Retinal phenotype of patients with hereditary defects in lipid metabolism

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To investigate whether mutations in genes associated with lipid metabolism are a risk factor for retinal pathology such as the early formation of drusen

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Ocular structural change, deposit and degeneration NEC
Study type	Observational non invasive

Summary

ID

NL-OMON50963

Source
ToetsingOnline

Brief title
Lipid metabolism-related proteins and the structure of the retina

Condition

- Ocular structural change, deposit and degeneration NEC

Synonym
Hereditary disorders of lipid metabolism

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Age-related macular degeneration, Drusen, Lipid metabolism, Retina

Outcome measures

Primary outcome

The presence or absence of drusen on slitlamp evaluation or optical coherence tomography.

Secondary outcome

Morphology of the drusen

Other optical coherence tomography characteristics such as choroidal thickness, choroid vessel density, retinal layer thickness.

Other peripheral and central retinal abnormalities

Visual acuity (Visus)

Study description

Background summary

Age-related macular degeneration (AMD) is the leading cause of blindness in adults over 50 years old, which will affect an estimated 14.9-21.5 million people in Europe alone by 2040. One of the earliest signs of AMD is the formation of drusen, which are deposits of extracellular debris, photoreceptor remnants and lipids, between the retinal pigment epithelium (RPE) and Bruch*s membrane beneath the retina. The pathological role of drusen remains poorly understood, as do the consequences of their formation for the course of the disease. Although the formation of Drusen typically begins after the age of 55, a clinical subtype of AMD termed Early Onset Drusen (EOD) is known to begin at an earlier age, often unbeknownst to the patient.

Genome-wide association studies on AMD identified significant correlations with several genes, of which complement C3 (C3) is the best known. Several genes related to lipid metabolism were also identified in these studies including: Apolipoprotein E (APOE), ATP binding cassette subfamily A member 1 (ABCA1) and LDL receptor (LDLR). Since lipid accumulation has been described in drusen, we hypothesize a role for these genes in the formation of drusen and thus the early stages of AMD. This is supported by research suggesting that the number of drusen is increased in retinas of mice with mutations in lipid-related proteins. Research into this mechanism has been limited to mouse studies mainly

and human studies are rare.

Our aim is to study the role of lipid metabolism-related genes in the formation of drusen and AMD by investigating whether individuals with specific mutations develop drusen at an early age and are thus at greater risk of developing AMD. This will lead to increased knowledge of the role of these genes in the disease. Furthermore, this study could lead to a recommendation to perform early screening for retinal abnormalities in this rare group of patients.

Study objective

To investigate whether mutations in genes associated with lipid metabolism are a risk factor for retinal pathology such as the early formation of drusen

Study design

Patients will be invited for a single visit to the ophthalmology outpatient clinic to undergo a non-invasive ophthalmological screening which will include assessment of visual acuity, slit-lamp examination, retinal photography (autofluorescence imaging, color fundus photographs) and optical coherence tomography (OCT) imaging of the macula.

Study burden and risks

Burdens for the patients are limited to a single visit to the ophthalmology department in the AMC, lasting around 60 minutes. This visit will include a non-invasive ophthalmological screening which will include the use of mydriatic drops to enlarge the pupils, which is required for the photographs. These drops may cause a temporary reduction of visual acuity lasting around 3 hours during which the patient is not allowed to drive a car. This effect is fully reversible and there is only a minimal risk of adverse allergic reactions.
There are no other physical risks associated with the investigations performed.
If the patient gives consent to being contacted again should any pathology of the eyes be discovered (for example glaucomatous cupping of the optic disc) we will do so and, depending on the nature of the pathology, recommend referral to an ophthalmological clinic for further diagnostics/treatment.
Benefits for individuals include a unique contribution to the knowledge of AMD, as well as a thorough screening for ocular pathology with the possibility of having early diagnosis of pathological changes and treatment thereof.
The results of the study will further elucidate the pathophysiological mechanisms of drusen-formation, and correspondingly increase knowledge of AMD. Identification of a causal role of these genes in AMD could lead additional therapeutic options for its treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age 18 and above
Patients with mutations in genes encoding proteints associated with lipid metabolism, including but not limited to: hom-ABCA1, LDL receptor, apo E2E2, as well as patients suffering from a-beta lipoproteinemia.

Exclusion criteria

Age under 18

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-12-2021
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	29-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22154
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL76299.018.21
OMON	NL-OMON22154
OMON	NL-OMON25132