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EMS Myth #2

Thrombolytic therapy is the standard of care for acute ischemic stroke

Like most practitioners of emergency medicine, I was surprised to see the American Heart Association (AHA) increase the level of its recommendation of recombinant tissue plasminogen activator (tPA) for acute ischemic stroke in its *Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiac Care*. I had followed the literature and agreed that it looked like a promising therapy. But, I thought, it was certainly not the standard of care for current medical practice. As an ED and EMS director at the time, I quickly prepared a stroke team and began to plan for routine thrombolytic therapy for appropriate patients. In fact, I administered tPA to a patient with acute ischemic stroke who subsequently experienced resolution of

his symptoms. However, shortly thereafter, I received a letter from my supervisor, who advised that our collective medical institutions would not provide tPA for stroke until additional scientific evidence was available. This was soon followed by a letter from our medical malpractice insurance carrier stating we would not be covered for malpractice litigation resulting from administering tPA for stroke. It was a confusing and frustrating time.

tPA for Stroke History

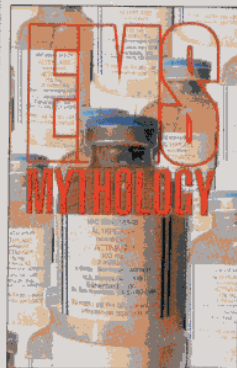
In the mid 1990s, the AHA launched a campaign to promote awareness of stroke. The goal of this campaign was to encourage both clinicians and patients to think of stroke (cerebrovascular accident) as an emergency on par with myocardial infarction. This initiative came to be known as the *brain attack* campaign, capitalizing on the term *heart attack's* wide recognition among the public. The impetus behind the brain attack campaign was the development of thrombolytic drugs for use in stroke. These drugs, if given

to ischemic stroke patients within three hours of the onset of symptoms, appeared to decrease subsequent stroke morbidity. Thus, with a definitive therapy finally available for stroke care, patients were encouraged to immediately seek emergency care when the possible signs or symptoms of a stroke occurred. EMS providers across the United States and Canada quickly rallied to the campaign. Many EMS systems initiated prehospital thrombolytic screening protocols, and patients were taken to hospitals with designated stroke teams. The stroke teams were a consortium of emergency physicians, neurologists, neuroradiologists and neurosurgeons who agreed to quickly respond to, evaluate and treat stroke patients who arrived at their hospitals.

The AHA published brain attack literature that stated, "A clot-busting drug that helped revolutionize heart attack treatment, tPA holds enormous potential for the treatment of ischemic stroke, which accounts for 70 to 80 percent of all strokes. It is estimated that tPA could be used in 400,000 stroke cases per year to save lives, reduce disability and reverse paralysis." When first approved in 1996 for the treatment of ischemic stroke, tPA was classified by the AHA as a Class II-B intervention (acceptable, safe and useful but optional). However, in their *Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiac Care*, tPA for ischemic stroke was upgraded to a Class I intervention (always acceptable, proven safe and definitely useful). This upgrade was based on a large study of tPA in ischemic stroke by the National Institute of Neurological Diseases and Stroke (NINDS).²

The Scientific Evidence

The recommendations to upgrade tPA from Class II-B to Class I were based upon a single study (the NINDS trial). There has been considerable criticism of the NINDS trial for various methodological reasons. The most striking of these was the fact that in that trial, many more patients in the 90–180-minute treatment group had milder stroke scores at baseline compared to those in the placebo. That is, patients with less severe initial symptoms received tPA, while patients with more severe symptoms did not. It would seem intuitive, therefore, that patients in the treatment group would fare better, as they were not as ill to start with. Another criticism of the study was that the proportion of patients enrolled in the 0–90-minute treatment group was artificially increased through statistical methods. Many researchers feel



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that chance alone could explain the benefits seen in the NINDS trial. Furthermore, approximately 20% of patients initially diagnosed with stroke were subsequently found *not* to have had strokes. Thus, these patients were exposed to the significant risks of tPA without any potential for benefit. Finally, even assuming clinical effectiveness, the clinical impact of administering tPA only benefited less than half of 1% of ischemic stroke patients.

A second study was conducted in the Cleveland, OH area.⁷ In this study, every stroke patient treated at one of 29 non-VA hospitals in Cleveland over a one-year period was enrolled. In this group of 3,948 patients, only 70 (1.8%) received tPA. In actuality, less than 1% of patients in the study group actually met the NINDS eligibility criteria to receive tPA. The results of the Cleveland study were quite the opposite of the NINDS study: In Cleveland, the rate of intracerebral hemorrhage in tPA recipients was 15.7%, twice that of the NINDS trial. Their mortality rate was 15.7%, compared to 7.2% in the untreated control group. Although it was not a randomized controlled trial, the Cleveland study results posed a stark contrast to those of the NINDS trial, and are worrisome.

