Ophthalmic imaging in RVCL

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

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

Summary

ID

NL-OMON42291

Source
ToetsingOnline

Brief title
Ophthalmic imaging in RVCL

Condition

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

Synonym
Retinal Vasculopathy with Cerebral Leukodystrophy, RVCL

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Afdelingsfonds project BRIGHTER studie

Intervention

Keyword: Optical coherence tomography, Retinal vasculopathy with cerebral

leukodystrophy, RVCL

Outcome measures

Primary outcome

Differences between the opthalmic findings in RVCL patients and controls.

Secondary outcome

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Study description

Background summary

Retinal Vasculopathy with Cerebral Leukodystrophy (RVCL) is a monogenic neurovascular disorder caused by heterozygous TREX1 mutations, and is characterized primarily by progressive loss of vision due to a retinal vasculopathy. In addition, a wide range of cerebral and systemic conditions, including intracerebral mass lesions and white matter lesions with associated focal neurological symptoms and cognitive impairment, migraine (primarily without aura), Raynaud*s phenomenon, anaemia and liver and kidney dysfunction can be detected. The consecutive disease stages of RVCL, especially the early stages, remain to be identified. Storimans et al. described retinopathy in a Dutch family. Retinopathy including central and peripheral microangiopathy, areas of capillary non-perfusion, haemorrhages, cotton wool spots and occlusion of large retinal vessels were reported in 22 of the 110 family members. Years later the affected family members turned out to be TREX1 mutation carriers.
It is hypothesized that RVCL patients, like patients with neurodegenerative diseases, undergo a prolonged presymptomatic period where histological changes are progressively accumulating without overt signs and symptoms.
Apart from fundoscopy and fundus imaging, optical coherence tomography (OCT) nowadays plays a key role in monitoring the health status of the retina. The OCT is a non-invasive imaging test that uses back-reflected infrared light to take cross-section pictures of the retina. The OCT is 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. In patients with neurodegenerative diseases like Alzheimer*s disease (AD) it has been reported that OCT visualized generalized reduction of the peripapillary retinal nerve fiber layer (RNFL) thickness and total macular volume has been reported. OCT might show abnormalities in RVCL without clear presence of symptoms related to RVCL.

So far, no studies with OCT in combination with fundus imaging have been performed in patients with RVCL. Retinopathy may also be present in a presymptomatic stage and this could assist in the search for adequate treatment of early stages in the disease.

Study objective

To detect ophthalmic differences between patients and controles. To detect (early) changes in the retina in (pre)symptomatic RVCL 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 RVCL 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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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

DNA-proven patients with RVCL or patients with a strong clinical suspicion for RVCL in combination with MRI-scan abnormalities highly suggesting RVCL 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 not 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:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-06-2015
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	09-03-2015
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	NL51446.058.14