

Building a “brain attack” team to administer thrombolytic therapy for acute ischemic stroke

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Abstract

BEFORE TISSUE PLASMINOGEN ACTIVATOR (tPA) WAS LICENSED for use in Canada, in February 1999, the Calgary Regional Stroke Program spearheaded the development and organization of local resources to use thrombolytic therapy in patients who had experienced acute ischemic stroke. In 1996 special permission was obtained from the Calgary Regional Health Authority to use intravenously administered tPA for acute ischemic stroke, and ethical and scientific review boards approved the protocols. After 3 years our efforts have resulted in improved patient outcomes, shorter times from symptom onset to treatment and acceptable adverse event rates. Areas for continued improvement include the door-to-needle time and broader education of the public about the symptoms of acute ischemic stroke.

Tissue plasminogen activator (tPA) was approved for the treatment of acute ischemic stroke in the United States in 1996 and in Canada in February 1999. Before Canadian approval, several Canadian centres, including Calgary, had gained early experience by participating in clinical trials of tPA for acute ischemic stroke. By special arrangement with the local health authority, Calgary began a program of open-label thrombolytic therapy for stroke in 1996.

The barriers to using tPA for acute ischemic stroke are dominated by the short time window: the drug must be administered within 3 hours of stroke onset. Patients must fulfill strict inclusion criteria because of the risk of symptomatic intracerebral hemorrhage. Another major impediment is the lack of public understanding of what the symptoms of stroke are. In the United States only 47% of randomly surveyed adults could identify a cardinal stroke symptom.¹ If patients do not recognize their symptoms and get to hospital rapidly, they cannot be treated with thrombolytic therapy.

The organizational approaches to solving the time problem and other barriers required a team approach. Because tPA for acute stroke was licensed only recently, only a few centres have had the opportunity to develop programs for acute stroke. We describe the development of the acute stroke service in Calgary and our initial experience with intravenously administered tPA.

Program development

The Calgary Regional Health Authority began restructuring health care services in the early 1990s. In January 1996 all neurosurgical and neurological staff and services were centralized to the Foothills Medical Centre. This allowed us to organize acute stroke care at one hospital around a multidisciplinary team that included the stroke team, the department of neurology, the department of diagnostic imaging, the department of emergency medicine, the stroke unit and emergency medical services (EMS). A protocol modelled after that used in the National Institute of Neurological Disorders and Stroke rt-PA Study² was developed applicable to the Calgary region. A pilot study, followed by ongoing treatment if safety concerns were met, was approved by the Medical Advisory Committee of the Calgary Regional Health Authority. After the first 20 patients an internal audit was conducted to assess the safety and complication rate of intravenous tPA therapy for acute ischemic stroke.

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Review

Synthèse

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We identified 5 Rs constituting the essential elements of acute stroke care: recognition (the time taken by patients to recognize their symptoms and call for help), reaction (the time taken for EMS to respond), response (the time from emergency department admission and assessment to CT scanning), reveal (the time for the stroke team to respond) and reperfusion (the time taken to start thrombolytic therapy) (Fig. 1). Target interval times are given in Table 1. This approach is similar to the “Code Stroke” pathways developed elsewhere.³ Special provisions were arranged with the Calgary Regional Health Authority for funding of a “blocked bed” on the stroke unit. This bed, virtually filled by a “ghost” patient, can be physically filled at any time with a real patient who has had a stroke.

