Ophthalmic Imaging in HCHWA-D

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To detect ophthalmic differences between patients and controles. To detect (early) changes in the retina in (pre)symptomatic HCHWA-D disease carriers, in order to find a *biomarker* for disease stage and progression.

Ethical review	Approved WMO
Status	Pending
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON40430

Source
ToetsingOnline

Brief title
Ophthalmic Imaging in HCHWA-D

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders
- Central nervous system vascular disorders

Synonym
Hereditary Cerebral Hemorrhage With Amyloidosis-Dutchtype; amyloid angiopathy; Katwijkse ziekte

Research involving
Human

Sponsors and support

Primary sponsor: Oogheelkunde
Source(s) of monetary or material Support: Afdelingsfonds project BRIGHTER studie

Intervention

Keyword: HCHWA-D, Optical coherence tomography, Retinopathy

Outcome measures

Primary outcome

Differences between the opthalmic findings in HCHWA-D patients and controls.

Secondary outcome

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Study description

Background summary

Hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D) is a rare autosomal dominant disease with repeated intracerebral hemorrhage and cognitive decline caused by a single base mutation at codon 693 of the amyloid precursor protein (APP) gene. This mutation leads to extensive amyloid deposition in the meningocortical arterioles. Levy et al. described this disease in several families who are originally from the Dutch beach villages Katwijk and Scheveningen. These cerebral amyloid deposits in HCHWA-D consist of amyloid beta (Aβ), which links up with other cerebral β-amyloidosis as Alzheimer*s disease (AD) and sporadic cerebral amyloid angiopathy (sCAA).
It is hypothesized that HCHWA-D patients, like patients with Alzheimer disease, undergo a prolonged presymptomatic period where histological changes are progressively accumulating without overt signs and symptoms such as intracerebral hemorrhage or vascular cognitive impairment. Detecting early non-invasive markers in apparently presymptomatic carriers would be a major step towards identifying the effects of cerebrovascular amyloid deposition in this stage of the disease and is important to future research in disease-modifying therapy for HCHWA-D (also called Dutch-type hereditary CAA) and other amyloidosis such as sCAA and AD.
One could suggest that if the cerebral vessels are affected, retinal vessels may also show abnormalities. Anatomically and developmentally, the retina is known as an extension of the central nervous system. There are only a few articles published about retinopathy in patients with cerebral amyloidosis. Furthermore, retinal abnormalities have been reported in patients with neurodegenerative diseases like AD. These studies suggest that AD is accompanied by loss of retinal ganglion cells and therefore retinal abnormalities could be demonstrated. The Aβ and APP gens are expressed in

retina at the level of the ganglion cell layer (GCL) and retinal nerve fiber layer (RNFL). A generalized reduction of the peripapillary RNFL thickness in patients with AD has been reported. In addition, a reduced total macular volume was shown in patients met AD that correlated with the severity of the disease. These findings were visualized by optical coherence tomography (OCT), which is a non-invasive imaging test that uses back-reflected infrared light to take cross-section pictures of the retina. The OCT is frequently used for detecting age related macular degeneration (AMD), which is a leading cause of severe central visual acuity loss in one or both eyes in people over 50 years of age. In AMD, amyloid depositions can be found in the macular region which relate to the atrophy of the retinal pigment layer.
So far, no studies with OCT (as a marker of thickness of the GCL and RNFL and macular region) in combination with fundus imaging have been performed in patients with HCHWA-D. Since both AD and HCHWA-D are related to Aβ deposition and APP gene, we suggest that in HCHWA-D patients also retinal abnormalities will be found.

Study objective

To detect ophthalmic differences between patients and controles.
To detect (early) changes in the retina in (pre)symptomatic HCHWA-D disease carriers, in order to find a *biomarker* for disease stage and progression.

Study design

We will perform an observational cross-sectional diagnostic study in HCHWA-D mutation carriers versus age and sex matched control subjects. The study will take place at the Leiden University Medical Center (LUMC).

Ophthalmic examination will be performed in all subjects, including:
• Visual acuity test
• Intraocular pressure
• Slit lamp examination
• Fundoscopy
• Fundus photography
• OCT-scan

Mydriasis is required for fundoscopy and fundus photography. Therefore mydriatic and cycloplegic eye drops (Tropicamide 0.5% eye drops and Phenylephrine hydrochloride 5.0% eye drops) will be given to all subjects. It takes approximately 15 to 20 minutes prior for these eye drops to have maximum effect and dilate the pupil. These eye drops have a duration of effect of approximately 5 to 8 hours.

The fundus photographs will be assessed according to classification of diabetic retinopathy. The OCT scans will be evaluated according to the classification of

AMD described by Ferris the 3rd en colleagues.

The total duration of all the tests will be approximately 1.5 hour.

Study burden and risks

For the ophthalmological tests the pupils will be dilated, which temporarily gives a slightly decreased vision and/or mild to moderate photofobia for 5-8 hours.

Contacts

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Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

DNA-proven patients with HCHWA-D or patients with a strong clinical suspicion for HCHWA-D in combination with MRI-scan abnormalities highly suggesting HCHWA-D. Patients must be willing to be informed about their test results and (clinical) diagnosis.

Exclusion criteria

Direct family members of the patients whom genetic testing is not performed and/or are nog willing to be informed about their test results and (clinical) diagnosis;
Age-related Macular Dystrophy (AMD);
Diabetic Mellitus;
Macular dystrophies;
Eye traumas;
Glaucoma

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2014
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Date:	22-10-2014

Application type:	First submission
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	NL47259.058.14