Intravenous Thrombolysis for Acute Ischemic Stroke in Patients with Thrombocytopenia

Ashkan Mowla, MD, FAHA, FAAN,* Haris Kamal, MD,* Navdeep S. Lail, MBBS,* Caila Vaughn, PhD,* Peyman Shirani, MD,* Sandhya Mehla, MD,* Hamidreza Rajabzadeh-Oghaz, MS,† Christopher Deline, MD,* Marilou Ching, MD, MPH,* Annemarie Crumlish, CCRC,* and Robert N. Sawyer, MD*

Objective: To determine the safety of intravenous (IV) recombinant tissue plasminogen activator (rtPA) in patients with acute ischemic stroke (AIS) who had a platelet count <100,000 /mm^3. *Methods:* We reviewed the charts of all patients who received IV rtPA for AIS during a 9.6-year period at our stroke center. Those with platelets <100,000/mm^3 were identified. Head computed tomography scans performed in 24-36 hours postthrombolysis were reviewed to evaluate the rate of symptomatic intracranial hemorrhage (sICH). *Results:* A total of 835 patients received IV rtPA for AIS during this period. A total of 5 patients were identified to have a platelet count <100,000/mm^3. One of them (20%) developed sICH post-IV tPA administration .The mean platelet count of those 5 patients was 63,000 ± 19,000/mm^3. To the best of our knowledge, only 21 thrombocytopenic patients have been reported to receive IV rtPA for AIS in the medical literature. Combining our 5 cases with 21 patients previously reported, we have 26 AIS patients who had a platelet count <100,000/mm^3 and received IV rtPA, with 2 of them developing sICH (7.7 %). Comparing the rate of sICH among this group with the patients with normal platelet count in our cohort, there was no statistically significant difference (7.7% versus 6.04%, *P* value = .73). *Conclusion:* IV rtPA for AIS might be safe in patients with platelet count <100,000/mm^3 and it is reasonable not to delay IV rtPA administration while waiting for the platelet count result, unless there is strong suspicion for abnormal platelet count. **Key Words:** IV rtPA—stroke—thrombocytopenia—ICH.

Introduction

Intravenous (IV) recombinant tissue plasminogen activator (rtPA) is the only Food and Drug Administration-approved pharmacological therapy for acute ischemic stroke (AIS).[1] A platelet count <100,000/mm^3 is considered as a contraindication for IV rtPA administration in AIS because of a possible increase in the risk of bleeding complications, particularly intracranial hemorrhage (ICH). This threshold was not determined through randomized trials or large prospective studies, but was derived from expert panel consensus.[2] To the best of our knowledge, only a few AIS patients who received IV rtPA and had platelet

From the *Stroke Division, Department of Neurology, University at Buffalo, State University of New York, Buffalo, New York; and †Department of Mechanical and Aerospace Engineering, University at Buffalo, State University of New York, Buffalo, New York.

Received January 5, 2017; revision received February 26, 2017; accepted March 21, 2017.

Address correspondence to Ashkan Mowla, MD,FAHA, FAAN, Stroke Division, Department of Neurology, University at Buffalo, State University of New York, 100 High Street, Buffalo, NY 14203. E-mail: mowla_a@yahoo.com.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2017.03.021

count <100,000/mm^3 have been reported in the medical literature thus far.[3-6] Because of very little data available on this group of patients, it is unclear whether this is a legitimate threshold for withholding IV tPA administration and whether clinicians should wait for platelet count result prior to IV rtPA administration for AIS. We sought to determine the safety of IV rtPA in such patients through a retrospective chart review study in a large-volume comprehensive stroke center along with review of the previous literature.

Methods

The medical records of patients who received IV rtPA for AIS at our tertiary academic medical center, or were transferred to our center after IV rtPA administration at an outside facility, from January 2006 until August 2015, were reviewed retrospectively. Patients were identified through a computerized database of IV rtPA for AIS, maintained by the Stroke Division of the Department of Neurology. All patients were treated based on the standard protocol adopted from the American Heart Association/American Stroke Association within 4.5 hours of ischemic stroke onset.[7] The following demographics were abstracted from the medical records for each patient: age, gender, medical history, National Institutes of Health Stroke Scale (NIHSS) at presentation, and NIHSS within 24-36 hours post-rtPA administration.

