Thrombolysis for Acute Ischemic Stroke in Taiwan

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Over the past 20 years, there have been several major advances in the care of patients with cerebrovascular diseases. The most important breakthrough is the use of intravenous thrombolysis for acute ischaemic stroke. Since the Department of Health of Taiwan approved the indication of tissue plasminogen activator (tPA) for acute ischemic stroke at the end of 2003, over 1,000 patients have been given intravenous thrombolytic therapy in Taiwan. However, many important, unresolved problems still exist concerning tPA therapy in Taiwan, even in the whole world.

First, in America and Europe, the current tPA dose for acute ischemic stroke is 0.9 mg/kg. However, low-dose tPA (0.6 mg/kg) for acute ischemic stroke was approved in Japan in 2005. Later many post-marketing studies in Japan also confirmed that low-dose therapy had similar outcomes compared with regular-dose therapy in Western patients. Meanwhile, information on the benefit/risk profiles in the thrombolytic treatment of acute ischemic stroke in Chinese people was rare. In view of this, the Taiwan Stroke Society initiated a multicenter, observational study, the Taiwan Thrombolytic Therapy for Acute Ischemic Stroke (TTT-AIS) study, and found the standard-dose group had significantly higher rates of symptomatic intracerebral hemorrhage (SICH) and mortality, twice that of those in the lower-dose group; and significantly lower independence rate compared with the lower-dose group; especially among patients ≥ 70 years old. However, there was a different result reported by China, and even conflicting and inconclusive results from country to country in Asia. About dosage and ethnicity issues in tPA, we need randomized controlled clinical trials to settle the controversies.

Second, in light of the proportion of older patients is rapidly arising in our society, one would ask is thrombolysis safe in the elderly? In Europe, tPA is not recommended for stroke patients older than 80 for fear of excessive risk of SICH. Yet, studies from North America have revealed no association between age greater than 80 years old and risks of SICH. Taiwan followed the European license. Recently, there were two studies which stressed this topic and had different results again. One from Europe, it concluded odds for improved outcomes in patients with ischaemic stroke who receive thrombolysis were similar in those aged ≤ 80 and > 80, and age alone should not be a barrier to thrombolysis. Another from US, it showed that the presence of intracerebral hemorrhage (ICH) was associated with higher mortality rates but not the use of thrombolysis among those > 80 years; however, the use of thrombolysis was associated with high risk of ICH. So although thrombolysis in the elderly population is not prohibited in US, physicians must be careful for the
potential complication of ICH. Still, inferences of these points should be cautious because these were not randomized studies. According to the TTT-AIS study\(^5\), there are interactions between age and tPA dose, should we use a different dose of tPA for different age categories? More extensive data from randomized controlled trials would more conclusively answer this topic.

Third, not only in Taiwan but also in all other countries there are still a room for increasing the percentage of patients receiving tPA treatment. According to an analysis of the National Inpatient Sample database from US for the years 2000-2006, a very low rate of thrombolysis in the total cohort was found (1.51\%)\(^6\). Various phases of barriers to thrombolysis have been identified, includingprehospital delay and in-hospital delay. Aggressive, combined educational programs aimed at the general public, general practitioners, and medical and paramedical hospital staff can reduce prehospital delay\(^9\). Establishment of a primary stroke center (PSC) at a community hospital has been shown to be able to significantly decrease in-hospital delay\(^10\). The article published in this issue of Acta Neurologica Taiwanica by Sung SF et al showed the same results\(^11\). Following the establishment of the PSC, they achieved a 2.3-fold increase in the proportion of stroke patients treated with tPA. However, like other studies, there are also some areas of weakness. This study was observational, and selection bias was a possibility. Besides, the sample size was small.

Lastly, more and more studies provide compelling evidences that either a PSC or a comprehensive stroke center (CSC) saves lives and improves outcomes for patients with ischemic stroke\(^12\). Currently more and more stroke centers are organized in Taiwan. However, some questions will be faced immediately, such as what’s the most suitable criteria of PSC or CSC in Taiwan? What organizations can fairly certify stroke centers? How many stroke centers do we need in view of the cost-effectiveness\(^17\)? And do we have any program to preferentially transfer patients with acute stroke to the nearest PSC? We believe neurologists and health-care leaders in Taiwan will finally find their ways.

REFERENCES


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