Intravenous Thrombolysis for Stroke Patients with G6PD Deficiency

Xiaoyan Wu, MD,*,[1] Ruying Fu, MD,†,[1] Yamei Tang, PhD,‡ Li Shi, MD,* Xiaoming Rong, PhD,‡ Jianjun Guo, MD,* Jie Li, MD,* and Qingyu Shen, MD, PhD*,‡

Background and Purpose: No reports regarding the safety of thrombolysis in acute stroke patients with a G6PD deficiency have been published to date. Here we aimed to evaluate the safety of intravenous thrombolysis for G6PD-deficient stroke patients. *Methods:* We enrolled each patient with acute ischemic stroke who arrived in our stroke unit within the therapeutic window and received systemic thrombolysis using recombinant tissue plasminogen activator (rt-PA), between January 2015 and March 2016. The primary clinical outcome was measured 3 months after treatment, and defined as a "good" outcome by a modified Rankin Scale (mRS) score of 0-2. Major safety outcomes were incidences of intracranial hemorrhage (ICH) or mortality at 90 days. *Results:* A total of 96 individuals were analyzed, of which 20 patients were G6PD deficient. The rates of ICH after rt-PA treatment were 12% the in G6PD-deficient group versus 15% in G6PD non-deficient group, and the incidences of symptomatic intracranial hemorrhage were also similar between the G6PD-deficient and non-deficient cohorts. No hemolysis crisis occurred, and no significant difference in mortality rate was found between the 2 groups. The overall rate of a good outcome at 3 months after stroke in the whole cohort was 60%, whereas 50% of patients achieved an excellent outcome (mRS 0-1) in the G6PD-deficient cohort, and 42% in the G6PD non-deficient group. *Conclusions:* Thrombolytic therapy for patients with G6PD deficiency seems to pose a similar risk of ICH and clinical outcome to those with G6PD non-deficiency. **Key Words:** Thrombolysis—glucosephosphate dehydrogenase deficiency—stroke—safety.

From the *Department of Neurology, Zengcheng District People's Hospital of Guangzhou, Sun Yat-sen University, Guangzhou, Guangdong Province, China; †Department of Neurology, The Fifth Affiliated Hospital of Sun Yat-sen University, Sun Yat-sen University, Zhuhai, Guangdong Province, China; and ‡Department of Neurology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong Province, China.

Received October 9, 2017; revision received February 10, 2018; accepted February 28, 2018.

Grant support: Dr. Shen was supported by the National Natural Science Foundation of China (No. 81471290) and the Natural Science Foundation of Guangdong Province (S2015A030313755 and S15140500000869).

Address correspondence to Qingyu Shen, MD, PhD, Department of Neurology, Zengcheng District People's Hospital of Guangzhou, Sun Yat-sen University, No. 1, Guangming East Road, Guangzhou, Guangdong Province 511300, China. E-mail: 13609710406@126.com.

[1] Both authors contributed equally to the study.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.02.060

Introduction

Intravenous thrombolysis using recombinant tissue plasminogen activator (rt-PA), which dissolves blood clots, is a recommended therapy for acute ischemic stroke within 4.5 hours of stroke onset.[1,2] However, the potential risk of intracranial hemorrhage (ICH), especially symptomatic intracerebral hemorrhages, which is a devastating event resulting in high risk of mortality, has limited the clinical use of rt-PA for acute stroke. Prior studies have indicated that risk factors for thrombolysis include oral anticoagulant treatment, patient's age greater than 80 years, imaging findings of early ischemic changes, high blood pressure, and a National Institutes of Health Stroke Scale (NIHSS) score higher than 25 points, due to the significantly increased risk for ICH.[3-7] However, none of these previous studies reported the safety and potential efficacy of thrombolytic treatment for patients with G6PD deficiency. G6PD deficiency is a very common X-linked genetic disorder that can cause hemolytic crisis,[8] affecting more than 400 million people worldwide.[9] Due to fear of either hemolysis or increased bleeding risk, most physicians tend to seek conservative alternate treatments such as antiplatelet drugs, rather than thrombolysis, in G6PD-deficient patients who are experiencing acute stroke even within the therapeutic window. However, whether intravenous thrombolytic treatment should be contraindicated for G6PD-deficient individuals is still ambiguous, and its potential effectiveness also remains to be determined. Therefore, in this study we aimed to investigate the clinical and safety-related outcomes of intravenous thrombolysis using intravenous tissue-type plasminogen activator in stroke patients with G6PD deficiency.

