Intravenous Tissue Plasminogen Activator Thrombolysis in Patients With Diabetes Mellitus and Previous Stroke

To the Editor:

We have read with great interest the article entitled “Is it time to reassess the SITS-MOST criteria for thrombolysis?,” which appeared in Stroke. The authors studied retrospectively a cohort of patients with acute stroke who received thrombolysis with intravenous (IV) tissue-type plasminogen activator (tPA) and established 2 subgroups for comparison: the patients fulfilling published Safe Implementation of Thrombolysis in Stroke-MONitoring STudy (SITS-MOST) inclusion criteria and the patients not fulfilling such criteria (labeled as non-SITS-MOST).

The importance of IV thrombolytic therapy for acute stroke is unquestionable. However, the proper selection of patients for IV tPA administration is especially relevant both to improve treatment efficacy and to decrease hemorrhage risk. In clinical practice, following very strict selection criteria may preclude treatment of specific patient groups that could benefit from IV tPA. Therefore, specialists have developed different approaches to increase the number of patients to be treated with IV tPA. In addition, the recent European Cooperative Acute Stroke Study (ECASS) III trial results reveal a statistically significant benefit of IV tPA in the 3- to 4.5-hour time window after acute stroke. According to these data, the rate of IV tPA use has increased in medical centers, although there are some issues that still remain controversial.

We consider that the results presented by Rubiera et al concerning IV tPA-treated patients with diabetes mellitus (DM) and previous stroke are very interesting. The authors describe their study outcomes in relation to SITS-MOST and non-SITS-MOST patients. The statistical comparison of both patient subgroups indicate that IV tPA-treated patients with DM and previous stroke show a lower 24-hour clinical improvement, a lower clinical improvement at discharge, a lower functional independency, and a higher rate of mortality. These differences may be due to 3 principal factors. First, DM is frequently associated with micro- and macrovascular complications; in fact, chronic microvascular damage secondary to long-standing DM may predispose vessels to rupture in the setting of ischemia, increasing the risk of hemorrhagic transformation after IV tPA. Besides, hyperglycemia has been related to poor functional outcome and elevated rates of intracerebral hemorrhage in patients treated with IV tPA. Although it is present in a significant proportion of nondiabetics, hyperglycemia is found more commonly in patients with pre-existing diabetes. Second, DM is associated with diminished fibrinolytic capacity and increased concentration in blood of plasminogen activator inhibitor-1, and patients with DM often display impaired response to antithrombotic treatment. Finally, patients with DM show higher prevalence of large vessel atherothrombotic stroke, and it has been reported that IV tPA could have less efficacy for this stroke subtype than for other stroke subtypes. All these factors somehow explain why patients with DM treated with IV tPA usually have worse prognoses.

Although the sample size in the study of Rubiera et al is not large enough to establish definite conclusions, their results suggest that SITS-MOST inclusion criteria may be too strict. We agree with the authors’ opinion and, in addition, we believe that the stratification of patients who could benefit from IV tPA therapy is a major issue. Of course, some of the SITS-MOST inclusion criteria may be reassessed, but we consider that a personal clinical history of DM and previous stroke must still contraindicate the administration of IV tPA; therefore, it is fundamental to perform further well-designed studies to define better this issue.

Disclosures

None.

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Stroke. 2009;40:e707; originally published online October 29, 2009; doi: 10.1161/STROKEAHA.109.564898

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/40/12/e707

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