When it came time to reevaluate the role of tPA in ischemic stroke, the AHA appointed nine scientists/clinicians to a consensus panel. Of the nine who were assigned to formulate AHA's 2000 recommendations for stroke treatment, six had ties to the manufacturer of tPA or associated firms. Although the AHA required the panelists to file conflict-of-interest statements, it has thus far refused to release these statements to the public.

EMS Implications

Many emergency medicine organizations have been alarmed about the AHA's upgrading of tPA for ischemic stroke to a Class I intervention. The AHA has, in essence, made tPA a standard of care based upon the results of a single study. Basing a standard of care on the results of a single study is not sci-

entifically sound. With this in mind, the Canadian Association of Emergency Physicians issued a position paper that stated, "Thrombolytic therapy should be restricted to use in the context of formal research protocols, or in a closely monitored program."⁸ In its position paper, the American Academy of Emergency Medicine stated, "It is the position of the American Academy of Emergency Medicine that objective evidence regarding the efficacy, safety, and applicability of tPA for stroke is insufficient to warrant its classification as a standard of care."⁹ The American College of Emergency Physicians, taking a slightly softer stance, stated, "Since the NINDS trial, there has not been a second randomized, double-blinded, placebo-controlled study to validate its findings. There is insufficient evidence at this time to endorse the use of tPA in clinical practice."¹⁰

EMS is caught in the middle. While many in emergency medicine are reluctant to embrace tPA for ischemic stroke, it remains a Class I recommendation by the AHA. As with many controversial therapies, there are quality clinicians who say it works, while others say it kills. Regardless, the AHA's claim that tPA for stroke "saves lives" has been tempered. When confronted by evidence that tPA in ischemic stroke does not reduce mortality, former AHA President Rose Marie Robertson, MD, withdrew the AHA statement that tPA for ischemic stroke "saves lives." Despite the protocols, stroke intervention teams and early recognition, it is estimated that only 4,000-6,000 patients with ischemic stroke receive tPA annually, compared to the 400,000 originally estimated by the AHA in 1996.

Recently, because of the outcry of criticism related to the NINDS trial and the AHA's endorsement of tPA, NINDS has appointed an independent panel to reevaluate its trial. Those results are expected in a few months.

Conclusion

EMS personnel should be included in any planning for stroke-intervention therapy in their communities. If only a limited number

of facilities are offering thrombolytic therapy for stroke, EMS vehicles may incur increased transport and hospital times that may adversely affect system performance. For the most part, tPA for stroke is primarily a hospital issue. Although this issue may be adequately addressed with additional studies, at best it remains a somewhat questionable therapy. Because of the ongoing controversy, EMS personnel must stay informed as to the status of this therapy. At the moment, regardless of its proponents' claims, thrombolytic therapy for acute ischemic stroke is *not* the accepted standard of care. Unbiased research in the future should help clarify this very sensitive issue. ■

References

1. American Heart Association, *Annual Report 1999*. Dallas: AHA, 2000.
2. Marler JR, Tilley BC, Lu M, et al. Early stroke treatment associated with a better outcome: The NINDS rt-PA stroke study. *Neurology* 55:1,649-1,655, 2000.
3. Katzen IL, Furlan AJ, Lloyd LJ, et al. Use of tissue-type plasminogen activator for acute ischemic stroke: The Cleveland area experience. *JAMA* 283:1,151-1,158, 2000.
4. Canadian Association of Emergency Physicians, *Position Statement for Thrombolytic Therapy for Acute Ischemic Stroke*, www.caep.ca/002.policies/002-01.guidelines/thrombolytic.htm.
5. American Academy of Emergency Medicine, *Position Statement on the Use of Intravenous Thrombolytic Therapy for the Treatment of Stroke*, www.aem.org/positionstatements/thrombolytictherapy.shtml.
6. American College of Emergency Physicians, *Use of Intravenous tPA for the Management of Acute Stroke in the Emergency Department*, www.aem.org/positionstatements/thrombolytictherapy.shtml.
7. Lenzer J. Alteplase for stroke: Money and optimistic claims buttress the "brain attack" campaign. *British Medical Journal* 324:723-726, 2002.
8. Lenzer J. Controversial stroke trial is under review following BMJ report. *British Medical Journal* 323:1,131, 2002.

Next Month: EMS Myth #3

Critical Incident Stress Management and related interventions are effective in managing EMS-related stress.

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