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Macular Pigment and Glaucoma Trial

Submission date
11/09/2013

Recruitment status
No longer recruiting

Registration date
02/10/2013

Overall study status
Completed

Last Edited
09/10/2017

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
The eye condition glaucoma is a leading cause of blindness worldwide. With the rapidly growing and ageing global population, there will be an increase in the number of individuals affected by glaucoma. The prevalence of glaucoma is estimated to increase from 60 million in 2010 to 80 million by 2020. Current treatment options are limited to halting disease progression and do not restore lost visual function. It is well recognised that vision impairment (reduced visual function) from glaucoma is a major contributing factor to falls and car accidents. Disability glare impairs vision when light scatters within the eye. This occurs when there is a bright light on a background of low light levels resulting in the loss of image contrast and difficulty seeing dull objects near the source of glare. Disability glare is commonly experienced by glaucoma patients and has been shown to be present even in those who are mildly affected by the disease .The use of tinted glasses is of no benefit in disability glare and may in fact cause further visual impairment. Macular pigment is believed to play an important role in visual performance including glare sensitivity. Macular pigment (MP) is highly concentrated at the macula, the central area of the retina responsible for central vision. The macular pigment optical density (MPOD) in an individual's eye can be measured using a macular densitometer. MPOD decreases with increasing age. There is evidence that dietary MP supplementation can lead to normal MPOD in healthy individuals and those with age-related macular degeneration (AMD). It has been shown that when healthy individuals or those with AMD were supplemented with dietary MP, their visual performance improved. Glaucoma patients commonly complain of disability glare and the cause of this is poorly understood. Individuals with AMD also suffer from disability glare and have reduced MPOD. This prompted us to explore the role of MP in glaucoma patients. It has recently been demonstrated that individuals with glaucoma have reduced MPOD compared to healthy age-matched controls. The aim of this study is to investigate the effects of dietary MP supplementation on the MPOD and visual function of glaucoma patients.

Who can participate?
Individuals attending the Eye Clinic at the Mater Misericordiae University Hospital or Mater Private Hospital for the management of their glaucoma, aged over 18, and healthy individuals with no history of glaucoma

What does the study involve?
All glaucoma participants undergo a series of non-invasive vision-related tests and fill out questionnaires at their first clinic visit. Participants are randomly allocated to receive either a

dietary MP supplement (MacuShield®) or placebo (dummy).The placebo only contains sunflower oil but looks exactly like MacuShield®. Each glaucoma participant takes one capsule daily, preferably with a meal for a duration of 6 months. At the end of the 6 months, all glaucoma participants return for repeat of their vision-related tests and questionnaires. Healthy individuals with no history of glaucoma are also invited to come in for the same testing as the glaucoma participants for comparison. However, the healthy controls do not undergo intervention and do not require further follow-up visits.

What are the possible benefits and risks of participating?
Participants may or may not receive any direct benefit from taking part in the study. However, information obtained during the course of the study may improve the understanding of glaucoma. It is hoped that the treatment that you get may reduce your glare symptoms. However, this cannot be guaranteed. The information from this study may help to improve the treatment of future glaucoma patients. MacuShield® is a natural product that is widely available over the counter. There are no long-term side effects to MacuShield® and it has been tested safe for human consumption in a large study in Ireland. The only documented and uncommon short-term side effect of lutein supplementation in humans has been carotenodermia, which is a harmless and reversible skin hyperpigmentation (darkening of skin).

Where is the study run from?
The study takes place at the Institute of Ophthalmology, Dublin, Ireland. Study subjects will be recruited from the Mater Misericordiae University and Mater Private Hospitals.

When is the study starting and how long is it expected to run for?
October 2013 to December 2014

Who is funding the study?
Howard Foundation and MacuVision Europe Ltd

Who is the main contact?
1. Prof. Colm O'Brien
cobrien@mater.ie
2. Dr James Loughman
james.loughman@dit.ie

Study website
http://www.dit.ie/optometry/people/jamesloughman/research/

Contact information

Type(s)
Scientific

Contact name
Prof Colm O'Brien

Contact details
Institute of Ophthalmology
No. 60, Eccles Street
Dublin
Ireland

7
+ 353 (0)1 885 8616
cobrien@mater.ie

Type(s)
Scientific

Contact name
Dr James Loughman

Contact details
Dublin Institute of Technology
Kevin Street
Dublin
Ireland
8
-
james.loughman@dit.ie

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Macular Pigment and Glaucoma Trial: a placebo-controlled, double-masked study

Study objectives
This is a research study looking at the effects of oral dietary macular pigment (MP) supplementation in an individual with glaucoma. MP is a naturally occurring pigment located at the back of the eye. MP plays an important role to maintain good visual function including glare sensitivity. We have found that patients with glaucoma have reduced MP levels in their eye, which is a new finding [Igras E, Loughman J, Ratzlaff M, O'Caoimh R, O'Brien C. Evidence of lower macular pigment optical density in chronic open angle glaucoma. Br J Ophthalmol. 2013;97(8): 994-8]. Studies have shown that oral dietary MP supplement can increase MP profiles to a normal level and improve glare sensitivity in healthy individuals and those with age-related macular degeneration. Individuals with glaucoma commonly suffer from glare and the cause of this is poorly understood. Here, we would like to study whether dietary MP supplementation will reduce glare symptoms among individuals with glaucoma. We would also like to understand whether dietary MP supplementation has any impact on glaucoma and the individual's quality of life.

The specific objectives of this research are as follow:
1. Establish the macular pigment optical density (MPOD) response to dietary MP supplementation in glaucoma patients
2. Investigate the visual response to dietary MP supplementation in glaucoma patients
3. Identify the relationship between MP and visual function in glaucoma patients compared to normal subjects

Objective 1: Establish the MPOD response to dietary MP supplementation in glaucoma patients
To our knowledge, the association of MPOD and glaucoma has not previously been explored unlike that of age-related macular degeneration (AMD). Our research group has recently published findings from our pilot study that showed glaucoma patients have reduced MPOD, which is a new and exciting finding. Dietary MP supplementation has been shown to increase MPOD in healthy subjects and patients with AMD. There has been no published data on the relationship between dietary MP supplementation and MPOD response in glaucoma. Here, we would like to investigate MPOD response to dietary MP supplementation in glaucoma patients. We hypothesise that the MPOD of glaucoma patients will increase following dietary MP supplementation as such a desirable response has previously been shown in healthy subjects and patients with AMD. To our knowledge, this will be the first study to establish MPOD response to dietary MP supplementation in glaucoma patients.

Objective 2: Investigate the visual response to dietary MP supplementation in glaucoma patients
There is evidence that MP may play a role in visual performance and this is attributed to its preferential spectral absorption for short wavelength blue light. The capability of MP to attenuate longitudinal chromatic aberration and to reduce scattered short wavelength light in the background improves retinal image quality and target contrast respectively allowing better visual performance. It has previously been shown that dietary MP supplementation increases MPOD and improves visual performance in individuals with AMD. The relationship between MPOD and visual function among healthy volunteers has also been demonstrated by other clinical trials. We aim to study whether a positive increment in MPOD following dietary MP supplementation in glaucoma patients will translate to an improvement in visual function such as visual acuity, visual field, glare disability, contrast sensitivity and PRT.

Objective 3: Identify the relationship between MP and visual function in glaucoma patients compared to normal subjects
We also propose to investigate the baseline relationship between MPOD and glaucoma. The glaucoma structure-function relationship will be assessed using the heterochromatic flicker photometry, spectral domain optical coherence tomography (SD-OCT, RTVue-100) and standard automated perimetry Humphrey field analyzer (HFA) Swedish Interactive Threshold Algorithm (SITA) 24-2 and 10-2 tests. The heterochromatic flicker photometry instrument measures the MPOD while the SD-OCT (RTVue-100) will assess the retinal ganglion cell complex thickness (GCCT), macular peripapillary retinal nerve fiber layer thickness (mpRNFLT) and central foveal thickness (CFT). There is evidence that individuals with progressing glaucoma as determined by visual field loss have reduced macular thickness on optical coherence tomography (OCT). Even in the absence of visual field loss, glaucoma patients have significantly lower GCCT and circumpapillary RNFLT when compared to healthy individuals. In our study, the macular visual field will be recorded using Humphrey 10-2 test. Na et al recently showed that the GCCT has a greater structure-function association with the macular visual field than that of the mpRNFLT. Here, we plan to investigate the association of glaucoma-related structural parameters in particular GCCT with that of MPOD. There have been studies that compared MPOD to central foveal thickness as measured by OCT in healthy subjects. Liew et al and van der Veen et al found a significant and positive relationship between MPOD and central foveal thickness while studies carried out by Nolan et al and Kanis et al showed no relation. These conflicting findings may be

explained by methodological differences. Here, we would like to understand the relationship between MPOD and visual function and the underlying retinal structures related to glaucoma. Results obtained from glaucoma patients can be compared to those obtained normal subjects (healthy controls).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee board (Mater Misericordiae University Hospital & Mater Private Hospital), 31/05/2013, ref: 1/378/1535

