.
  - Indicated to treat:
    - Acute PE obstructing blood flow to a lobe or multiple lung segments.
    - Acute PE accompanied by unstable hemodynamics.

**Contraindications (Genentech, 2018)**

- **General**
  - Active internal bleeding
  - Recent (within 3 months) severe head trauma or intracranial/intraspinal surgery
  - Intracranial conditions that may increase the risk of bleeding such as intracranial neoplasm, arteriovenous malformation, or aneurysm
  - Bleeding diathesis
  - Current severe uncontrolled hypertension

- **Acute ischemic stroke (in addition to the above general contraindications):**
  - Current intracranial hemorrhage
  - Subarachnoid hemorrhage

- **Acute myocardial infarction or pulmonary embolism (in addition to the above general contraindications):**
  - History of recent stroke

**Administration (Genentech, 2018)**

- Reconstitute using the accompanying sterile water for injection without preservatives.
  - Avoid excessive agitation during dilution; don’t shake, mix gently.
  - Use aseptic technique.
  - Don’t reconstitute more than eight hours before use.
  - Don’t use bacteriostatic water for injection.
  - Don’t add other medications to alteplase solution.
  - Solution will appear colorless to pale yellow after reconstitution

- 50 mg vials are vacuum sealed. Don’t use if vacuum is not present; administer using either polyvinyl chloride bag or glass vial and infusion set.
- 100 mg vials do not contain a vacuum seal.
- *Consult package insert for complete instructions on medication preparation, reconstitution and administration.*

**Nursing Considerations**

*The following recommendations are based on the care of acute ischemic stroke (AIS) patients, unless otherwise noted (Powers et al., 2019).***

- Prior to administration
  - Carefully lower blood pressure (BP) to maintain systolic BP less than 185 mmHg and diastolic BP less than 110 mmHg before initiating fibrinolytic therapy.
  - Due to an increased risk of intracranial bleeding, check INR, aPTT and blood glucose prior to administration.
- Alteplase should not be administered to patients who have received a full dose of low-molecular-weight heparin (LMWH) within the prior 24 hours.
- In AIS patients without recent use of oral anticoagulants or heparin, alteplase can be started prior to coagulation study results. Discontinue alteplase if pretreatment INR is greater than 1.7 or aPTT is elevated (Genentech, 2018).
- IV aspirin should not be administered within 90 minutes after the start of IV alteplase in AIS patients.
  - For PE patients who are hemodynamically unstable, discontinue any prior anticoagulant therapy before and during the thrombolytic infusion to minimize risk of bleeding (Tapson & Weinberg, 2020).
  - Assess for exclusion criteria/contraindications.
  - Admit to the intensive care unit (ICU) for monitoring.
- **During administration**
  - Maintain strict bedrest during treatment.
  - Measure BP and perform neurological assessment every 15 minutes during infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after treatment.
    - Increase frequency of BP measurements if systolic BP greater than 180 mm Hg or if diastolic BP greater than 105 mm Hg; administer antihypertensive as needed to maintain these levels.
  - If patient develops a severe headache, acute hypertension, nausea or vomiting, or has a worsening neurological examination, stop the alteplase administration and obtain an emergency CT scan.
  - Avoid invasive procedures and I.M. injections, and perform venipunctures carefully and only as required, avoiding internal jugular and subclavian venous punctures.
  - IV aspirin should not be administered within 90 minutes after the start of IV alteplase when treating AIS patients.
  - Closely monitor the patient for bleeding and frequently assess all puncture sites.
  - If serious bleeding occurs, stop the alteplase infusion immediately.
  - Monitor for hypersensitivity and discontinue alteplase immediately if signs develop.
  - Extravasation of alteplase can cause ecchymosis or inflammation. If this occurs, stop the infusion and apply local therapy.
- **After administration**
  - Monitor BP and perform neurologic assessment every 15 minutes during infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after treatment.
  - After the initial 24 hours, monitor vital signs, control blood pressure, and perform neurological assessments frequently, per hospital policy.
  - Maintain BP less than 180/105 mmHg for at least 24 hours after treatment in AIS patients.
  - For AIS patients, hold antiplatelet or anticoagulation therapy and invasive procedures for 24 hours following administration.
  - For AMI and PE patients, concomitant IV unfractionated heparin is recommended near the end or immediately following alteplase infusion when the PTT or thrombin time returns to twice normal or less to prevent re-occlusion (Genentech, 2018; Gibson & Levin, 2020; Tapson & Weinberg, 2020)
Monitor for serious adverse events, such as bleeding and angioedema.

- Concomitant use of angiotensin-converting enzyme (ACE) inhibitors may increase the risk of orolingual angioedema.
- Concomitant use of anticoagulants and drugs that inhibit platelet function increase the risk of bleeding.
- Delay insertion of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if patient can be managed without them.
- For AIS patients, obtain follow-up CT or MRI scan 24 hours after treatment before starting anticoagulants or antiplatelet agents.

Adverse reactions (Genentech, 2018)

- Bleeding can occur one or more days after infusion – see management below.
  - A dose greater than or equal to 150 mg should not be used to treat AMI as it has been associated with increased intracranial bleeding.
- Hypersensitivity (anaphylactic reactions, laryngeal edema, rash and shock) may occur during and up to 2 hours after infusion.
- Cholesterol embolization may present as acute renal failure, spinal cord infarction, retinal artery occlusion, bowel infarction, rhabdomyolysis, “purple toe” or livedo reticularis.
- Re-embolization of deep venous thrombi (DVT).

Management of Symptomatic Bleeding Within 24 Hours After Administration of IV Alteplase (Powers, et al., 2019)

- Stop alteplase infusion.
- Obtain CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match.
- Obtain emergent non-enhanced head CT.
- Per order, administer cryoprecipitate (includes factor VIII): 10 U infused over 10-30 minutes (onset in 1 hour, peaks in 12 hours); administer additional dose for fibrinogen level less than 150 mg/dL.
- Per order, administer tranexamic acid 1 g (or 10 to 15 mg/kg) once; administer at a rate not to exceed 100 mg/minute (over about 10-20 min) OR E-aminocaproic acid 4-5 g over 1 hour, followed by 1 g per hour IV for 8 hours or until bleeding is controlled.
- Obtain hematology and neurosurgery consult.
- Manage BP, intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP), temperature, and glucose.

Management of Orolingual Angioedema Associated with IV Alteplase (Powers, et al., 2019)

- Maintain airway.
- Intubation may not be needed if edema is limited to anterior tongue and lips.
- Edema involving larynx, palate, floor of mouth, oropharynx with rapid progression (within 30 minutes) poses higher risk of respiratory compromise requiring intubation.
- Awake fiberoptic intubation is preferred.
- As ordered, perform the following:
  - Discontinue IV alteplase infusion and hold ACE-inhibitors.
  - Administer IV methylprednisolone 125 mg.
  - Administer IV diphenhydramine 50 mg.
Administer ranitidine 50 mg IV or famotidine 20 mg IV.

If there is an increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL.

Administer icatibant (selective bradykinin B₂ receptor antagonist), 3 mL (30 mg) subcutaneously in abdomen; additional 30 mg doses may be given at 6-hour intervals not to exceed 3 injections in 24 hours.

References:


