Cerebral Haemorrhage associated Inflammation: a PET/MRI Study

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To assess the association between secondary brain injury in intracranial haemorrhage and the involved inflammatory response. We want to correlate perihematomal inflammation, serum inflammation markers, increased blood-brain-barrier leakage and...

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

Summary

ID

NL-OMON49603

Source
ToetsingOnline

Brief title
CHIPS

Condition

- Central nervous system vascular disorders

Synonym
cerebral hemorrhage, hemorrhagic stroke

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: hemorrhage, inflammation, intracranial hemorrhage, stroke

Outcome measures

Primary outcome

Primary outcome is perihematomal oedema (measured as oedema extension distance on MRI at day 7), which will be correlated with perihematomal uptake of 18F-DPA-714 on PET imaging at day 3 as a measure of neuroinflammation.

Secondary outcome

Secondary study parameters are the association between and the perihematomal uptake of 18F-DPA-714 on PET imaging at day 3 and blood barrier leakage Ktrans as measured with DCE-MRI on day 7. Furthermore the correlation with serum inflammation markers (comparing day 1, 3 and 7 to baseline) will be assessed.

Study description

Background summary

Spontaneous intracerebral haemorrhage yearly affects over 6000 patients in the Netherlands. It is the deadliest stroke subtype, with a 30-day case-fatality of 40%. Of patients surviving, only few gain independence. However, effective treatment options are still lacking. This is reflected in het prognosis which has not improved over the last 30 years. Inflammation is known to play a vital role in the development of secondary brain injury related to intracranial haemorrhage. The release of blood products in the brain parenchyma leads to an activation of the immune system. This subsequently leads to destruction of the blood brain barrier and the formation of perihematomal oedema. In vivo studies linking serum inflammatory markers, blood brain barrier disruption and perihematomal oedema with perihematomal inflammation are lacking.
The CHIPS study strives to assess this relation in patients with acute, spontaneous intracerebral haemorrhage through blood sampling and MRI and PET-CT imaging. This will provide essential insights for the development of new treatment procedures to ameliorate secondary brain injury in intracranial

haemorrhage.

Study objective

To assess the association between secondary brain injury in intracranial haemorrhage and the involved inflammatory response. We want to correlate perihematomal inflammation, serum inflammation markers, increased blood-brain-barrier leakage and perihematomal oedema.

Study design

Prospective, observational cohort study which will be executed at the Radboud University Medical Centre (Radboudumc).

Study burden and risks

Over the course of 1 week patients will undergo; 4x blood sampling (day 0, 1, 3 and 7), 1x a PET-CT scan (day 3) and 1x a MRI scan with intravenous contrast (day 7). The total time-invest for the individual patient will be approximately 2 hours and 20 minutes.
This risk of these procedures are negligible and the burden is considered minimal.
The main negative consequences of performing vena puncture are local pain or bruising. The protocol of the MRI-scan includes administration of intravenous contrast, just as the PET-CT uses an intravenous radioactive tracer. The use of these products can result in local symptoms as redness of the skin or a warm feeling. Furthermore few patients experience side effects as nausea or headache. Those are usually mild and occur in <1% of the patients. Very seldom an allergic reaction can occur. Lastly, incidental findings on the MRI/PET-CT need to be considered. In case of incidental clinical significant findings, the patient*s treating physician will be notified as soon as possible to take appropriate measures.

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

1. Age >= 18 years;
2. Supratentorial non-traumatic ICH confirmed by CT, without a confirmed causative lesion on admission CT-angiography (e.g. aneurysm, AVM, DAVF, cerebral venous sinus thrombosis) or other known underlying lesion (e.g. tumour, cavernoma);
3. Minimal haemorrhage volume of 10mL;
4. Inclusion within 24 hours after symptom onset;
5. Patient*s or legal representative*s informed consent.

Exclusion criteria

1. Severe infection at admission, requiring antibiotic treatment;
2. Use of immunosuppressive or immune-modulating therapy at admission;
3. Pre-stroke modified Rankin Scale score >= 3;
4. Severe ICH, unlikely to survive the first 72 hours (defined as Glasgow Coma Scale score < 6 at time of consent);
5. Pregnancy or breast-feeding;
6. Standard contraindications to MRI;
7. Administration of a radionuclide within 10 physical half-lives prior to study enrolment;
8. Known prior allergic reaction to gadolinium contrast or one of the constituents of its solution for administration;
9. Severe renal impairment (eGFR <30ml/min/1.73m);

10. Planned neurosurgical haematoma evacuation

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-04-2021
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	04-01-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL74920.091.20