CEREBRAL HEMORRHAGE

1. Primary hemorrhage. Nevertheless, acute intracerebral lowering to decrease the risk of so-called spontaneous or studies have shown the effectiveness of blood pressure to 20% of the stroke burden worldwide. Treatment of arterial coagulopathy, neoplasm, or vasculopathy accounts for 10%

2. Progress for treatment of acute intracerebral hemorrhage. This hope was generated because of uncontrolled or functional outcome in the larger phase III study. Whether this will turn out to be correct when prospectively studied will be answered by STICH II. Unlike subcortical bleeding, hemorrhages with a deep location did not benefit at all in STICH. However, these hemorrhages have a propensity to rupture into the ventricles and, according to animal studies and open series outcome, seem to improve when the blood is cleared from the ventricles more rapidly.

3. Intracerebral hemorrhage with rupture into the ventricles is the most frequent cause of intraventricular hemorrhage, more frequent than intraventricular hemorrhage from aneurysm rupture or the rare bleedings from intraventricular arteriovenous malformations or tumors. A recent study showed that 45% of intracerebral hemorrhages rupture into the ventricles. Patients with larger hematomas and caudate or thalamic locations tend to bleed more often into the ventricles, and patients with intraventricular extension have a worse outcome. The volume of intraventricular hemorrhage is an important determinant of outcome in supratentorial intracerebral hemorrhage.

4. In this issue of Stroke, Naff et al report the results of a phase II trial to clear blood from the ventricles in patients with small supratentorial intracerebral hemorrhage (<30 mL) and massive intraventricular bleeding. All patients had an extraventricular drainage and were randomized within 24 hours to receive 3 mg/3 mL of recombinant tissue-type plasminogen activator (rtPA) or 3 mL of normal saline injected via the extraventricular drainage into the ventricular spaces every 12 hours until CT evidence of clot resolution was sufficient to remove the catheter. With 18% per day, the blood clot resolution was significantly higher in the rtPA–treated patients compared to 8% per day for the placebo–treated patients (P<0.001), and treatment duration was shorter. Mortality and complications such as bleeding events were similar in both treatment arms, although there was a

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trend toward more bleedings with use of rtPA. Mortality was 19% in the rtPA–treated group and 23% in the placebo group. Ventriculitis occurred among 8% and 9%, respectively, and symptomatic bleeding was reported for 23% of the rtPA–treated group and 5% of the placebo group. There was also a trend toward better clinical outcome at 30 days. The prespecified functional outcome measures were all improved in the rtPA group: Glasgow Outcome Scale was <2 (57% rtPA versus 64% placebo); modified Rankin Scale score was <4 (52% rtPA versus 27% placebo); National Institutes of Health Stroke Scale score was <10 (54% rtPA versus 29% placebo); and Barthel Index was >80 (19% rtPA versus 18% placebo).

Questions that arise or remain after this successful phase II study are whether rtPA is the right thrombolytic agent and whether the right dose has been selected. Most of the work using animals has been performed with urokinase, and most of the reported patients before this study were treated with urokinase, even by the principal investigators of this study. Experimental and clinical work has shown that rtPA might be toxic, enhances edema formation, and might potentially not be the best choice among thrombolytic agents. The principal investigators of this trial were forced to terminate an earlier study because commercial withdrawal of urokinase in the United States precluded additional enrollment of patients. Was the choice of rtPA in this study a regulatory issue, or is there a good scientific reason for the selection of rtPA?

Nevertheless, the investigators have made a great achievement and they have to be congratulated for this successful phase II trial. With their study they have given more than a glimpse of hope to patients with cerebral hemorrhage and complications with rtPA. This could be a signal that the expected benefit of rtPA might easily turn into harm. Let us hope that this will not be the case!

Disclosures

None.

References


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CLEAR Intraventricular Hemorrhage: More Than a Glimmer of Hope
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