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Analysis of eye vasculature anatomy and function using a novel non-invasive imaging device

Submission date
26/09/2018

Recruitment status
No longer recruiting

Registration date
04/10/2018

Overall study status
Completed

Last Edited
21/11/2023

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
The retina, found in the back of the eye, is responsible for vision, by transforming a light stimulus in an electrical one that can be interpreted by our brain. The retina needs a rich blood supply and its effective autoregulation is key to its normal function. In diabetes mellitus (DM), there is some evidence of an early impairment of the vessel autoregulation, which inflammation may contribute to. With a novel non-invasive imaging device (OCT-Angiography) we are able to visualize the retina microvasculature (small blood vessels around the retina) and study its response to external stimuli. In this study, we will compare the response of retinal vessels between healthy individuals and the ones with type 1 diabetes.

Who can participate?
Patients with type 1 diabetes mellitus with no eye involvement, and a similar sample of healthy subjects

What does the study involve?
The participants will be subjected to test that cause a dilation or constriction of the retinal vessels, and the response compared between the two groups.

Participants will be asked to complete two tests (hypoxia challenge test and handgrip test), which cause a dilation or constriction of the blood vessels in the retina. The responses to both tests will be monitored using an imaging device and the results will be compared between both groups. Tear and blood samples will be taken from both groups. This will take around two hours and only one study visit will be required from all participants.

What are the possible benefits and risks of participating?
All participants will benefit with a comprehensive ophthalmological examination and counselling. In case of any abnormality, possibility of medical follow-up will be offered. The tests performed are safe and standardised for clincal research. There are no known risks to participants taking part in this study.

Where is the study run from?
Hospital de Santa Maria, Lisbon (Portugal)

When is the study starting and how long is it expected to run for?
February 2018 to November 2019

Who is funding the study?
1. AstraZeneca (UK)
2. Faculty of Medicine of the University of Lisbon (Portugal)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
469/17

Study information

Scientific Title
Retinal Vascular Function Analysis using Optical Coherence Tomography Angiography

Acronym
RV_OCTA

Study objectives
Aim 1: To describe the effects of hypoxia in ocular hemodynamics using OCT-A.
Hypothesis 1: A reduced inspired fraction of oxygen induces a detectable retinal vascular response – i.e. vasodilation.

Aim 2: To compare the retinal vessel density between T1D patients without DR and a cohort of age and gender-matched healthy individuals.
Hypotheses:
2.1. The retinal vessel density in diabetic patients with no evidence of DR on fundus examination is significantly lower than in healthy subjects.
2.2. The retinal vessel density in diabetic patients with no evidence of DR is related with duration of disease and/or HbA1c.

Aim 3: To describe the retinal vascular response to HCT in T1D patients without DR, in comparison with age and gender-matched healthy individuals.
Hypotheses:
3.1. The retinal vascular response of T1D patients without DR in response to a hypoxic stress is different than the physiologic vasodilation observed in healthy individuals.
3.2. here is a relationship between the duration of disease and/or HbA1c and retinal vascular response to hypoxia.

Aim 4: To describe the retinal vascular response to isometric handgrip test in T1D patients without DR, in comparison with age and gender-matched healthy individuals.
Hypotheses:
4.1. The retinal vascular response of T1D patients without DR in response to isometric exercise is different than the physiologic vasoconstriction observed in healthy individuals.
4.2. There is a relationship between the duration of disease and/or HbA1c and retinal vascular response to handgrip test.

Aim 5: To compare inflammatory cytokines (IL-1β and TNF) concentration in tears and in circulation between T1D patients without DR and a cohort of age and gender-matched healthy individuals.
Hypotheses:
5.1. Inflammation biomarkers are increased in T1D patients even with no evidence of DR, when compared to healthy subjects.
5.2. There is a relationship between inflammation biomarkers concentration and retinal vascular response to HCT/handgrip test.
5.3. There is a relationship between the duration of disease and/or HbA1c and inflammatory cytokines' concentration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Lisbon Academic Medical Center (CAML), 06/03/2018, Ref. 469/17

