Kissimmee, Florida, February 2006) suggest that the Merci procedure is also safe and effective in failed thrombolysis patients. The Merci procedure is currently being performed in over 150 centres in the US. It is estimated that over 3,000 patients have been treated with the device to date.

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Evidence based thrombolysis

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Evidence Based Medicine is a method of decision making when we decide which option is the best for a given patient in a given situation by considering the most reliable scientific evidence from clinical research. The level of scientific evidence depends on the amount and the quality of research data regarding the intervention in question. Systematic reviews of randomized controlled trials give the strongest scientific evidence.

Atherothrombotic disease may affect several organs, like the brain, the heart and the lower extremities causing ischemic stroke, myocardial infarction or gangrena of the extremities. To dissolve the occluding clot, i.e. thrombolysis may save the ischemic tissue from permanent damage, therefore seems to be a promising approach to treat atherothrombotic diseases. Thrombolysis may have other indications like pulmonary embolism, deep vein thrombosis of the extremities and there are some possible neurological applications like acute ischemic stroke, intraventricular hemorrhage, intracerebral hemorrhage and cerebral sinus/deep vein thrombosis.

Based on Cochrane reviews, thrombolysis may be beneficial in deep vein thrombosis of the lower extremities, but the optimal drug, dose and route of administration has to be determined in future trials. There is not enough evidence to decide if surgery or thrombolysis is better to treat acute limb ischemia. A meta-analysis of randomized controlled trials did not find enough evidence to decide if thrombolysis or heparin treatment is better for patients with pulmonary embolism.

Of the possible applications in central nervous system (CNS) disorders, there is no available evidence from randomized trials regarding the efficacy and safety of thrombolytic therapy in dural sinus thrombosis. There are only cohort studies describing rtPA or urokinase use in intraventricular or deep cerebral hemorrhages. Most trials in CNS disorders were performed in ischemic stroke and the Cochrane review of Wardlaw et al (2003) gives the best overview: thrombolytic treatment resulted in significant net reduction in death and disability, in an increase in death, and an increase in hemorrhagic complications. The outcome seemed better with earlier application and if rtPA was the thrombolytic agent.

rtPA has been licensed for intravenous use in patients within 3 hours of stroke onset. The currently ongoing IST-3 trial will help to decide several unsettled issues, like the possible expansion of the 3-hour time window, inclusion of people over 80 years of age, and those with mild and severe stroke signs.

PETER SANDERCOCK

Use of thrombolysis outside the 'classical' indication: should we or shouldn't we?

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It is now 12 years since the publication of the modest-sized 624-patient National Institute of Neurological Disorders and Stroke (NINDS) trial of iv rt-PA, that led to the FDA approval in 1996 of thrombolysis. As thrombolytic therapy is one of the very few effective treatments for acute stroke, wider implementation would be desirable. Yet, there is a major mismatch between expert opinion and guidelines (which support thrombolysis for selected patients within 3 hours of onset) and clinical practice. rt-PA for stroke has not been widely implemented in clinical practice; large-scale surveys suggest only 1-2% of stroke patients in developed countries receive it. Two factors are responsible in part for the poor implementation: the paucity of data on the effects of rt-PA treatment in many categories of stroke patients, especially the elderly and those who present more than 3 hours after onset; and the continuing debate over the evidence under-pinning licensed use (e.g. Australian Emergency Medicine physicians have refused to endorse the current Australian Governmental approval for rt-PA treatment for stroke because of ongoing debate over the trial data). Unless additional trial evidence establishes benefit for a wider variety of patients outside the current licence, especially among the elderly, the implementation – and public health impact - of this treatment will remain very limited.