Acute ischaemic stroke

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ABSTRACT Stroke is the third most common cause of death worldwide. About 80% of strokes are ischaemic. The only reliable way of distinguishing cerebral infarction from haemorrhage is with neuroimaging, most commonly CT scanning in the UK. The last decade has produced a number of RCTs clarifying former areas of management uncertainty. Three interventions have been shown to be beneficial in acute stroke: admission to a stroke unit; early aspirin; and intravenous thrombolysis. Aspirin and stroke service admission should be available to all patients, thrombolysis is of benefit to a select minority of patients. Accurate diagnosis, investigation, and management of physiological variables such as BP, temperature, glycaemia, and oxygen saturation should improve outcome. Multiprofessional guidelines exist and, when used with education, audit, and other areas of clinical governance, improve the basic standards of care. The National Sentinel Audits of Stroke have repeatedly shown that care is suboptimal. Secondary prevention with anti-platelet drugs (or warfarin in the case of atrial fibrillation), statins, and antihypertensive drugs, reduce recurrent strokes and other vascular events. Patients with 70–99% stenosis of the ipsilateral carotid bulb or internal carotid artery may benefit from early carotid endarterectomy.

KEYWORDS Aspirin, haemorrhage, infarction, neuroimaging, prevention, stroke, thrombolyises.

LIST OF ABBREVIATIONS angiotensin-converting enzyme (ACE), blood pressure (BP), Chinese Acute Stroke Trial (CAST), computed tomography (CT), diffusion-weighted imaging (DWI), International Stroke Trial (IST), lacunar infarction (LACI), National Institute of Health Stroke Score (NIHSS), numbers needed to treat (NNT), magnetic resonance angiograms (MRA), magnetic resonance imaging (MRI), magnetic resonance venograms (MRV), partial anterior circulation infarction (PACI), posterior circulation infarction (POCI), primary intracerebral haemorrhage (PICH), randomised controlled trials (RCT), recombinant tissue plasminogen activator (rt-PA), Safe Implementation of Thrombolysis in Stroke (SITS-MOST), subarachnoid haemorrhage (SAH), total anterior circulation infarction (TACI) transient ischaemic attack (TIA), World Health Organization (WHO).

DECLARATION OF INTERESTS No conflict of interests declared.
DIAGNOSIS

Stroke is a clinical diagnosis and should be suspected if there is a sudden onset (usually within seconds) of a focal neurological deficit usually occurring in individuals with established vascular disease or risk factors. Three-quarters of all strokes occur in those over 65 years of age. National audits have consistently shown the physical examination to be inadequate, often neglecting the assessment of sensory modalities, visual fields and parietal signs such as neglect and dysphasia. The National Institute of Health Stroke Score is useful particularly if considering thrombolysis. The Oxford Community Stroke Project classification helps to identify cause and allows some cautious prediction of outcome (see Table 1).

INVESTIGATIONS

Cerebral haemorrhage and infarction can only be reliably distinguished with neuroimaging. In the UK this is most commonly done using unenhanced CT scanning. The Royal College of Physicians guidelines recommend CT scanning within 24 hours of symptom onset although many departments are rightly striving for immediate scanning. Computed tomography scanning should be done as an emergency if any of the following are present: a depressed level of consciousness, anticoagulation or known coagulopathy, severe headache at onset, papilloedema, neck stiffness or unexplained fluctuation or progression of symptoms, or if there is potential for thrombolysis. Some MRI sequences are particularly useful in identifying haemosiderin deposits of old haemorrhage, for patients presenting late, when the characteristic hyperdense CT appearance of haemorrhage may have become hypodense (usually after ten days). In cerebral infarction early CT scans may appear normal. There are now increasingly recognised early CT signs of ischaemia, and training is available on the British Association of Stroke Physician’s website (www.basp.ac.uk). Diffusion-weighted imaging is particularly useful for detecting small infarcts not visible on CT scanning. Early MRI may not always recognise cerebral haemorrhage. Magnetic resonance angiograms and MRV allow non-invasive imaging of vessels. Colour Doppler ultrasonography is most commonly used to image carotid vessels and calculate the degree of stenosis.

