Letter to the Editor

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Letter by Chao et al Regarding Article, “Standard-Dose Intravenous Tissue-Type Plasminogen Activator for Stroke Is Better Than Low Doses”

To the Editor:

We read with great interest the results of Liao et al reporting that standard-dose intravenous tissue-type plasminogen activator (tPA) for stroke had more favorable outcome than low-dose tPA without increasing the risk of symptomatic intracranial hemorrhage (SICH).1 They concluded that 0.9 mg/kg should be the optimal dose of tPA for Asians to treat acute ischemic stroke.

The authors in the study reported there was no significant difference in the rate of SICH between 0.5 to 0.7 and 0.85 to 0.95 groups; and SICH in 0.7 to 0.85 group was even greater than in 0.85 to 0.95 group. For functional independence (mRS, 0–2) at 3 month, 0.7 to 0.85 mg/kg group did also significantly worse than 0.85 to 0.95 mg/kg group. However, they evaluated and compared the safety and efficacy only with analysis adjusted for sex, history of hyperlipidemia, and independent status before the stroke. It is a pity that age was not included for the adjustment during the analysis even though age is one of the most important prognostic factors for patients with acute stroke.2 Moreover, age-adjusted analysis is missing in the comparison of outcome between the groups of 0.7 to 0.85 mg/kg and 0.85 to 0.95 mg/kg, neglecting the fact that the median age in the patients with dose of 0.7 to 0.85 mg/kg group was 5 years older than that of the patients with dose of 0.85 to 0.95 mg/kg group. Therefore, we cannot agree that 0.9 mg/kg should be the optimal dose of tPA for Asians.

Age is the one of the most important factors to predict the occurrence of SICH and the outcome.2,3 First, for the safety, in our study in Taiwan, in which most of the patients were also ethnic Han population, there was a significant trend of increasing SICH with age (P=0.002).2 There were few numbers of SICH in the younger patients, but SICH increased dramatically when patients aged over 70 years. If we did not consider the age effect, the rate of SICH was comparable among patients receiving each dose of tPA (0.6 mg/kg, 0.7 mg/kg, 0.8 mg/kg, and 0.9 mg/kg). However, after taking age into consideration, in patients aged >70 years, there was a significant trend of increasing SICH. Second, for the efficacy, in patients aged >70 years, we found lesser good functional outcome (P=0.0179) and a trend of increasing mortality (P=0.0971) at 3 months with increasing doses of tPA.3

Third, the authors did not report how did the physicians in China decide the dose of tPA for acute ischemic stroke, and there was a marked imbalance of the number of patient among different dosage groups. The number of patients who received low dose is small (n=75, 8.5% for 0.5–0.7 mg/kg group; n=131, 14.8% for 0.7–0.85 mg/kg group; and n=678, 76.7% for the standard dose). For patients who received the lower dose, we may speculate that it is because of the unreported comorbidity, such as poor renal or liver function, or because of the inexperience of the physician in charge in conducting thrombolytic therapy.

Finally, Asians consist of different ethnic groups. Indians, Indonesians, and so on are ethically different from Chinese, Korean, and Japanese, and coagulation status in the latter is slightly different from the former as well. The results from a study in Chinese people may not be appropriate to extrapolate them to all Asians.

Disclosures

None.

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