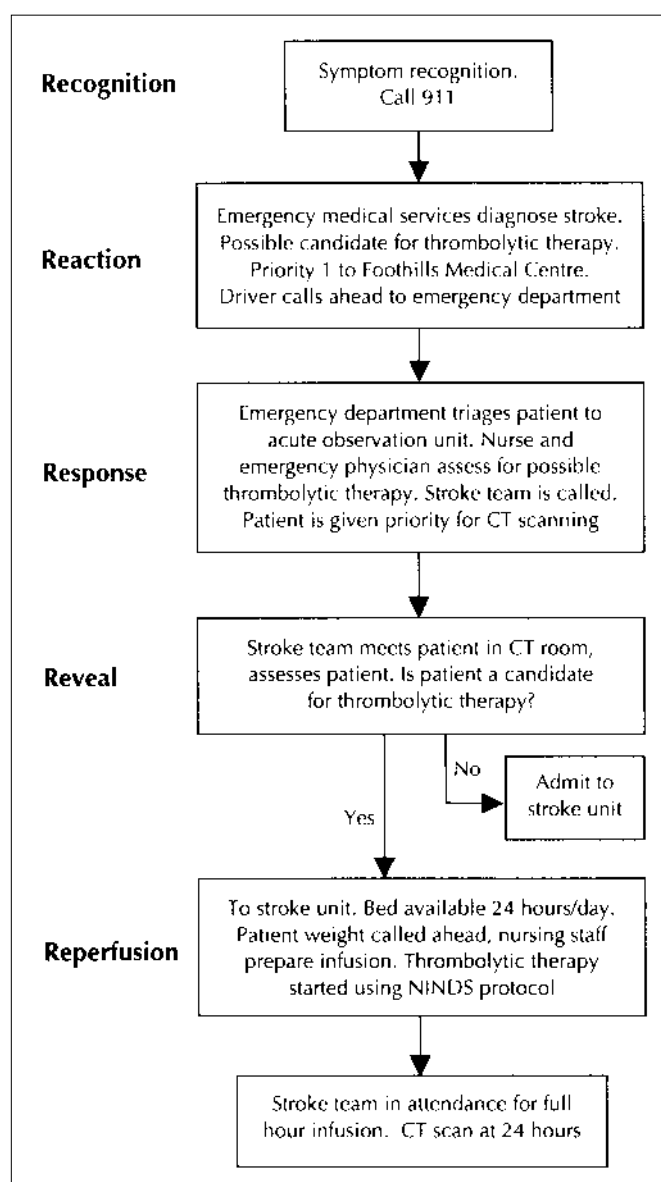


Fig. 1: Management of acute ischemic stroke at the Foothills Medical Centre, Calgary. tPA = tissue plasminogen activator, NINDS = National Institute of Neurological Disorders and Stroke.²

If the patient is a candidate for thrombolysis, he or she is moved immediately from the emergency department to the stroke unit, and another blocked bed is created instantly. The unit is called in advance to prepare the tPA infusion based on the patient's weight. The development of the blocked bed allowed for rapid removal of patients with acute stroke from the emergency department. Although patients were treated in a stroke unit in Calgary, the emergency department or intensive care unit would be logical alternatives in other institutions.

In cooperation with the Heart and Stroke Foundation of Alberta/North West Territories, a campaign was launched to educate the public about the symptoms of stroke. Specifically, people who might experience any of the cardinal symptoms of stroke — sudden onset of one-sided weakness (face, arm or leg), sudden onset of sensory loss (face, arm or leg), sudden difficulty speaking or understanding speech, or sudden loss of vision — were instructed to call 911 and inform the dispatcher that they were having a stroke. Local radio stations, television stations and newspapers participated in the education campaign.

EMS were asked to change their dispatch procedures for a possible stroke. En route, the driver was asked to alert the emergency department. Paramedics were taught a quick stroke assessment examination to identify patients who might be candidates for thrombolytic therapy. The dispatch priority for acute stroke was changed to a level 1 emergency (lights and sirens). All patients with onset of symptoms of acute stroke within the previous 3 hours were to be brought to Foothills Medical Centre, bypassing other hospitals.

The emergency department staff were asked to triage stroke as a life-threatening emergency, with a nurse and emergency physician making a preliminary assessment and arranging for plain cranial CT scanning. By arrangement with the diagnostic imaging department, the patient with acute stroke was given priority for CT scanning. On the patient's arrival in the emergency department, the stroke team, stroke unit and neurology service were all contacted automatically.

The stroke team, composed initially of the neurology resident on call and the neurologist on call, with support from one of us (A.M.B.), now also has a stroke nurse-practitioner and 1 of 4 neurologists (2 staff, 2 fellows). The team meets the patient in the emergency department or at the CT scanner and assesses the patient for possible thrombolysis.

