

New laboratory parameters for the detection of stroke-related complications after rupture of an intracranial aneurysm: role of small cell membrane fragments in the blood and cerebrospinal fluid

Submission date 02/06/2014	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 16/06/2014	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 16/06/2014	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Spontaneous subarachnoid haemorrhage (bleeding on the surface of the brain) accounts for about 5% of all cases of stroke. Although the initial death rate has been reducing over the past two decades, long-term outcomes still remain disappointing because of many complications in the course of the disease despite best intensive care. Delayed cerebral ischemia (insufficient blood flow to the brain) is a common complication and occurs in about 20-40% of patients and may progress to cerebral infarction (blockage of blood vessels). The causes of this serious complication remain poorly understood. While traditionally attributed to the narrowing of large brain vessels (referred to as vasospasm), recent research has indicated that delayed cerebral ischemia may instead result from many factors. Recently, small membrane fragments, called cellular microparticles, have been identified as players in these mechanisms. In a small-scale study, our research group was able to detect increased cellular microparticle release into the blood circulation in patients with subarachnoid hemorrhage. Further, we found a strong correlation with the occurrence of delayed ischemic complications. Therefore, we propose that the generation of cellular microparticles is due to dysfunction of blood vessels after subarachnoid hemorrhage, and has an impact on the occurrence of delayed cerebral ischemia. Changes in the load of cellular microparticles may happen before delayed cerebral ischemia and detection of these abnormalities can help to identify patients at risk.

Who can participate?

Men and women aged between 18-75 years with signs and symptoms of a subarachnoid hemorrhage that started within 48 hours before screening.

What does the study involve?

In this study we will find out the changes in cellular microparticle load by flow cytometry, an established cell counting and characterization method, in the blood circulation. We will perform

an array of statistical tests and delayed cerebral ischemia is assessed by magnetic resonance imaging according to a standardized procedure. Functional outcome is assessed with a set of tests 3 months later.

What are the possible benefits and risks of participating?

Participation of the patients in this study will not interfere with their usual standard of care, and therefore patients may not directly benefit from this study themselves. However, their participation may help others who find themselves in the same position in the future. Frequent collections of blood and cerebrospinal fluid samples are necessary to guide intensive care treatment of patients suffering from subarachnoid hemorrhage. We believe that the additional withdrawal of 5-15 ml of blood per sampling required for our analyses poses no extra risk for our patients. On the other hand, a clear benefit for all patients is the regular follow-up with standardized tests.

Where is the study run from?

The Center for Neurology and Neurosurgery of Innsbruck Medical University (Austria).

When is the study starting and how long is it expected to run for?

Recruitment starts in June 2014. The study will run for 36 months.

Who is funding the study?

Austrian Science Fund (FWF), Austria.

Who is the main contact?

Dr Ronny Beer

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

KLI-375-B00

Study information

Scientific Title

Novel biomarkers for delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage: cellular microparticles revisited

Study objectives

It is hypothesised that the generation of cellular microparticles is a consequence of the microvascular dysfunction after subarachnoid hemorrhage, and has an impact on the occurrence of delayed cerebral ischemia. Further, it is hypothesized that changes in microparticle burden precede the emergence of delayed cerebral ischemia and detection of these abnormalities can help to identify patients at risk.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Institutional Review Board of Innsbruck Medical University (Austria); 28/02/2014; ref. AN4091 292/4.6 (3328a)

Study design

Prospective observational cohort study

Primary study design

Observational

Secondary study design

Cohort study

Study setting(s)

Other

Study type(s)

Screening

Participant information sheet

Not available in web format yet, please use the contact details below to request patient information material.

Health condition(s) or problem(s) studied

Aneurysmal subarachnoid hemorrhage/neurocritical care

Interventions

Objective 1 will be to examine by flow cytometry the temporal evolution of endothelial, platelet-, leukocyte-, and erythrocyte-derived microparticles in patients with aneurysmal subarachnoid hemorrhage and control patients in the systemic circulation, and where applicable in the

cerebrospinal fluid (drawn from external ventricular drainage catheter) and in blood drawn from the internal jugular vein, as well as intracranial arteries if it is necessary to advance the microcatheter distally during angiography. Sampling of body fluids is performed at predefined, standardized time-points (i.e., daily from treatment days 17 and every other day thereafter until treatment day 14, and at treatment day 21).

Objective 2 will investigate the clinical course and outcome of the study cohort focusing on the occurrence of cerebral vasospasm and delayed cerebral ischemia. Therefore, clinical and neuroimaging investigations follow a stringent time-dependent protocol (neurological assessments will be completed every 6 hours or upon evident clinical deterioration from admission until day 21; neuroimaging studies will be performed at admission [baseline] to confirm the diagnosis, after aneurysm repair [i.e., within 24 hours], at day 8 ± 2 , day 14 ± 2 , day 21 ± 2 and day 90 ± 7 ; additional neuroimaging studies indicated at the discretion of the treating physicians are permitted). All patients will be followed for at least 3 months.

Objective 3 will correlate the potential qualitative and quantitative changes in cellular microparticle load with the occurrence of cerebral vasospasm and/or delayed cerebral ischemia, as well as with functional outcome assessed 3 months after the ictus.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

Prognostic value of cellular microparticles for the occurrence of cerebral infarction attributable to delayed cerebral ischemia (i.e., not adjudicated to lesions arising from the aneurysm repair procedure, intracerebral hemorrhage or ventricular drain encephalomalacia) assessed by magnetic resonance imaging (MRI) at day 21 ± 2 .

Secondary outcome measures

Association of cellular microparticles with patient morbidity and mortality at the 3-month follow-up visit. Other (exploratory) endpoints, derived from the clinical database, might be analyzed on data-driven considerations.

Overall study start date

01/06/2014

Completion date

31/05/2017

Eligibility

Key inclusion criteria

1. Patients of either sex aged between 18-75 years
2. Signs and symptoms of SAH with an onset within 48 hours before screening irrespective of World Federation of Neurological Surgeons (WFNS) grade (IV) at admission
3. A computed tomography (CT) scan shows an aneurysmal bleeding pattern in combination with

the presence of an appropriate aneurysm at CT angiography or digital subtraction angiography (DSA)

4. Women of childbearing potential must have a negative serum pregnancy test

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

63 patients are required (per protocol)

Key exclusion criteria

1. Definite contraindication to magnetic resonance imaging (MRI) (e.g., pacemakers)
2. History of trauma, cerebral vascular malformation or other non-aneurysmal source of bleeding
3. Moderate to severe cerebral vasospasm at screening
4. Known coagulopathies, long-term therapy with platelet aggregation inhibitors or oral anticoagulants
5. Severe concomitant diseases as well as patients in whom death seems imminent

Date of first enrolment

01/06/2014

Date of final enrolment

31/05/2017

Locations

Countries of recruitment

Austria

Study participating centre

Neurological Intensive Care Unit

Innsbruck

Austria

6020

Sponsor information

Organisation

Austrian Science Fund (FWF) (Austria)

Sponsor details

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Sponsor type

Government

Website

<http://www.fwf.ac.at/en/index.asp>

ROR

<https://ror.org/013tf3c58>

Funder(s)**Funder type**

Government

Funder Name

Austrian Science Fund (FWF) (Austria), ref: KLI-375-B00

Alternative Name(s)

Fonds zur Förderung der Wissenschaftlichen Forschung, FWF Der Wissenschaftsfonds, FWF Austrian Science Fund, Der Wissenschaftsfonds FWF, Österreichischer Wissenschaftsfonds, FWF, FFWF, FWF EN

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Austria

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration