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Improving the experience of physical activity in people with severe lung disease using dietary nitrate supplementation with beetroot juice

Submission date
12/07/2022

Recruitment status
No longer recruiting

Registration date
02/08/2022

Overall study status
Completed

Last Edited
18/12/2024

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
People with a lung disease called chronic obstructive pulmonary disease (COPD) who need to use oxygen at home are usually limited in what they can do on a day-to-day basis. In COPD, breathlessness and fatigue during daily activities are usually due to a combination of lung problems, the heart having to work harder and the muscles not being very good at using oxygen. Nitrate is a natural product found in green leafy vegetables and beetroot. There is evidence that increased nitrate in your diet can improve the way that blood vessels function and make muscles work more efficiently. Beetroot juice drinks are a good source of nitrate. In a previous study, we showed that a single dose of a nitrate-rich beetroot drink enabled people with COPD who need to use oxygen to walk further. We now want to see if taking this drink regularly for a longer period of time can improve your daily experience of physical activity (how much you can do and how difficult it feels). This study will look at the effect of three months' use of a dietary beetroot juice drink with nitrate, compared to a dummy or placebo beetroot drink. The placebo beetroot drink looks and tastes the same as the beetroot drink, but the nitrate has been removed. We want to see if this will improve the experience of physical activity in people with COPD who need to use oxygen. We will also be looking to see if this improves other measurements such as exercise capacity and blood vessel function. If the study shows that this form of dietary supplementation improves the experience of physical activity, it might become part of the routine treatment for people with this condition.

Who can participate?
People with COPD who need to use supplemental oxygen

What does the study involve?
Participants will be asked to attend three appointments at the Royal Brompton Hospital, two at the beginning of the study (1 week apart) and one at the end of the study 3 months later. The study visits will include a blood test, spirometry test, non-invasive blood vessel function test (EndoPAT test) and walk test. Outside of study visits, participants will be asked to wear a small activity monitor for a week at the beginning and end of the study. After the second visit participants will be randomised into two groups and each given small 70ml beetroot juice drinks

to drink every day for 3 months. One group will have beetroot juice containing nitrate and one group will have beetroot juice which has had the nitrate removed, both drinks are identical in appearance and taste and neither the participant nor the researcher will know which group participants are in.

What are the possible benefits and risks of participating?
You may or may not benefit directly from this study, but the results may help doctors in the future treat people who have COPD and need to use oxygen. Most of the procedures in this study, such as the recording of your weight, height, hip, waist, body composition, wearing activity monitors and blood pressure present no risk to you. Other procedures, such as taking blood samples, can cause mild discomfort. The risks of taking a blood sample include slight discomfort when the needle is inserted and possible bruising or localised infection. These procedures will only be carried out by an experienced health professional under sterile conditions to minimise all these risks. There are also no major side effects associated with taking the beetroot juice drink. Some people find the taste unpleasant and occasionally experience mild stomach discomfort, but this usually settles down after a few days. Most people notice that their urine becomes darker or orangey-red, because of the natural red pigment in the beetroot juice.

Where is the study run from?
The Respiratory Clinical Research Facility at the Royal Brompton Hospital (London, United Kingdom), Glenfield Hospital in Leicester (UK), and Royal Sussex County Hospital in Brighton (UK).

When is the study starting and how long is it expected to run for?
June 2022 to September 2025

Who is funding the study
National Institute for Care and Health Research (NIHR) (United Kingdom)

Who is the main contact?
Ms Alexis Perkins (Trial Manager) (United Kingdom)
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Contact information

Type(s)
Scientific

Contact name
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Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
315107

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 53147, IRAS 315107

Study information

Scientific Title
Dietary nitrate supplementation to enhance daily physical activity in hypoxic COPD: A randomised controlled trial

Acronym
ON-PACE

Study objectives
Primary: In people with COPD who are hypoxic and on home oxygen therapy, dietary nitrate supplementation will improve the experience of physical activity. Secondary: In people with

COPD who are hypoxic and on home oxygen therapy, dietary nitrate supplementation will improve endothelial function.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/06/2022, Wales REC 6 (Meeting Room, Level 2, Wales National Pool, Sketty Lane, Swansea SA2 8QG, United Kingdom; +44 (0)7920 565664; wales.REC6@wales.nhs.uk), ref: 22/WA/0180

Study design
Double-blind parallel-group randomized controlled interventional trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease

Interventions
On-PACE is a double-blind parallel-group randomised controlled trial to demonstrate the superiority of dietary nitrate supplementation with beetroot juice to matched placebo conducted at a single centre – Royal Brompton Clinical Research Facility with three home oxygen services serving as patient identification sites.
Cohort: people with severe COPD who need to use home oxygen. 102 participants will be recruited
There are three in-person study visits as well as several phone calls.
Pre-screening:
The clinical team looking after patients with home oxygen treatment will review the patient's eligibility for the study and will contact the participant. If patients agree, the clinical team will either pass their details on to the study centre at Royal Brompton Hospital or ask them to directly contact the team at Royal Brompton Hospital.
All the study visits will be at Royal Brompton Hospital.
Visit 1 (Screening/Baseline):
Review eligibility and informed consent obtained. Baseline measures include an ECG, CAT score, FACIT score, EQ 5D, MAP, spirometry and FeNO measurement as well as height and weight - BMI. eMRC dyspnoea score. A diet questionnaire will be carried out. Blood pressure values will be collected.
Blood will be drawn for FBC, U&Es, BNP, Endothelin 1, prostacyclin, nitrate/nitrite levels and Arginine/Asymmetric dimethylarginine (ADMA).
Endothelial function will be assessed using the Endopat device.
Participants perform two incremental shuttle walk tests - the better result of these is used to determine the ESWT speed to be used. They will be given a McRoberts MoveMonitor to wear for one week on their waist.
Visit 2 (baseline 2) one week later:
Participants return the MoveMonitor and complete the PROactive physical activity (c-PPAC) questionnaire. ESWT will be performed on the participant’s usual ambulatory oxygen flow rate.

