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Improving the diabetic heart's energy efficiency

Submission date
17/04/2023

Recruitment status
No longer recruiting

Registration date
04/05/2023

Overall study status
Completed

Last Edited
25/04/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Heart failure (HF) is the most common initial presentation of cardiovascular disease in diabetes. Before HF develops, patients with diabetes often exhibit adverse subclinical changes on imaging. A major cause of cardiac dysfunction in type 2 diabetes (T2D) is impaired cardiac energy metabolism. The heart has a very high energy demand while having minimal energy-storing capacity. Abnormal mitochondria are a major source of reactive oxygen species (ROS) production, which can induce cellular damage. Mito-Q is a supplement that could provide insight into the effects of reducing mitochondrial oxidative stress in patients with T2D. The study's aim is to evaluate, in vivo, the efficacy of modulating myocardial energetics through Mito-Q supplementation in patients with diabetes to reverse the subclinical diabetic heart disease process.

Who can participate?
Adults with T2D

What does the study involve?
Participants will attend 2 study visits. They will have blood taken and a cardiac MRI scan at each visit. Participants randomised to the supplement arm will be given Mito-Q supplement to take for 16 weeks as directed. At 8 weeks, the research team will follow up with these participants by phone. Participants randomised to the no supplement arm will take no supplement for 16 weeks.

What are the possible benefits and risks of participating?
There are no direct benefits for participants. Participants may find the insertion of the cannula for the MRI and blood-taking uncomfortable. There is a risk of an adverse reaction to the contrast dye and stress drug used in the cardiac MRI scan; however, appropriately trained staff will always be in attendance.

Where is the study run from?
The study is run from the Advanced Imaging Centre at the Leeds General Infirmary at the Leeds Teaching Hospitals Trust (UK)

When is the study starting and how long is it expected to run for?
August 2020 to December 2024

Who is funding the study?
The Wellcome Trust; Grant Codes: 221690/Z/20/Z (UK)

Who is the main contact?
Dr Henry Procter, H.Procter@leeds.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
308132

Central Portfolio Management System (CPMS)
55661

Study information

Scientific Title
Improving the diabetic heart's energy efficiency (IDEE)

Acronym
IDEE

Study objectives
Mito-Q will restore the energy balance of the heart and will promote improvements in myocardial perfusion, oxygenation and contractile function in the diabetic heart, thus reversing the subclinical cardiomyopathic process in type 2 diabetes (T2D).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/04/2023, East Midlands- Nottingham 1 Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham NG1 6FS, UK; +44 (0)207 104 8271; Nottingham1.rec@hra.nhs.uk), ref: 23/EM/0074

Primary study design
Interventional

Study design
Single-centre prospective randomized open-label mechanistic study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
This is a single-centre, prospective, randomized, open-label mechanistic study. Type 2 diabetes (T2D) patients will be randomly assigned in a 1:1 ratio to receive either Mito-Q 40mg od for 16 weeks or receive no additional treatment.

Patients will be identified from Yorkshire local GP practices and enrolled and followed up in a single centre at Leeds Teaching Hospitals NHS Trust.
Study duration: 16-week open-label study period.

Setting: Tertiary cardiac centre – Leeds General Infirmary and University of Leeds
Study population: 70 adult T2D patients (35 per drug arm).

Potential participants will be invited to the Advanced Imaging Centre (AIC) at the Leeds General Infirmary for a screening/ baseline visit (Visit 1). At this visit, they will be given the PIS to read through, and given the opportunity to ask questions. If they are interested in participating, their consent will be taken in written form. Each participant will then have a series of non-invasive tests. At this baseline visit, the following assessments will be done:

Visit 1 (Baseline; week 0) - approximately 3 hours
• Review of medical history and concomitant medications

• Review of patients' history of diabetes and complications
• Review of inclusion/exclusion criteria
• Collection of demographic data
• Height and weight
• Urine pregnancy test in women of childbearing potential
• Written informed consent
Baseline assessments
• Vital signs
• Physical examination
• 12-lead ECG
• Blood pressure
• Venepuncture (fasting sample): 20mls for the assessment of NTproBNP, HbA1c levels
• Multiparametric MRI
• Randomization
• Dispense Mitoquinone and issue patient diary

At this visit, participants will be randomized to receive either Mitoquinone or receive no additional treatment over the standard treatment patients were receiving. Participants will continue to take their previously prescribed medications throughout the study. The randomisation to either arm (Mitoquinone or no additional supplementation) will be performed by the investigators using an online block randomization tool. They will use a validated randomisation programme and will securely back up both the randomisation seed and the randomisation allocation. We will use randomization to reduce the risk of our findings being related to chance. Otherwise, as this mechanistic study is not a drug trial randomization would not be required.

