Alteplase Injection for Acute Ischemic Stroke

Alteplase (tissue plasminogen activator, recombinant; tPA) is approved by the U.S. FDA for intravenous thrombolysis in acute ischemic stroke within 3 hours of the onset of stroke symptoms. Use the following drug information to increase your understanding of this agent and provide safe patient care.

Inclusion criteria (Powers, et al., 2018)

- Diagnosis of ischemic stroke causing measurable neurological deficit
- 18 years of age or older
- Onset of symptoms < 3 hours
    - Includes patients with severe stroke and patients with mild but disabling stroke symptoms
    - Equally effective in patients < 80 and > 80 years of age
- For select patients with symptom onset 3- to 4.5- hours:
    - 80 years of age or less
    - No history of diabetes mellitus and prior stroke, no current oral anticoagulant use, NIHSS score ≤ 25, no anticoagulants, cerebral imaging showing ischemia involving less than one third of middle cerebral artery (MCA) territory
- Blood pressure (BP) that can be lowered safely (< 185/110 mm Hg) with antihypertensive agents.
- Initial glucose > 50 mg/dL
- Non-contrast computed tomography (NCCT) showing early mild-moderate ischemic changes.
- Patients taking mono-antiplatelet therapy or combination therapy (i.e. aspirin and clopidogrel) and patients with end-stage renal disease on hemodialysis and normal aPTT are eligible for therapy.

Contraindications (Powers, et al., 2018)

- Unclear time and/or unwitnessed symptom onset and last known baseline state > 3 or 4.5 hours
- Current or history of intracranial hemorrhage
- CT scan showing hypoattenuation or hypoperfusion representing irreversible injury
- Recent (within 3 months) ischemic stroke, severe head trauma, or intracranial/intraspinal surgery
- Subarachnoid hemorrhage
- Gastrointestinal (GI) malignancy or GI bleed within 21 days of stroke event

- Intracranial conditions that may increase the risk of bleeding such as intracranial neoplasm, arteriovenous malformation, or aneurysm
- Coagulopathy: Platelet count < 100,000/mm^3, INR > 1.7, aPTT > 40 seconds, or PT > 15 seconds
- Low molecular weight heparin (LMWH) treatment doses within the previous 24 hours
- Current use of anticoagulant with INR > 1.7 or PT > 15 seconds
- Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated laboratory tests
- Concurrent use of glycoprotein IIb/IIIa receptor inhibitors
- Infective endocarditis
- Aortic arch dissection
- Intra-axial intracranial neoplasm – lesions located within the brain tissue

Note: See current clinical practice guidelines for complete list of recommendations for treatment with parenteral alteplase and relative indications.

Pregnancy Risk Category: C

Dosage and Administration

Available forms: 50-mg vial, 100-mg vial

Dosage: Dose is calculated based on patient weight (0.9 mg/kg) with a maximum total of 90 mg over 60 minutes. Ten percent of total dose given as an IV bolus over 1 minute, followed by an IV infusion of the remainder of the dose over 1 hour.

Administration:

- May be administered IV or intra-arterially (intra-arterial administration is an off-label route).
- May be given to eligible patients even if endovascular therapies (EVTs) are being considered.
- *Consult package insert for complete instructions on medication preparation, reconstitution and administration.*

Nursing Considerations

- **BEFORE** administration:
  - Carefully lower blood pressure (BP) to maintain systolic BP < 185 mmHg and diastolic BP < 110 mmHg **before** initiating fibrinolytic therapy (Powers, et al., 2018).
  - Due to an increased risk of intracranial bleeding, check INR, PTT and blood glucose prior to administration.

  - Assess for exclusion criteria/contraindications.
  - Explain use and administration of the drug to the patient and the family; tell them to report adverse reactions immediately.
  - 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 SBP > 180 mm Hg or if DPB > 105 mm Hg; administer antihypertensive as needed to maintain these levels.
  - If any change in neurological status or symptoms occurs, such as severe headache, acute hypertension, nausea or vomiting, or worsening neurological examination, the alteplase administration should be stopped and a CT scan obtained.
  - Avoid invasive procedures and I.M. injections, and perform venipunctures carefully and only as required, avoiding internal jugular and subclavian venous punctures.
  - Closely monitor the patient for internal bleeding and frequently assess all puncture sites.
    - If serious bleeding occurs, stop the alteplase infusion immediately.
- **AFTER** administration:
  - Monitor BP and neurologic status every 5 minutes for the first 15 minutes after administration, then every 15 minutes for 2 hours, every 30 minutes for 6 hours, and hourly for 16 hours after treatment. After the initial 24 hours, monitor vital signs, control blood pressure, and perform neurological assessments frequently per your facility's policy.
  - Maintain BP < 180/105 mmHg for at least 24 hours after treatment.
  - Hold antiplatelet or anticoagulation therapy and invasive procedures for 24 hours following administration.
  - 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.

- Obtain follow-up CT or MRI scan 24 hours after treatment before starting anticoagulants or antiplatelet agents.

Adverse reactions

- Bleeding (most common)
- Orolingual angioedema
- Arrhythmias
- Hypotension
- Edema
- Cholesterol embolization
- Venous thrombosis
- Re-embolization of deep venous thrombi (DVT) in patients with pulmonary embolism
- Nausea
- Vomiting
- Hypersensitivity reactions

Management of Symptomatic Bleeding Within 24 Hours After Administration of IV Alteplase (Powers, et al., 2018)

- Stop alteplase infusion.
- Obtain CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match.
- Obtain emergent nonenhanced head CT.
- Per order, administer cryoprecipitate (includes factor VIII): 10 U infused over 10-30 minutes (onset in 1 hour, peaks in 12 hour); administer additional dose for fibrinogen level < 200 mg/dL.
- Per order, administer tranexamic acid 1000 mg IV infused over 10 min OR Ɛ-aminocaproic acid 4-5 g over 1 hour, followed by 1 g IV 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., 2018)

- 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 B_2 receptor antagonist), 3 mL (30 mg) subcutaneously in abdomen.

References:

Demaerschalk, B., Kleindorfer, D., Adeoye, O., Demchuk, A., Fugate, J., Grotta, J. … Smith, E. (2016). Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke, (47),* 581-641.

Genetech. (2017, September). Activase Prescribing Information. Retrieved from Activase.com: http://www.gene.com/download/pdf/activase_prescribing.pdf

Powers, W.J., Rabinstein, A.A., Ackerson, T., Adeoye, O.M., Bambakidis, N.C., Becker, K.,…Tirschwell, D. L., (2018). 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke. *Stroke, 49,* e46-e99.

Wolters Kluwer Health. (2018, August). Alteplase Recombinant Injection. Retrieved from Facts & Comparisons: https://fco.factsandcomparisons.com/lco/action/doc/retrieve/docid/fc_dfc/5548433