MANAGEMENT

Three interventions have been shown, by RCT, to be of benefit in acute ischaemic stroke.

International Stroke Trial (IST) and CAST, two of the largest RCTs, have shown that aspirin (300 mg and 160 mg, respectively) given soon after a stroke (orally or rectally) reduces the risk of further cerebral infarction and death or dependence, although the overall benefits are small (NNT = 90). The International Stroke Trial also showed that regular use of heparin reduced thromboembolic complications, but this is offset by an...
increased risk of systemic and cerebral haemorrhage. Routine use of early prophylactic heparin is not recommended.

Trials have consistently shown that stroke services work, preventing death and disability (NNT=18). These trials often pre-dated the regular use of thrombolysis, antiplatelet therapy, and the many secondary prevention therapies. No one feature can be identified, but education, audit, and the use of guidelines, with an emphasis on consistent management, may outweigh the purely pharmacological benefits of drugs.

Intravenous thrombolysis with 0.9 mg/kg of alteplase, an rt-PA, was given a provisional license in the UK in 2003 for the treatment of acute ischaemic stroke. SITS-MOST, a post-marketing audit has shown thrombolysis works well outside the trial situation. It must be given within three hours of symptom onset. The inclusion and exclusion criteria are listed in Table 2. Currently only about 5% of strokes meet these criteria but service redesign may increase this number considerably as has been seen in some European and North American centres. Benefits can be considerable (NNT=16 for reduced dependency) but 1 in 30 patients will have a severe intracerebral haemorrhage which may prove fatal. Introducing a thrombolysis service requires a major investment in service development and education involving potential patients, primary care staff, ambulance staff, and hospital services. The benefits of a thrombolysis service may outweigh that of pure thrombolysis, with all patients benefitting from improved early assessment, imaging, and physiological monitoring.

In the early phases of stroke, high temperature, low blood pressure, low oxygen saturation, and hyperglycaemia are all associated with worsening outcomes. Whether this represents a direct effect on neuronal physiology leading to cell death, or reflects the severity of the stroke and its complications, is uncertain. It makes physiological sense to maintain these parameters within normal limits if at all possible, although trial evidence for this is lacking. Hypotension may reflect dehydration or sepsis, and hypoxia commonly reflects pneumonia or pulmonary embolism. Pyrexia should instigate a search for sepsis and responds to paracetamol.

SECONDARY PREVENTION

There is a growing body of evidence about secondary prevention. Aspirin reduces further vascular events by about 20%. The usual maintenance dose is 75–150 mg per day. Higher doses are associated with a greater risk of side-effects. Clopidogrel, 75 mg per day, is as effective and can be used as an alternative in those genuinely intolerant to aspirin. There is emerging evidence that a combination of aspirin and dipyridamole may have additional benefits over aspirin alone. Trials of the combination of aspirin and clopidogrel have shown that haemorrhagic complications offset any benefits and this combination should only be used with care in ischaemic stroke after recent acute coronary syndrome.

Anticoagulation is not recommended for patients in sinus rhythm. In those with atrial fibrillation it reduces the risk of further stroke by 67%, from an annual risk of about 12%. Because of the possible risk of causing haemorrhage into a friable early infarct, anticoagulation is usually delayed for the first two weeks. It can be given earlier if there is rapid recovery or in TIA. The risk–benefit balance becomes complex, particularly in elderly patients (greater risk of haemorrhage) and in those with a history of falls, previous haemorrhage, dementia, or poor compliance.

