Usefulness of Checking Platelet Count Before Thrombolysis in Acute Ischemic Stroke

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Background and Purpose—Thrombolysis for acute ischemic stroke is strikingly time sensitive. Current guidelines require confirmation of a platelet count ≥100,000 before thrombolysis; however, obtaining this laboratory test may delay treatment.

Methods—We queried our hospital database to identify patients with ICD-9 codes consistent with acute ischemic stroke from 2000 to 2005 and to determine platelet counts in these patients. Medical charts of patients with platelet counts <100,000 were reviewed to determine whether the patient had a known history of thrombocytopenia or conditions associated with thrombocytopenia.

Results—A total of 1752 patients were identified, and 82 (4.7%) had a platelet count <100,000 at stroke onset. Only 6/1752 (0.3%) had a platelet count <100,000 which was not suspected based on initial history. All of these 6 patients had only mildly decreased platelet counts.

Conclusions—An unsuspected platelet count <100,000 was found in 0.3% of patients at stroke presentation. In patients without a history of thrombocytopenia or predisposing factors, the benefit of earlier thrombolysis may outweigh the bleeding risk of inadvertently treating a patient with thrombocytopenia. (Stroke. 2007;38:000-000.)

Key Words: platelet count ■ stroke ■ thrombolysis

Clinical trials of thrombolysis for acute ischemic stroke (AIS) clearly show that faster treatment improves the odds of a good outcome.¹ Unfortunately, evaluation of patients before administration of tissue plasminogen activator (tPA) is complex and time-consuming. The comprehensive protocol for tPA use, based on the National Institute of Neurological Disorders and Stroke (NINDS) trial which established the effectiveness of tPA, specifies a number of inclusion and exclusion criteria, including confirmation that the platelet count is ≥100,000.² This study aims to determine the frequency of thrombocytopenia at presentation among patients with AIS. If finding a platelet count <100,000 is sufficiently infrequent, then risk-benefit analysis may support starting thrombolysis before platelet count results are available.

Methods

We queried our hospital database to identify all patients ≥18 years old with ICD-9 codes consistent with a diagnosis of AIS (433.x1, 434.x1, 436) from 2000 to 2005. This strategy has been shown to accurately identify stroke patients when compared with a gold standard of chart review.³ A computerized search of hospital laboratory records was undertaken to locate patients in this cohort with a platelet count <100,000 at some time during their hospitalization. Medical charts of these patients were systematically reviewed to confirm the diagnosis of AIS, to identify those with platelet count <100,000 at stroke onset, and to determine whether the patient had a known history of thrombocytopenia or conditions associated with thrombocytopenia (defined as metastatic cancer, hematologic malignancy, bleeding of any type within the preceding one month, or presentation with sepsis or shock) at the time of initial evaluation. For the latter determination, record review was limited to the emergency department records, admission note, and pre-existing laboratory and chart data immediately available at patient presentation. This study was approved by our institution’s research review board.

Results

A total of 1752 patients with ICD-9 codes consistent with AIS and available laboratory data were identified. Of these, 212 patients had a platelet count <100,000 at some time during their hospitalization, and 82 (4.7%) had a platelet count <100,000 at stroke onset. Record review indicated a diagnosis other than AIS in 9 of these 82 patients (11%). Incorrect diagnoses included intracerebral hemorrhage (n=4), metabolic derangement (n=2), subdural hematoma (n=1), hypertensive encephalopathy (n=1), and traumatic brain injury (n=1). Of the 73 remaining patients, 62 had known thrombocytopenia at the time of stroke onset based on a reported history of low platelet count or prior laboratory data available at presentation. Five patients without known thrombocytopenia had a medical history of conditions associated with thrombocytopenia (metastatic cancer, n=2; hematologic malignancy, n=1; recent bleeding, n=1; and septic shock, n=1) at the time of presentation. Only 6/1752 (0.3%) had a platelet count <100,000 not suspected based on initial
history. All of these 6 patients had only mildly decreased platelet counts (>65,000).

Discussion
The pivotal NINDS tPA study excluded patients with a platelet count <100,000 from enrollment. This decision was undoubtedly made to limit hemorrhagic risk in the setting of a trial of a drug known to cause bleeding complications. The NINDS inclusion/exclusion criteria, developed for use in a research study, have since been widely adapted to clinical practice, and adherence to these criteria is recommended in treatment guidelines. However, an evidence-based analysis of a proposed treatment exclusion criteria would ideally consider (1) the likelihood the criteria is present in the target population, (2) the risk of complications from using the treatment in patients with the exclusion, and (3) any potential loss of benefit incurred by the procedures needed to identify those patients with the exclusion criteria.

Regarding these issues, several points can be made. First, in real-world practice, determination of the platelet count is a frequent cause of treatment delay. In contrast to glucose, which can be measured by paramedics in the field using widely available point-of-care testing devices, platelet-count measurement requires venipuncture and blood collection, careful specimen-labeling, transportation to a central laboratory where automated equipment is available, sample analysis, and communication of results to the treating physician. Delay can be introduced at numerous points along this pathway. Second, we found an unsuspected platelet count <100,000 in only 0.3% of patients at stroke presentation. There are no reliable data on the absolute risk of administering tPA to a patient with thrombocytopenia. However, positing a worst-case scenario, in which every patient with thrombocytopenia treated with tPA has a fatal hemorrhage and would otherwise have had an excellent outcome, then empiric treatment might cause harm to 3 per 1000 treated.

Is this potential harm outweighed by the benefit of increasing the speed of thrombolysis to the other 997 per 1000 stroke patients? On a theoretical basis, Saver found that each minute of untreated AIS is associated with the loss of 1.9 million patients. More practically, analysis of stroke tPA trials shows a powerful effect of time-to-treatment on outcome, especially in the first 90 minutes after onset. Even short delays, applied systematically to large populations, may have a major impact on overall disability burden. Further research to more precisely characterize the effect per unit time delay in treatment would be helpful to better assess the risk-benefit ratio of strategies to streamline thrombolytic administration. Our study has several limitations. First, the population studied was not limited to patients presenting within the thrombolytic time-window, but rather included all patients with AIS. However, it seems unlikely that thrombocytopenia should be more or less frequent in patients presenting early compared with later after onset. Second, our study used ICD-9 codes to identify patients with AIS from an administrative database, and thus there is some risk of misclassification. In the report of Kokotailo et al, which supported use of ICD-9 codes for identification of stroke patients, an accuracy rate of 86% was found for AIS compared with the gold standard of chart review. In our study, detailed medical record review of the cohort with thrombocytopenia showed 11% had a diagnosis other than AIS, consistent with this previously reported level of accuracy. Finally, it is possible that documentation in the emergency department records or admission note of either known thrombocytopenia or a history of a condition associated with thrombocytopenia represented information not available immediately at stroke presentation. Caution must therefore be exercised when the patient is unable or family members unavailable to provide a reliable and complete medical history. This last limitation is particularly significant given that stroke patients are frequently unable to provide a complete history because of their neurological deficits.

In conclusion, an unsuspected platelet count <100,000 is extremely rare in patients with AIS. This finding should not, however, distract from efforts to reduce laboratory delays in AIS patients. Rapid laboratory results would allow thrombolysis to be discontinued promptly even after initiation in patients subsequently found to have thrombocytopenia; furthermore, measurement of coagulation studies remains necessary in patients on anticoagulants or with other suspected causes of coagulopathy.

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References
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