A diary will be given to the patient to complete.
Random allocation to study arm.
Trial intervention will be delivered to their home and participants start to take daily active /placebo beetroot juice.
4-week phone call:
Used to reinforce compliance/collect information about any adverse events. It will also be used to check the delivery of the study intervention (beetroot juice/placebo)
8-week phone call:
Used to reinforce compliance/collect information about any adverse events.
11-week phone call:
MoveMonitor posted to participants in week 10. A phone call to remind participants to wear the monitor for a week up till the final study visit.
Visit 3 week 12
Participants return for an end-of-study assessment.
We will collect empty bottles for compliance count and ask directly about compliance and adverse events. Diet questionnaire.
Participants will have an ECG, complete the CAT score and MRC dyspnoea score and have their weight measured. Repeat baseline blood tests. Adverse events will be collected.
Participants will return the MoveMonitor to allow an analysis of physical activity data and complete the PROactive physical activity (c-PPAC) questionnaire. After a rest period, the EndoPat measure of endothelial function will be performed as well as checking blood pressure. They will then perform an ESWT on their usual oxygen and exit the trial.

Intervention Type
Supplement

Primary outcome(s)
Experience of difficulty with physical activity measured using the difficulty domain of the clinic visit PROactive COPD tool, c-PPAC, at baseline and 3 months

Key secondary outcome(s))
Current secondary outcome measures as of 28/05/2024:

1. Experience of the amount of physical activity measured using the amount domain of the clinic visit PROactive COPD tool, c-PPAC, at baseline and 3 months
2. Exercise capacity measured using an endurance shuttle walk test (ESWT) at baseline and 3 months
3. Oxygenation and heart rate during exercise measured using a pulse oximeter during ESWT at baseline and 3 months
4. Mean arterial pressure, reactive hyperaemia index (RHI) and PAT-Augmentation Index (AI@75) measured using an EndoPAT-RHI system (Itamar Medical) at baseline and 3 months
5. Step count/day measured using a Mcroberts MoveMonitor worn for 7 days at baseline and 3 months
6. Quality of life measured using both COPD assessment (CAT) score and EQ-5D-5L questionnaire at baseline and 3 months
7. Fatigue measured using the FACIT score at baseline and 3 months
8. BNP, blood nitrite/nitrate levels and other blood markers of endothelial function (ADMA, Endothelin 1, Prostacyclin) measured using blood sampling and analysis (including ECFC isolation (alternatively named BOEC) and neutrophil isolation) at baseline and 3 months

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Previous secondary outcome measures:

1. Experience of the amount of physical activity measured using the amount domain of the clinic visit PROactive COPD tool, c-PPAC, at baseline and 3 months
2. Exercise capacity measured using an endurance shuttle walk test (ESWT) at baseline and 3 months
3. Oxygenation and heart rate during exercise measured using a pulse oximeter during ESWT at baseline and 3 months
4. Mean arterial pressure, reactive hyperaemia index (RHI) and PAT-Augmentation Index (AI@75) measured using an EndoPAT-RHI system (Itamar Medical) at baseline and 3 months
5. Step count/day measured using a Mcroberts MoveMonitor worn for 7 days at baseline and 3 months
6. Quality of life measured using both COPD assessment (CAT) score and EQ-5D-5L questionnaire at baseline and 3 months
7. Fatigue measured using the FACIT score at baseline and 3 months
8. BNP, blood nitrite/nitrate levels and other blood markers of endothelial function (ADMA, Endothelin 1, Prostacyclin) measured using blood sampling and analysis at baseline and 3 months

Completion date
20/09/2025

Eligibility

Key inclusion criteria
1. Adults aged 18 years and over
2. Diagnosis of COPD
3. Under care of home oxygen service
4. Documented oxygen assessment meeting NICE criteria:
4.1. PaO2< 7.3 or < 8 if pulmonary hypertension
4.2. Increase in exercise capacity if ambulatory oxygen only

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. Inability to consent
2. Systolic blood pressure below 120mmHg
3. Exacerbation within the last four weeks
4. Use of nitrate-based medication

Date of first enrolment
01/09/2022

Date of final enrolment
31/01/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Brompton & Harefield NHS Foundation Trust
Royal Brompton Hospital
Sydney Street
London
United Kingdom
SW3 6NP

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
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United Kingdom
SE1 7EH

Study participating centre
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SE5 8AB

Study participating centre
Glenfield Hospital
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LE3 9QP

Study participating centre
Brighton and Sussex University Hospitals NHS Trust
Royal Sussex County Hospital
Eastern Road
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BN2 5BE

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR131548

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
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			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes