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Feasibility of providing additional oxygen in patients with resistant high blood pressure and obstructive sleep apnoea

Submission date
24/02/2021

Recruitment status
No longer recruiting

Registration date
11/03/2021

Overall study status
Completed

Last Edited
17/07/2025

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Obstructive sleep apnoea (OSA) is common affecting 1 in 4 adults to some extent. Whilst sleeping, patients with OSA have repeated episodes of narrowing of their throat leading to loud snoring, pauses in breathing, and disturbed sleep. Patients with OSA often feel sleepy in the daytime and often have high blood pressure. OSA is particularly common in patients who have persistently high blood pressure despite the use of medications, termed difficult-to-treat hypertension. Resistant hypertension affects up to 1 in 20 adults and increases the risk of heart attack and stroke.

The standard treatment for OSA is a tight-fitting face mask, called CPAP. Whilst CPAP is very effective, patients often struggle to use CPAP, especially those with few symptoms, such as many of those with difficult-to-treat hypertension and OSA. New treatments to reduce blood pressure are needed for patients with difficult-to-treat hypertension and OSA to reduce the risk of heart attacks and stroke. Overnight oxygen is easier to deliver than CPAP, not requiring a tight-fitting face mask and we recently showed that overnight oxygen can improve morning blood pressure in patients with OSA. However, it is not known whether oxygen can be used as a treatment for resistant hypertension in OSA. We aim to see if overnight oxygen is acceptable and suitable for use in patients with OSA and resistant hypertension. It is important to know this to help design larger studies to test if it is an effective treatment.

Who can participate?
Adults over 18 years, from the specialist cardiology hypertension clinic who have high blood pressure which is not controlled on at least one medication. We are not looking for participants with known OSA.

The study was initially designed to recruit patients with high blood pressure despite using at least three medications for blood pressure, but recruitment of these patients was not feasible and the protocol was amended.

What does the study involve?
To reduce the number of hospital visits, the study will be explained to a potential participant in a virtual appointment by telephone or video-call. They will have been sent the Informed Consent form along with this Patient Information Leaflet by email so they will have copies of these for their reference during that call. If they agree to participate in this virtual appointment, the researcher will document this in the consent form and provide them with a copy for their records. With their permission, the team will review their medical notes to check that they are suitable for this study. Following this, there are two stages to this study, an initial stage looking at whether the participant has OSA, and then a stage when the team will ask the participant to use supplemental oxygen for two weeks. This study will involve extra appointments outside of normal clinic appointments.

Stage 1 involves two virtual appointments lasting approximately 20 minutes. Following stage 1, if the participant is suitable for Stage 2, they will have two face-to-face appointments lasting 1-2 hours. In the event face-to-face visits are not permitted, these will instead be virtual. The study will involve sleeping two nights wearing a sleep study kit in Stage 1 and using extra oxygen for two weeks in Stage 2.

Stage 1 of the study will involve virtual appointments. One of the researchers will arrange a telephone call or video call. The participant will have the opportunity to ask any questions that they may have about the study. The team will ask them some questions about any medical problems and write down details of their current medications. The team will then arrange for them to collect, or post-out a home sleep study kit, home blood pressure monitor and a participant to them. Once they have received these, the team will arrange a second telephone call or videocall to run through how to use these. They will then be asked to use the overnight sleep kit for two nights whilst they sleep.
This is a small device worn on your chest which connects to an oxygen probe which is worn on a finger and nasal prongs which sit in the nose. Once they have finished using your sleep kit for two nights, the participant will be asked to return the equipment to the team in a stamped addressed envelope.
Once we have received your sleep kit, the study team will explain the results to the participant. If this does not show OSA, they will not be suitable to go onto Stage 2 of the study and their participation in the study will end. If the study does show that the participant has OSA, they will be able to continue on to Stage 2 of the study.
Occasionally, the sleep studies do not provide suitable recordings to make a diagnosis. In which case there will be the opportunity to repeat the sleep studies up to twice. In this case, the team will again either arrange collection or postage of the sleep kit with the participant.