Over 100 neuroscience nurses on the acute neuro-observation unit were trained and certified in tPA administration in addition to basic stroke care in April and May 1996. The inclusion and exclusion criteria and the procedures for intravenous administration of tPA to patients with acute stroke were printed on a pocket-size card and distributed to all members of the department of neurosciences and the emergency department (Fig. 2).

In the expectation of an increase in the number of patients with transient ischemic attack (TIA) who would be seen in the emergency department as a result of rapid triage by EMS, a walk-in TIA clinic was scheduled every

weekday afternoon. All patients with TIAs had a CT scan and were seen the same day or the following day in the stroke prevention clinic after direct referral from the emergency department.

All information regarding treated patients was collected prospectively.

We used the results of the original Oxfordshire Community Stroke Project cohort⁴ to estimate expected outcome.

Results

The first patient was treated with intravenously administered open-label tPA on Apr. 2, 1996. No safety concerns were identified at the internal audit after 20 patients had been treated. From the inception of the stroke program through Jan. 31, 1999, 69 patients were treated with intravenously administered tPA. The mean age was 69.3 years, 55% were male, 59% had a past history of hypertension, and 41% had atrial fibrillation. The median score on the National Institutes of Health Stroke Scale⁵ was 15. A total of 39% of the patients with total anterior circulation syndrome made an independent recovery at 3 months, as compared with 4% of the Oxfordshire patients.⁴ Similarly, 69% of the Calgary patients with partial anterior circulation syndrome, 50% of those with posterior circulation syndrome and 100% of those with lacunar syndrome achieved an independent outcome, as compared with 55%, 68% and 66% respectively of the Oxfordshire patients. The mean length of hospital stay was only 10.2 days, and 48% of the patients were discharged to home or to home with care.

From April 1997 to March 1998, 1127 patients with stroke were admitted in Calgary for treatment or investigation (Table 2). Of the 1127 patients, 731 had ischemic stroke. A total of 468 (64%) were admitted to Foothills Medical Centre; 29 (6%) of these patients were treated with intravenously administered tPA.

We have previously reported detailed outcome data.⁷ In brief, our outcomes were comparable to those achieved in published randomized trials, but treating patients who vio-

lated the stated strict inclusion criteria resulted in a rate of symptomatic hemorrhage of 25%. Despite initial concerns and published guidelines,⁸ none of the patients with symptomatic hemorrhage required craniotomy. However, 83% of the patients with symptomatic hemorrhage were dead at the 90-day follow-up.

EMS was the only group to have treatment times equal to or less than our target times (Table 1). Once the patient arrived at the hospital, it took a mean time of 46.1 (range

Table 1: Time intervals from symptom onset to treatment for 69 patients with acute ischemic stroke who received thrombolytic therapy in Calgary from April 1996 to January 1999

Interval	No. of patients	Time, min*			
		Target	Mean	Median	Range
Symptom onset to emergency department	63†	75	55.8	47	15–125
Symptom onset to CT scanning	68‡	125	101.2	100	40–160
Emergency department to CT scanning	63†	30	46.1	37	5–130
Emergency department to treatment	63†	60	101.8	100	45–330
CT scanning to treatment	68‡	30	55.6	45	20–315
Symptom onset to treatment	69	135	157.1	160	100–405

*Times are approximately normally distributed.

†Six patients had a stroke while they were inpatients.

‡One patient was treated without a CT scan for presumed myocardial infarction.

Table 2: Types of stroke at Calgary Regional Health Authority (CRHA) adult acute care hospitals from April 1997 to March 1998*

Stroke type†	CRHA total	Foothills Medical Centre	Peter Lougheed Centre and Rockyview Hospital
Ischemic stroke‡	731	468	263
Transient ischemic attack§	158	81	77
Subarachnoid hemorrhage¶	72	71	1
Intracerebral hemorrhage**	157	129	28
Total	1118††	749	369

*Source: corporate data, CRHA health records.

†International Classification of Diseases, Ninth Revision, Clinical Modification⁶ codes for most responsible diagnosis: †433, 434, 436; §435; ¶430; **431, 432.

