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Oxidative stress and obstructive sleep apnoea; effect of withdrawing continuous positive airway pressure therapy

Submission date
26/06/2012

Recruitment status
No longer recruiting

Registration date
01/08/2012

Overall study status
Completed

Last Edited
04/01/2019

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Obstructive sleep apnoea (OSA) is a condition that causes interrupted breathing during sleep. It is unknown why patients with moderate/severe OSA develop high blood pressure, raised heart rate, reduced endothelial function, and probably an increased incidence of vascular events. The main purpose of this study is to find out whether OSA, and the brief falls in oxygen levels that it causes, lead to the release of what are called 'free oxygen radicals' in the blood. These substances are known to be released into the blood (and also be excreted into the urine) following short periods of low oxygen. It is thought they may eventually, over years, contribute to the furring up of arteries (atherosclerosis) and thus high blood pressure, heart attacks and strokes. At the moment there is no convincing evidence that OSA does this, and the current study has been designed to try and provide proof, one way or the other.
In order to answer this question we are asking some of the subjects to stop their continuous positive airway pressure (CPAP) breathing apparatus for a maximum of 14 nights to allow the sleep apnoea to return. Samples taken at the end of this period without CPAP will be compared with the ones taken at the beginning whilst on CPAP; and with another group of subjects who will not be stopping their CPAP, but carrying on as normal during the 14 days. In this way we should be able to identify if the brief falls in oxygen levels lead to an increase in these 'free oxygen radicals'.

Who can participate?
People aged 20-75 with obstructive sleep apnoea who have been treated with CPAP for more than 12 months.

What does the study involve?
The first stage of the study involves assessing the current severity of patients' sleep apnoea. In order to do this patients will be asked to stop using their CPAP machine for four consecutive nights and measure their overnight oxygen levels at home with a small device (oximeter) that they wear on a finger overnight. This would be on the fourth night after stopping their CPAP. If the patient's sleep apnoea does return enough on the fourth night then we would ask them to return to using their CPAP, and come to an evening appointment at the hospital to see one of

our research nurses about two weeks later. At this appointment we would take some basic details about the patient, and measure height, weight and neck size. We would also give them the Epworth Sleepiness score to fill in. We would show them how to take their blood pressure and heart rate with a machine they can take home with them. We would also explain how to use a portable sleep study device which they would also take home and use that night while sleeping with their CPAP. We would also give patients a bottle in which to collect the urine they pass overnight.
Patients would then come back the following morning to return the sleep study device which the research team would download and analyse. We would take a blood and fat sample after which the patients would then be randomly allocated to use either a normal CPAP machine and continue with CPAP, or a machine set at a lower pressure that will allow a return of sleep apnoea. These CPAP machines will be provided by the research team for the period of the study and patients will not be told which of the two machine types they have been given. Patients would then be free to return home.
Over the next 14 days/nights we would ask patients to record their blood pressure and heart rate three times, twice a day. In addition, the CPAP machine has a built-in oximeter and we would ask them to wear the oximeter probe each night too. After 14 days/nights we would ask patients to return with the BP and CPAP machines. We would repeat the measurements done at the first visit and the home sleep study, the overnight urine collection and, the following morning, the blood and fat samples. After that patients would be free to go (and return to using their own CPAP machine) and the study would be finished.

What are the possible benefits and risks of participating?
There are unlikely to be any benefits directly to patients. However, in the two previous studies, where subjects have discontinued CPAP for 14 nights, it has been interesting to see that some of them have not had a return of sleep apnoea for a few nights. It has been reassuring to the subject to know that they can stop CPAP for a few nights, safe in the knowledge that their sleep apnoea will not return. We would be able to tell patients how many nights it was before their sleep apnoea returned. We are not anticipating any risks other than the partial return of sleepiness, similar to that which patients probably experienced before treatment. Thus patients will be asked not to drive if they do experience significant sleepiness.

Where is the study run from?
Oxford Centre for Respiratory Medicine, Churchill Hospital, Oxford (UK).

When is the study starting and how long is it expected to run for?
September 2012 to August 2013.

Who is funding the study?
The study is being organised by the Oxford Sleep Unit. It is being funded from different sources including locally donated charitable funds. Funding from the British Heart Foundation is being applied for.

