Tranexamic acid in aneurysmal subarachnoid hemorrhage

The current evidence does not support the use of antifibrinolytic drugs in the treatment of people with aneurysmal subarachnoid hemorrhage, even in those who have concomitant treatment strategies to prevent cerebral ischemia. Results on short-term treatment are promising, but not conclusive. Further randomised trials evaluating short-term antifibrinolytic treatment are needed to evaluate its effectiveness [1].

A randomized controlled clinical trial was carried out to study the effect of tranexamic acid (AMCA, Cyklokapron; AB Kabi, Stockholm, Sweden) in the prevention of early rebleeding after the rupture of an intracranial aneurysm. The incidence of vasospasm, hydrocephalus, cerebral ischemic and thromboembolic complications, morbidity, and mortality was also evaluated. The series comprises 59 patients, 30 treated with tranexamic acid and 29 controls. The treatment was stopped if there was rebleeding, operation, or discharge from the hospital. There were 6 recurrent hemorrhages in 6 patients in the tranexamic acid-treated group and 11 recurrences in 7 patients in the control group. Recurrent hemorrhages occurred later in tranexamic acid-treated patients than in controls. Five patients in each group died from rebleeding. Five additional treated patients and 2 controls died from cerebral ischemic dysfunction. The results suggest that tranexamic acid may protect patients with ruptured aneurysms from rebleeding for 1 or 2 weeks, but that it also may produce cerebral ischemic complications [2].

Trials

A multicenter, prospective, randomized, open-label trial with blinded endpoint (PROBE) assessment. Adult patients with the diagnosis of non-traumatic SAH, as proven by computed tomography (CT) within 24 hours after the onset of headache, will be randomly assigned to the treatment group or the control group. Patients in the treatment group will receive standard treatment with the addition of a bolus of TXA (1 g intravenously) immediately after randomization, followed by continuous infusion of 1 g per 8 hours until the start of aneurysm treatment, or a maximum of 24 hours after the start of medication. Patients in the control group will receive standard treatment without TXA. The primary outcome measure is favorable functional outcome, defined as a score of 0 to 3 on the modified Rankin Scale (mRS), at 6 months after SAH. Primary outcome will be determined by a trial nurse blinded for treatment allocation. We aim to include 950 patients in 3 years.

The strengths of this study are: 1. the ultra-early and short-term administration of TXA, resulting in a lower dose as compared to previous studies, which should reduce the risk for delayed cerebral ischemia (DCI), an important risk factor in the long-term treatment with antifibrinolytics; 2. the power calculation is based on functional outcome and calculated with use of recent study results of our own population, supported by data from prominent studies; and 3. the participation of several specialized SAH centers, and their referring hospitals, in the Netherlands with comparative treatment protocols [3].

1)
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2)
Fodstad H, Forssell A, Liliequist B, Schannong M. Antifibrinolysis with tranexamic acid in aneurysmal subarachnoid hemorrhage: a consecutive controlled clinical trial. Neurosurgery. 1981 Feb;8(2):158-65. PubMed PMID: 7010203.

3)

Germans MR, Post R, Coert BA, Rinkel GJ, Vandertop WP, Verbaan D. Ultra-early tranexamic acid after subarachnoid hemorrhage (ULTRA): study protocol for a randomized controlled trial. Trials. 2013 May 16;14:143. doi: 10.1186/1745-6215-14-143. PubMed PMID: 23680226; PubMed Central PMCID: PMC3658919.