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Author(s)	Cheung, RTF
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RTF Cheung 張德輝

Cerebrovascular disease—advances in management

腦血管疾病處理的進展

Recent advances in the diagnosis and treatment of stroke have justified its management as a medical emergency. This article summarises current recommendations for the initial management of major types of stroke with emphasis on acute therapy for ischaemic stroke. Recommendations are based on the results of well-designed clinical trials. An acute stroke care team and an acute stroke unit should be established in all regional hospitals.

Diagnosis of stroke must be accurate. General management aims for prevention and treatment of neurological and systemic complications, whereas specific management varies according to the stroke type and the underlying pathogenic mechanisms. For selected patients with ischaemic stroke, intravenous recombinant tissue plasminogen activator or a modified viper venom within 3 hours of onset, or intra-arterial pro-urokinase within 6 hours may improve functional outcomes. Neurosurgical treatment is indicated for some patients with ischaemic or haemorrhagic strokes. Prevention of recurrence and rehabilitation are the core components of subsequent management.

中風的診斷和治療的新進展證明，將其作為緊急醫療情況處置是恰當的。本文總結了對於主要類型中風初步處理的最新建議，重點在局部缺血中風的緊急處置。處置建議基於設計良好的可用臨床試驗結果。所有地區醫院都應設立緊急中風護理組和緊急中風科。

中風的診斷必須準確，一般處理的目的在於預防和治療神經性和全身的併發症，特殊處理根據中風類型和潛在的致病機製而改變。在挑選出的局部缺血中風患者中，在肇端開始3小時內經靜脈輸送重組體組織纖維蛋白溶脢原催化劑或更改的毒液，或在6小時內經動脈輸送原尿激脢可以改善功能結果。對一些局部缺血或出血中風患者所進行的神經外科處置作了簡要說明。康復和預防復發是隨後處理的核心。

Key words:
Cerebral haemorrhage;
Cerebral infarction;
Subarachnoid haemorrhage;
Surgical treatment;
Thrombolysis

關鍵詞：
腦出血；
腦梗塞；
蛛網膜下腔出血；
外科治療；
血栓溶解

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Division of Neurology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong
RTF Cheung, PhD, FRCP (Edin)

Correspondence to: Dr RTF Cheung

Introduction

Stroke is not a cerebrovascular 'accident'. It is a consequence of cerebrovascular disease and a leading cause of death and disability—approximately one third of stroke patients die and another third survive with significant neurological deficits. Recently, there have been some breakthroughs in both diagnosis and treatment. Stroke should therefore be managed as a brain-threatening emergency—a 'brain attack'.

Stroke is defined as a syndrome with rapidly developing signs of focal or global disturbance in cerebral or visual functions due to non-traumatic vascular causes, with symptoms lasting for at least 24 hours, or having a rapidly fatal course.[1] The major pathological types of stroke are

Table 1. Patterns of neurological deficit according to the location of stroke[10]

Location	Pattern
Left (dominant) hemisphere	Aphasia, right hemiparesis and/or sensory loss, right homonymous hemianopsia, impaired conjugate gaze to right, dysarthria, dyslexia, dysgraphia, dyscalculia
Right (non-dominant) hemisphere	Left-sided visual-spatial neglect, left-sided weakness and/or sensory loss, impaired conjugate gaze to left, dysarthria, spatial disorientation, apraxia
Brain stem, cerebellum, or occipital lobe	Motor or sensory loss in all 4 limbs, cranial nerve deficits with or without limb weakness and/or sensory loss on opposite side of body, dysarthria, dysconjugate gaze, nystagmus, gait ataxia, amnesia, bilateral visual field defects
Small subcortical hemisphere or brain stem	Pure motor stroke with weakness of face and limbs on the same side without abnormalities of higher brain functions, sensation, or vision; pure sensory stroke with reduced sensation of face and limbs without abnormalities of higher brain functions, sensation, or vision; ataxia, hemiparesis; clumsy hand, dysarthria

ischaemic stroke (ISS or cerebral infarction), intracerebral haemorrhage (ICH or haemorrhagic stroke), and subarachnoid haemorrhage (SAH). A transient ischaemic attack (TIA) is essentially a mild ISS with symptoms resolving within 24 hours, of which the symptoms of most TIAs resolve in less than 1 hour.[2] The artificial cutoff of 24 hours between strokes and TIAs requires amendment because of the narrow time window for acute interventions in ISS (within 6 hours of onset). A TIA provides a warning of an increased risk of stroke and warrants aggressive measures of stroke prevention.[2] The management of traditionally defined TIA is identical to that of ISS.

