

tPA for Stroke – Potential Benefit, Risk and Alternatives



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Definitions

tPA stands for tissue Plasminogen Activator, a strong “clot dissolving” medicine.

Stroke occurs when an area of the brain is deprived of oxygen and nutrients because of a blocked blood vessel. Many sudden blockages are due to a blood clot, and can result in loss of function in the affected area of the brain. Common signs and symptoms of stroke include abrupt onset of one-sided weakness/numbness, and difficulty with vision, speaking, thinking or coordination. The National Institute of Health Stroke Scale (NIHSS) is a standardized way to measure the severity of a stroke on a 0-42 point scale (normal to worst).

Stroke mimic is a term used for medical problems that can present in a manner similar to stroke and not the result of a blocked blood vessel. Causes include aftereffects of seizures and migraine headaches, among others. Stroke mimics may be initially misinterpreted as a stroke.^{1,2}

Potential Benefit

The National Institute of Neurological Disorders and Stroke (NINDS) study suggested that 8 out of 18 stroke patients who receive tPA according to a strict protocol will recover by three months after the event without significant disability. This is compared to 6 out of 18 stroke patients (one-third) who recover substantially regardless of treatment.³ See illustration on next page.

Potential Risk

As with most treatments, there are risks associated with tPA administration. Studies vary in predicting the likelihood of complications, which include bleeding into the brain, other types of serious bleeding (e.g., gastrointestinal), and death. Here is a recap of those research findings:

- The NINDS study suggested that bleeding into the brain occurred in about 1 out of 18 patients receiving tPA (specifically, 5.8%). When this occurred, there was a 45 percent fatality rate.
- Several studies suggested treatment with “clot-dissolving” medications increases the number of patients who die following a stroke.^{4,5,6,7,8,9}
- Subsequent studies demonstrated that using tPA more liberally than is recommended in the NINDS protocol resulted in a higher rate of intracranial hemorrhage.^{10,11,12,13}

Complications are more likely when tPA is used in patients over 70 years old, those with more severe stroke (NIHSS over 15), or those with glucose over 300 mg/dl.

Balancing Benefits and Risks and Alternatives

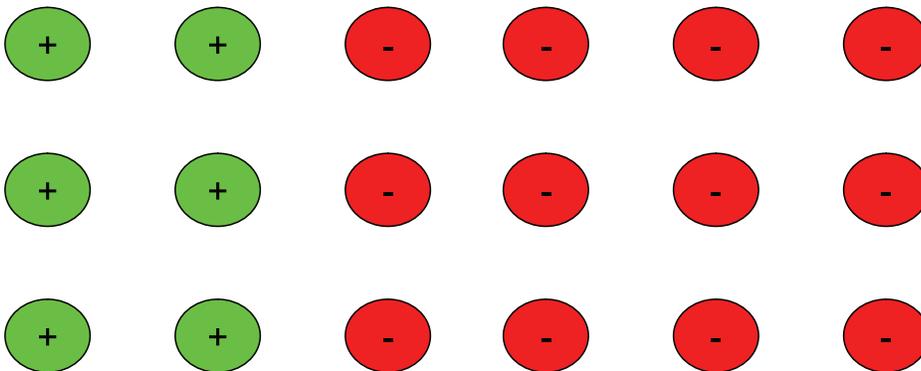
It is important for physicians and patients (or family members) to weigh the possibility of benefit (improved function at 3 months) against the possibility of harm (severe bleeding or death). Stroke symptoms alone are insufficient to definitely diagnose stroke and, in patients with a stroke mimic, tPA use results only in potential adverse effects without any possibility of benefit.

Alternative treatments with proven benefit for patients with stroke include aspirin and care in a specialized unit where staff members pay careful attention to a variety of basic aspects of care.^{14,15} Several other experimental treatments, including invasive de-clotting procedures, may prove to be beneficial.

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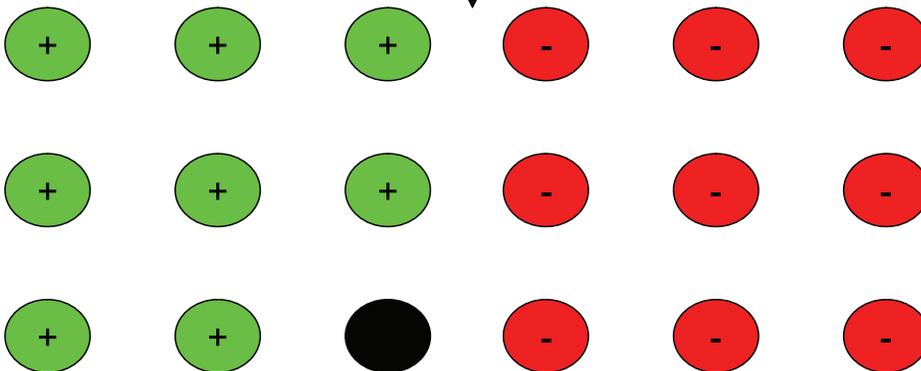


when minutes count



tPA within 3 hours

by NINDS protocol



Legend:

- = good recovery
- = poor/no recovery
- = brain bleed/45% die

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Disclaimer

Treatment of stroke cases must be individualized. In fact, stroke experts do not always agree on the treatment plan given a specific situation. Thus, this educational tool should be viewed as a guideline that will undoubtedly evolve with further research and experience. It was approved by the American Academy of Emergency Medicine Board of Directors on March 11, 2007.

Endnotes

- 1 Libman R, et al. Conditions that mimic stroke in the Emergency Department: Implications for acute stroke trials. Arch Neurol 52:1119-1122, 1995.
- 2 Allder SJ, et al. Limitations of clinical diagnosis in acute stroke. Lancet 1999;354:1523.
- 3 The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 333:1581-1587, 1995.
- 4 Hacke, W., et al. Intravenous Thrombolysis With Recombinant Tissue Plasminogen Activator For Acute Hemispheric Stroke, The European Cooperative Acute Stroke Study (ECASS). JAMA 274(13):1017, 1995
- 5 Multicenter Acute Stroke Trial-Italy (MAST-I) Study Group. Randomized controlled trial of streptokinase, aspirin, and combination of both in treatment of acute ischemic stroke. Lancet 346:1509-1514, 1995.
- 6 Donnan GA. Streptokinase for acute ischemic stroke with relationship to time of administration: Australian Streptokinase (ASK) Trial Study Group. JAMA 276(12):961-6, 1996.
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- 8 Hacke W, Kaste M, Fieschi C, et al. Randomized double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet 352:1245-1251, 1998.
- 9 Clark WM, et al. Recombinant tissue-type plasminogen activator (Alteplase) for ischemic stroke 3 to 5 hours after symptom onset. The ATLANTIS Study: a randomized controlled trial. Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke. JAMA 282(21):2019-26. 1999.
- 10 Katzan I, et al. Use of tissue-type plasminogen activator for acute ischemic stroke: The Cleveland area experience. JAMA 283:1151-1158, 2000.
- 11 Tanne D, et al. Intracerebral hemorrhage after intravenous t-PA for hyperacute ischemic stroke in clinical practice: rate and predictors. Cerebrovasc Dis 8(suppl 4):48, 1998.
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- 14 Gubitz G, Sandercock P, Counsell C. Antiplatelet therapy for acute ischaemic stroke. Cochrane Database Syst Rev. 2000:CD000029.
- 15 Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database Syst Rev. 2002:CD000197.