Does Prior Antiplatelet Treatment Increase the Risk of Hemorrhagic Transformation and Unfavorable Outcome on Day 90 after Intravenous Thrombolysis in Acute Ischemic Stroke Patients?

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Background: The effect of prior antiplatelet (AP) therapy on the risk of hemorrhagic transformation (HT), and on functional outcomes of acute ischemic stroke (AIS) after intravenous thrombolysis (IVT), is not known. We performed a retrospective analysis to determine whether history of AP therapy is associated with post-thrombolysis HT and poor prognosis in AIS patients. *Methods:* Data pertaining to 145 patients with AIS, who underwent IVT between October 2008 and January 2015, were analyzed. The patients were divided into 2 groups based on whether or not they had received prior AP therapy. Neurological outcomes at 24 hours and 3 months after IVT therapy were assessed. Intergroup difference in cost of treatment was also evaluated. A multivariate logistic regression model was used to identify independent predictors of post-thrombolysis HT. *Results:* Among 145 patients, 23 (15.8%) had received prior AP therapy. On multivariate analyses, older age (odds ratio [OR]: 1.084; confidence interval [CI], 1.028-1.144) and prior AP therapy (OR: 3.318; CI, 1.172-9.398) were found to be independent predictors of HT. *Conclusion:* In this study, prior AP therapy was independently associated with post-thrombolysis HT in AIS. **Key Words:** Acute ischemic stroke—prior antiplatelet therapy—intravenous thrombolysis—hemorrhagic transformation.

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Introduction

Intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator is considered to be the most effective therapy for acute ischemic stroke (AIS).[1] However, post-thrombolysis intracerebral hemorrhage (ICH) is a serious complication that constrains its wider clinical use.[2] An early trial reported a 30% incidence of post-thrombolytic ICH among AIS patients who had received prior antiplatelet (AP) therapy.[3] However, due to inconsistencies in the available evidence,[4,5] the association between prior AP therapy and post-thrombolysis ICH in patients with AIS is subject to controversy. We performed a retrospective, observational study to determine whether history of AP treatment prior to thrombolytic therapy was associated with an increased risk of ICH and poor prognosis.

Methods

Ethics Statement

Written informed consent was obtained from all the patients prior to their enrollment in the study. The study protocol was approved by the Ethics Committee at the local hospital. The study was conducted according to principles enshrined in the Declaration of Helsinki.

Selection of Patients

The study was conducted between October 2008 and January 2015. Data including 145 patients with AIS who received intravenous recombinant tissue plasminogen activator (alteplase, .9 mg/kg up to a maximum of 90 mg; 10% of total dose as a bolus and the rest over 1 hour) were obtained according to the standard guideline.[1] Patients were selected if they met the following criteria: (1) age older than 18 years, (2) diagnosis of AIS based on clinical and imaging findings, and (3) IVT therapy administered within 6 hours of onset of AIS. Patients who did not meet the criteria as per standard IVT guidelines were excluded from the study.

All patients underwent a computed tomography scan of the head between 24 and 36 hours after IVT therapy, and on attaining an increase in the National Institutes of Health Stroke Scale (NIHSS) score by more than 4 points. We categorized hemorrhagic transformation (HT) occurring within 24 hours of thrombolysis into hemorrhagic infarction and parenchymal hemorrhage (PH), on the basis of imaging criteria defined in the European Cooperative Acute Stroke Study II.[6] Symptomatic intracerebral hemorrhage was defined as a local or remote parenchymal hematoma (PH2 type), associated with an increase in NIHSS score or leading to death.[3]

Neurological Outcomes

Neurological deficit was evaluated prior to administration of IVT therapy, and repeated at 24 hours and 90 days after IVT therapy, as per NIHSS score and modified Rankin Scale (mRS) score, by an experienced vascular neurologist.

Statistical Analysis

All statistical analyses were performed using SPSS V.17.0 (SPSS Inc., Chicago, IL). Fisher's exact test was used to compare the dichotomous variables in the 2 groups, while independent samples 2-tailed *t*-test or Mann–Whitney *U*-test was used for continuous variables. A multivariable logistic regression model was used to assess the association between prior AP use and HT. All tests used an alpha level of .05 as the criteria for statistical significance.

Results

Baseline Characteristics

A total of 145 patients (mean age 64.3 ± 11.6 years) were enrolled in the study, of whom 94 (64.8%) were males. The median NIHSS score was 11 (interquartile range 7-15), and the mean interval between symptom onset and treatment was 188.7 ± 48.4 minutes. Twenty-three patients (15.9%) had a history of AP treatment; 29 patients (20%) sustained symptomatic ICH after IVT; and 56 patients (38.6%) had an mRS score of 0-1. The baseline characteristics of the patients by study group are presented in Table 1.

Table 1. *Patient demographics and baseline characteristics*

Characteristics	AP patients (N = 23)	Non-AP patients (N = 122)	*P*
Female (%)	9 (39.1)	42 (34.4)	.665
Age (years)	70.0 ± 8.7	63.2 ± 11.8	.009
DNT (min)	195.9 ± 50.6	187.3 ± 48.0	.435
Initial stroke severity (NIHSS score)*	14 (7-16)	11 (7.0-14.25)	.180
Hypertension	14 (60.9)	74 (60.7)	.985
Diabetes mellitus	5 (21.7)	24 (19.7)	.820
Hyperlipidemia	10 (43.5)	29 (23.8)	.051
Smoking	7 (30.4)	36 (39.5)	.929
Atrial fibrillation	10 (43.5)	41 (33.6)	.363
Prior stroke or TIA	7 (30.4)	18 (14.8)	.068
Baseline glucose level (mmol/L)	8.4 ± 4.0	7.8 ± 3.3	.687
SBP (mmHg)	151.1 ± 15.5	150.7 ± 20.3	.917
DBP (mmHg)	83.7 ± 2.3	85.0 ± 11.9	.621
Costs in hospital (RMB)	20,031.6 ± 17,108.0	18,177.2 ± 28,140.2	.805
Hospitalization (days)	16.4 ± 6.5	14.07 ± 6.9	.2013

Abbreviations: AP, antiplatelet; DBP, diastolic blood pressure; DNT, door-to-needle time; NIHSS, National Institutes of Health Stroke Scale; RMB, Renminbi; SBP, systolic blood pressure; TIA, transient ischemic attack.

*Median (interquartile range).