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Central Retinal Enrichment Supplementation Trials - enrichment of macular pigment in subjects with age-related macular degeneration (AMD)

Submission date
17/07/2012

Recruitment status
No longer recruiting

Registration date
22/08/2012

Overall study status
Completed

Last Edited
23/10/2017

Condition category
Eye Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Age-related macular degeneration (AMD) is an eye disease which affects the central part of the retina at the back of the eye, known as the macula. The macula is responsible for fine detail, central and colour vision. AMD affects central vision, making those affected unable to see what they are looking directly at and unable to perform daily tasks such as reading, driving and recognising faces. AMD is caused by harmful blue light (present in sunlight and artificial light) and damaging unstable molecules, known as free radicals, which are caused by oxygen intake. Because we need light to see and oxygen to breathe, the damage caused by blue light and free radicals is unavoidable. It is part of the ageing process. Research suggests that a pigment found at the macula known as macular pigment may help prevent AMD. Macular pigment is made up of three naturally occurring pigments known as carotenoids. These macular carotenoids are lutein, zeaxanthin and meso-zeaxanthin. We believe that macular pigment functions as an antioxidant which quenches the harmful free radicals, and as a blue light filter which filters the damaging high energy blue light. Research has shown that this protective pigment may be increased by taking dietary food supplements that contain these three important carotenoids.

Who can participate?
People who have been diagnosed with the early stages of AMD (AMD which has not yet affected their vision), who do not have diabetes and who are not currently taking any eye-related dietary supplements which contain the macular carotenoids.

What does the study involve?
The study involves five visits to the Vision Research Centre throughout a 24-month period. Each study visit will take around two and half hours. Study visits will involve various vision tests. They are non-invasive. Study visits will also include a blood sample taken by a trained professional. This blood sample will be assessed in our lab for amounts of the important carotenoids found in the blood. Study volunteers will be randomly allocated to take either a supplement containing lutein, meso-zeaxanthin and zeaxanthin plus vitamin C, vitamin E, zinc and copper, or a

supplement containing lutein and zeaxanthin plus vitamin C, vitamin E, zinc and copper once a day for 24 months. Neither the study organisers nor the volunteers will know which tablet each person is allocated.

What are the possible benefits and risks of participating?
The study volunteers will be provided with a summary of their physical measurements (such as height, weight, blood pressure) and advice with regard to the response required (e.g., lifestyle modification for those who are overweight), as appropriate. Information leaflets on lifestyle changes (e.g., advice on healthy eating, regular physical activity and stopping smoking) will be provided at the study centre. In the case of measurements that may require immediate action, for example if the participants blood pressure is dangerously high, the participant will be advised to go directly to their GP or local hospital, and any assistance needed to make these arrangements will be provided by an appropriate member of the study team. We anticipate that the proposed research will benefit a wide range of people, including those with AMD and the general population, with respect to vision and visual performance in the long term. We foresee no major risks to volunteers participating in this research. There is of course a risk that the status of the volunteers AMD will worsen given that he or she will have AMD. There is a designated Data Safety and Monitoring Committee established, which will review data during the study to ensure that no unforeseen risk presents as a consequence of participation in this study.

Where is the study run from?
The study will be run from the Macular Pigment Research Groups Vision Research Centre at the Waterford Institute of Technology, Waterford, Ireland.

When is the study starting and how long is it expected to run for?
The study will start in September 2012 and each patient will be enrolled for 24 months. It may take us up to a year to recruit all the patients for this study and so the expected finish date could be May 2016.

Who is funding the study?
The study is funded by the European Research Council (Belgium)

Who is the main contact?
Miss Sarah ORegan
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Study website
http://www.mprg.ie

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
281096

Study information

Scientific Title
Enrichment of macular pigment in subjects with age-related macular degeneration (AMD)

Acronym
CREST AMD

Study objectives
Age-related macular degeneration (AMD) is the leading cause of blindness in the developed world. The macula, the central part of the retina, is responsible for optimal spatial vision. There is a growing body of evidence that a lack of a dietary pigment at the macula, known as macular pigment, is associated with increased risk of AMD.

