Tissue Plasminogen Activator Prescription and Administration Errors within a Regional Stroke System

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Background: Intravenous (IV) tissue plasminogen activator (tPA) utilization in acute ischemic stroke (AIS) requires weight-based dosing and a standardized infusion rate. In our regional network, we have tried to minimize tPA dosing errors. We describe the frequency and types of tPA administration errors made in our comprehensive stroke center (CSC) and at community hospitals (CHs) prior to transfer. *Methods:* Using our stroke quality database, we extracted clinical and pharmacy information on all patients who received IV tPA from 2010-11 at the CSC or CH prior to transfer. All records were analyzed for the presence of inclusion/exclusion criteria deviations or tPA errors in prescription, reconstitution, dispensing, or administration, and for association with outcomes. *Results:* We identified 131 AIS cases treated with IV tPA: 51% female; mean age 68; 32% treated at the CSC, and 68% at CHs (including 26% by telestroke) from 22 CHs. tPA prescription and administration errors were present in 64% of all patients (41% CSC, 75% CH, $P < .001$), the most common being incorrect dosage for body weight (19% CSC, 55% CH, $P < .001$). Of the 27 overdoses, there were 3 deaths due to systemic hemorrhage or ICH. Nonetheless, outcomes (parenchymal hematoma, mortality, modified Rankin Scale score) did not differ between CSC and CH patients nor between those with and without errors. *Conclusion:* Despite focus on minimization of tPA administration errors in AIS patients, such errors were very common in our regional stroke

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Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the University of Utah. [1]

REDCap is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry, (2) audit trails for tracking data manipulation and export procedures, (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources.

[1] Paul A. Harris, Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, Jose G. Conde, Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support, J Biomed Inform 2009;42:377-381.

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system. Although an association between tPA errors and stroke outcomes was not demonstrated, quality assurance mechanisms are still necessary to reduce potentially dangerous, avoidable errors. **Key Words:** Errors—tPA—thrombolysis—stroke—systems of care.

Introduction

Systemic intravenous (IV) tissue plasminogen activator (tPA) remains the only U.S. Food and Drug Administration-approved treatment for acute ischemic stroke (AIS). Administration of tPA in AIS requires patient-specific weight-based dosing of .9 mg/kg (not to exceed 90 mg total dose) infused over 60 minutes with 10% of the total dose administered as an initial IV bolus over 1 minute based on the National Institute of Neurological Disorders and Stroke (NINDS) t-PA trial protocol.[1] The most devastating complication encountered during tPA therapy is bleeding.[2] It is thus important to have a systematic approach to tPA administration so that it is done accurately, reducing the possibility of error.

As part of our systems-based approach to AIS care, we attempt to minimize tPA dosing and administration errors. For example, we systematically weigh patients at our comprehensive stroke center (CSC) to accurately calculate tPA dose and pharmacy discards extra tPA prior to administration. When performing phone- and telestroke-based consults, we ask the same of our community hospitals (CHs). Additionally, all patients accepted to our CSC after tPA administration are met by a multidisciplinary team that includes an emergency department (ED) physician or critical care pharmacist who checks the dosing accuracy of tPA. Through this system, we observed frequent tPA medication errors in patients presenting to our hospital after or during tPA infusion. This motivated us to systematically study the frequency, types, and effects of deviations to the standard tPA protocol among patients treated in our region and whether these errors have led to worse outcomes.

Methods

The University of Utah has a prospective registry of stroke patients treated with IV tPA either at our CSC or at a CH prior to transfer to us (drip-and-ship). Using this database, we retrospectively studied consecutive patients treated with tPA for presumed AIS from January 2010 to December 2011. We excluded patients treated via telephone or telestroke consult who were not subsequently transferred to the CSC.

In-house treatment at the CSC is managed by the brain attack team including an ED nurse, ED physician, pharmacist, neurology resident, and either a vascular neurology attending or a neurocritical care intensivist. The CH staff includes an ED physician and nurse; none have consulting neurologists available for acute stroke cases. Stroke consultation to the CH was provided by the CSC stroke attending via telephone or telestroke. At the CSC, a sling scale is used to obtain an accurate weight for each stroke patient. The tPA order and dosing were verified by the ED pharmacist from 0700 to 0100 or by the central pharmacy from 0100 to 0700 and mixed in the IV center. Both at the CSC and via telephone/telestroke to the CHs, the standard protocol for treating these patients during this period was based on criteria established by the 2007 American Heart Association guidelines.[3]

Clinical information, including demographics, medical history, modified Rankin Scale (mRS) scores at discharge and at follow-up (when available), and discharge location, was abstracted from each patient's chart. The National Institutes of Health Stroke Scale (NIHSS) score was prospectively recorded (86%) or retrospectively extracted (14%) using a validated method.[4] Referring hospital and use of telemedicine or telephone consultation were recorded for all transferred patients. tPA mixing and delivery data were retrospectively collected from air transport records, nursing records, and pharmacy data. Three School of Pharmacy faculty pharmacists with extensive experience in preparing tPA reviewed the charts to determine the presence and nature of the administration errors and graded them using the University Health System Consortium Patient Safety Net scale for medication errors.[5] The pharmacists used uniform definitions for tPA medication errors to provide consistency in record review. Per CSC stroke protocol, all patients received follow-up neuroimaging (computed tomogaphy or magnetic resonance imaging) approximately 24 hours after tPA treatment; these were read by board-certified neuroradiologists. For this study, 2 separate vascular neurologists determined the presence of parenchymal hematoma (PH) as defined by European Cooperative Acute Stroke Study (ECASS) criteria[6]; differences in ratings were adjudicated by discussion.

Inclusion/exclusion criteria deviations based on the 2007 American Heart Association guidelines[7] were recorded but not counted as errors. tPA administration to patients with low NIHSS were intentional violations of a relative exclusion criteria and thus were not counted as errors. Possible tPA errors included prescription errors (wrong dose ordered by >1 mg, inaccurate body weight by >1 kg, an agent other than alteplase, prescription sent to the wrong area, total dose exceeding 90 mg, or prescription written on an incorrect patient); reconstitution error (incorrect diluents other than sterile water, incorrect volume); dispensing error (prolonged delivery to