Stroke

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The prominence of stroke on the political agenda is rising to reflect its importance as the third leading cause of death worldwide. However, an article in The Guardian on the day of the conference showed that there is still a long way to go to influence some politicians about this public health perspective, given 'Frank Dobson's well-known aversion to [public health] and what he [sees] as its 'pointy-headed academics'. The professions allied to medicine constituted one quarter of the 300 delegates, reflecting their partnership in contemporary, multidisciplinary stroke care. However, the conference organiser, Professor Charles Warlow (Professor of Medical Neurology, University of Edinburgh), lamented the dearth of neurologists in the audience and suggested that a marker of real success would have been parity in the numbers of attending neurologists and geriatricians.

The patient's perspective

Amongst all these health professionals, however, there was one barrister at the conference. Now retired from the bar, Mr Donal O'Kelly (Director, Different Strokes, London) gave a vivid account of his personal experience of having a brainstem stroke. He did not spare the health service from criticism: from the paramedic who assured him that his condition was not serious (which made him instantly realise it was), to successfully avoiding compulsory inpatient rehabilitation by his dapper appearance in outpatients wearing a suit and tie, his 'graveyard humour' highlighted the importance of expertise in the management and rehabilitation of people affected by a stroke. In September 1996 he launched Different Strokes, a charity set up by younger stroke survivors for younger stroke survivors, to promote self-help and foster mutual support. When asked if there were too many organisations offering patients information and support, Donal O'Kelly felt that a little competition was no bad thing. After an animated discussion, he concluded, 'As a barrister, I was used to talking to judges. It's been much nicer talking to a live audience'.

The population perspective

Most of the other speakers considered populations rather than individuals. Their themes followed a coherent sequence from quantification of the impact of stroke, analysis of risk factors for its development, judicious use of diagnostic tests and rigorous evaluation of potential therapies to strategic secondary prevention. Topics presented were firmly based in pragmatic, clinical epidemiology in which 'physicians must be content to end not in certainties, but rather in statistical probabilities. The modern [physician] thus has a right to feel certain, within statistical constraints, but never cocksure. Absolute certainty remains for some theologians – and like-minded physicians'.

Impact of stroke

World Health Organisation data reveal that worldwide 4.5 million people die each year due to stroke. Even though stroke is the most common cause of adult disability in the UK (prevalence of 5–8 per 1,000 in people over the age of 25) and accounts for £500 million (12%) of the NHS and Social Services budget, there are inadequacies in the planning and delivery of stroke care. The target of the government's White Paper Saving lives: our healthier nation (July 1999), for the reduction of coronary heart disease and stroke, disappointing because it fails to target the specific age group with the greatest burden of stroke. Nevertheless, case fatality is declining in the UK as a whole, despite clear inequity in the provision of care between units across the country, probably due to the effectiveness of organised
inpatient stroke unit care and changes in risk factor prevalence.

Risk factors for stroke

Beyond our knowledge of well-established risk factors for ischaemic heart disease and stroke lie some fashionable areas of uncertainty. For example, the observed associations between various infections and vascular disease have led to intriguing hypotheses, but the existing evidence for a causal association is rather tenuous. The implication of *Chlamydia pneumoniae, Helicobacter pylori* and cytomegalovirus in the aetiology of stroke has been inferred from studies of cardiovascular disease. Unsurprisingly, a stronger association has been described in pathological studies of atherosclerotic tissue than in epidemiological studies of serological markers of these infections. But pathological studies have been flawed by the use of a variety of techniques to examine different markers in different tissues from highly selected groups of patients. The challenge for epidemiological studies has been to account successfully for the high seroprevalence of these indirect infectious markers, adjust correctly for other factors confounding the perceived association with vascular disease, and assemble suitable prospective cohorts of patients with appropriate controls. The bulk of research has concerned *Chlamydia pneumoniae*, but its role as an epiphenomenon has not been dismissed, so we still do not know whether this organism is 'an innocent bystander, or a silent assassin'.