Macular pigment contains the carotenoids lutein, zeaxanthin and meso-zeaxanthin (MZ). The typical western diet contains around 60 carotenoids, and 18 have been identified in human serum. However, only three carotenoids are found at the macula, indicating the unique biological selectivity for their uptake at this location. The function of macular pigment remains undetermined. It is likely that the accumulation of macular pigment has evolved because of its optical and antioxidant properties. For example, macular pigment limits retinal oxidative damage passively (through filtration of blue light) and actively (by quenching free radicals). Furthermore, its optical properties suggest a key role for macular pigment in enhancing visual performance and supporting optimal vision by reducing the effects of chromatic aberration and light scatter.

Recent research has shown that macular pigment can be augmented by dietary supplementation in most (but not all) subjects, suggesting that the macular concentrations of these carotenoids are suboptimal in many people. Our research group has discovered that a dip in the central portion of this pigment, seen in around 12% of individuals, is an undesirable feature of its spatial profile and may be linked to an inability to generate MZ at the macula. Significantly, central dips

in macular pigment are more common in patients with AMD. We have also identified that enrichment of macular pigment, including reconstruction of undesirable central dips, can be achieved by inclusion of MZ in a dietary supplement. We propose to uniquely enrich macular pigment, with all three macular carotenoids, and assess its impact on visual performance and experience in subjects with AMD. This ground-breaking study will advance our understanding of the protective and optical hypothesis of macular pigment, and potentially prevent or delay blindness due to AMD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee, Waterford Institute of Technology, Ireland, 02/11/2010, ref: 10/JN /01

Study design
Single-centre double-blind randomised controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
http://www.wit.ie/images/uploads/Research_PDF /CREST_AMD_Patient_information_leaflet_23rd_July_2013.pdf

Health condition(s) or problem(s) studied
Age-related macular degeneration (AMD)

Interventions
Current interventions as of 21/01/2014:
Intervention 1: 10 mg lutein, 10 mg meso-zeaxanthin and 2 mg zeaxanthin plus 500 mg vitamin C, 400 IU of vitamin E, 25 mg zinc and 2 mg copper.
Intervention 2: 10 mg lutein and 2 mg zeaxanthin plus 500 mg vitamin C, 400 IU of vitamin E, 25 mg zinc and 2 mg copper.

One tablet to be taken per day, preferably with a meal, for the duration of the study.

Previous interventions:
Intervention 1: a soft-gel carotenoid combination formulation containing 10 mg meso-Z, 10 mg L and 2 mg Z in a sunflower oil suspension.
Intervention 2: soft-gel placebo control containing sunflower oil.

One tablet to be taken per day, preferably with a meal, for the duration of the study.

Intervention Type
Supplement

Primary outcome measure
Contrast sensitivity at 24 months of supplementation. The level of significance for changes will be set at 0.05

Secondary outcome measures
Current secondary outcome measures as of 28/01/2014:
1. Contrast sensitivity (measured using the Functional Vision Analyzer and the LogMAR ETDRS test chart [Test Chart 2000 Pro])
2. Glare disability (measured with the Functional Vision Analyzer)
3. Photostress recovery (measured by threshold contrast sensitivity before and after a 10-second exposure to blue photostress lamp)
4. Macular pigment (measured using customised heterochromatic flicker photometry [Macular Metrics II Maculux] and dual wavelength autofluorescence [Heidelberg Engineering Spectralis])
5. Visual acuity (measured using the LogMAR ETDRS test chart [Test Chart 2000 Xpert])
6. Light scatter (measured using the Oculus C-Quant)
7. Foveal architecture (measured using the Heidelberg Engineering Spectralis)
8. AMD morphology (based on retinal grading at the Reading Centre, Moorfields Eye Hospital)
9. Serum carotenoid concentrations (measured by high performance liquid chromatography analysis)
10. Cognitive function (measured using the Cambridge Cognition CANTAB [Cambridge Neuropsychological Test Automated Battery] software)
11. Reading acuity (measured using the Radner Reading Chart)
12. Reading speed (measured using the Radner Reading Chart)

