

Stroke

Keypoints

- Stroke is a significant cause of UK morbidity and mortality – the most important cause of adult disability, and the third leading cause of death.
- Specialist acute and rehabilitation management on a Stroke Unit is associated with improved outcomes, though effective rehabilitation can also be provided by a co-ordinated, multidisciplinary early supported discharge service.
- Stroke is associated with a high risk of recurrence, particularly within the first month. Therefore, effective prevention strategies should be applied early.
- Hypertension is the most prevalent modifiable risk factor for primary and secondary prevention, how best to manage blood pressure in the immediate post-stroke period is still unclear.

Background

Stroke is the most common life-threatening neurological condition, the third most common cause of death, and the most important cause of adult disability in the United Kingdom representing 4.4% of National Health Service costs notwithstanding costs to social services and individual patients and carers. New strokes affect over 120,000 patients per annum in the United Kingdom with 30,000 people suffering recurrent strokes. Importantly, the risk of recurrence is 'front-loaded' with 15% of transient ischaemic attack or minor stroke patients suffering a disabling stroke within one month. Therefore, acute stroke is a medical emergency, and a combination of public education and effective pre-hospital triage should facilitate rapid access to stroke unit care.

Assessment

A detailed clinical assessment, comprising history, examination, and neuroradiological and cardiovascular investigation, should establish the neurological deficit (e.g. by use of the National Institutes of Health Stroke Scale). Also, it should exclude non-stroke diagnoses, distinguish ischaemic from haemorrhagic stroke; define aetiology, particularly future modifiable vascular risk factors; provide prognostic information and identify an acute treatment population.

Acute Treatment

To date, only systemic intravenous thrombolysis with recombinant tissue plasminogen activator has been approved for the hyperacute treatment of acute ischaemic stroke [1], though the short therapeutic window (3 hours) and the need to exclude haemorrhagic stroke limit its general

usage. Unfortunately, other proposed neuroprotective treatments to prevent ischaemia and reperfusion-induced cell death lack efficacy.

Nonetheless, measures to optimise perfusion and metabolism may be important to salvage potentially viable 'penumbral tissue'. These include: maintenance of adequate oxygenation; prevention of aspiration pneumonia and other infective complications; avoidance of hypo- and hyperglycaemia; and prevention of venothromboembolic complications, though prophylactic anticoagulation should not be routinely prescribed. Aspirin, however, in a dose of 300mg daily should initially be prescribed for all cerebral infarct, but not haemorrhage, patients irrespective of their initial blood pressure levels, as this will have a small but significant effect in reducing recurrent ischaemic stroke, death and dependency but with a small (although significant) risk of haemorrhage.

Blood pressure management in the immediate post-stroke period is less clear for the 80% of acutely hypertensive patients, as well as the 40% of patients on pre-existing antihypertensive therapy. In the acute stroke period, there is evidence that both relative hypotension and hypertension may be associated with poor outcome [11]. In the presence of global cerebrovascular dysautoregulation, theoretical mechanisms mitigate against acute intervention, except in a minority of indications listed in existing guidelines, where arbitrary blood pressure levels for intervention have been defined:

- Hypertensive encephalopathy
- Cardiac, vascular or other urgencies (e.g. acute myocardial infarction, unstable angina, severe left ventricular failure, aortic dissection, acute renal failure)
- Concurrent or intended coagulant therapy (thrombolysis)
- Severe hypertension associated with intracerebral haemorrhage (>180/105mmHg)
- Severe hypertension associated with ischaemic stroke (>200/120mmHg)

Therefore, the recommendation for the majority of hypertensive patients in the immediate post-ictal period is that pre-existing treatment is stopped, where relevant, that blood pressure is monitored, and treatment re-introduced or started de novo at one to two weeks following stroke. For the minority of acute stroke patients where relative hypotension (systolic BP <140mmHg) may be detrimental, current recommendations suggest the identification and treatment of potentially reversible causes (e.g. myocardial ischaemic, arrhythmias, sepsis), adequate hydration, and the consideration of pressor therapy. However, ongoing trials of candidate depressor (ACEI, ARB, Labetalol, Nitrates) and pressor (Phenylephrine) agents will specifically address these questions. Ongoing rehabilitation should continue to be provided in a geographically defined stroke unit within a hospital by a co-ordinated multidisciplinary team with specialist expertise in stroke and rehabilitation [2], though subsequent rehabilitation may be provided effectively by early supported discharge services [3].