Imaging of stroke

The increasing availability of various brain imaging techniques and a contemporary focus on the hyper-acute treatment of cerebral ischaemia have created a considerable burden for those who bear the brunt of acute stroke care in district general hospitals. These busy clinicians could ease their problems by establishing a prioritised, focused strategy of investigation suited to the stroke throughput and available imaging resources in their individual hospitals. As an analysis of the data from the International Stroke Trial (IST) has not shown a trend for survival according to the timing of the first dose of aspirin, there is no urgency to confirm a clinical diagnosis of uncomplicated ischaemic stroke with computed tomography (CT) if aspirin is the only intended therapy. The combined results of the IST and the Chinese Acute Stroke Trial (CAST) show that aspirin can be started safely pending a CT in these patients (and, reassuringly, aspirin appears to cause neither harm nor benefit for the few who on subsequent CT turn out to have a haemorrhagic stroke, if the aspirin is then stopped). Whilst magnetic resonance imaging (MRI) and diffusion-weighted imaging (DWI) have their relative strengths, their poor specificity for ischaemic stroke, expense and limited availability currently preclude them from routine practice.

The treatment of acute ischaemic stroke

The rational potential interventions for ischaemic stroke are aimed at vessel occlusion (reperfusion and prevention of further thrombosis), neuroprotection (N-methyl-D-aspartate (NMDA), glutamate, glycine and gamma-aminobutyric acid (GABA) receptors, magnesium, free radical scavengers, suppression of cerebral metabolism and oedema) and further management (blood pressure alteration, and nutrition). There is considerable uncertainty about the correct treatment of intracerebral haemorrhage, the management of stroke patients' comorbidity, and many questions about the choice of drugs, their dosage and timing of administration. With questions outnumbering answers (in the form of completed clinical trials and systematic reviews in the Cochrane Library), the future evaluation of therapies for stroke in clinical trials will rely on increased public awareness and 'stroke-aware hospitals' with a change in their existing structure and process of care.

Secondary prevention

Because a reduction in the rate of recurrent stroke is quantitatively the most important outcome of secondary prevention, it has been the focus of a multitude of observational cohort studies of secondary prophylaxis and, increasingly, clinical trials of various treatments. Observational and trial data support a direct and continuous relationship between a lower usual diastolic blood pressure and a lesser relative risk of recurrent stroke (approximately 40% relative risk reduction for every 5 mmHg lowered), with further data awaited from the PROGRESS trial. Although statins do appear to decrease the risk of all strokes in studies of coronary heart disease secondary prevention, the trial data are sparser for cholesterol reduction in stroke and transient ischaemic attack (TIA) patients (especially the elderly and those with lower baseline cholesterol levels), with more conclusive results awaited from the Heart Protection Study and the Cholesterol Treatment Trialists' overview. The current focus of the antiplatelet debate is not on their overall efficacy, but the choice of agent and dose. There appears to be some rather weak evidence behind adding dipyridamole to aspirin for patients with ongoing transient ischaemic attacks. Clopidogrel has been shown to be as effective (possibly more so) than aspirin in one direct comparison, but at 400 times the price of aspirin, cost-conscious clinicians may be reluctant to use it.

In attempting to predict which patients may benefit the most from an intervention, risk factor modelling is more accurate at appropriately targeting therapy than subgroup analyses derived from clinical trial data. For example, analyses of data from clinical trials of carotid endarterectomy have identified patients at a greater annual risk of stroke (early in their clinical course, with several recent TIAs and an irregular plaque morphology), lower annual
risk of stroke (amaurosis fugax and collapse of the internal carotid artery on angiography) and with a higher operative risk of stroke and death (older, hypertensive women). By weighting these prognostic indicators appropriately, examining the relationship between the score and absolute risk reduction from surgery, and internally validating the model, a threshold for an intervention can be derived. Although this appears to contravene the 'prevention paradox': that most 'cases' arise in people at moderate rather than high risk, targeting a small number of high-risk patients may be a clinically effective strategy in absolute terms for carotid endarterectomy.

Summary

Clearly, progress is being made in the investigation and evaluation of therapies for stroke, and the last two decades have seen stroke medicine come of age. The challenge now is to maintain this momentum with government support, transfer research findings into routine clinical practice and increase public awareness. This conference should have inspired its audience to do so, with clear evidence and good humour.

References

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