Visit 2 (phone visit for drug tolerance assessments; week 8, +/- 5 days) - approximately 5-10 minutes
• Check the current medication list and patient clinical status
• Check study supplementation compliance (diary review)
Visit 3 final visit (week 16, +/- 5 days) - approximately 3 hours
Final assessments
• Height and weight
• Vital signs
• Physical examination
• 12-lead ECG
• Blood pressure
• Venepuncture (fasting sample): 20mls for the assessment of NTproBNP, HbA1c
• Multiparametric MRI
End of the study
Collected blood will be tested for N-terminal pro–B-type natriuretic peptide and glaciated haemoglobin (HbA1c) levels.
The participant will have two types of MRI scans, MR spectroscopy and a cardiac MRI scan. The MR spectroscopy will measure fat in the heart and determines the energy levels of your heart at rest. The participants will then be given a dobutamine infusion through a cannula in the arm, to increase the heart rate and 'stress' the heart. The MR spectroscopy measurements will then be repeated when the heart is stressed with dobutamine.
Following the spectroscopy scans the participant will have an MRI scan to assess cardiac function. This is the traditional MR scan which is used routinely in clinical practice for assessing the structure and function of your heart.

The participants will need to lie very still on their backs as movement can blur the images. The participants will be asked to breathe in and out and hold their breath for several seconds for some of the scans. As part of this scan, the participants will also be given dobutamine to perform stress imaging, and will also be given a contrast dye (called gadolinium) through a cannula in their arm. The dye makes the images of your heart and blood flow more visible.
Both dobutamine and gadolinium are used routinely in MR scans in hospitals.
Participants will be given diaries to complete while they are on Mitoquinone. The diary for taking Mitoquinone should take 5 to 10 minutes a week to complete, as all is required is filling in the date and answering yes or no to if they took the drug that week.
If a participant has to discontinue the supplement due to side effects, the patient's initial data from visit 1 will be retained, but they would not attend visit 3.

Intervention Type
Supplement

Primary outcome(s)
Change in myocardial resting PCr/ATP ratio (a sensitive indicator of myocardial energy levels) measured using MRI after 16 weeks of treatment

Key secondary outcome(s)
The following secondary outcomes measured using MRI are assessed at 16 weeks:
1. Percent difference in myocardial PCr/ATP from rest to stress
2. Myocardial blood flow (rest and stress myocardial blood flow)
3. Global longitudinal strain
4. Biventricular ejection fraction
5. Diastolic function (mitral inflow E/A ratio)

Completion date
10/12/2024

Eligibility

Key inclusion criteria
1. Men and women >18 years of age
2. T2D patients with the ability and willingness to provide written informed consent and to comply with the requirements of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
72

Key exclusion criteria
1. Any type of diabetes other than T2D
2. Cardioverter defibrillator or a pacemaker implant
3. Cardiac amyloidosis
4. Known heart failure
5. Established significant renal impairment on routine clinical assessments (eGFR <60 ml/min/m2)
6. Participation in a clinical trial of an investigational medicinal product (CTIMP) in the preceding 12 weeks
7. Known hypersensitivity to dobutamine or gadolinium or any other contra-indications to MRI
8. Female participants who are pregnant, lactating or planning pregnancy during the course of the study
9. Known prior allergic reaction to mitoquinone

Date of first enrolment
20/07/2023

Date of final enrolment
08/08/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Sponsor information

Organisation
University of Leeds

ROR

https://ror.org/024mrxd33

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Protocol file	version 2.0	23/03/2023	03/05/2023	No	No