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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

Registration date
16/06/2014

Overall study status
Completed

Last Edited
16/06/2014

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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 2040% 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 1875 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

Protocol serial number
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

Study type(s)
Screening

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(s)
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.

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

Completion date
31/05/2017

Eligibility

Key inclusion criteria
1. Patients of either sex aged between 1875 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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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)

ROR
https://ror.org/013tf3c58

Funder(s)

Funder type
Government

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

Alternative Name(s)

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Austria

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes