Serum complement levels and the relation between zinc and Age-Related Macular Degeneration.

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1. To determine if zinc supplementation in AMD patients has a direct measurable effect on the complement system explaining the mechanism through which this substance exerts its influence on AMD progression.2. To determine whether this proposed…

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

Summary

ID

NL-OMON35087

Source
ToetsingOnline

Brief title
Zink supplementation in AMD

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders
- Immune disorders NEC

Synonym
AMD, Macular Degeneration

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMD, complement, zinc

Outcome measures

Primary outcome

The primary outcome is the serum level of activation fragment C3d and complement component C3, C3d/C3 ratio will be calculated. This ratio is the activity marker of alternative complement pathway.

Secondary outcome

The secondary outcome is the correlation between this supposed drop in serum level C3d and Y402H polymorphism status in CFH.

Study description

Background summary

Zinc and antioxidants supplementation can delay the progression of age-related macular degeneration (AMD). The strongest genetic association for development of AMD has been found with the complement factor H (CFH) gene, which encodes a regulator of an innate immune system, the complement cascade. Compared to controls, AMD patients have a higher level of complement-mediated inflammation as demonstrated by subretinal complement deposits (drusen). The AREDS study has demonstrated that zinc supplementation may prevent the progression of AMD and preserve visual function in 21% of patients. In addition, it has been demonstrated that zinc has the ability to temper activation of the complement cascade by direct binding to active complement molecules.

Study objective

1. To determine if zinc supplementation in AMD patients has a direct measurable effect on the complement system explaining the mechanism through which this substance exerts its influence on AMD progression.
2. To determine whether this proposed effect of zinc is influenced by the genetic status, regarding the Y402H polymorphism in CFH, enabling us to identify subgroups of patients more

susceptible to the beneficiary effect of zinc.

Study design

51 AMD patients, 17 heterozygous and 17 homozygous carriers of the risk CFH genotype (CT and CC) as well as 17 homozygous nonrisk (TT) genotype will be enrolled. These groups will receive 50 mg oral zinc supplements during 3 months. Serum level of complement component C3 and activation fragments C3d will be analyzed prior, during and post treatment. In case the zinc supplementation in AMD patients has a positive effect on complement parameters, we will like to obtain one venous blood extraction, approximately two months after the ending of the zinc.

Intervention

All participants of the study will receive daily oral 50 mg zinc as zinc sulfate and 1 mg copper as cupric sulphate for 3 months.

Study burden and risks

All participants of this 5 month study will be preselected from EUGENDA, a multi centre database for clinical and molecular analysis of age-related macular degeneration. At the first visit, after signing informed consent forms, each patient will undergo a routine ophthalmological examination, a determination of best corrected visual acuity using ETDRS charts. Furthermore, all patients will be examined by non invasive SD-OCT retina imaging. Zinc supplement will be given during the period of 3 months. In order to measure and monitor changes in serum complement levels at every visit (in total 4) venous blood will be collected. In order to detect a symptoms that may indicate ongoing infection at every visit the patient will undergo an interview (approximately 5 minutes). In case the zinc supplementation in AMD patients has a positive effect on complement parameters, approximately two months after the ending of the zinc one more venous blood extraction (in total 5) and 5 min. interview will be obtained.

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

• Men and women >= 50 years of age.
• AMD patients previously included in the EUGENDA database.
• Previously genotyped for Y402H (rs1061170) gene variation (from EUGENDA database).
• Patients with extensive small drusen, intermediate drusen, large drusen, advanced neovascular AMD without neovascular activity in one or both eyes or geographic atropy in one or both eyes.
• Informed consent.

Exclusion criteria

• Active leakage from CNV due to AMD.
• Ongoing anti/VEGF treatment.
• Ongoing infection.
• Subretinal hemorrhages.
• History of any vitreous hemorrage within 12 weeks.
• Other ocular disorders that may confound the interpretation of the study results.
• Systemic or local steroid treatment within the last three months.
• Use of any antibiotica.
• Prolonged use of diuretics.
• Supplemental use of iron (38-65 mg/day of elemental iron).

• Use of zink and vitamin supplements one month prior to the study.
• Systhemic diseases that may influence complement levels (atypical haemolytic uraemic syndrome (aHUS), membranoproliferative glomerulonephritis type 2 (MG2)).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-06-2010
Enrollment:	51
Type:	Actual

Ethics review

Approved WMO

Date:	20-04-2010
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

ID: 22306
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL31655.091.10
OMON	NL-OMON22306