Expanded Modes of Tissue Plasminogen Activator Delivery in a Comprehensive Stroke Center Increases Regional Acute Stroke Interventions

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**Background and Purpose**—We sought to evaluate whether a comprehensive stroke center could work with regional hospitals to increase the use of tissue plasminogen activator (tPA) in acute stroke.

**Methods**—In 30 months, 142 patients seen at the Mid America Brain and Stroke Institute received tPA. Site of presentation, protocol selection, and outcomes were analyzed.

**Results**—We found that 18.2% (142 of 781) of all ischemic strokes received tPA. Of those, 70% (99 of 142) were transferred from hospitals within 100 miles of Kansas City (Mo). Mortality rate was 12.7% (18 of 142). Symptomatic hemorrhage rate was 9.2%.

**Conclusions**—A comprehensive stroke center can serve as a hub for a regional network and increase the number of stroke interventions with acceptable outcomes. (Stroke. 2003;34:e58-e60.)

Key Words: stroke, ischemic ■ stroke units ■ thrombolysis ■ tissue plasminogen activator

In many areas of the United States, stroke victims are most likely to present to hospitals without stroke protocols or physicians familiar with the use of tissue plasminogen activator (tPA). This can result in missed opportunities to treat appropriate patients. This is a report of 142 patients who received tPA at the Mid America Brain and Stroke Institute at Saint Luke’s Hospital in Kansas City (Mo). Seventy percent were referred from regional hospitals.

**Subjects and Methods**

Three tPA protocols are used at the Mid America Brain and Stroke Institute. The National Institute of Neurological Disorders and Stroke (NINDS) tPA trial inclusions and exclusions are followed for patients treated within 3 hours.\(^1\) Informed consent is obtained for off-label use of tPA, and a 6-hour window is used for intra-arterial (IA) tPA. Patients with mild strokes presenting within 3 hours are treated according to the NINDS protocol for intravenous (IV) tPA at 0.9 mg/kg.\(^1\) More severe strokes (National Institutes of Health Stroke Scale [NIHSS] >10) seen within the 3 hours get IV tPA at 0.6 mg/kg, followed by angiography and IA tPA at 20 to 25 mg if a clot is located.\(^2\) IA tPA alone is reserved for patients in the 3- to 6-hour window or those who are not candidates for IV tPA therapy. To take advantage of early arrival by patients at regional hospitals, IV tPA can be initiated there in phone consultation with neurologists at Saint Luke’s, and transfer by helicopter or ambulance for subsequent angiography can be arranged. Patients presenting beyond the 3-hour window can be transferred for IA tPA.

Over 30 months, 781 stroke victims were admitted, and 142 patients received tPA in one of the protocols described. Data from those cases were analyzed to determine the site of origin, mortality rate, symptomatic hemorrhage rate, admission and discharge NIHSS scores, and time from onset to treatment.

**Statistical Analysis**

Categorical data are reported as frequencies and differences between treatment groups and were compared by use of a χ² or Fisher’s exact test. Continuous data are reported as mean±SD, and differences between treatment groups were tested by use of analysis of variance. The primary analysis using a paired t test evaluated the in-hospital change in NIHSS between admission and discharge for each treatment protocol.

**Results**

**Site of Origin and Protocol Selection**

We found that 18.2% of stroke victims (142 of 781) received tPA: IV tPA in 36% (52 of 142), IV followed by IA tPA in 25% (35 of 142), and IA tPA in 39% (55 of 142). Seventy percent (99 of 142) were referred from hospitals within 100 miles of Kansas City (Figure 1). More than half of the referring hospitals have <60 beds. The referring hospitals initiated IV tPA in 37.3% of the cases (53 of 142), and 21 of those went on to get IA tPA.

**Time to Treatment**

The mean times from onset to treatment were as follows: IV (0.9 mg/kg), 119 minutes; IV (0.6 mg/kg) followed by IA tPA, 120.5 minutes; and IA tPA, 210.6 minutes.
Outcomes

The mean admission NIHSS in patients who received only IV tPA was lower at 8.3±5.3 compared with 16.9±8.7 for combination IV/IA tPA and 16.5±8 for IA tPA alone. All groups had significantly improved NIHSS scores at discharge (Figure 2). Overall in-hospital mortality rate was 12.7% (18 of 142): IV tPA, 5.8%; IA tPA, 14.2%; and IV/IA, 20%.

<table>
<thead>
<tr>
<th></th>
<th>IV tPA (n=52)</th>
<th>IV/IA tPA (n=35)</th>
<th>IA tPA (n=55)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality rate</td>
<td>3 (5.8)</td>
<td>7 (20.0)</td>
<td>8 (14.6)</td>
<td>0.128</td>
</tr>
<tr>
<td>Symptomatic hemorrhage</td>
<td>1 (1.9)</td>
<td>4 (11.4)</td>
<td>8 (14.55)</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Symptomatic hemorrhage occurred in 9.2%: IV tPA, 1.9%; IV/IA tPA, 11.4%; IA tPA, 14.6% (the Table).

Discussion

The use of tPA in 18.2% of ischemic strokes in this series represents a significantly higher intervention rate than is generally reported. Hospitals in Cleveland reported tPA use in 1.8% of cases. Organized regional networks in Illinois and Calgary have reported tPA use in 6% of ischemic strokes. In Houston, a network of 1 university medical center and 3 community hospitals was able to treat 9% of ischemic strokes with IV tPA over 4 years. The high intervention rate at the Mid America Brain and Stroke Institute is due partly to the regional network of hospitals that works with stroke team neurologists on the management and transfer of patients. The network (Figure 1) that has developed has been an emergent process without formal organization or triage plan. It is a result of education programs, feedback from Saint Luke’s neurologists to referring physicians, easy access and transfers to Saint Luke’s stroke team, helicopter transport, and standardized orders and protocols for use in the referring hospitals. National and local media reports of successful stroke intervention at Saint Luke’s have raised the level of public and professional awareness in the surrounding communities.

Figure 1. Regional hospital stroke referral network surrounding Saint Luke’s Hospital Stroke Center in Kansas City, Mo.

Figure 2. Admission and discharge NIHSS in 3 treatment groups. P≤0.0001 for all 3 groups.
The availability of several tPA protocols also increases the intervention rate. The 6-hour window for intra-arterial tPA allows many more patients to be treated. Physicians in the regional hospitals have become proficient in initiating IV tPA before transfer. Evidence indicates that the earlier the treatment with tPA, the better the outcome. The 2-hour time-to-treatment times in both IV tPA groups in this series could not have been accomplished without the initiation of therapy in the regional hospitals. Many of these cases would have fallen outside the 3-hour window if they had been transferred without initiation of treatment.

Comparison of outcomes in this report to the literature is challenging because most references report experience with 1 tPA protocol. The in-hospital mortality rate in this series was 13% compared with 16% in the Houston report and 13% 30-day mortality in the Standard Treatment with Alteplase to Reverse Stroke (STARS) study, both IV tPA protocols. The mortality rates of 20% with IV/IA tPA and 14.6% with IA tPA in this report are comparable to other series. Suarez et al reported 16% mortality in a series of 45 cases of IV/IA thrombolysis with 16% in-hospital mortality; Prolyse in Acute Cerebral Thromboembolism II (PROACT II), using IA prourokinase, reported 25% mortality at 90 days. The median NIHSS in the PROACT II trial at 17 was comparable to the admission NIHSS in both the IV/IA (16.9) and IA (16.5) tPA groups in this report.

The symptomatic hemorrhage rate of 1.9% in the IV tPA group in this report is lower than that reported by NINDS (6.4%), STARS (3.3%), and Houston (5.6%). The symptomatic hemorrhage of 11.4% in the IV/IA tPA group and 14.6% in the IA tPA group compares well with the 18% hemorrhage rate in a series of similar cases reported by Kidwell et al.

This report indicates that the use of tPA can be increased when regional hospitals work with a comprehensive stroke center offering consultation and intra-arterial thrombolysis. This network may serve as a model for other regions in the country attempting to link primary and comprehensive stroke centers for improved intervention rates.

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References

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