There is a near-linear relationship between mean arterial blood pressure and incidence of stroke, implying that hypertension causes stroke. Recent trials show that reducing blood pressure reduces the risk of further vascular events. There is uncertainty as to when to introduce antihypertensives after a stroke; ongoing trials should clarify this. Most guidelines recommend starting therapy one or two weeks after the stroke. Long-acting ACE inhibitors, such as ramipril and perindopril (with

<table>
<thead>
<tr>
<th>Exclusion</th>
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<tr>
<td>&gt;3 hours from onset of symptoms.</td>
<td>&lt;3 hours from symptom onset.</td>
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<tr>
<td>Severe stroke (NIHSS &gt;25).</td>
<td>Cerebral haemorrhage excluded with imaging.</td>
</tr>
<tr>
<td>Very large infarction on CT scan.</td>
<td>18–80 years.</td>
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<tr>
<td>Seizure at onset.</td>
<td>Consent for alteplase (if possible).</td>
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<tr>
<td>History suggestive of subarachnoid haemorrhage.</td>
<td>Neurological deficit &gt; 30 minutes.</td>
</tr>
<tr>
<td>Heparin in preceding 48 hours.</td>
<td>Unit specialising in stroke care.</td>
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<tr>
<td>Previous stroke and diabetes.</td>
<td>Not rapidly improving.</td>
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<td>Stroke in previous three months.</td>
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<td>BP &gt;185 systolic or &gt;110 diastolic.</td>
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<td>Glucose &lt;2.8 or &gt; 22.</td>
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<td>Platelets &lt;100.</td>
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<td>Other: including warfarin, previous cerebral or subarachnoid haemorrhage, recent gastrointestinal bleed, surgery, pancreatitis, or pericarditis.</td>
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TABLE 2 Criteria for thrombolysis in ischaemic stroke.
indapamide), are beneficial even in those with near-normal blood pressure.

There is a less powerful relationship between serum cholesterol and stroke when compared with ischaemic heart disease. Trials have shown that lowering cholesterol with statins reduces vascular events and strokes. The recent SPARCL study showed that atorvastatin, 80 mg, reduces the incidence of stroke and vascular events in TIA and stroke patients without previous heart disease by 2% over five years. Current guidelines recommend treating all stroke patients with a serum cholesterol above 3·5 mmol/l with the equivalent of 40 mg of simvastatin.

Patients with an anterior circulation TIA or stroke who have made a good recovery may benefit from a carotid endarterectomy if the ipsilateral bulb or internal carotid artery is (70–99%) stenosed. Lesser degrees of stenosis may also benefit if local surgical morbidity is low, particularly as the procedure can be done under local anaesthetic. There is strong evidence that patients are at high risk of recurrent stroke in the first week after a TIA or stroke, particularly if they are elderly, hypertensive, and symptoms last more than 60 minutes. Such patients should have early endarterectomy.

In common with other vascular diseases, lifestyle advice should be given and documented. Such advice includes stopping smoking, reducing salt intake, taking regular exercise, eating more fruit and vegetables, reducing body mass and curbing excessive alcohol consumption, if required. Such advice stresses the need for the patient’s active participation in secondary prevention. Rehabilitation is started early, with patients sitting out of bed as soon as possible. All staff should be well versed in setting both long- and short-term goals. Patients recovering rapidly should be discharged with early supported discharge, and all patients should receive physiotherapy, occupational therapy, and speech and language therapy if required. National audits have shown disappointingly low involvement of psychologists and social workers in multidisciplinary teams. Good stroke management is consistent, multiprofessional, guideline-driven, and audit-managed and should be the right of all stroke patients.

**KEYPOINTS**

- Cerebral haemorrhage can only be distinguished from cerebral infarction by neuroimaging.
- The clinical diagnosis of stroke is based on a clear history of sudden onset of a focal neurological deficit, often with a background of vascular disease.
- As soon as cerebral haemorrhage has been excluded antiplatelet therapy, usually aspirin 300 mg stat., followed by 75–150 mg per day, should be started.
- Alteplase (rt-PA) is conditionally licensed in the UK for the treatment of cerebral infarction, but must be given within three hours of symptom onset.
- Patients admitted through a stroke service consistently do better than those admitted through general wards.