Images and official reports of all brain imaging obtained (computed tomography [CT] and magnetic resonance imaging [MRI] based) were reviewed. MRI of brain is usually performed after IV thrombolysis (IVT) in our center. A subset of patients with platelet count <100,000/mm^3 from this cohort was identified. We were blinded to the information on whether the treating physicians were aware of platelet count result at the time of treatment or they found out about the low platelet count after IVT. Follow-up CT or MRI within 24-36 hours of IV rtPA administration and medical records were also reviewed to determine the number of patients with ICH and symptomatic intracranial hemorrhage (sICH) in this subset. sICH was defined as ICH with an increase in NIHSS of at least 4 points.[8]

Two authors (H.K. and A.M.) independently searched Ovid Medline, PubMed, and Google Scholar for all relevant previously published articles or abstracts in English, using the search terms "Stroke," "thrombolysis," "rtPA," "thrombocytopenia," and "off-label use." The reference list in all articles was checked for additional data sources. Our Health Sciences Institutional Review Board approved the study.

Results

A total of 835 patients who received IVT for AIS during a 9.6-year period were identified. Fifty-one patients (6.1%) were found to have sICH. The demographics of the patients are outlined in Table 1. The platelet count data were not available for 2 patients. A total of 5 patients (.6%) were found to have a platelet count <100,000/mm^3 at the time of IVT. Of these 5, 3 (60%) revealed acute infarction on their postthrombolysis brain MRI and MRI of the brain was not performed in 1 patient as she passed away soon after thrombolysis. The mean age of the patients was 75 ± 18 years. The mean platelet count was 63,000 ± 19,000/mm^3 (range: 38,000-85,000/mm^3). The cause of thrombocytopenia was reported to be cancer and chemotherapy in 1 patient and liver cirrhosis in another patient There were no data available on the cause of low platelet count in the other 3 patients. One patient developed sICH within 3 hours of IV rtPA administration and expired on the same day because of a large sICH (Fig 1). She was a 92-year-old female who had an NIHSS of 5 on admission and was treated with IV rtPA after 165 minutes of symptom onset. She did not have any history of coagulopathy or bleeding disorders. Later on, platelet count was found to be 48,000/mm^3 at the time of IV rtPA administration. The cause of low platelet count was not clear in this patient. Table 2 shows the characteristics of the patients with thrombocytopenia.

Discussion

In our retrospective study, one of the patients who were treated with IV rtPA for AIS and had platelet count <100,000/mm^3 at the time of IVT developed sICH. She did not have any history of coagulopathy or bleed disorders. A web search in Medline, PubMed, and Google Scholar until July 2016 revealed 21 reported cases of IV rtPA given for AIS in patients with platelet count <100,000/mm^3. The previous largest case series reported 10 patients with platelet count <100,000 mm^3 who received IV rtPA despite this contraindication were identified.[3] None of them developed sICH post-IVT. In the Helsinki Stroke Thrombolysis Registry, Meretoja et al found 7 patients who were treated with IVT for AIS. Only 1 (14.35%) of those patients developed sICH.[4] No more detail is available on this patient. In another retrospective chart review study, Brunner and colleagues showed that the risk of SICH stroke does not appear to be increased following IVT after AIS in patients with abnormal baseline coagulation. Particularly, they found 3 patients with platelet count <100,000/mm^3 and none of them was reported to have sICH post-IVT.[5] In addition, 1 more patient was found to have a platelet count <100,000/mm^3 in another single-center registry; this patient did not develop sICH post-IVT.[6] Combining our 5 cases with the 21 cases previously reported in the literature, we have 26 AIS patients who had a platelet count <100,000/mm^3 and who received IV rtPA, with 2 of them developing sICH (7.7%). Comparing the rate of sICH among this group with the patients with normal platelet count in our cohort, there was no statistically sig-