Ultra-early tranexamic acid after subarachnoid hemorrhage. A prospective, randomized, multicenter study.

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To evaluate whether SAH patients treated by state-of-the-art SAH management with additional ultra-early and short term TXA administration have a significantly higher percentage of favourable outcome after six months (score 0-3 on the Modified Rankin…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON46921

Source
ToetsingOnline

Brief title
ULTRA

Condition

- Central nervous system vascular disorders
- Vascular haemorrhagic disorders

Synonym
brain hemorrhage from a weak spot in an cerebral artery, hemorrhage in the subarachnoid space

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,nationaal fonds

Intervention

Keyword: functional outcome, subarachnoid hemorrhage, tranexamic acid, ultra-early

Outcome measures

Primary outcome

Clinical outcome evaluated with a modified Rankin Scale score after six months,

dichotomized into favourable and unfavourable outcome.

Secondary outcome

1. If patient has deceased: the date and cause of death

2. Cause of poor outcome

3. Possible or definite rebleed, rebleed volume, and time interval with first

hemorrhage

4. Rebleed during endovascular or surgical treatment

5. Thromboembolic events during endovascular treatment

6. Delayed cerebral ischemia (DCI)

7. Extracranial thrombosis

8. Treatment for hydrocephalus (therapeutic lumbar puncture, lumbar or

ventricular drainage or definitive shunt)

9. Hemorrhagic complications (intra- and extracranial)

10. Time interval from last hemorrhage to TXA administration

11. Discharge location

12. Infarctions and infarctions volumes on MRI imaging at six months after

endovascular treatment

13. Health-care costs between discharge and six months after hemorrhage

14. Quality of life six months after hemorrhage

15. Gender

16. WFNS grade at admittance

Study description

Background summary

Approximately 50% of all patients with a subarachnoid hemorrhage (SAH) die due to the hemorrhage or subsequent complications. There are several major causes for this course, such as in-hospital rebleed in 21.5% which most frequently occurs within the first 6 hours after the primary hemorrhage (*ultra-early rebleed*). A major part of the patients with a rebleed die during hospital admission and when they survive, they develop more severe cognitive dysfunctions. Reducing the rebleeds by ultra-early administration of tranexamic acid (TXA) could be a major factor in improving the functional outcome after SAH.

Study objective

To evaluate whether SAH patients treated by state-of-the-art SAH management with additional ultra-early and short term TXA administration have a significantly higher percentage of favourable outcome after six months (score 0-3 on the Modified Rankin Scale) compared to the group treated by up-to-date SAH management without additional TXA.

Study design

Multicenter, prospective, randomized, open label treatment with blind endpoint assessment.

Intervention

TXA group: standard treatment with additional administration of 1 g TXA intravenously in ten minutes, immediately after the diagnosis SAH, succeeded by continuous infusion of 1 g per 8 hours until a maximum of 24 hours. Control group: standard treatment with no TXA administration. Both groups undergo a standardized and validated interview at discharge and six months after

hemorrhage to assess the modified Rankin Scale score, and both groups receive a questionnaire to evaluate health-care costs and quality of life.

Study burden and risks

Subjects are randomly allocated to ultra-early TXA therapy or standard treatment. Complications are minor and the expected benefit is large compared with separate studies done with antifibrinolytic medications. In these studies, the safety of the use of these medications in this study population is confirmed.
In this patient group there are adequate, disoriented and comatose patients on admission, so a part of the studied patients are incapacitated when undergoing the study. To extrapolate the conclusions of this study to clinical protocols it is necessary to include patients with a SAH in all different severity grades. Weighing carefully the benefits versus the burden and risks, it is assumed that patients will benefit from ultra-early TXA administration with minimal burden during therapy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Admission to one of the participating study centers or the participating referring hospitals;
• CT-confirmed SAH with most recent ictus less than 24 hours ago
• Age 18 years and older

Exclusion criteria

• No proficiency of the Dutch or English language
• No loss of consciousness after the hemorrhage with World Federation of Neurological Surgeons (WFNS) grade 1 or 2 on admission in combination with a perimesencephalic hemorrhage
• Bleeding pattern on CT compatible with a traumatic SAH
• Treatment for deep vein thrombosis or pulmonary embolism
• History of blood coagulation disorder (a hypercoagulability disorder)
• Pregnancy checked with a pregnancy test in women in their childbearing period
• History of severe renal (serum creatinin > 150 mmol/L) failure
• Imminent death within 24 hours

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-07-2013
Enrollment:	950
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cyklokapron
Generic name:	Tranexamic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	14-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-000343-26-NL
CCMO	NL39577.018.12
Other	NTR 11024

Study results