Secondary Prevention

All ischaemic stroke patients should have an individualised strategy of evidence-based secondary prevention. Hypertension will be considered in a specific section, but measures should include:

- (1) Aspirin. Aspirin should be continued in all cerebral infarct patients for the first 2 weeks and then, following the National Institute for Health and Clinical Excellence recommendations, Dipyridamole-MR, where tolerated, should be additionally prescribed at a dose of 200mg twice daily. Clopidogrel should be reserved for genuinely Aspirin-intolerant patients.
- (2) Statin therapy is recommended for all patients with cerebral infarction with a total cholesterol >3.5mmol/l, unless contraindicated. Its benefits in patients with cerebral haemorrhage have yet to be clearly defined.
- (3) Anticoagulation. Specific preventative measures are required in patients with cerebral infarct with persistent or paroxysmal atrial fibrillation, who should be anticoagulated with warfarin, unless contraindicated, with a target International Normalised Ratio of 2.5 (range 2.0 to 3.0), following exclusion of haemorrhage by neuroimaging [4]. Furthermore, all patients with a symptomatic carotid stenosis >70% (without near occlusion) and some patients with a stenosis of 50 to 69% should be considered for carotid endarterectomy [5], which should ideally be undertaken as soon as possible after last symptoms [6].
- (4) All patients should receive lifestyle advice, including smoking cessation, regular exercise, appropriate diet, and avoidance of excess alcohol.

Intracerebral Haemorrhage

Specific treatments for intracerebral haemorrhage are few, with no evidence supporting immediate neurosurgical intervention, at least for supratentorial haemorrhage [7]. The outcome of ongoing trials of recombinant activated factor VII use in cerebral haemorrhage are eagerly awaited. [8].

Hypertension and Stroke

Primary Prevention: Hypertension is the most prevalent modifiable risk factor for both primary ischaemic and haemorrhagic stroke, with clear evidence that antihypertensive therapy reduces this risk [9]. Current guidelines recommend that blood pressure be lowered to a target of <140/85mmHg (<130/80mmHg for diabetic patients). The main determinant of benefit from blood pressure-lowering drugs is the achieved level, rather than the agent used, though specific antihypertensive drug classes may benefit special patient groups. In particular, in older patients, beta-blocker based regimes appear to be less effective than alternatives in respect of stroke prevention in the primary, secondary and acute settings.

Secondary Prevention:

Furthermore, in stroke survivors, the risk of recurrent fatal and nonfatal stroke and other cardiovascular events is high. It is recommended that blood pressure reduction should be attempted in both normotensive and hypertensive patients, probably with an ACEI and/ or Thiazide or thiazide-like therapy regime, provided that there is no contraindication and that such

blood pressure reduction is tolerated [9], and provided at least one to two weeks have elapsed following stroke onset [10]. It is important to note that benefits are reported in both normotensive and hypertensive patients with modest blood pressure reductions (10/5mmHg) with a target BP of <130/80 mmHg.

Conclusions

Stroke is an important cause of reduced life expectancy and disability-free life expectancy in the United Kingdom. Hypertension is the most prevalent modifiable risk factor, and should be appropriately managed as part of an overall prevention strategy, which includes antithrombotic therapy, statin therapy, lifestyle modification, and anticoagulation and carotid surgery in selected patients. The management of acute blood pressure change following stroke remains a matter of debate, though ongoing trials should provide important information about the efficacy and safety of blood pressure manipulation in the immediate post-ictal period.

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