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Background and Rationale:

Ischemic stroke is the most common type of stroke accounting for about 40,000 cases annually in Canada. In the great majority of cases, the cause is an acute occlusion of intracerebral arteries caused by thrombus originating either from proximal arterial atherothrombotic lesions or from an intracardiac source. Because thrombolytic therapy has been shown to restore vessel patency rapidly in different vascular beds, its use in acute cerebral ischemia appears reasonable as the brain is particularly sensitive to ischemia. Although several drugs (tissue plasminogen activator, urokinase, pro-urokinase, streptokinase) have been tested in this clinical context, only tissue plasminogen activator (t-PA) has been approved for treatment of acute ischemic stroke in Canada.

Indications:

- Acute ischemic stroke within 3 hours of symptom onset and with a clinically meaningful neurologic deficit.
- Baseline brain CT or other diagnostic imaging method (MRI) showing no evidence of intracranial hemorrhage

Contra-Indications:

- Minor or rapidly improving neurological symptoms or signs
- Uncontrolled hypertension (systolic pressure >185mmHg and/or diastolic pressure >110mmHg). Aggressive treatment necessary to lower blood pressure (e.g. Nitroprusside infusion).
- Low platelet count (<100,000/mm³)
- Major surgery or trauma in past 2 weeks
- Seizure at stroke onset if no clinical evidence of associated ischemic deficit
- Glycemia < 2.7 mmol/L or > 22.2 mmol/L
- Active internal bleeding
- Anticoagulant use with elevated activated partial thromboplastin time or INR >1.4
- Presence of symptoms suggesting pericarditis
- Pregnant or lactating women

Physicians using this treatment should be experienced in acute stroke management and CT scan interpretation and be treating patients in an appropriate hospital setting to closely monitor the neurological and hematological status of the patient.

Dose Regimen and Monitoring:

Based on favorable clinical evidence, the recommended dose of intravenous t-PA is 0.9mg/kg (maximum of 90mg) with 10% of the total dose given as an initial bolus and the remainder given over 60 minutes. Expert personnel (physicians, nurses), is required for clinical monitoring and management of potential complications. The risk of intracranial hemorrhage is increased approximately ten fold in patients treated with tPA the risk being maximal during the first 36 hours after treatment.

Doses of t-PA greater than 0.9mg/kg, uncontrolled hypertension (>185/110), severity of initial neurological deficit or obvious and major early infarct signs (clear evidence of extensive hypodensity or substantial edema with mass effect) on the pretreatment CT scan all may be associated with an increased risk of intracranial hemorrhage. Close clinical monitoring with regular and frequent neurological signs, as well as blood pressure monitoring (keep BP <180/105mmHg) and avoidance of any antithrombotic agents including antiplatelets in the first 24 hours after administration of t-PA is strongly suggested. Although no special hematological monitoring is required, a CBC, PT, PTT, INR, fibrinogen and brain CT are suggested between 24-36 hours post-administration.

Clinical Guide: Thrombolysis for Acute Ischemic Stroke

The recently published CASES study (Canadian Alteplase Stroke Effectiveness Study) has confirmed the effectiveness and safety of intravenous t-PA in routine clinical practice for acute ischemic stroke. Presently, intravenous streptokinase is not recommended for treatment of acute ischemic stroke and intra-arterial thrombolytic therapy is still investigational.

Although no clinical trial data are available on the use of tPA after 3 hours in patients with vertebrobasilar ischemic disease, case reports have documented good recovery with both intravenous and intra-arterial therapy given as late as 6-12 hours after symptoms onset in selected patients. Clinical expertise is required however, no recommendations can be provided at this time regarding this delayed use of thrombolytic therapy.

Management of Bleeding Complications:

For suspected major bleeding or intracranial hemorrhage:

- Stop infusion if still in progress
- Stat fibrinogen, CBC w/platelet, PT, PTT, FDP
- Type and cross 4 units PRBCs, 6 units cryoprecipitate, 2 units FFP, 1 unit platelets
- Stat CT scan without contrast of head if intracranial hemorrhage suspected

See corresponding section in Thrombolytic Therapy for Venous Thromboembolic Disease (VTE) guidelines.

References:

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