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Stroke Management in the Decade of the Brain

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Stroke has been the third (fourth in 1995) leading cause of death in Singapore since 1970, accounting for 10% to 12% of all deaths, and a crude death rate of 50 to 60/100,000. While the number of patients dying from stroke has been rising, the age and sex-standardised mortality rates have declined dramatically[1]. The number of patients admitted annually to Singapore hospitals for stroke has been escalating; this trend can be expected to continue as the population ages. While there is as yet no efficacious treatment that can be administered uniformly to all stroke patients, clinical trials have provided much-needed new information, opening new avenues for management of what has previously been thought to be an untreatable disease.

Contrary to the unfavourable results of emergency carotid surgery or embolectomy, clinical trials of pharmacological reperfusion of ischaemic stroke have yielded cautiously encouraging results[2]. The two latest published trials of fibrinolytic agents - National Institute of Neurological Diseases and Stroke (NINDS) recombinant Tissue Plasminogen Activator (rTPA) trial, and the European Co-operative Acute Stroke Study (ECASS) - have suggested the possible benefit of intravenous rTPA administered within 3 and 6 hours respectively of stroke onset. While there was a better outcome in treated patients, the risk of symptomatic haemorrhage suggests caution. Centres embarking on a thrombolysis program should have adequate neurological, neurosurgical, neuroradiological and neurointensive care facilities available on a 24-hour basis. It is still uncertain which subtype of stroke should receive thrombolysis, the preferred route of administration, the best agent, or the optimal time window. The streptokinase trials (Australian Streptokinase Trial AST, Multicentre Acute Stroke Trial-Italy MAST-I, and Multicentre Acute Stroke Trial-Europe MAST-E) yielded largely unfavourable results. The outcome after thrombolysis may be better in those with early recanalisation. ECASS II and the Australian Urokinase Stroke Trial (AUST) may provide further information when they are completed a few years from now. The utility of fibrinogenolytic agents such as snake venom, particularly Ancrod, is undergoing clinical trials.

Trials of neuroprotectant drugs have generally yielded disappointing results - most trials either showed no efficacy or were stopped prematurely because of deleterous complications or unacceptable side-effects[3]. It appears that benefit will probably be seen only with early treatment, and the new and on-going trials tend to include only those patients randomisable within 6 hours of onset of stroke symptoms. More neuroprotectant trials have been planned or are on-going and the results of these are eagerly awaited.

The recurrence rate of stroke after an ischaemic stroke or transient ischaemic attack ranges from 5% to 10% annually. Antiplatelet drugs are presently the mainstay of therapy to reduce recurrence. A meta-analysis[4] has suggested that 40 vascular events will be avoided per 1,000 stroke or TIA patients treated with antiplatelet agents over a 3-year period; benefit is seen in both men and women. However, the minimum effective dose of aspirin, the most widely used antiplatelet agent, is still uncertain. The recently concluded mega-trials of 20,000 patients each - International Stroke Trial (IST) and Chinese Aspirin Stroke Trial (CAST) - recommend that all ischaemic stroke patients be started on aspirin as early as possible. Ticlopidine, another antiplatelet agent, is at least as good as aspirin, as suggested by the Ticlopidine Aspirin Stroke Study (TASS); it is FDA approved for use in those who have failed aspirin, or who are aspirin intolerant. Clopidogrel was tested in the study of Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE); it may be a safer alternative to ticlopidine. The additional benefit of dipyridamole is being debated after the recent publication of the European Stroke Prevention Study (ESPS) II. The role of anticoagulants is uncertain and will probably be further clarified after the completion of the Warfarin Aspirin Recurrent Stroke Study (WARSS) and the second Fraxiparine in Ischaemic Stroke Study (FISS-bis).

The benefits of carotid endarterectomy in patients with severe symptomatic carotid stenosis of 70% to 99% and who have a minor stroke or transient ischaemic attack (TIA), have been clearly demonstrated in the North American Symptomatic Carotid Endarterectomy Trial (NASCET), European Carotid Surgery Trial (ECST) and Veterans Administration (VA) trial[5]. In centres with low surgical and angiographic morbidity and mortality, the risk of recurrent stroke may be reduced from 26% to 9% at 2 years of follow-up. There is as yet no evidence of benefit of surgery for moderate or mild carotid stenosis over medical

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treatment. The role of carotid or vertebral artery angioplasty and stenting is still under investigation. The early clipping of ruptured intracranial aneurysms has reduced the risk of rebleed; coils may be inserted into some aneurysms unsuitable for surgery to promote thrombosis. Obliteration of arteriovenous malformations (AVMs) by surgery, neuroradiological insertion of "glue", and radiosurgery by gammaknife have been shown in carefully selected cases to reduce recurrent haemorrhage.

The benefits of non-pharmacologic therapy should however, not be forgotten. These include the avoidance of iatrogenic hypotension, adequate sugar and fever control, prophylaxis for deep venous thrombosis, and early rehabilitation. Stroke Units refer to a geographical co-location of stroke patients in a hospital ward, or a multi-disciplinary team of specialists who attend to all stroke patients in a hospital. Stroke Units have been found to reduce death at one year by 17%, hospital stay by 8%, death or dependency by 31%, and death or institutionalisation by 25%[6]. These benefits were independent of the patient's age, sex, stroke severity or variations in stroke unit organisation. This benefit can be easily realised by a reorganisation of the stroke services in a hospital, without inflating costs of stroke care. Such a stroke team would comprise physicians, nurses, therapists, medical social workers, dietitians, stroke nurse educators, and other health care professionals who can contribute to the better care of the stroke patient.

The problems of stroke care will continue to plague every community. Recent advances have begun to show that there are realistic therapeutic options for stroke patients, especially if offered early, and in the setting of a Stroke Unit. It is time to thrust aside the nihilism that has long dogged those caring for stroke patients, and to persist with efforts to reduce the tremendous costs stroke has on patients, families and the society at large.

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