Methods

Participants

All patients with acute ischemic stroke admitted within 4.5 hours of symptom onset to the inpatient department, and who consequently underwent thrombolysis between January 2015 and March 2016, were included. On admission, noncontrast brain computed tomography (CT) scans were available to the whole cohort. Patients were eligible if they arrived at the hospital within 4.5 hours of symptom recognition, and if they were aged between 18 and 80 years old. Patients with initial CT scans which revealed ICH or visible large acute stroke more than one third of middle cerebral artery territory, history of ICH, manifested severe liver or kidney disease, platelet count below 100,000/mm^3, current use of anticoagulants with abnormal coagulation function (INR >1.7, activated partial thromboplastin time >40 seconds, or prothrombin time >15 seconds), stroke or serious head-spinal surgery or trauma in the past 3 months, gastrointestinal-urinary tumors or bleeding within the previous 21 days, severe trauma or major surgery in the past 14 days, lumbar puncture or endovascular puncture at a noncompressible site within the previous 7 days, pregnancy, blood glucose less than 3.0 or more than 20.0 mmol/L, systolic blood pressure above 180 mm Hg or diastolic blood pressure above 100 mm Hg, or other disorders with increased risk of bleeding were excluded.[10,11] The present study was approved by the ethical committees of our institutions, and written informed consents were obtained by all the patients or appropriate surrogates.

All the enrolled individuals received intravenous alteplase (Boehringer-Ingelheim, Germany) .9 mg/kg body weight to a maximum 90 mg, with 10% as initial bolus, and 90% in 1-hour infusion. No antiplatelet or anticoagulant agents were allowed within the first 24 hours, and systolic blood pressure was maintained within specified values (<180 mm Hg).

Procedure and Clinical Assessment

The following baseline characteristics were recorded: age, sex, the time from arrival to delivery of thrombolysis, early infarction signs on CT, history of stroke, coronary artery disease, atrial fibrillation, hypertension, diabetes mellitus, medication, current smoking habits, systolic and diastolic blood pressure, platelet count, hemoglobin, activated partial thromboplastin time, prothrombin time, the score from the NIHSS at admission, and pre-event modified Rankin Scale (mRS). Blood samples were collected from each enrolled individual, and G6PD enzyme activity was recorded using fluorescent spot tests following the manufacturer's instruction (Micky Ltd, Guangzhou, China). Cerebral CT scans were performed at baseline and 24 hours after rt-PA administration for each enrolled individual. All neuroimaging data were reviewed by 2 independent, certified, and experienced neuroimaging specialists. ICH and symptomatic intracranial hemorrhage (sICH) were defined according the European Cooperative Acute Stroke Study II (ECASS II) Criteria.

Clinical assessment was performed by 2 experienced stroke neurologists. Stroke severity was assessed using NIHSS scoring at baseline, 24 hours, day 7, and on day 14 (or earlier if discharged early from the stroke unit). A favorable outcome was defined as a decrease in NIHSS score by 4 or greater or NIHSS score of 0 on day 14 after stroke onset. mRS assessment was used to evaluate functional outcome on admission, and 90 (±10) days after thrombolysis treatment via telephone interviews. An excellent outcome was defined as an mRS score of 0-1 without clinically significant disability, a good outcome was a score of 0-2 with no or slight disability, and a poor outcome was a score of 4-6 with severe disability or death. Safety outcomes were ICH, sICH, or mortality, which were assessed at 3 months post-treatment.