Study design
Interventional non-randomised controlled study

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied

Type 1 diabetes mellitus without diabetic retinopathy

Interventions
This study will involve type 1 diabetes (T1D) patients without diabetic retinopahty (DR), and a demographically similar control group. Both groups will be subjected to two standardized tests:
1. Hypoxia Challenge Test
2. Handgrip Test
Both tests are expected to induce a physiologic retinal vascular response, with vasodilation in the former and vasoconstriction in the latter. OCT-Angiography will be performed before and during each test to comparatively characterise retinal microvasculature response and its detailed anatomy. Tears and venous blood samples will be collected from all subjects, and IL-1β and TNF concentrations will be measured to investigate if these are associated with a different vascular response pattern between groups. The total duration of the protocol is expected to be approximately 2 hours per patient, and a single visit is needed as all measurements will be performed during that visit.

Intervention Type
Behavioural

Primary outcome(s)
To assess aims 1, 3, 4 and 5:
1. Macular vessel density, assessed using ocular coherence tomography angiography built-in software after the HCT test at the single study visit
2. Peripapillary vessel density, assessed using ocular coherence tomography angiography built-in software after the handgrip test at the single study visit

To assess aim 2:
1. Macular vessel density, assessed using ocular coherence tomography angiography built-in software at the single study visit
2. Peripapillary vessel density, assessed using ocular coherence tomography angiography built-in software at the single study visit

To assess aim 5:
1. Inflammatory cytokine (TNF and IL-1β) concentration in tear and blood samples, assessed using ELISA at the single study visit

Key secondary outcome(s))
To assess all aims:
1. Metabolic data regarding diabetic disease:
1.1. HbA1c values, assessed using a standard laboratory test with a blood sample at the single study visit
1.2. Length of disease, assessed using a chart review of the patient at the single study visit

To assess aims 1, 3, 4 and 5:
1. Changes in cardiorespiratory parameters in relation to macular and peripapillary vessel density change:
1.1. Heart rate, assessed using a polygraph and an oximeter from a single finger throughout the single study visit
1.2. Electrocardiography RR-interval variability, assessed using polygraph and an oximeter from a single finger during the HCT test at the single study visit
1.3. Arterial pressure, assessed using a polygraph and an oximeter from a single finger

throughout the single study visit
1.4. Oxygen desaturation index, assessed using polygraph and an oximeter from a single finger during the HCT test at the single study visit
1.5. Respiratory rate, assessed using a polygraph with a respiratory band during the HCT test at the single study visit

To assess aims 2 and 5:
1. Inflammatory cytokine (TNF and IL-1β) concentration in tear and blood samples, assessed using ELISA at the baseline

Completion date
30/11/2019

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Healthy
3. Type 1 diabetes

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
48

Key exclusion criteria
1. Presence of significant lens opacities (Lens Opacities Classification System III stage 2 or more)
2. High refractive error (spherical equivalent below -6.50 or above +4.00 diopters)
3. History of glaucoma or ocular hypertension
4. Neuro-ophthalmic disease
5. Previous intraocular surgery
6. Untreated hypertension (systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg)
7. Treated hypertension
8. Nephropathy
9. Other documented microvascular complication
10. Local or systemic inflammatory diseases

11. Taking vasoactive drugs
12. Smokers of more than 20 cigarettes per day
13. Pregnancy (urine pregnancy test performed if deemed necessary)
Subjects will be asked to abstain from alcohol and caffeine for at least 6 hours before the study to reduce the possible autonomic effects and measurement bias.

Date of first enrolment
20/10/2018

Date of final enrolment
30/11/2018

Locations

Countries of recruitment
Portugal

Study participating centre
Hospital Santa Maria
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Sponsor information

Organisation
Centro de Estudos Ciências da Visão - FMUL

ROR
https://ror.org/01c27hj86

Funder(s)

Funder type
Not defined

Funder Name
Bolsa de Investigação Fundação AstraZeneca / Faculdade de Medicina da Universidade de Lisboa

Results and Publications

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2018		Yes	No
Results article		03/06/2020	21/11/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes