Stroke. 2017 Jul;48(7):1877-1883.

Low- Versus Standard-Dose Alteplase in Patients on Prior Antiplatelet Therapy: The ENCHANTED Trial (Enhanced Control of Hypertension and Thrombolysis Stroke Study).

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Abstract

BACKGROUND AND PURPOSE: Many patients receiving thrombolysis for acute ischemic stroke are on prior antiplatelet therapy (APT), which may increase symptomatic intracerebral hemorrhage risk. In a prespecified subgroup analysis, we report comparative effects of different doses of intravenous alteplase according to prior APT use among participants of the international multicenter ENCHANTED study (Enhanced Control of Hypertension and Thrombolysis Stroke Study).

METHODS: Among 3285 alteplase-treated patients (mean age, 66.6 years; 38% women) randomly assigned to low-dose (0.6 mg/kg) or standard-dose (0.9 mg/kg) intravenous alteplase within 4.5 hours of symptom onset, 752 (22.9%) reported prior APT use. Primary outcome at 90 days was the combined end point of death or disability (modified Rankin Scale [mRS] scores, 2-6). Other outcomes included mRS scores 3 to 6, ordinal mRS shift, and symptomatic intracerebral hemorrhage by various standard criteria.

RESULTS: There were no significant differences in outcome between patients with and without prior APT after adjustment for baseline characteristics and management factors during the first week; defined by mRS scores 2 to 6 (adjusted odds ratio [OR], 1.01; 95% confidence interval [CI], 0.81-1.26; *P*=0.953), 3 to 6 (OR, 0.95; 95% CI, 0.75-1.20; *P*=0.662), or ordinal mRS shift (OR, 1.03; 95% CI, 0.87-1.21; *P*=0.770). Alteplase-treated patients on prior APT had higher symptomatic intracerebral hemorrhage (OR, 1.82; 95% CI, 1.00-3.30; *P*=0.051) according to the safe implementation of thrombolysis in stroke-monitoring study definition. Although not significant (*P*-trend, 0.053), low-dose alteplase tended to have better outcomes than standard-dose alteplase in those on prior APT compared with those not using APT (mRS scores of 2-6; OR, 0.84; 95% CI, 0.62-1.12 versus OR, 1.16; 95% CI, 0.99-1.36).

CONCLUSIONS: Low-dose alteplase may improve outcomes in thrombolysis-treated acute ischemic stroke patients on prior APT, but this requires further evaluation in a randomized controlled trial.