

Clinical controversies

Thrombolysis in Stroke, USA, 2005

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As in Israel, the opinion of the American emergency medicine community is divided on the use of thrombolysis in acute stroke. Interestingly, the neurologic community is also divided. The NINDS and other studies have been subject to different interpretations and reinterpretations. The truth as to the efficacy of thrombolysis in stroke is in the eyes of the beholder. Many emergency physicians accept the data that thrombolysis can produce an improved outcome in certain patients, in certain settings. Why aren't these physicians universally in favor of stroke thrombolysis? What factors influence this decision?

Dr. Leibman is concerned that the risk of hemorrhage is unacceptably high. Graham (1) and Lang (2) used meta-analysis and evidence based reviews respectively to show that tPA improved long-term outcomes but at the cost of increased hemorrhage and early death. Crucial to that success is giving the tPA without protocol violations - that is within the time frame of three hours to people without contraindications. Scott and Silbergleit showed that, in a US four-hospital system, emergency physicians could do this without a stroke team (3).

The increased incidence of early death from hemorrhage is acceptable to Dr. Drescher but not to Dr. Leibman. Whether this is a valid tradeoff for improved outcome is the issue. In actuality, the individual patient with the stroke should make this determination. In my experience most, but not all, patients (or family members) desire the chance of a better recovery in spite of the risk.

Another concern of Dr. Leibman is the seeming difficulty of getting patients to the ED, screened, and treated, within the three-hour window. In the US, 15% is thought to be a reasonable goal for the percentage of patients with strokes admitted to a hospital who are thrombolysed. This was not done in Cleveland but is done at Hartford Hospital and other US centers with an interest in stroke treatment. It was done in Helsinki.(4) Admittedly this requires both public education and an aggressive treatment by interested individuals in the ED. It can be done.

An important adage mitigating against the universal approval of thrombolysis is "primum non nocere". When we order a thrombolytic we increase the risk of intracerebral hemorrhage beyond what would occur in the absence of thrombolysis in the hope of incurring an overall benefit in large groups of patients. Brain hemorrhage is a major, frightening, adverse event that is iatrogenic. Nevertheless, we administer other therapies with similar potential adverse effects.

Some emergency physicians question the motives of those who promote thrombolysis. The research efforts that have demonstrated efficacy for thrombolysis have been "industry sponsored" by pharmaceutical companies that stand to make many millions of dollars if their drugs are widely used. Emergency physicians have seen thousands of dollars spent on gifts, lavish meals at expensive restaurants, and even paid trips to exotic locations that provide the pharmaceutical companies the opportunity to "educate" us. They are skeptical of the motivation, and thus of the drug and because it is now very expensive. In the USA, stroke centers - like trauma centers twenty years ago - are a new concept. Then, as now, the emergency departments being designated as centers were not thought by all to have altruistic motives; the suspicion that they were taking patients from those quite able to care for them was voiced.

The majority of American and Israeli emergency physicians work in an environment totally unlike that of any controlled clinical trial. Most do not have the benefit of a stroke team. They are too busy with full rooms, hallways, and waiting rooms to have the luxury of concentrating on a single patient. They face the constant specter of being interrupted by patients seemingly more in need of immediate care because of cardiac arrest, gunshot wounds, and other critical conditions that have defined treatment regimens. Neurologists do not assist them and neuroradiologists do not interpret their CT scans. They may not have the latest generation scanners in their hospital.

Given the above what is the outlook for acceptance of thrombolysis in acute stroke asks Dr. Leibman? Thrombolysis will be successful when the public demands it (which they increasingly do in the US), when the right questions are almost always asked, when the CT scan is correctly read, and when the correct dose of the lytic is

administered in a timely fashion. This will be greatly facilitated by new clinical information systems. Computer based algorithms will allow the history of the stroke and factors contraindicating thrombolysis to be taken by nursing or paramedical personnel. Mandatory fields will not allow the medication to be ordered until all of the necessary questions have been asked. Teleradiology will allow the CT scan to be read by a qualified radiologist twenty-four hours per day. When these developments are widespread so will be thrombolysis of stroke, unless...

A confounding variable is the increasing use of invasive, intra-arterial, methods of stroke treatment. Intra-arterial thrombolysis, stenting, and clot retrieval devices are already in use at selected stroke centers. Only time will tell if these, analogous to coronary angioplasty, will become widespread and synonymous with the best care. If so, the specialized knowledge and equipment required will take a number of years to propagate.

References

1. Graham GD. Tissue plasminogen activator for acute ischemic stroke in clinical practice: a meta-analysis of safety data. *Stroke* 2003;34(12):2847-2850
2. Lang ES. Evidence-based emergency medicine. Use of thrombolytic therapy in patients with acute ischemic stroke. *Annals of Emergency Medicine* 2002;39(3):296-298
3. Scott PA, Silbergleit R. Misdiagnosis of stroke in tissue plasminogen activator-treated patients: Characteristics and outcomes. *Annals of Emergency Medicine* 2003;42(5):611-618
4. Kaste M. Reflection and Reaction: Approval of alteplase in Europe: will it change stroke management? *The Lancet* 2003;2(4):207-208