HCHWA-D a monogenetic model for intracerebral hemorrhage

Published: 04-09-2013
Last updated: 24-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON38982

Source
ToetsingOnline

Brief title
HCHWA-D a monogenetic model for intracerebral hemorrhage

Condition

- Neurological disorders congenital
- Central nervous system vascular disorders
- Vascular haemorrhagic disorders

Synonym
familial amyloid angiopathy, HCHWA-D

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Amyloid Angiopathy, Cerebral, HCHWA-D, Hemorrhage

Outcome measures

Primary outcome

There are several primary study parameters. The main parameters are triggers of ICH, presence of the *spot sign* on CT, hematoma progression on CT, amyloid and microvascular changes on 3T/7T MRI, recurrence rate and clinical outcome.

Secondary outcome

Not applicable

Study description

Background summary

Although intracerebral hemorrhage (ICH) is a frequent subtype of stroke, the research in this field has received far less attention than ischemic stroke. One frequent cause of lobar hemorrhage in the elderly is sporadic cerebral amyloid angiopathy (sCAA). sCAA is characterized by the deposition of amyloid-* peptide and degenerative changes in the capillaries, arterioles, and small and medium sized arteries of the cerebral cortex, leptomeninges, and cerebellum. Hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D) is an autosomal dominant form of CAA, in which the amyloid angiopathy is pathologically and biochemically similar to sCAA. The disease is characterized by (repeated) intracerebral hemorrhage and cognitive decline. Since in patients with HCHWA-D the genetic background is known it offers a unique opportunity to investigate in vivo the role of these vascular amyloid depositions on ICH progression, recurrence rate and outcome.

Study objective

The overall aim of this study is to investigate the pathophysiology of ICH by investigating intracerebral hemorrhage in HCHWA-D patients. By investigating triggers for ICH, hematoma expansion, recurrence rate and outcome in HCHWA-D related ICH we expect not only to better understand HCHWA-D related ICH but also to increase insight in the pathophysiology of sCAA related ICH.

Study design

Our study is an observational cohort study. The design of the studies considering triggers, the spot sign, hematoma expansion, and 3T/7T MRI are prospective, the design of the study considering recurrence rate and final outcome is retrospective. The study on triggers of ICH has a case-cross over design.

Study burden and risks

The potential risks are limited. The risk of the additional CT scan is a low dosage of radiation (the radiation dose of one non-contrast CT is 0,8 to 1,1 mSv). The risks of MRI are minimal (risk of every day life), because there are no known consequences to the health of the participant. The mutation carriers may benefit from more insight into hemorrhages related to their disease, especially the part on triggers and hematoma growth. Patients with sCAA are needed as comparison for patients with HCHWA-D. By investigating possible modifying factors such as hypertension, coagulation factors and cholesterol we hopefully will discover new targets for treatment of ICH in patients with HCHWA-D. Moreover, this study could eventually lead to much more insights about both sCAA and pICH in general and will be of importance to define endpoints for future intervention trials.

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

HCHWA-D patients
1. Age * 18y
2. Written informed consent from the patient or in case the patients is not able to give informed consent from his/her legal representative (see appendix 2 for the evaluation of the (mental) ability of the patient to give informed consent).
3. Presence of the amyloid precursor protein codon 693 mutation or a hemorrhage pattern on CT or MRI suspect for amyloid angiopathy and first degree relative with HCHWA-D.
sCAA patients
1. Age * 18y
2. Written informed consent from the patient or in case the patients is not able to give informed consent from his/her legal representative (see appendix 2 for the evaluation of the (mental) ability of the patient to give informed consent).
3. Probable CAA based on the modified Boston criteria and no family history of HCHWA-D (see appendix 1) 15 In case there is doubt about a possible familiar type of sCAA a DNA test will be offered to the patients to test for HCHWA-D.

Exclusion criteria

* Age < 18 years
* For the 3T and 7T MRI study:
- Claustrophobia
- Renal failure (only for the contrast enhanced substudy of 7T MRI)
Possible other contra-indications for MRI (for example pacemakers and defibrillators, nerve stimulators, intracranial clips, intraorbital or intraocular metallic fragments, cochlear implants, ferromagnetic implants, hydrocephalus pump, intra-uterine device, an iron wire behind the teeth, permanent make-up, tattoos above the shoulders) will be discussed by the investigator with the MRI technician under supervision of professor A. Webb of the C.J. Gorter Center for High-field MRI.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-09-2013
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	04-09-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	02-12-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-01-2015
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-11-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL44719.058.13