Study design
Single-centred randomised placebo-controlled double-masked study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information can be found at: http://www.dit.ie/optometry/people/jamesloughman/research/patientinformation/

Health condition(s) or problem(s) studied
Glaucoma and disability glare

Interventions
120 glaucoma participants
Treatment arm - MacuShield® (N=60)
Placebo arm (N=60)
Duration of intervention: 6 months

At baseline, all glaucoma participants will undergo detailed vision assessments such as visual acuity, slit- lamp examination, standard automated perimetry tests, measurement of macular pigment optical density (MPOD), optical coherence tomography scans, glare and contrast sensitivities and photostress recovery time, and fill out vision-related and dietary questionnaires. After the baseline assessments, glaucoma participants will be randomised (1:1) to receive a dietary MP supplementation (MacuShield®) or placebo for 6 months. Each daily dose of MacuShield® contains 10mg Lutein, 10mg meso-Zeaxanthin and 2mg Zeaxanthin in a softgel capsule. The intervention consists of a daily oral consumption of one softgel capsule for a period of 6 months. The placebo will look identical to MacuShield® in its preparation size, colour, smell and taste. It will contain no active ingredients but sunflower oil only.

Sixty age-matched healthy controls will also be recruited for comparison but they will not undergo any intervention.

Intervention Type
Supplement

Primary outcome measure
1. Macular pigment optical density (MPOD) response to dietary macular pigment (MP) supplementation in glaucoma patients. MPOD will be measured using the Macular Densitometer.
2. Visual response to dietary MP supplementation. Visual function assessments include the measurements of best corrected visual acuity (Logmar ETDRS chart), macular visual field test (Humphrey 10-2), glare and contrast sensitivities (Optec 6500 device) and photo-stress recovery time (MDD-2 Macular Adaptometer).

Measured at baseline and repeated again at 6 months after intervention.

Secondary outcome measures
1. Relationship between MP and visual function in glaucoma patients and healthy controls
2. Effect of MP supplementation on vision-related quality of life

Scores from the GAL-9 and TyPE SPEC (vision-related quality of life) questionnaires will be compared before and after dietary MP supplementation.

Overall study start date
01/10/2013

Completion date
31/12/2014

Eligibility

Key inclusion criteria
1. Glaucoma patients or healthy controls aged 18 years and above
2. Either gender
3. Able to give informed consent, make the required study follow-up visits and adhere to study protocol

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

120 glaucoma participants and 60 age-matched healthy controls

Key exclusion criteria
1. Underlying ocular disease such as age-related macular degeneration, diabetic retinopathy or moderate to significant cataract (using Lens Opacity Classification System III grading)
2. Best corrected visual acuity of worse than 6/12 in the test eye
3. Previous ocular surgery other than for cataract extraction or glaucoma drainage procedure
4. Any individual who has a blue-light filter intraocular lens
5. Individuals who already are taking dietary MP supplementation

Date of first enrolment
01/10/2013

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
Ireland

Study participating centre
Institute of Ophthalmology
Dublin
Ireland
7

Sponsor information

Organisation
The Howard Foundation (UK)

Sponsor details
c/o HFH Group
PO Box 1187
Cambridge
United Kingdom
CB22 5WB

Sponsor type
Charity

Website
http://www.howard-foundation.com/trustees.htm

ROR
https://ror.org/03ywwjy69

Funder(s)

Funder type
Charity

Funder Name
The Howard Foundation (UK) (Reg UK Charity No. 285822)

Funder Name
MacuVision Europe Ltd

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?
Results article	results of pilot study	01/08/2013		Yes	No
Results article	baseline results	01/10/2015		Yes	No
Other publications	cross-sectional analysis of baseline data	01/07/2018		Yes	No