Among Caucasians, ISS accounts for 80% to 85% of all strokes, ICH accounts for 10% to 15% of strokes, and the remaining 5% are due to SAH.[3,4] Previous local studies have reported different figures for the Hong Kong population—specifically, 60% to 65% for ISS and 30% to 35% for ICH.[5,6] A recent local study, however, found rates of ISS (78.3%), ICH (21.4%), TIAs (5.2%), and SAHs (0.2%), which are more similar to those found in Caucasians.[7]

Overall management of stroke is multifaceted and includes primary prevention, management of acute stroke, prevention and treatment of systemic or neurological complications, rehabilitation, and secondary prevention. This article is a brief review of the initial management of major types of stroke during the first few days after onset, with emphasis on acute therapy for ISS. Readers should refer to other articles for discussions of aetiology and pathogenesis of stroke and rehabilitation after stroke, as well as primary and secondary prevention of stroke.[8,9] The recommendations reported herein are based on currently available data from clinical trials. When evidence is not available from clinical trials, consensus statements from expert groups have been adopted as the guidelines for treatment.

Initial evaluation

Stroke should be suspected in all patients presenting with sudden onset of focal neurological symptoms and signs, including:

(1) Weakness, paralysis, incoordination, and/or sensory loss of the arm and/or leg;
(2) Facial weakness, asymmetry, and/or sensory loss;
(3) Dysarthria or aphasia;
(4) Monocular or binocular visual loss;
(5) Ataxia, poor balance, clumsiness, or difficulty in walking;
(6) Vertigo, double vision, nausea, or vomiting; and
(7) Stupor or coma, confusion, agitation, or seizures.[10]

The pattern of deficits reflects the site of stroke (Table 1). Differential diagnoses include cranio-cervical trauma, focal seizures, drug intoxication, brain tumour, encephalitis, brain abscess, subdural haematoma, hypoglycaemia, migraine with focal neurological symptoms, and syncope. Clinical features alone cannot reliably differentiate between ISS and ICH. Subarachnoid haemorrhage, however, may be preceded by some characteristic clinical features (Box 1), which serve as warning symptoms. Differential diagnoses also include migraine, tension headache, meningitis, cervical spine injury or arthritis, and whiplash injury.[11]

Management of stroke starts with an accurate diagnosis and classification of stroke types from studying the history of patients, physical examination, and investigations.[4,11,12] The general medical examination should focus on the cardiovascular system. A complete

Box 1. Characteristic presenting features of subarachnoid haemorrhage

Sudden severe headache
Nausea and/or vomiting
Photophobia
Phonophobia
Neck stiffness

Table 2. The National Institutes of Health Stroke Scale (abbreviated version)[13]

Item	Score
Level of consciousness	0 (alert), 1 (arousable), 2 (obtunded), 3 (coma)
Orientation	
two questions	0 (both correct), 1 (one correct), 2 (neither correct)
two commands	0 (both correct), 1 (one correct), 2 (neither correct)
Eye movements	0 (normal), 1 (partial), 2 (forced deviation or total gaze paresis)
Visual fields	0 (normal), 1 (partial), 2 (complete), 3 (bilateral hemianopsia)
Facial palsy	0 (normal), 1 (minor), 2 (partial), 3 (complete or bilateral)
Left arm motor	0 (no drift), 1 (drift), 2 (some effort against gravity), 3 (no effort against gravity), 4 (no movement)
Right arm motor	0 (no drift), 1 (drift), 2 (some effort against gravity), 3 (no effort against gravity), 4 (no movement)
Left leg motor	0 (no drift), 1 (drift), 2 (some effort against gravity), 3 (no effort against gravity), 4 (no movement)
Right leg motor	0 (no drift), 1 (drift), 2 (some effort against gravity), 3 (no effort against gravity), 4 (no movement)
Limb ataxia	0 (absent), 1 (one limb), 2 (two or more limbs)
Sensory	0 (normal), 1 (mild to moderate), 2 (severe or total sensory loss)
Language	0 (normal), 1 (mild to moderate), 2 (severe aphasia), 3 (mute)
Dysarthria	0 (normal), 1 (mild to moderate), 2 (severe)
Extinction or inattention	0 (absent), 1 (one modality), 2 (two or more modalities)

