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Investigating the effects of dietary nitrate in patients with stable angina

Submission date
05/11/2015

Recruitment status
No longer recruiting

Registration date
05/11/2015

Overall study status
Completed

Last Edited
13/05/2021

Condition category
Circulatory System

[_] 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
Coronary heart disease (CHD), also known as ischemic heart disease, is one of the leading causes of death worldwide. CHD develops because of the build-up of fatty deposits (plaque) on the walls of the coronary arteries (the arteries that supply the heart with oxygen-rich blood). When arteries are blocked or narrowed, the heart does not receive enough blood to function properly, which can cause pain and tightness in the chest (angina), or even lead to a heart attack. There are several types of angina, the most common being stable angina (where the pain is brought on by an obvious trigger, such as exercising). An angioplasty is a common procedure in which a thin tube (catheter) is placed in the narrowed blood vessel. A small balloon on the tip of the catheter is gradually inflated to reopen the artery and flatten the blockage against the artery wall. A mesh-like tube (stent) is often placed inside the artery to keep it open (percutaneous coronary intervention). In about 5-10% of patients, the part of the artery that was reopened in the angioplasty can become narrowed again (restenosis). Nitrate is a chemical which plays an important part in regulating blood pressure and blood flow. It is commonly found in green leady vegetables and beetroot. Recent studies have shown that including nitrate in the diet could help to prevent or reduce restenosis. The aim of this study is to find out whether drinking nitrate-rich beetroot juice can help to prevent restenosis in patients who have had a percutaneous coronary intervention.

Who can participate?
Adults between 18 and 85 years with stable angina who are having an angioplasty

What does the study involve?
Participants are randomly allocated to one of two groups. Starting one day after their surgery, participants in the first group are given 70ml of beetroot juice containing a concentration of 4-5mmol nitrate every day for 6 months. Starting one day after their surgery, participants in the second group are given 70ml nitrate-depleted beetroot juice (where the nitrate has been removed from the juice) to drink every day for 6 months. At the end of the 6 months, participants in both groups are scanned to find out if there is any sign of restenosis.

What are the possible benefits and risks of participating?
Participants in the nitrate group could potentially benefit from an improvement to their

cardiovascular (heart and blood vessels) health. There are no notable risks of participating in this study.

Where is the study run from?
William Harvey Research Institute, Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?
November 2015 to April 2018

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
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02529189

Protocol serial number
20060

Study information

Scientific Title
A randomised, double-blind, placebo-controlled study investigating the effects of dietary nitrate on vascular function, platelet reactivity and restenosis in stable angina

Acronym
NITRATE-OCT

Study objectives

The aim of this study is to investigate whether dietary nitrate might be useful in preventing restenosis in patients who have undergone elective angioplasty.

Ethics approval required
Old ethics approval format

Ethics approval(s)
City Road & Hampstead Research Ethics Committee, 22/05/2015, ref: 15/LO/055

Study design
Prospective randomised single-centre double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Participants are randomly allocated to one of two groups:

Group 1: Participants receive 70ml beetroot juice concentrate containing 4-5mmol nitrate to drink daily, starting one day after their angioplasty procedure for 6 months.
Group 2: Participants receive 70ml beetroot juice which is nitrate-depleted to drink daily, starting one day after their angioplasty procedure for 6 months.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Late-lumen loss within the stent is measured using optical coherence tomography (OCT) at 6 months.

Key secondary outcome(s))
1. Improvement in endothelial function assessed by flow-mediated dilatation of the brachial artery at baseline and 6 months
2. Reduction in target vessel revascularisation (TVR), restenosis rate (diameter >50%) and in-segment late loss is measured using angiography at 6 months (+/- 1 month)
3. Reduction in major adverse cardiac events (i.e. MI, death, CVA, TVR) is measured using via a telephone call at 6, 12 and 24 months
4. Reduction in plaque size as assessed using OCT at 6 months (+/- 1 month)
5. Reduction in inflammatory markers and changes in plasma xanthine oxidase activity, hsCRP

and IL-6 is measured using ELISAs at baseline, 6 and 12 months
6. Reduction in platelet count is measured using a blood test at baseline, 6 months and 12 months

Completion date
02/04/2018

Eligibility

Key inclusion criteria
1. Aged between 18 and 85
2. Able and willing to provide informed consent
3. Patients undergoing successful PCI procedure
4. Patients with stable angina diagnosed by a cardiologist on optimal medical therapy, undergoing an angioplasty to treat residual symptoms

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Unstable ischaemic heart disease, with an episode of chest pain less than 24 hours
2. In patients who have had previous coronary artery bypass surgery (CABG), if they are undergoing angioplasty within a non--native vessel
3. Patients undergoing angioplasty with a bio--absorbable stent
4. Current diagnosis of or treatment for malignancy, other than non-melanoma 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 (tested by urine HcG measurement)
10. History of alcohol or drug abuse within the past 6 months
11. A history of heart failure NYHA class 3-4 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. Patients 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
15. A history of chronic viral hepatitis (including presence of hepatitis B surface antigen or hepatitis C antibody or other chronic hepatic disorder) or HIV
16. Abnormal liver function due to acute or chronic liver conditions 3 x upper limit of normal at screening
17. Renal impairment with creatinine clearance (eGFR) of 30ml/min at screening
18. If patients are on mouthwash, they must be willing to stop using this at least 1 week before the start of the study and throughout the duration that they are involved within the study

Date of first enrolment
02/11/2015

Date of final enrolment
02/04/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
William Harvey Research Institute
Barts and the London
Queen Mary University of London
Charterhouse Square
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Sponsor information

Organisation
Queen Mary University of London

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	20/12/2016	10/04/2019	Yes	No