††Nine patients were admitted directly to long-term care or the Alberta Children's Hospital and are not included in this total.

Table 3: Improvement in time intervals over time

Interval	Mean time, min		Mean of difference (and 95% confidence interval), min*
	Apr 1996–Aug 1997	Sept 1997–Jan 1999	
Symptom onset to emergency department	63.3	48.6	15.0 (3.2 to 26.9)
Symptom onset to CT scanning	113.3	89.7	23.6 (9.8 to 37.3)
Emergency department to CT scanning	51.1	41.6	9.6 (–4.4 to 23.5)
Emergency department to treatment	105.2	98.7	6.5 (–14.3 to 27.2)
CT scanning to treatment	54.4	56.7	–2.3 (–22.0 to 17.4)
Symptom onset to treatment	167.8	147.4	20.3 (2.3 to 38.4)

*Generated by means of a 2-sample t-test.

5–130) minutes to obtain a CT scan and a further mean time of 55.6 (range 20–315) minutes to start tPA treatment. The total mean time from symptom onset to treatment was just over 2.5 hours (minimum 100 minutes). The times improved over the study period (Table 3). Only 1 patient (1%) was treated between midnight and 7 am; 27 (39%) were treated on a weekend or holiday.

Interpretation

The main barrier to developing an acute ischemic stroke service — availability of beds and nursing — was overcome by the development of the blocked bed and an accompanying salary for a neuroscience nurse. EMS were the first to

have their protocols operational, and although our records are incomplete they indicate that, over the 3 years, only a handful of patients were mistakenly sent to a hospital other than the Foothills Medical Centre.

The neurology staff identified early on that they wanted to take responsibility for clinical decisions while on call, with the stroke team functioning in a consultative role. This arrangement has worked particularly well, with each attending neurologist participating actively in thrombolytic therapy.

Over 1 year, only 6% of patients with ischemic stroke admitted to Foothills Medical Centre and 4% of patients with ischemic stroke in the region were treated with tPA. These results compare favourably with those reported for Houston⁹ but leave much to be desired. Prospective information col-