Box 2. Hunt and Hess Scale for subarachnoid haemorrhage[11]

Grade 1	Asymptomatic or mild headache only
Grade 2	Moderate to severe headache Nuchal rigidity Oculomotor palsy
Grade 3	Confusion, drowsiness Mild focal neurological signs
Grade 4	Stupor Hemiparesis
Grade 5	Coma, moribund Extensor posturing

neurological examination should be performed, including the Glasgow Coma Scale, the National Institutes of Health Stroke Scale (NIHSS) [Table 2], and the Hunt and Hess Scale for suspected SAH (Box 2).[4,11-13] The severity and nature of the neurological deficits documented reveals the extent of ongoing brain injury and forecasts the prognosis.

Admission to an acute stroke unit reduces the risk of death, lessens disability, and lowers the need for long-term institutionalised care.[14,15] A stroke unit is a geographically defined facility within a hospital that specialises in caring for patients with stroke. In this unit, cardiac and neurological monitoring should be available, whereas the facility for invasive monitoring is optional. Initial evaluation also includes assessment of vital signs, estimation of the most likely aetiology, and screening for any complications.

Box 3. Recommended initial investigations for stroke[4]

- Computed tomography of the brain without contrast
- Electrocardiography
- Chest X-rays
- Complete blood count, prothrombin time, partial thromboplastin time, serum electrolytes, urea and creatinine, blood sugar, liver function tests
- Fasting blood sugar and lipids
- Arterial blood gas levels when hypoxia suspected*
- Lumbar puncture for subarachnoid haemorrhage if computed tomography of the brain is inconclusive*
- Cervical spine X-rays if patient is comatose or trauma is suspected*
- Electroencephalography for seizures*

* Under certain other circumstances

Initial investigations

The recommended initial investigations for stroke are listed in Box 3.[4] Early computed tomography (CT) signs of ISS include loss of the insular ribbon, obscuration of the lentiform nucleus, and cerebral hypodensity or early sulcal effacement.[4,11,12] The hyperdense artery sign reveals the site of ongoing ischaemia. Computed tomography signs of early infarction are often associated with more serious ischaemic injury, poor outcome, and a greater risk of haemorrhage transformation.[16,17] Magnetic resonance imaging (MRI) is more sensitive than CT in detecting small subcortical or cortical infarctions, or lesions in the posterior fossa. The age of the haematoma can also be estimated by MRI.[4,12] Magnetic resonance imaging, however, has some short-comings: it is not commonly available, acute haemorrhage may be missed, and MRI cannot be used for patients with claustrophobia, a pacemaker, or metallic implants. Cerebral angiography, transcranial Doppler, and duplex ultrasound examination of the cervical arteries can be helpful for detecting arterial diseases such as atherosclerosis and dissection.[17] Transthoracic and transoesophageal echocardiography and Holter monitoring are similarly useful in screening for cardiogenic embolism and aortic plaques.[4] Special haematological and serological tests are also indicated

when hypercoagulability, antiphospholipid antibody syndrome, or vasculitis are suspected.

General management

General management at the acute stage comprises regular neurological observation and attention to vital signs and potential complications (Table 3).[4,11,12] Adequate oxygen saturation is important. Hypoxia may occur secondary to airway obstruction, hypoventilation, aspiration pneumonia, and/or atelectasis. Hyperbaric oxygen may be useful for some patients with stroke secondary to an air embolism or Caisson's disease.[4] Corticosteroids are not recommended for cerebral oedema or increased intracranial pressure (ICP).[18,19] Osmotherapy (mannitol), hyperventilation, and neurosurgical procedures are indicated in response to high ICP.[4]

Anticonvulsants should be prescribed to prevent recurrent seizures in patients with ISS or ICH and should be given to all patients with SAH during the immediate post-haemorrhage period.[4,11,12] An elevation in blood pressure is commonly observed, however, pharmacological treatment should be avoided unless hypertension is severe (systolic pressure >220 mm Hg in ISS, or mean pressure >130 mm Hg in ICH) or thrombolytics are used.[4,12,16] Since hyperthermia aggravates brain damage, infection should be treated vigorously, and hyperpyrexia should be controlled.[4,20] Euglycaemia should also be maintained. Early mobilisation and low dose subcutaneous heparin can prevent deep vein thrombosis and pulmonary embolism.[4] Good nursing care, early physiotherapy, cautious feeding, and adequate nutrition can all lower the risk of subsequent medical complications.

