

Effects of inorganic nitrite on cardiac and skeletal muscle

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| Submission date 02/12/2015 | Recruitment status No longer recruiting | <input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol |
| Registration date 02/12/2015 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results |
| Last Edited 12/03/2018 | Condition category Circulatory System | <input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 leafy 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
Polwarth Building
Foresterhill
Aberdeen
United Kingdom
AB25 2ZD

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 VO₂ 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

United Kingdom

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 |