Thrombolysis for stroke in India: Miles to go…..

J. M. K. Murthy

Department of Neurology, The Institute of Neurological Sciences, CARE Hospital, Exhibition Road, Nampally, Hyderabad - 500 001, India

Stroke is a major health problem worldwide and is associated with high mortality and dependence.[1] In the next 30 years the burden of stroke will grow mostly in developing countries rather than in developed countries.[2] World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (WHO MONICA) project[3] data showed relatively large geographical differences in stroke-related case-fatality rates, with the rates in less developed countries among the highest in the world.

The major development in the treatment of acute ischemic stroke has been the introduction of thrombolysis therapy (intravenous tissue plasminogen activator, tPA),[4] which has radically changed the perception and management of stroke patients. Cochrane meta-analysis[5] shows that thrombolysis therapy reduces death or dependence by an odds ratio (OR) of 0.66 (95% confidence interval (CI) 0.53-0.83) with no significant increase in adverse effects (OR 1.13; CI 0.86-1.48) for patients treated within 3h of the onset of an ischemic stroke. This translates to one extra patient being alive and independent for every seven patients treated. The safety of routine clinical use of tPA within 3h of stroke onset has been confirmed in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SISTS-MOST).[6] This study was designed to control for symptomatic intracerebral hemorrhage, mortality and independence when compared to randomized controlled trials. Thrombolysis therapy has a very favorable economic profile; the therapy results in a net cost savings.[7-10] When compared with standard acute stroke care, thrombolysis therapy provides, on average, greater health benefits (in terms of average quality adjusted life years, QALYs) at reasonable medical costs.[11-14] The anticipated savings that would result from even modest, feasible increase in use of thrombolysis therapy is likely to be enormous.[15]

In spite of good clinical efficacy and favorable economic profile, even in industrialized nations thrombolysis therapy is underutilized, only a very small proportion, 2%, of stroke patients are actually being treated.[7,16] A more recent published data show a treatment range of 5-11% of incident ischemic stroke in USA and West European nations.[17,18] The proportion of patients receiving thrombolysis therapy in acute stroke is pathetically low in India.[19] The only incidence study of stroke in India determined an incidence of 163 per 100,000 populations per year (Dr. N. C. Borah personal communication). The expected number of incident ischemic strokes in India is 14, 43, 528 per year (assuming ischemic stroke account for 80% of all strokes and Indian population in 2005: at 1, 107 millions).[20] Anticipated cost savings and health benefits (in terms of average QALYs) of thrombolysis therapy in India, even if a small proportion of patients are treated, will be enormous. The Indian regulatory authority has approved tPA for use in acute ischemic stroke. There are centers with infrastructure and resources to give tPA widespread across the country.[18] It is feasible to give intravenous tPA for acute ischemic stroke in India as shown by Padma and her colleagues[21] in this issue of the journal and also by others.[19,22] However there are several barriers for safe and effective implementation of thrombolysis therapy in acute ischemic stroke in India.

Most of the centers with infrastructure and resources to give thrombolysis therapy are in urban India, where as 80% of the population lives in rural India where the resources to give thrombolysis therapy are virtually nonexistent.[19] Indian Collaborative Acute Stroke Study, urban hospital-based, has shown 7-24% of patients present to hospital within three hours of onset of stroke (unpublished data, 2004). One of the major reasons for the late arrival is delay in transportation.[23-25] There is hardly any ambulance service for transportation of the patients from rural India. Even in urban India transportation to the nearest hospital may not be in time. In an urban hospital-based study in northwest India one of the factors for early arrival to stroke unit was living within a 10-km radius from the hospital.[25]

The knowledge of stroke is quite low among the population. In a study in northwest India, majority (73%) of the subjects (including both patients and
relatives) interviewed did not realize that the symptoms were due to stroke and only a third of the study cohort correctly identified the brain as the affected organ in stroke. In this study self-recognition of stroke symptoms by patients was only 27%.26 Low-threat perception of stroke was an independent factor for the late arrival of patients at the hospital in a study from north India.24 Most of the rural patients with stroke attending a university hospital in south India were not aware of the importance of the time window in stroke management.25 Like with epilepsy, cultural beliefs may have an influence on treatment seeking behavior among patients with stroke. In a study on the knowledge of stroke in northwest India, 7% of the study population believed that oil massage would improve stroke victims and another 3% believed in witchcraft, faith healing, homeopathic and ayurvedic treatment.27

The economic burden and loss of productivity caused by stroke in India has not been appreciated or explored. The in-hospital stroke care including intravenous tPA are likely to be exorbitant and beyond the reach of a common man, tPA drug (75 mg) cost INR 55,500 (US$ 1217) accounts for 0.5% of per capita GNP (source: Boehringer Ingelheim). Almost all the state governments in India are not in a position to provide free thrombolysis therapy to the eligible patients. Health insurance systems are limited and are still not popular. Patients have to virtually bear the costs from their own personal savings. In a study in south India, all the seven patients eligible for thrombolysis therapy belonged to a lower socioeconomic status from rural India and could not afford the therapy.23 In an urban hospital in northwest India of the 23 eligible patients, only five patients actually received the drug, the remainder being unable to afford the treatment due to the expense of the drug.22

The strategies to increase the use and awareness of thrombolysis therapy should include: 1) equipping the practicing physicians in the community with the practical knowledge of stroke management, including the importance of window period and the benefits of thrombolysis therapy and 2) educating the public about stroke warning symptoms, risk factors, the mortality and dependence associated with stroke and importance of time window for thrombolysis treatment. For the safe implementation of thrombolysis in stroke in India, Indian Stroke Association has recently launched both SITS-International Stroke Thrombolysis Register (SITS-ISTR) and SITS in Non European World (SITS-NEW). Even after increasing the awareness of stroke and thrombolysis among the people, in India still the affordability and poor healthcare infrastructure in the community for the safe implementation of thrombolysis remain formidable barriers for some time to come. Guwahati Neurological Research Center in Assam has initiated a novel approach, Stroke Help Card, to make stroke care affordable. Holder of the card by paying INR 499 (US$ 11) (valid for one year) can have access to acute stroke care including thrombolysis therapy (Dr. N. C. Borah personal communication).

References