Acute treatment of ischaemic stroke

An unstable ischaemic penumbra provides an opportunity for acute intervention within the therapeutic time window.[21] Four types of antithrombotics are available to treat thromboembolic occlusion of cerebral vessels: plasminogen activators (thrombolytics), defibrinogenation, anticoagulants, and antiplatelet agents. Thrombolytic agents convert plasminogen to plasmin, which cleaves fibrinogen and fibrin. Tissue plasminogen activator , urokinase (UK) and pro-urokinase (pro-UK) are 'specific' in binding selectively to the fibrin clot, whereas streptokinase (SK) is 'non-specific' and binds to both fibrin and fibrinogen.

Of the thrombolytics studied to date, only intravenous administration of recombinant tissue plasminogen activator (rtPA) has been shown to be effective in managing acute ISS, in terms of better functional outcome and a trend towards reduced mortality.[22-27] Specifically, the evidence indicates that one extra patient will have an excellent functional outcome for every eight patients receiving rtPA.[22] The benefit applies to different pathogenic subtypes of ischaemic strokes and is sustained at 1 year poststroke.[28,29] Table 4 summarises the inclusion and exclusion criteria used in the National Institute of Neurological Disorders and Stroke rtPA Stroke Study Group Trial. The rtPA dose given was 0.9 mg/kg (with a maximum 90 mg) with 10% as a bolus dose and 90% infused over 1 hour.

Heparin, warfarin, aspirin, or other antithrombotic agents should be withheld for 24 hours after treatment with rtPA. Nevertheless, intravenous rtPA treatment

Table 3. Common complications of stroke and recommended management[4,11,12]

Complications	Management
Neurological	
Cerebral oedema	Hyperventilation, osmotherapy (mannitol)
Hydrocephalus	Neurosurgical shunting
High intracranial pressure	Hyperventilation, osmotherapy, neurosurgical monitoring
Haemorrhagic transformation	Conservative, reverse bleeding tendency
Seizures	Electroencephalography, anticonvulsants
Systemic	
Aspiration	Tube feeding, frequent suction
Hypoventilation	Avoid sedatives, mechanical ventilation
Pneumonia	Antibiotics, chest physiotherapy, oxygen
Myocardial ischaemia	Avoid hypoxia, nitrates, consult cardiologist
Cardiac arrhythmias	Avoid electrolyte disturbance, consult cardiologist
Deep vein thrombosis	Subcutaneous heparin, early mobilisation
Pulmonary embolism	Subcutaneous heparin, early mobilisation
Urinary tract infection	Avoid indwelling catheter, antibiotics
Decubitus ulcers	Regular turning, air mattress
Malnutrition	Cautious oral feeding or tube feeding, parenteral nutrition
Contractures	Early physiotherapy and mobilisation
Stiff joints	Early physiotherapy and mobilisation

Table 4. Inclusion and exclusion criteria used in the National Institute of Neurological Disorders and Stroke rtPA Stroke Study Group Trial[22]

Inclusion
Ischaemic stroke within 3 hours of onset
Measurable deficit on the National Institutes of Health Stroke Scale
No intracranial haemorrhage, tumour, aneurysm, arteriovenous malformation, nor early changes of a major cerebral infarction on computed tomography of the brain
Exclusion
Pregnancy; minor
History of intracranial haemorrhage
Previous stroke or major head trauma within 3 months
Myocardial infarction within 3 months
Pericarditis within 6 weeks
Gastrointestinal bleeding or urinary tract haemorrhage within 3 weeks
Major surgery within 2 weeks
Arterial puncture at a non-compressible site within 1 week
Anticoagulated or received heparin within 2 days
Renal, liver, or other organ failure
Rapidly improving or minor symptoms
Symptoms of infarction of entire middle cerebral artery territory
Seizure at the onset of stroke
Complete loss of brain stem reflexes or coma
Features of subarachnoid haemorrhage
Systolic blood pressure >185 mm Hg or diastolic blood pressure >110 mm Hg
Elevated partial-thromboplastin time or prothrombin time
Platelet counts <100 000/mm^3
Hypoglycaemia (<50 mg/dL) or hyperglycaemia (>400 mg/dL)

carries a high (3% to 6%) risk of symptomatic haemorrhagic transformation (SHT),[22,24,30] and mortality rates of up to 60% within 6 weeks have been observed in patients with SHT.[22] Benefits associated with rtPA use have not been seen when stroke patients were treated between 3 and 6 hours after onset or when a higher dose of rtPA was used.[23,24,31] Factors associated with a higher risk of SHT or a poor outcome include increasing time from onset, uncontrolled hypertension, a higher dose of rtPA, advanced age, severe stroke (NIHSS >20), and early infarct signs on CT scan.[22,28]