Measured at baseline, 6, 12, 18 and 24 months

Previous secondary outcome measures:
1. Glare disability: measured by the Functional Vision Analyzer)
2. Photostress recovery (measured by threshold contrast sensitivity before and after a 10 second exposure to blue photostress lamp)
3. Macular pigment (measured using customised heterochromatic flicker photometry [Macular Metrics II Maculux] and dual wavelength autofluorescence [Heidelberg Engineering Spectralis])
4. Visual acuity (measured using Snellen letters [Thomson chart])
5. Light scatter (measured using the C-Quant)
6. Foveal architecture (measured using the Heidelberg Engineering Spectralis and the Zeiss Visucam 200)
7. Serum carotenoid concentrations (measured by high performance liquid chromatography analysis)
8. Cognitive function (measured using the Cambridge Cognition CANTAB [CAmbridge Neuropsychological Test Automated Battery] software)
9. Reading acuity (measured using LogRAD [Log Reading Acuity])
10. Reading speed (measured using the Radner Reading Chart)

Measured at baseline, 6, 12, 18 and 24 months

Overall study start date

01/09/2012

Completion date
31/05/2016

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/01/2014:
1. Early stage AMD in at least one eye (between one and eight on the AREDS severity scale)
2. Corrected distance visual acuity of ≥ 6/12
3. Spectacle prescription of ≤ ±5D
4. Have not taken eye-related dietary supplements containing the macular carotenoids (lutein, zeaxanthin and/or meso-zeaxanthin)
5. No other ocular pathology
6. No diabetes

Previous inclusion criteria:
1. Early stage non-visually consequential AMD in at least one eye (between one and eight on the Wisconsin severity scale) and no visually consequential (or late stage) AMD in the fellow eye
2. Corrected distance visual acuity of ≥ 6/12
3. Spectacle prescription of ≤ ±5D
4. Have not taken eye-related dietary supplements containing the macular carotenoids (lutein, zeaxanthin and/or meso-zeaxanthin) in the previous twelve months
5. No other ocular pathology
6. No diabetes

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
75 subjects and 75 controls

Key exclusion criteria
Current exclusion criteria as of 21/01/2014:
1. No early stage AMD in at least one eye (between one and eight on the AREDS severity scale)
2. Presence of late stage AMD in either eye
3. Corrected distance visual acuity of < 6/12
4. Spectacle prescription of > ±5D
5. Recent history of carotenoid supplementation
6. Presence of other ocular pathology
7. Diabetes

Previous exclusion criteria:
1. No early stage non-visually consequential AMD in at least one eye (between one and eight on

the Wisconsin severity scale)
2. Presence of visually consequential (or late stage) AMD in either eye
3. Corrected distance visual acuity of < 6/12
4. Spectacle prescription of > ±5D
5. Recent history of carotenoid supplementation
6. Presence of other ocular pathology
7. Diabetes

Date of first enrolment
01/09/2012

Date of final enrolment
31/05/2016

Locations

Countries of recruitment
Ireland

United Kingdom

Study participating centre
Waterford Institute of Technology
Waterford
Ireland
NA

Sponsor information

Organisation
European Research Council (ERC)

Sponsor details
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Sponsor type
Not defined

Website

http://erc.europa.eu/

ROR
https://ror.org/0472cxd90

Funder(s)

Funder type
Government

Funder Name
European Research Council (ERC) ref: 281096

Alternative Name(s)
ERC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/04/2014		Yes	No
Results article	results	01/12/2015		Yes	No
Results article	results	01/10/2017		Yes	No