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Effect of dietary nitrate ingestion in stable angina

Submission date	**Recruitment status**	[X] Prospectively registered
21/01/2015	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/01/2015	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/10/2020	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The opening up of blocked coronary arteries using a balloon that is passed through the artery and inflated (called angioplasty) has been a revolutionary technique for improving survival in people with heart disease. However, over time, in 5-10% of patients the treated artery becomes blocked, a phenomenon called restenosis. Recent evidence suggests that dietary nitrate, a chemical found naturally in high levels in green leafy vegetables including beetroot, has a range of biological effects in the body that might reduce restenosis. In this study we will investigate the effects of increasing dietary nitrate intake in patients having balloon angioplasty. The aim of this study is to determine whether increasing dietary nitrate intake, by eating vegetables that has a high nitrate content, might improve long term outcome in patients who have undergone balloon angioplasty. It has been shown previously that nitrate exerts effects on arteries that might prevent a heart attack. This study will test whether dietary nitrate might be useful in preventing arteries from becoming blocked in patients who are at risk of this happening.

Who can participate?
Adults aged at least 18 with stable angina and single/multiple coronary artery stenosis (i.e. narrowing) having elective balloon angioplasty surgery

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 are given 4 mmol potassium nitrate capsules at least one month before and no more than three months before angioplasty surgery. Those in group 2 are given a placebo (potassium chloride). Blood samples are taken from each participant before they take the capsules and then at regular time periods over the next 24 hours in order to measure the amount of nitrite in the blood. Urine and saliva samples are also taken before the participants take the capsules and then 3 and 24 hours later in order to monitor the conversion of nitrate to nitrite and for assessment of bacteria in the mouth (oral). White cell activity and vascular function is also assessed by flow cytometry and pulse wave velocity respectively.

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

Where is the study run from?
Barts and The London (UK)

When is the study starting and how long is it expected to run for?
February 2015 to September 2015

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Krishnaraj Rathod

Contact information

Type(s)
Scientific

Contact name
Dr Krishnaraj Rathod

Contact details
Barts and The London
Queen Mary's School of Medicine and Dentistry
Rutland Place
Charterhouse Square
London
United Kingdom
EC1M 6BQ

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18250

Study information

Scientific Title
Investigation of the effect of dietary nitrate ingestion in stable angina

Study objectives
Consuming oral nitrate in the form of capsules improves blood levels of nitrate and therefore nitric oxide in individuals with hardening of blood vessels and blockages of vessels.

Ethics approval required

Old ethics approval format

Ethics approval(s)
NRES Committee London - London Bridge, 06/11/2014, ref: 14/LO/1708

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Treatment

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

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

Interventions
Patients will be randomised to receive 4 mmol KNO3 or matched KCl capsules (placebo) with 250 ml of low nitrate containing water. This will occur at least 1 month and no more than 3 months prior to angioplasty.

As this is a cross-over study, all patients will receive both the treatment and placebo capsules at different parts of the study.

The whole duration of the study will be a maximum of 3 months with both limbs being conducted no sooner than 1 week apart and no later than 1 month apart.

Intervention Type
Other

Primary outcome measure
Assessment of circulating nitrite levels over a 24h period

Secondary outcome measures
N/A

Overall study start date
01/02/2015

Completion date

30/09/2015

Eligibility

Key inclusion criteria
1. Age between 18-80
2. Stable angina diagnosed on coronary angiography
3. Not taking any additional vitamin or food supplements
4. Long term use of antiplatelet agents such as aspirin, clopidogrel, or anticoagulants such as warfarin, plus a statin for a period of no less than one year
5. A previous history of known ischaemic heart disease, diabetes and stroke is acceptable as long as the subject's condition is deemed stable at time of recruitment into the trial by the practitioner at time of screening

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
Planned Sample Size: 16; UK Sample Size: 16

Key exclusion criteria
1. Patients already on organic nitrate treatment (Nicorandil, ISMN, GTN)
2. Previous history of myocardial infarction (MI) or systolic dysfunction
3. Previous coronary artery bypass surgery (CABG)
4. Current diagnosis of or treatment for malignancy, other than nonmelanoma skin cancer
5. Current life threatening condition other than vascular disease that may prevent a subject completing the study
6. Use of an investigational device or investigational drug within 30 days or 5 half lives (whichever is the longer) preceding the first dose of study medication
7. Patients considered unsuitable to participate by the research team (e.g., due to medical reasons, laboratory abnormalities, or subject's unwillingness to comply with all study related procedures)
8. Severe acute infection, or significant trauma (burns, fractures)
9. Pregnancy. If there is any suggestion that a participant might be pregnant, a pregnancy test will be performed before recruitment
10. History of alcohol or drug abuse within the past 6 months
11. A history of heart failure NYHA class 24 or severe LV dysfunction LVEF<30% regardless of symptom status

12. Systemic autoimmune disease such as rheumatoid arthritis, connective tissue disease, or other conditions known to be associated with chronic inflammation such as inflammatory bowel disease
13. Subjects who have donated > 500mls blood within 56 days prior to study medication administration
14. Anaemia with Hb <10g/dl, or any other known blood disorder or significant illness that may affect platelet function, and coagulation. Known essential hypertension on antihypertensive medication is not a contraindication
15. Any non stable dosing of ongoing medication regimens throughout the study trial
16. A history of chronic viral hepatitis (including presence of hepatitis B surface antigen or hepatitis C antibody or other chronic hepatic disorder)
17. Abnormal liver function due to acute or chronic liver conditions 3 x upper limit of normal at screening
18. Renal impairment with creatinine clearance (eGFR) of <50ml/min at screening
19. BMI <18.5 or > or = 40kg/m2
20. Any patient requiring insulin (whether they are suffering from Type 1 or Type 2 diabetes mellitus)

Date of first enrolment
01/02/2015

Date of final enrolment
30/09/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
William Harvey Research Institute
Barts and The London
London
United Kingdom
EC1M 6BQ

Sponsor information

Organisation
Queen Mary University of London

Sponsor details
Rutland Place
Charterhouse Square

London
England
United Kingdom
EC1M 6BQ

Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

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