Advantages of a Combined Approach to Recanalization Therapy

To the Editor:

We agree with Ciccone et al’s article regarding the myths of arterial therapy and Mattle’s accompanying editorial that advocates further controlled trials involving endovascular strategies in acute stroke. IV recombinant tissue plasminogen activator (rt-PA) therapy remains the standard of care for patients presenting within 3 hours of symptom onset. Yet, whereas 13% to 21% of patients will have recanalization of middle cerebral artery occlusions during the first hour of IV rt-PA treatment, patients with National Institutes of Health Stroke Scale (NIHSS) of 10 or greater often have persistent arterial occlusions at angiography.

A comparison trial of IV rt-PA alone and intra-arterial (IA) therapy using thrombolytics and devices is one possible approach to stroke treatment, but in such a trial, IA therapy will be placed at a disadvantage because of inherent delays in this treatment paradigm. In PROACT II, the average time to randomization was 4.7 hours with an average hospital arrival to intra-arterial pro-UK infusion time of 3 hours.

A second approach is to start IV rt-PA in eligible patients as quickly as possible, and then take patients with an appropriate level of neurological deficit or with documented large vessel occlusions to angiography for possible IA thrombolytic therapy and/or devices aimed at recanalizing the artery. The EMS trial was a randomized pilot trial comparing the combined IV/IA approach to IA rt-PA therapy alone. Recanalization of middle cerebral artery occlusions was greater with a combined approach (82%) than with IA therapy alone (50%), supporting that early IV thrombolytic may be important for achieving early recanalization.

Subsequent NINDS-funded trials of combined therapy, IMS I and II, demonstrated improved outcomes at 3 months in modified Rankin Scale (mRS) of 0 to 1, mRS 0 to 2, NIHSS, Barthel Index, and mortality in patients with a NIHSS ≥10 treated with a combined approach when compared to comparable historical placebo treated controls. Furthermore, compared to IV rt-PA treated historical controls, IMS II found a benefit with combined treatment for Barthel Index and Global Test Statistic at 90 days and similar rates of symptomatic ICH. Complications related to angiography and treatment in the IMS II trial was <4%.

Although the early trials of combined therapy are promising, a direct comparison of IV rt-PA alone and the combined approach is needed. IMS III is a prospective, randomized, controlled trial that attempts to combine the advantages of IV rt-PA and IA recanalization therapy. Eligible patients receive 0.6 mg/kg of IV rt-PA and subsequent angiography. If no clot is seen at angiography, no further treatment is administered. Patients with persistent large vessel arterial occlusion are eligible for intraarterial thrombolytic therapy as well as devices aimed at recanalization. The trial is currently ongoing and has a planned enrollment of 900 patients.

Disclosures

None.

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