NORSTROKE
Norwegian Stroke Research Co-operation
Centre for Neurovascular Diseases
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The Norwegian Sonothrombolysis in Acute Stroke Study

Randomised Trial of Contrast-enhanced Sonothrombolysis in acute ischemic stroke

NOR-SASS (EudraCT Nº 2012-000323-41)

Background:

New therapeutic approaches for patients with acute ischemic stroke are imperative. Several small studies have confirmed the ability of ultrasound to facilitate the activity of fibrinolytic agents within minutes of exposure to a thrombus and to blood that contains rt-PA. The mechanisms of ultrasound-enhanced thrombolysis (sonothrombolysis) include disaggregation on non-cross linked fibrin stands, promotion of fluid around the thrombus, arterial dilation and increased uptake and penetration of rt-PA into the thrombus. Sonothrombolysis can be further enhanced with intravenous contrast agents (gaseous microspheres). When exposed to ultrasound, the microspheres oscillate producing fluid jets that erode the thrombus surface and thereby accelerate clot lysis.

A recent meta-analysis of six randomized (n=224) and three nonrandomized (n=192) clinical studies showed that sonothrombolysis with high frequency is safe and associated with a nearly 3-fold increased likelihood of complete recanalization and a 2-fold higher likelihood of functional independence at 3 months.
In previous studies, however, only patients with an identified thrombus in the major intracranial arteries were included. No studies have examined the effect of sonothrombolysis in patients with minor stroke, or the effect in a general stroke population eligible or not eligible for thrombolysis. There are also no data on sonothrombolysis in combination with Tenecteplase.

Design:

NOR-SASS is a prospective randomized, open-label, blinded endpoint trial. Patients with acute ischemic stroke with symptom onset within 4,5 hours and with no contraindications to sonothrombolysis with contrast agent (Sonovue) are included. Patients eligible for iv thrombolysis are randomized 1:1 to Tenecteplase or Alteplase and then 2:1 to either sonothrombolysis or no sonothrombolysis. Patients not eligible for iv thrombolysis are randomized 2:1 to either sonothrombolysis or no sonothrombolysis.

Hypothesis:

- Sonothrombolysis is a safe treatment for patients receiving iv thrombolysis (Alteplase/Tenecteplase) and for patients not eligible for iv thrombolysis.
- Sonothrombolysis achieves higher recanalization rates than iv thrombolysis alone and is effective in both proximal as well as distal clots.
- Clinical efficacy of sonothrombolysis is superior to that of standard iv thrombolysis and superior to no treatment in patients not eligible for iv thrombolysis.

Aims:

The scientific aims of the study are to assess the effect of sonothrombolysis on clinical short-term and long-term outcome, the safety of the chosen algorithm and the effect on recanalization of sonothrombolysis versus Alteplase/Tenecteplase/no specific treatment without sonothrombolysis.

The clinical aim is to implement a new treatment option, which may remove clots rapidly and safely and thereby may improve outcome among patients with acute ischemic stroke.

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