Intravenous Thrombolysis With Low-Dose Recombinant Tissue Plasminogen Activator in Acute Ischemic Stroke

To the Editor:

We read with interest the study by Toyoda et al1 regarding intravenous thrombolysis with low-dose tissue plasminogen activator (IV tPA) in Japanese patients with acute ischemic stroke (IS). We want to discuss some important issues raised by this study.

Data regarding thrombolysis in Asia are scarce. Only a small proportion of patients with acute IS are thrombolyzed in Asia and the treatment approach remains largely conservative.2 Patients’ late arrival, treatment costs, and limited access to neuroimaging are some of the major contributing factors.

A major concern has been the anticipated higher rates of tPA-related symptomatic intracranial hemorrhage among Asians due to racial differences in coagulation–fibrinolysis factors.3 A clinical trial4 with low-dose IV tPA (0.6 mg/kg) in Japanese patients with IS showed the clinical outcomes to be comparable with standard dose IV tPA (0.9 mg/kg) used in the Western population.5 These findings have caused some controversies in Asia and variable IV tPA dose regimens are being followed.

Being ethnically closer to the Japanese, low-dose IV tPA certainly appears an attractive option to reduce the treatment cost as well as bleeding complications. Accordingly, we adopted the low-dose IV tPA regimen at our tertiary center in 2000.6 However, our rates of functional independence barely matched with the Japan Alteplase Clinical Trial (J-ACT)4 and National Institute of Neurological Diseases and Stroke5 trials. Furthermore, we observed considerably higher rates of symptomatic intracranial hemorrhage. On the contrary, much better results were reported in an Asian study using the standard dose IV tPA.7 We revised our IV tPA regimen to the standard dose in 2006 and observed significantly better functional outcomes (modified Rankin scale 0 to 1 in 59% cases) and low (1.7%) symptomatic intracranial hemorrhage, much better as compared with the current report1! Interestingly, another recent Asian center reported similar results.8 Although difficult to substantiate, we believe that low-dose IV tPA results in lower rates of recanalization. Furthermore, low-dose IV tPA might cause a delayed recanalization and increase the risk of symptomatic intracranial hemorrhage.

We want to emphasize that the recent reports6–8 provide preliminary evidence that standard dose IV tPA is effective as well as safe in Asian patients with IS. Our results, even on their own, could be generalized to represent an Asian sample due to a good mixture of multiple ethnicities in Singapore.

In conclusion, we agree that a low-dose IV tPA regimen could be appropriate for Japanese patients with IS. However, the results from other Asian populations provide a compelling reason to re-evaluate the thrombolysis regimen in Japan, especially when there has never been a head-to-head comparison of low-dose and standard dose IV tPA. Owing to the rapid improvements in socioeconomic conditions, healthcare facilities, and public awareness, thrombolysis services in patients with acute IS are expected to improve. We propose a larger study (or even a registry) across Asia to alleviate the prevailing hesitations among stroke neurologists as well as the controversies related to the IV tPA dose.

Disclosures

None.

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