Stage 2 involves two face-to-face visits, a baseline and a follow-up visit. The team will phone the participant ahead of this appointment to check that they are well and to run through a COVID-19 safety check list. At baseline visit the participant will be asked to complete a questionnaire about their sleep and how it impacts their daily life. The participant's blood pressure, heart rate, height, weight and neck circumference will be measured. The team will also take a 1ml blood sample from the participant's earlobe to measure the levels of carbon dioxide in their blood.
The participant will be provided with an oxygen concentrator, tubing and given a choice of a face-mask or nasal prongs and shown how to use this. They will be asked to turn the oxygen concentrator on immediately before going to sleep and to turn it off immediately when they wake up in the morning. They will be provided with a pulse oximeter, which is a small device worn like a wrist-watch, and shown how to use this. They will then be instructed to sleep using both the oxygen concentrator and pulse oximeter for the next 14 nights.
In the event face-to-face visits are not permitted, this visit will instead be virtual. In this case, the blood test will not be done and the team will supply all of the equipment the participant will

need ahead of this visit. If this appointment is virtual, the team will supply the participant with a single use tape measure and ask them to record your own height, weight and neck circumference if possible. After 14-17 nights, the team will arrange for the participant to come back to have a follow-up visit. At their follow-up visit they will again be asked to complete a questionnaire about their sleep and how this impacts their daily life. The team will measure the participant's blood pressure and heart rate and will also take a repeat blood sample from their earlobe as on the first face-to-face visit. The team will collect the oxygen concentrator, pulse oximeter, blood pressure machine will not be taken.

What are the possible benefits and risks of participating?
Benefits: Taking part in this study may show that the participant has undiagnosed OSA. If this identified, the team can discuss the participant's options for treating OSA at the end of the study.
Risks: Stage 2 of this study involves the use of oxygen therapy. Oxygen is a flammable gas. When using oxygen therapy during Stage 2, it is important that no-one smokes in the house and that the oxygen or air concentrator does not come into contact with naked flames (e.g. candles) as this would pose a fire risk. Oxygen therapy can cause a dry or blocked nose. Rarely oxygen therapy can cause nose bleeds or morning headaches.
The blood tests taken as part of the study can be slightly painful but should not be any more painful than normal blood tests. There is also a very low risk of tissue damage although this is very unlikely and the test will be conducted by an experienced clinician.

Where is the study run from?
Oxford University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
February 2021 to December 2023

Who is funding the study?
Academy of Medical Sciences (UK)

Who is the main contact?
Christopher Turnbull, Christopher.Turnbull@ouh.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
279286

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 48021, IRAS 279286

Study information

Scientific Title
The feasibility of supplemental oxygen in patients with resistant hypertension and obstructive sleep apnoea

Acronym
FOXOSA

Study objectives
Current study hypothesis as of 04/04/2023:
1. To assess if screening for obstructive sleep apnoea is feasible in patients with difficult-to-treat hypertension
2. To assess if supplemental oxygen therapy is feasible in patients with difficult-to-treat hypertension identified to have obstructive sleep apnoea during the first stage of the study

Previous study hypothesis:
1. To assess if screening for obstructive sleep apnoea is feasible in patients with resistant hypertension
2. To assess if supplemental oxygen therapy is feasible in patients with resistant hypertension identified to have obstructive sleep apnoea during the first stage of the study

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/02/2021, East of England - Essex Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8106; essex.rec@hra.nhs.uk) ref: 21/EE/0010

Study design
Interventional non-randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Home

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Obstructive sleep apnoea in patients with difficult-to-treat hypertension

Interventions
Current interventions as of 04/04/2023:
This is a single-arm, non-blinded study to assess the feasibility of screening for obstructive sleep apnoea in patients with difficult-to-treat hypertension and to assess the feasibility, tolerability and safety of oxygen in patients with uncontrolled high blood pressure and OSA. Oxygen has not been tested in this way and this feasibility data is needed to see if this is an acceptable treatment for patients. This will provide useful information as to the promise of using oxygen as a treatment for OSA.

The study is divided into two stages, with Stage 1 identifying the prevalence of OSA in patients with resistant hypertension in a tertiary hypertension clinic, and Stage 2 assessing the feasibility of supplemental oxygen in participants with resistant hypertension who were identified to have OSA in Stage 1.

