Acute management of stroke — I: ischaemic stroke

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Abstract

The adage that 'Time is Brain' remains a cornerstone of acute stroke treatment, and reflects the importance of timely diagnosis and treatment in order to minimise long-term consequences. The greatest advance in the management of ischaemic stroke has come in the form of reperfusion strategies, the success of which relies upon appropriate patient selection and the prompt initiation of therapy. The benefits of intravenous thrombolysis up to 4.5 hours are now firmly established, with trials underway to determine whether certain subgroups may benefit from thrombolysis beyond this timeframe. Intra-arterial thrombolysis has been used for decades but data on its efficacy and safety are limited. Novel methods of reperfusion, such as mechanical clot retrieval and stenting, have high recanalisation rates with acceptable safety and should be considered in patients with mid- to large-sized artery occlusion. Multi-modal reperfusion therapies, which use a combination of pharmacological and endovascular techniques, are showing encouraging results.

Keywords Clot retrieval; neuroprotection; stroke; thrombolysis

Royal College of Anaesthetists CPD Matrix: 2F01

Learning objectives

After reading this article you should be able to:

- describe the initial assessment and management of acute ischaemic stroke
- identify patients eligible for intravenous thrombolysis
- describe the criteria for endovascular intervention in stroke patients

Introduction

Ischaemic stroke can lead to devastating long-term neurologic sequelae. Prompt initiation of therapy aims to minimise irreversible damage. There are four interventions that improve the outcome after a stroke: management within a stroke unit, intravenous thrombolysis, aspirin within 48 hours, and decompressive hemicraniectomy for malignant middle cerebral artery (MCA) stroke. Of these interventions, thrombolysis is the most established although its use is limited by a narrow time-window. Several strategies have been developed to improve access to thrombolysis both at pre-hospital and in-hospital levels. In addition, the use of novel methods of reperfusion, such as intra-arterial thrombolysis and mechanical clot retrieval are rapidly expanding. In this brief review, we will discuss recent and exciting advances in the treatment of acute ischaemic stroke.

Emergency department assessment

The initial management of acute stroke focuses on stabilisation of the airway, breathing and circulation, followed by an assessment of neurological deficits and co-morbidities to identify patients eligible for thrombolysis (Tables 1 and 2). A concise history of the symptom onset, in particular with regards to when the patient was last seen well, should be obtained. Clinical features suggestive of stroke mimics should be identified (Table 1). The distinction between ischaemic and haemorrhagic stroke relies on imaging findings, although progressive neurological deficits or severe hypertension (systolic blood pressure >230 mmHg) are suggestive of haemorrhagic stroke. A focused and detailed neurological examination facilitates anatomical localisation, and thereby provides the basis for interpreting the imaging findings and potentially identifying the underlying causes.

Emergency investigations include blood glucose, electrolytes with renal function tests, full blood examination, cardiac markers, coagulation profile and ECG. Because time is critical, thrombolytic therapy should not be delayed while waiting for blood results (although hypoglycaemia must be excluded). Several biomarkers have been studied to predict infarct volume and prognosis (S100B, NSE and d-Dimer), however their clinical utility is limited by inadequate specificity.

A non-contrast CT brain must be obtained urgently to exclude intracerebral haemorrhages or structural lesions mimicking a stroke (e.g. subdural haematoma). The findings in ischaemic stroke will depend on the timing of the scan from the ictus, the severity and location of the ischaemia. Early signs of ischaemia include evidence of intravascular thrombus and cerebral oedema (i.e. loss of normal grey-white matter differentiation). A cerebral and/or neck CT angiogram should be considered in cases of arterial dissection and carotid or vertebral occlusive disease. Brain haemodynamic measurements with CT or MRI perfusion allow the identification of viable tissue at risk of infarction (penumbra). Diffusion weighted imaging, a novel technique to identify any restriction in water diffusion in brain tissue, is the most reliable tool for detecting acute ischaemic stroke as early as 30 minutes from symptom onset. Conventional MRI sequences are most useful for assessing the extent and age of subacute and chronic infarcts.

Stroke unit management (see Box 1 for summary)

Rapid triage of patients to a stroke unit has been shown to improve functional outcome and to reduce mortality (>20%) compared with treatment in a general medical ward. A stroke unit provides geographically localised care involving a multidisciplinary team of medical, nursing and allied health staff with expertise in stroke management. Physiological monitoring is an important aspect of stroke unit management. Routine

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Features of conditions mimicking stroke

Condition	Clinical features
Migraine with aura (complicated migraine)	Gradual onset of spreading deficits often associated with headaches
Hypertensive encephalopathy	Severe hypertension, headache, cortical blindness, seizures and vasogenic oedema
Seizure	Positive symptoms, amnesia for the event +/−Todd's paresis and tongue biting
Hypoglycaemia	History of diabetes, low serum glucose, decreased level of consciousness +/− focal deficits
Conversion disorder	Lack of concern, neurological findings in a non-vascular distribution, inconsistent examination
Drug toxicity	Lithium, phenytoin, carbamazepine

Table 1

supplemental oxygen is required acutely in stroke patients if oxygen saturation drops below 95%. Hypertension should not be treated in the first 48 hours unless extreme (>220/120 mmHg) or required for other indications (e.g. aortic dissection). If thrombolysis is given, the blood pressure should be maintained at less than 185/110 mmHg for the first 24 hours. Cardiac monitoring is indicated for early identification and treatment of atrial fibrillation or acute coronary syndrome. Hyperglycaemia and hyperthermia should be treated vigorously as they are independent adverse prognostic factors.

Reperfusion therapy

Intravenous thrombolysis

Numerous large, randomised, controlled clinical trials have established the benefit of intravenous thrombolysis with tissue plasminogen activator (r-tPA) at a dosage of 0.9 mg/kg within 4.5 hours from the stroke onset. Treatment given within 1.5 hours approximately doubles the odds of near-complete recovery compared to administration at 3.0—4.5 hours. Current imaging studies aim to establish whether patients with a salvageable ischaemic penumbra may benefit from thrombolysis beyond the 4.5-hour time-window. Strict adherence to r-tPA administration and post-treatment protocols minimises the risk of complications. The main side effects are intracranial haemorrhage (about 7% of cases), gastrointestinal bleeding, allergic reactions and hypotension. Predictors of intracranial haemorrhage are time of thrombolysis and the size of the core infarct. Current research focuses on enhancing the efficacy of thrombolysis by using agents with longer half-lives and higher fibrin-specificity, and on extending the time-window by selecting the patients on the basis of neuroimaging parameters.

Management of acute stroke

- Intravenous thrombolysis is an effective treatment for acute ischaemic stroke when given <4.5 hours after symptom onset
- Strict adherence to the treatment protocols minimizes the risk of haemorrhagic complications
- Mechanical clot retrieval and intra-arterial thrombolysis beyond the 4.5-hour window may be beneficial in highly selected cases
- Early decompressive hemicraniectomy in individuals (<60 years old) with hemispheric strokes and severe oedema increases survival, but not neurological recovery

Box 1

Intra-arterial thrombolysis

The delivery of thrombolytic agent directly to the thrombus reduces the risk of systemic side effects. The evidence for the use of intra-arterial thrombolysis is still limited (PROACT I, PROACT II and MELT) and not superior or safer to systemic thrombolysis.

Exclusion criteria for thrombolytic treatment of acute ischaemic stroke

Historical

- Stroke/head trauma in previous 3 months
- Any history of intracranial haemorrhage
- Major surgery over the last 14 days
- GI or urinary tract bleeding in previous 21 days
- Myocardial infarct in previous 3 months
- Arterial puncture at non-compressible site in previous 7 days
- Dabigatran within 4 hours (relative)

Clinical

- Spontaneously clearing stroke symptoms
- Only minor and isolated neurologic signs
- Seizure at onset *if* thought to be Todd's paresis
- Symptoms suggestive of SAH
- Persistent BP >185/110
- Active bleeding or acute trauma
- NIHSS >25

Laboratory

- Platelets <100/mm^3
- Glucose <2.8 mmol/litre
- INR >1.7
- Elevated aPTT

CT brain

- Haemorrhage
- Multilobar infarction involving >1/3 of the cerebral hemisphere

aPTT, activated partial thromboplastin time; BP, blood pressure; CT, computed tomography; GI, gastrointestinal; INR, international normalized ratio; NIHSS, National Institutes of Health Stroke Scale; SAH, subarachnoid haemorrhage.

Table 2

Intra-arterial thrombolysis is an option for acute middle cerebral artery occlusions within 6 hours of symptom onset in patients who have contraindications to systemic thrombolysis. Patients with basilar artery occlusive strokes have a mortality rate of 90% without recanalisation, and as such small case series have also supported the use of intra-arterial thrombolysis in selected patients with basilar thrombosis within 24 hours of symptom onset.

Mechanical clot retrieval

Several devices and techniques aiming to aspirate the occluding clot have been trialled. The use of these devices may extend the treatment window beyond the conventional 4.5-hour window and are an option for patients with contraindications to rt-PA. The combination of systemic/intra-arterial thrombolysis and mechanical thrombectomy appears to have a higher rate of recanalisation compared to intravenous rt-PA alone (80% vs 46%). Nevertheless, recanalisation is not invariably associated with a favourable outcome, possibly due to intracerebral haemorrhage with revascularisation of the ischaemic core. In addition, endovascular approaches are costly and require highly specialised centres. Patients with proximal vessel occlusions, severe neurological deficits (National Institutes of Health Stroke Scale >18), a viable penumbra on MRI and good functional premorbid status might benefit the most, but further controlled clinical studies are required.

Antiplatelet agents

Aspirin 100–300 mg daily should be started within 48 hours of stroke onset to reduce the risk of early recurrent ischaemic stroke and, to a mild extent, to reduce mortality and unfavourable outcome. In patients with dysphagia, aspirin 300 mg should be administered rectally or by enteral tube. There is currently no evidence to support the early use of clopidogrel, dipyridamole or intravenous abciximab.

Neuroprotection

A large number of neuroprotective strategies (glutamate and calcium antagonists, corticosteroids and free radical scavengers) have proved effective in experimental models but have failed to translate into clinical practice. Possible reasons for this discrepancy include dosing issues, poor drug penetration into the ischaemic penumbra, and outcome evaluation. The SAINT-I trial demonstrated reduced disability and rate of r-tPA-related haemorrhage after administration of the free radical trapping agent NXY-059. However, such beneficial effects were not confirmed in subsequent studies. Hypothermia is an alternative neuroprotective strategy effective in animal models and feasible in the clinical setting. However, initial trials have shown increased incidence of medical complications without significant benefits.

Decompressive surgery

Patients with MCA territory stroke complicated by severe cerebral oedema comprise a small proportion of stroke patients. Untreated, the mortality is up to 80%. Decompressive hemicraniectomy and duroplasty performed in individuals less than 60 years old within 48 hours of symptom onset increases survival to 80%, but this is often associated with severe disability.

Conclusion

Stroke is a clinical emergency requiring prompt medical intervention. Thrombolytic therapy with rt-PA is available but its use is currently limited. Strategies to increase patient access to rt-PA and improve the efficacy of thrombolysis are rapidly evolving. Lack of evidence from randomised controlled trials precludes the recommendation and widespread adoption of endovascular treatment in acute stroke. Further advances in neuroimaging techniques and endovascular interventions are likely to result in significantly improved outcomes for patients with ischaemic stroke. ◆

FURTHER READING

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