Who is the main contact?
Professor John Stradling
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1

Study information

Scientific Title
Oxidative stress and obstructive sleep apnoea; effect of withdrawing continuous positive airway pressure therapy: a randomised controlled trial

Study objectives
We hypothesise that the withdrawal of continuous positive airway pressure (CPAP) and the return of obstructive sleep apnoea (OSA), with consequent hypoxia/reoxygenation, will increase markers of oxidative stress and reduce markers of anti-oxidant reserve.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South West - Exeter, 02/10/2012, ref: 12/SW/0254

Study design
Single-centre randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact Magda Laskawiec-Szkonter, magda.laskawiec@ouh.nhs.uk to request a patient information sheet

Health condition(s) or problem(s) studied
Sleep apnoea

Interventions
Current interventions as of 07/05/2013:
Sham/placebo CPAP at subtherapeutic levels: subtherapeutic CPAP (<1cm H2O) nightly during sleep time for 2 weeks. Using a ResMed Autoset, the subtherapeutic pressure will be achieved by setting the CPAP machine to its lowest pressure, insertion of a flowrestricting connector at the machine outlet, and creation of six extra holes in the collar of the main tubing at the mask end to allow air escape, and to prevent rebreathing of CO2. This has been used successfully as a placebo in many studies and has no effect on the apnoeas and hypopnoeas. The ResMed Autoset device allows monitoring of simultaneous pulseoximetry to quantify the degree of hypoxia /reoxygenation occurring during the two week experimental period.

CPAP limb: Therapeutic CPAP will continue using the ResMed Autoset with simultaneous oximetry monitoring as well as the internal apnoea/hypopnoea counter to ensure continuing full abolition of OSA and hypoxia during the two week experimental period.

Previous interventions until 07/05/2013:
Sham/placebo CPAP at subtherapeutic levels: subtherapeutic CPAP (<1cm H2O) nightly during sleep time for 2 weeks. Using a ResMed Stellar 150, the subtherapeutic pressure will be achieved by setting the CPAP machine to its lowest pressure, insertion of a flowrestricting connector at the machine outlet, and creation of six extra holes in the collar of the main tubing at the mask end to allow air escape, and to prevent rebreathing of CO2. This has been used successfully as a placebo in many studies and has no effect on the apnoeas and hypopnoeas. The ResMed Stellar 150 device allows monitoring of simultaneous pulseoximetry to quantify the degree of hypoxia /reoxygenation occurring during the two week experimental period.

CPAP limb: Therapeutic CPAP will continue using the ResMed Stellar 150 with simultaneous oximetry monitoring as well as the internal apnoea/hypopnoea counter to ensure continuing full abolition of OSA and hypoxia during the two week experimental period.

Intervention Type
Procedure/Surgery

Primary outcome measure
Change in plasma malondialdehyde over the two weeks trial period, CPAP withdrawal (sham CPAP) versus control (continuing CPAP) E55

Secondary outcome measures

1. Other measures of oxidative stress
2. Blood pressure and heart rate
3. Overnight catecholamine secretion
4. Subjective sleepiness
5. OSA severity assessed by nocturnal respiratory disturbances (ODI/AHI from polygraphic sleep studies, and ODI/AHI from nightly monitoring)

Overall study start date
03/09/2012

Completion date
30/08/2013

Eligibility

Key inclusion criteria
1. Objectively confirmed obstructive sleep apnoea (at the time of original diagnosis) with an oxygen desaturation index (ODI, ≥4% dips) of >20 (this threshold will exclude subjects with borderline OSA, in whom there may be little experimental effect)
2. Currently >20/h oxygen desaturations (≥4% dips) returning during an ambulatory nocturnal pulse oximetry performed at the end of a 4-night period without CPAP, prior to entry into the study
3. Treated with CPAP for more than 12 months, minimum compliance 4h per night, AHI <10 with treatment (derived from CPAP download data)
4. Written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
42

Key exclusion criteria
1. Previous ventilatory failure (awake resting arterial oxygen saturation <93% or arterial PCO2 > 6kPa) or severe respiratory disorders other than OSA
2. Unstable, untreated coronary or peripheral artery disease, severe arterial hypertension (>180 /110mmHg), severe arterial hypotension (<90/60mmHg)
3. Previously diagnosed with Cheyne-Stokes breathing
4. Current professional driver
5. History of any sleep-related driving or other accident
6. Age <20 or >75 years at trial entry

7. Acute upper respiratory infection
8. Mental or physical disability precluding informed consent or compliance with the protocol
9. Non-feasible trial follow-up (for example, distance from follow-up centre, physical inability)

Date of first enrolment
03/09/2012

Date of final enrolment
30/08/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
Oxford University Hospitals NHS Trust (UK)

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Research and Development Department
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Sponsor type
University/education

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (UK) - application in progress

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?
Results article	results	01/09/2012		Yes	No
Results article	results	01/10/2015		Yes	No
Results article	results	02/02/2017		Yes	No