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Effects of inorganic nitrite on cardiac and skeletal muscle

Submission date	Recruitment status	[ ] Prospectively registered
02/12/2015	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
02/12/2015	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
12/03/2018	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Nitrate is a chemical which plays an important part in regulating blood pressure and blood flow. Naturally, it is found in green leady vegetables and beetroot, although inorganic (man-made) supplements are becoming more common. Studies have shown that increased dietary intake of nitrates could prove to be beneficial for cardiovascular health (heart and blood vessels). In the body, nitrates are used by the cells that line the walls of blood vessels to produce the chemical nitric oxide (NO). NO causes the veins and arteries in the body to dilate, helping oxygen-rich blood to circulate around the body and to the heart. As more oxygen is carried around the body, the heart does not need to work as hard, which is particularly advantageous if someone is suffering from heart disease. Chronic heart failure (CHF) is a long-term condition where the heart has become weakened and isn't able to pump blood around the body effectively. The aim of this study is to find out whether giving people suffering from CHF inorganic nitrate supplements could help to improve their condition.

Who can participate?
Adults who suffer from stable chronic (long-term) heart failure.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group are given capsules containing inorganic sodium nitrate to take orally (by mouth) every day for 2 months. Participants in the second group are identical looking capsules containing a placebo (dummy) every day for 2 months. At the start of the study and then again after 1 week and 2 months, participants in both groups have the level of nitrate in their blood measured. Participants also complete questionnaires and physical tests to measure how well their heart is working when they exercise.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Norfolk and Norwich University Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for?
April 2016 to April 2019

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Professor Michael Frenneaux

Contact information

Type(s)
Scientific

Contact name
Prof Michael Frenneaux

Contact details
University of Aberdeen
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Aberdeen
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Additional identifiers

EudraCT/CTIS number
2012-000788-26

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13080

Study information

Scientific Title
The effects of inorganic nitrite on cardiac and skeletal muscle: Physiology, pharmacology and therapeutic potential in patients with chronic heart failure

Study objectives
Oral inorganic sodium nitrate supplementation will increase plasma levels of nitrite which will improve cardiac function and exercise capacity in association with an improvement in cardiac energy status compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A Research Ethics Committee, 08/05/2012, ref: 12/SS/0037

Study design
Single-centre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Cardiovascular disease; Subtopic: Cardiovascular (all Subtopics); Disease: Heart Failure

Interventions
Participants are randomly allocated to one of two groups.

Intervention group: Participants asked to take 7mmol inorganic sodium nitrate orally for two months
Control group: Participants asked to take an identical placebo orally for two months

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Peak VO2O2 consumption/workload relation during submaximal exercise at baseline and 2 months.

Secondary outcome measures
1. Cardiac and skeletal muscle energetic status is measured using an MRI at baseline and 2 months
2. Change in peak VO2 on exercise testing is measured after 1 week of treatment
3. Fasting plasma glucose and insulin (HOMA), high sensitivity CRP is measured at baseline, 1 week and 2 months
4. Quality of life is measured using the Minnesota Living with Heart Failure Questionnaire score at baseline and 2 months

5. Nitrate/nitrite/nitroso-species levels, conjugated nitro-fatty acid levels are measured at baseline, 1 week and 2 months
6. Oxygen uptake/workload relation on exercise testing is measured at baseline, 1 week and 2 months
7. Parameters of diastolic and systolic function on transthoracic echocardiogram are measured at baseline and 2 months
8. Plasma N-terminal Pro BNP are measured at baseline, 1 week and 2 months
9. Six minute hall-walk distance is measured at baseline and 2 months
10. Skeletal muscle proteomics on skeletal muscle biopsy is measured at baseline and 2 months

Overall study start date
30/11/2015

Completion date
01/04/2019

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Patients who suffer from symptomatic but stable chronic heart failure despite maximal tolerated contemporary medication, of non-ischaemic aetiology, in sinus rhythm

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 56; UK Sample Size: 56; Description: We will aim for a final cohort of 56 patients who complete the study for the Primary Endpoint

Key exclusion criteria
1. Have been hospitalised for decompensated heart failure within the past three months.
2. Contra-indications for undergoing MRI.
3. Known G6PD deficiency or G6PD deficiency measured at screening in males of African, Asian or Mediterranean decent
4. Female subjects of childbearing potential
5. Valvular heart disease of moderate severity or greater
6. Predisposed to acute on chronic limb ischemia

Date of first enrolment
30/11/2015

Date of final enrolment
01/02/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Norfolk and Norwich University Hospital NHS Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Sponsor information

Organisation
Norfolk and Norwich University Hospital NHS Trust

Sponsor details
Colney Lane
Colney
Norwich
England
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NR4 7UY

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01wspv808

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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?
HRA research summary			28/06/2023	No	No