Future clinical trials are needed to determine the role of SK in acute ISS. Studies to date indicate that intravenous SK produces unacceptable rates of SHT.[25-27]

Thrombolytic therapy—issues and options

Many stroke patients present to the hospital more than 3 hours after onset. Only 3% to 4% of all stroke patients are candidates for rtPA in the USA, for example.[32] In addition, only 1% of the National Institute of Neurological Disorders and Stroke rtPA Stroke Study Group Trial population were Asian by race.[22] Thus, the risk-benefit ratio of rtPA therapy is uncertain in Asian populations. It is also unknown whether Asian patients require an adjustment in dosage. Although a local, randomised, placebo-controlled, double-blinded clinical trial is needed to confirm the efficacy and safety of rtPA in Hong Kong, it would be difficult to conduct such a trial because only a small percentage of patients are candidates for rtPA and haemorrhagic stroke is relatively more common in Hong Kong than in western countries.

Local intra-arterial infusion of a smaller dose of thrombolytic agent is a logical alternative.[16,33-36] There are a number of theoretical advantages with this approach. Firstly, the presence, site, and size of any occluding thrombus or thromboembolus can be confirmed. Secondly, use of a lower dose would reduce the risk of SHT. Thirdly, arterial recanalisation can also be confirmed. Intra-arterial infusion would, however, further delay thrombolysis since arterial angiography is needed, adding extra risk to the patient.

Anecdotal case reports and uncontrolled studies on local intra-arterial infusion of UK, pro-UK and rtPA are available.[16,33-36] A recently completed, randomised, phase III clinical study of 180 patients (from screening of 12 000 patients) showed that 40% of patients treated with pro-UK (9 mg infused over 2 hours) plus low dose intravenous heparin (2000 IU bolus followed by 500 IU/h for 4 hours) within 6 hours of a documented proximal middle cerebral artery (MCA) thromboembolic ISS had slight or no neurological disability at 90 days, when compared to a rate of 25% in patients treated with intravenous heparin alone. Futhermore, pro-UK increased the rate of SHT from 2% to 10%, whereas the mortality rate was unaffected.[36] Intra-arterial thrombolysis within 3 hours of onset remains an experimental treatment option as it has not been

shown to be more effective than intravenous rtPA in improving clinical outcomes following ISS.[16] Patients with stroke onset of between 3 and 6 hours previously may benefit from intra-arterial pro-UK.[36] Large, randomised, controlled clinical trials are needed to clarify the role of intra-arterial thrombolysis.

Another option which allows extension of the treatment time window beyond 3 hours is the 'bridging' technique of combining intravenous rtPA (at the lower dose of 0.6 mg/kg) and intra-arterial rtPA.[37]

Queen Mary Hospital studies

Special triage of stroke patients potentially eligible for acute thrombolysis and ongoing clinical trials on neuroprotectants has been undertaken at the Queen Mary Hospital accident and emergency department since July 1998.[38] Over a 30-month period, rtPA was given to 10 eligible patients after informed written consent was obtained from the patients and/or their relatives. In addition, 17 patients were recruited into ongoing clinical trials of neuroprotectants given within 6 hours of onset of stroke. Of seven patients treated with intravenous rtPA (0.8 mg/kg), two patients with severe deficits did not improve and died of massive stroke. Haemorrhagic transformation was seen in one of the two fatal cases. The remaining five patients made an excellent or complete recovery from their disabling stroke. All three patients treated with intra-arterial rtPA (total dose, 11 to 21 mg) had haemorrhagic transformation. This was asymptomatic for one patient who underwent a complete recovery. Transient deterioraton with subsequent complete recovery was seen in the second patient, after temporary ventricular drainage for obstructive hydrocephalus, whereas no improvement was seen in the third patient who succumbed to the massive MCA infarction. (Unpublished data. RTF Cheung).

Acute defibrinogenation in ischaemic stroke

A recent placebo-controlled trial of acute defibrinogenation involving 500 patients has been reported. Acute defibrinogenation (to a target fibrinogen level between 40 to 69 mg/dL) within 3 hours of stroke onset was achieved using intravenous infusion of ancrod, a modified viper venom, for 5 days.[39] A favourable outcome was seen in 42% of the patients treated with ancrod, compared with 34% of those treated with placebo. Symptomatic haemorrhage transformation was seen in 5.2% of the ancrod-treated patients compared with 2% of controls, however. The benefit of acute defibrinogenation in ISS remains to be confirmed and compared against the efficacy of intravenous rtPA in future studies.

Use of anticoagulants

Rapidly acting, parenteral anticoagulant agents may stop clot propagation, prevent recurrent embolism and help maintain perfusion to the ischaemic penumbra via collaterals.[4] The role of immediate or early anticoagulation in acute cardioembolic stroke remains unknown. Immediate anticoagulation carries an increased risk of SHT. Spontaneous haemorrhagic transformation is present in 30% to 40% of cardioembolic strokes, and bleeding usually occurs within the first 2 to 4 days.[40,41] In the International Stroke Trial, the benefit of early antithrombotic treatment with aspirin (300 mg/day) or two different doses of subcutaneous unfractionated heparin (5000 or 12 500 IU twice daily) within 48 hours of onset was assessed in patients with ISS.[42] Neither heparin regimen reduced the risk of death or level of dependency at 6 months.

Subcutaneous low-molecular–weight heparin (nadroparin) has been shown to be effective in preventing deep vein thrombosis and pulmonary embolism, whereas its benefit in ISS was suggested by the results of a small clinical trial.[43] In the first nadroparin stroke study, the treatment window was within 48 hours of onset. Elapsed time since awakening with symptoms was used for some patients however, and two thirds of patients were given treatment 24 hours or more after stroke onset.[43] The second nadroparin stroke trial was larger and better designed, using 24 hours post stroke as the treatment window. Benefits seen in the first study were not confirmed, however.[44] Similarly, treatment with a low-molecular–weight heparinoid, Org 10 172, did not confer a benefit for patients with ISS.[45] Further clinical trials are needed to determine the efficacy of subcutaneous low-molecular–weight heparins or heparinoids in ISS.[46]

For patients who need long-term anticoagulation for secondary prevention of stroke, the optimum time to commence treatment is uncertain. A popular strategy is to delay anticoagulation for 48 hours for small to moderate sized infarcts, and for 7 to 10 days for large infarcts.[10] Computed tomography of the brain should be repeated to exclude spontaneous haemorrhagic transformation before initiation of anticoagulation.

Antiplatelet agents

Antiplatelet agents (aspirin, aspirin plus dipyridamole, ticlopidine, and clopidogrel) are effective for prophylaxis against ischaemic events,[4,9] and early use of aspirin in ISS has been evaluated in two large trials, the International Stroke Trial and the Chinese Aspirin Stroke Trial.[42,47] Early use of aspirin (160 to

300 mg/day) within 48 hours of stroke onset could reduce 11 cases of recurrent ISS or death per thousand patients, and produce two additional cases of SHT.[47]

The glycoprotein IIb/IIIa receptor antagonists are effective adjuncts for high-risk patients undergoing coronary angioplasty with or without stenting. The Abciximab in Ischemic Stroke Investigators reported encouraging results from a randomised, double-blind, placebo-controlled, dose-escalation trial involving 74 patients treated within 24 hours of onset. Fifty four patients were treated with four escalating doses of intravenous abciximab and 20 patients with placebo.[48] The scheduled post-study CT brain scans detected asymptomatic parenchymal haemorrhages in 7% of the abciximab-treated patients and 5% of the placebo-treated patients. Another 11% of abciximab-treated patients had asymptomatic parenchymal haemorrhages on unscheduled brain imaging (CT or MRI) performed between days 2 and 35. No instances of SHT were noted. In contrast, however, a local study using a similar dosing regimen was suspended when one of the two Chinese patients died of SHT despite a 6-hour treatment window.[49]

Neuroprotectants

To date, none of the neuroprotectants—calcium channel blockers, inhibitors of glutamate release, glutamate receptor antagonists, barbiturates, opiate antagonists, free radical scavengers, or membrane active agents—has been found to be beneficial following ISS.[4,50] Results are still awaited from completed trials on neuro-protectants, however, and other studies are ongoing.[51] There is no evidence to support the use of haemodilution or volume expansion in ISS, and hypothermia is currently an investigational treatment modality.[4]

Neurosurgery

While surgical procedures to revascularise the ischaemic penumbra have not been shown to be effective in controlled trials, there is now renewed interest in neurosurgical management (decompressive craniectomy or infarctectomy) of malignant cerebral oedema due to large hemispheric infarction.[4,52] Monitoring of ICP, drainage of hydrocephalus, and decompressive posterior fossa surgery are considered appropriate management in special circumstances.

Specific management of haemorrhagic strokes

The site of ICH is influenced by the underlying cause.[3] In general, patients with ICH have greater deficits, lower levels of consciousness, and greater increases in ICP and blood pressure than patients with ISS. Close neurological observation is crucial. Severely elevated blood pressure should be treated to stop further bleeding and recurrent bleeding. Medical and neurosurgical therapies can control raised ICP (Table 3). Patients with a small ICH (<10 mL) or mild deficits, and moribund patients with brainstem or hemispheric haematoma should be treated medically.

Cerebellar haematoma should be surgically removed in deteriorating patients with brainstem compression or obstructive hydrocephalus.[12] Surgical removal of haematoma allows confirmation of the presence, as well as management of underlying aneurysm, arteriovenous malformation, or cavernous angioma in patients where the vascular lesion is accessible and there is a good chance of recovery.[12] Young patients with a moderate or large lobar haematoma whose condition is deteriorating, may be candidates for surgery. Neurosurgery is currently not recommended for any other patient groups pending more information from clinical trials. Although bleeding diatheses are uncommon causes of ICH, any bleeding tendency should be promptly detected and corrected by appropriate measures.[3]

Management of spontaneous subarachnoid haemorrhage

Spontaneous SAH is due to rupture of a berry aneurysm in most cases.[11] The major causes of death and disability include effects of the initial bleeding, recurrent SAH, and cerebral ischaemia due to vasospasm. Neurosurgical input is crucial. Management is complex and includes general and symptomatic treatment, treatment of raised ICP and hydrocephalus, prevention of recurrent SAH, and treatment of cerebral ischaemia.[11]

The incidence of rebleeding peaks in the first 24 hours (occurring in approximately 4% of patients) and markedly decreases after the first 4 weeks.[53] Rebleeding is preventable by clipping of the an-eurysm. Other useful measures include control of blood pressure, use of antifibrinolytic agents, and interventional neuroradiological procedures.[11] The incidence of cerebral vasospasm peaks between day 5 and day 14, with gradual resolution over 2 to 4 weeks.[54] Adequate hydration, calcium antagonists (nimodipine 60 mg orally every 4 hours for 21 days), transluminal angioplasty, hypervolaemic haemodilution, and induced hypertension (after aneurysm clipping) are effective measures for this complication.[11]

Conclusions

Effective treatments exist for major types of stroke, and strokes are highly preventable. The term brain attack emphasises that stroke requires management as a medical emergency. Stroke services should be organised, with formation of acute stroke care teams and the establishment of acute stroke units. The public, medical doctors, and health professionals need to know more about stroke and should be educated to view stroke as a medical emergency. Many people, however, do not currently recognise the presentation of stroke and/or know the best response to its occurrence.[55,56]

Specific management varies according to the type of stroke and the underlying pathogenic causes. Close monitoring of neurological state, attention to vital signs, and prevention and treatment of neurological and systemic complications is crucial in managing all types of stroke, however.

The traditional definition of TIA is now obsolete given the time window for treatment of ISS of 3 to 6 hours. Among appropriately selected patients with ISS, intravenous rtPA or ancrod within 3 hours of onset, or intra-arterial pro-UK within 6 hours improves functional outcomes. Early use of aspirin in ISS has a small benefit. Advanced neuroimaging techniques may further improve patient selection and extend the time window for treatment via direct visualisation of the ischaemic penumbra.[17] A combination of intravenous and intra-arterial thrombolysis or combining neuro-protective therapy with thrombolysis may also extend the time window for treatment beyond the current 3- to 6- hour limit.

New medical or surgical treatment for different types of stroke will emerge from the results of large randomised trials. Non-acute management of stroke should be focused upon prevention of recurrent stroke as well as rehabilitation of the patient with stroke.

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