Participants will have a total of four research appointments. This will consist of two virtual screening visits, conducted either by video conference or telephone and this will be followed by two face-to-face visits; a baseline and a follow-up visit. Patients can expect to be in the study for a minimum of 15 days to a maximum of 15 weeks from home polygraphy. Further study details are listed below.

If face-to-face appointments are not possible (due to site guidance in response to an increase in COVID-19 cases), Stage 2 will be carried out virtually with two virtual visits instead of two face-to-face visits.

As this is a feasibility study, no formal power calculation has taken place. We aim to enrol 20 patients which allow for screening failures and drop-outs should allow 6 patients to receive oxygen for 14 days. This will provide data screening prevalence of OSA, oxygen usage and safety data.

This study is planned to complete recruitment and follow-up within 1 year. There are no planned interim analyses.

Previous interventions:
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Intervention Type
Other

Primary outcome measure
1. % of participants with an Apnoea–Hypopnoea Index (AHI) >15, measured by home polygraphy at screening
2. % of participants using supplemental oxygen for an average of ≥6 hours/night measured by self report at 2 week follow up

Secondary outcome measures
1. Sleep apnoea related quality of life measured using Sleep Apnoea related Quality of Life Index (SAQLI) at baseline and 2 week follow-up visit
2. Overnight oxygen levels measured by oxygen desaturation index at screening polygraphy and night 14 oximetry
3. Blood pressure (sphygmomanometer) on days -2, -1 and 0, and Days 12, 13, 14
4. Carbon dioxide and base excess levels measured using average capillary PCO2 and base excess with supplemental oxygen at baseline and 2 week follow-up visit

Overall study start date
02/02/2021

Completion date
30/06/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 04/04/2023:
1. Participant is willing and able to give informed consent for participation in the trial
2. Male or Female, aged 18 years or above
3. Current diagnosis (at time of enrolment) of hypertension
4. Ambulatory blood pressure monitoring showing either systolic >135mmHg or diastolic >85mmHg on ambulatory blood pressure monitoring following observed administration of medications
5. Using one or more current regular anti-hypertensive medications for at least 4 weeks before trial entry
6. In the Investigator's opinion, is able and willing to comply with all trial requirements
7. Participant has access to a home computer and/or other device connected to the internet and an email account

Previous participant inclusion criteria:
1. Participant is willing and able to give informed consent for participation in the trial
2. Male or Female, aged 18 years or above
3. Current diagnosis (at time of enrolment) of resistant hypertension
4. Ambulatory blood pressure monitoring showing either systolic >145mmHg or diastolic >85mmHg on ambulatory blood pressure monitoring following observed administration of medications
5. Stable dose of three or more current regular anti-hypertensive medication for at least 4 weeks prior to trial entry
6. In the Investigator's opinion, is able and willing to comply with all trial requirements.
7. Participant has access to home computer and/or other device connected to the internet and an email account

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 20; UK Sample Size: 20

Key exclusion criteria
1. Significant renal or hepatic impairment
2. Scheduled elective surgery or other procedures requiring general anaesthesia during the trial

3. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant’s ability to participate in the trial
4. Participants who have participated in another research trial involving an investigational product in the past 12 weeks
5. Secondary causes of hypertension (other than OSA)
6. Excessive sleepiness with an ESS >16 (as assessed clinically prior to enrolment) or a history of sleepiness-related driving related accident
7. Professional drivers or vigilance critical occupation
8. Any prior use of CPAP
9. Current smoker or other cause of increased fire risk with oxygen therapy (i.e. relative smoking in the participant's residence)
10. An AHI of <=15 on both nights of screening polygraphy
11. Baseline capillary blood gas PCO2 > 6.5kPa, or if unavailable, awake saturations < 93% on overnight polygraphy (assessed at the face to face Baseline visit prior to proceeding with the visit)

Date of first enrolment
30/04/2021

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
John Radcliffe Hopsital
Oxford University Hospitals NHS Foundation Trust
Headley Way
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United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

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Sponsor type
University/education

Website
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ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research organisation

Funder Name
Academy of Medical Sciences; Grant Codes: SGL022\1063

Alternative Name(s)
The Academy of Medical Sciences

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/12/2025

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v2.0	20/01/2021	11/03/2021	No	Yes
Protocol file		20/01/2021	11/03/2021	No	No
HRA research summary			28/06/2023	No	No