<p style="text-align: center;">tPA in Acute Ischemic Stroke Please contact STROKE TEAM</p> <p>Procedures Prior to tPA Infusion</p> <ul style="list-style-type: none"> ◆ History and physical exam consistent with an acute ischemic stroke ◆ Pre-treatment tests: CBC, electrolytes, glucose, PT, PTT, fibrinogen, type and cross-match, ECG (results not required prior to tPA infusion unless suspected abnormality) ◆ Pre-treatment non-contrast head CT scan ◆ Attendance of the stroke physician to manage the case ◆ Compatibility with the inclusion criteria and contraindications (opposite page) <p>Procedures: tPA Infusion and Subsequent Management</p> <ul style="list-style-type: none"> ◆ Infuse tPA in a 0.9 mg/kg (maximum 90 mg) continuous IV infusion over 60 minutes with 10% of total dose as a bolus at the start of infusion ◆ Monitor in an acute care setting for signs of neurological change or bleeding <ul style="list-style-type: none"> ⇒ BP q15min x 2h then q30min x 6h then q1h x 16h ⇒ Neurovital signs q1h x 12h then q2h x 12h ⇒ Neurological examination (NIHSS or CNS score) q1h x 6h then q3h x 72h ⇒ Daily neurological evaluations after first 24h ⇒ NPO x 3h post infusion, then re-assess ⇒ Bedrest x 24h post infusion then re-assess ⇒ Maintain BP < 180/105 mm Hg; if clinical deterioration, <ol style="list-style-type: none"> 1. Discontinue tPA infusion 2. Immediate CT scan 3. Consider giving cryoprecipitate and platelets ◆ Repeat CT scan after 24h in all cases ◆ No IV heparin or ASA for 24h and repeat CT scan. ASA and/or heparin may be started after this period if the repeat CT scan is free of hemorrhage ◆ At 45 minutes into the infusion, check tongue, lips for evidence of angioedema. If present, consider discontinuing tPA and administration of antihistaminergics and corticosteroids 	<p>Inclusion Criteria</p> <ul style="list-style-type: none"> ◆ Acute ischemic stroke with clearly definable time of onset ◆ Patient presenting early enough so that thrombolytic infusion may be started within 3 hours from symptom onset <p>Absolute Contraindications</p> <ul style="list-style-type: none"> ◆ TIA or stroke with rapidly improving deficit ◆ History and examination compatible with subarachnoid hemorrhage ◆ BP > 185/110 mm Hg after 2 attempts to reduce BP to this level ◆ Pre-treatment CT scan showing: hemorrhage, mass effect or edema, tumour, or AVM ◆ Major surgery or trauma in the last 14 days ◆ Active internal bleeding ◆ Arterial puncture at a non-compressible site in the last 7 days ◆ History of hematological abnormality OR coagulopathy, OR anticoagulation for any reason (PT > 15sec, INR > 1.4, PTT > 40sec, platelets <100 x 10⁹/L) <p>Relative Contraindications</p> <ul style="list-style-type: none"> ◆ Decreased level of consciousness ◆ CT scan showing a large area of early infarct changes ◆ Intracranial surgery or intraspinal surgery < 2 months ◆ Stroke or head injury in the preceding 3 months ◆ History of GI or GU hemorrhage in the preceding 21 days ◆ Previous history of central nervous system bleeding ◆ Glucose < 2.7 mmol/L or > 22.2 mmol/L ◆ Seizure at stroke onset ◆ Pregnancy ◆ Endocarditis, acute pericarditis ◆ Serious underlying medical illness, including liver failure
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Fig. 2: Front (left) and back (right) of pocket-size card distributed to all members of the Department of Neurosciences and the Department of Emergency Medicine, Foothills Medical Centre, Calgary, for the intravenous administration of tPA. CBC = complete blood count, PT = prothrombin time, PTT = partial thromboplastin time, ECG = electrocardiography, IV = intravenous, BP = blood pressure, NIHSS = National Institutes of Health Stroke Scale, CNS = Canadian Neurological Scale, NPO = nothing by mouth, TIA = transient ischemic attack, AVM = arteriovenous malformation, INR = international normalized ratio, GI = gastrointestinal, GU = genitourinary.

lected over the third year of the program suggests that the main reason for not treating more patients is that either they do not arrive at hospital in time, or the time of symptom onset cannot be established reliably. Thrombolytic therapy will have little effect on stroke from a population standpoint if only 6% of patients can be treated. Since community surveys have shown that a substantial number of people cannot name even one symptom of stroke, public education about the symptoms and what to do about stroke can only increase the number of patients eligible for treatment.

The time from onset of symptoms to treatment is important. Animal data suggest that late reperfusion results in higher rates of hemorrhagic conversion.¹⁰ Treatment 3 to 6 hours after stroke onset is associated with a higher rate of symptomatic intracerebral hemorrhage than treatment before 3 hours.¹¹ Under 3 hours, the time from symptom onset to treatment is not predictive of hemorrhage.¹² However, patients who have early recanalization may have better outcomes.¹³ Our experience with EMS suggests that if the public can be taught to recognize stroke and react by calling 911, EMS will get them to the hospital promptly. The only group who had treatment times equal to or less than the target times in Calgary was EMS. Among patients arriving at hospital within 125 minutes of stroke onset in Cincinnati, 48% were treated, as compared with only 4% of those who arrived after 125 minutes.¹⁴ Other investigators have documented a mean door-to-needle time of 48 minutes.¹⁵ Thus, getting patients to hospital early is imperative.

The incremental improvements in treatment times over the study period suggest that there is a significant learning curve associated with the intravenous use of tPA for acute ischemic stroke. We are sobered by the fact that the improvement overall was gained primarily because patients reached the hospital faster. A major focus must now be on reducing the times from arrival to CT and from CT to treatment. The former can be as short as 5 minutes, which suggests that a target time of 30 minutes is both possible and reasonable. Neurologists took almost 1 hour to make the decision to start treatment. The fact that there was no improvement in CT-to-treatment times suggests that neurologists remain extremely cautious. This time is the most amenable to large improvement. With increased experience, it should be possible to meet this target.

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