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Asthma and obstructive sleep apnea

Submission date 14/10/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 21/10/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 28/04/2021	**Condition category** Respiratory	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Asthma is a common condition of variable airway obstruction due to inflammation, often caused by certain triggers. Obstructive sleep apnoea (OSA) is a condition in which the airway at the back of the throat is obstructed during sleep causing sufferers to snore and stop breathing. There are frequent awakenings and they never achieve a full night of good sleep. Severe sleepiness can impact enormously on their quality of life. Although both asthma and OSA are common and it would be inevitable that some patients will have both conditions, the overlap between the two seems to be more that would be expected by chance alone. This observation suggests there may be some link, possibly causative, between the two. This project aims to examine the feasibility of studying the overlap between asthma and (OSA); could asthma cause or worsen OSA? Could OSA cause or worsen asthma? We will describe various hypothetical physiological links between asthma and OSA. In addition, we will examine whether CPAP (a treatment for OSA) could have a beneficial effect on asthma?

Who can participate?
There are four groups of participant, all of which have to be at least 18: patients with OSA and asthma, asthma alone, OSA alone and healthy people with neither condition ('control subjects').

What does the study involve?
Patients receive appropriate standard treatment for their particular condition, which includes inhaled medication for asthma and continuous positive airways pressure (CPAP) delivered via a fitted mask over the nose at night for patients with OSA. They all have a number of breathing tests done, are asked to donate a saliva sample and complete a questionnaire about symptoms. These investigations are performed at the time of recruitment to the study for all participants. All participants are then treated with CPAP for one hour. The breathing tests are repeated one hour after the CPAP. For patients in whom it is clinically indicated (patients with OSA, with or without asthma) there is also a one month period of treatment with home CPAP. For these patients, the breathing tests and questionnaires are repeated once more after the treatment period.

What are the possible benefits and risks of participating?
The participants will not receive any immediate and direct benefits. The assessment by a specialist may lead to treatment being offered for the improvement of patients which may improve the long term lung function and thus the patient's quality of life. In future guidelines

for asthma control, it is hoped that screening for OSA in asthmatics can help in better treatment and control for asthma. There are no extra risks involved in taking part in the study, since the tests are routine and generally regarded as safe. Pulmonary function tests (PFT) are usually safe for most people. Many patients undergo the PFT without experiencing any complications. However, because the test may require patients to inhale and exhale rapidly, some patients may experience a feeling of lightheadedness. CPAP is a commonly used treatment to treat OSA in the Sleep clinic.. Side effects and other problems are usually minor, and they can be treated or fixed. Minor cases of dry mouth, nose congestion, runny nose, sneezing and sinusitis can occur. If they do the problem can usually be helped or resolved by adding a heated humidifier to the CPAP machine. All the procedures will be carried out following the current guidelines and performed only by the Respiratory and sleep consultants.

Where is the study run from?
Royal Victoria Infirmary and Freeman Hospital (UK)

When is study starting and how long is it expected to run for?
March 2015 to August 2017

Who is the main contact?
Dr. Graham Burns
Graham.Burns@nuth.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Graham Burns

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Additional identifiers

EudraCT/CTIS number

IRAS number
170309

ClinicalTrials.gov number

Secondary identifying numbers
REC reference: 16/NE/0021, IRAS project ID: 170309

Study information

Scientific Title
Asthma and obstructive sleep apnea. The association, physiological inter-relation and impact of therapy.

Study objectives
Asthma is associated with Obstructive Sleep Apnea (OSA) and the overlap between both diseases can worsen the state of patients clinically. CPAP improves OSA and can help people with asthma and OSA. We hypothesized that CPAP will improve airway physiology in people with asthma, this is because of improvements in airway physiology and/or acid reflux.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East - Newcastle & North Tyneside 2 Research Ethics Committee, 22/03/2016, ref: 16/NE/0021

Study design
Feasibility, observational cohort study

Primary study design
Observational

Secondary study design
Feasibility, Cohort study

Study setting(s)
Hospital

Study type(s)
Screening

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

Health condition(s) or problem(s) studied
Asthma and obstructive sleep apnea (OSA)

Interventions
This study aims to examine various postulated physiological links between asthma and obstructive sleep apnea.

There will be four groups of participant recruited from Respiratory and Sleep Clinics - patients with OSA and asthma, asthma alone, OSA alone and healthy people with neither condition ('control subjects')

Patients receive appropriate standard treatment for their particular condition: inhaled medication for asthma, continuous positive airways pressure (CPAP) delivered via a fitted mask

over the nose at night for patients with OSA. Subjects will also undergo a number of breathing tests and complete a questionnaire about symptoms. For (patients with OSA, with or without asthma) there will be a one month period of treatment with home CPAP and then the breathing tests and questionnaires will be repeated.

At recruitment (for all groups (asthma only, OSA only, Asthma and OSA and healthy control)
1. Assessment of reflux symptoms
1.1. Leicester cough questionnaire
1.2. Reflux Symptoms Index Questionnaire
1.3. Saliva pepsin test
2. Lung function tests:
2.1. Exhaled Nitric Oxide
2.2. Specific airway conductance (SGaw)
2.3. Forced Expiratory Volume in 1 second (FEV1)
2.4. Forced Expiratory Volume in 1 second Per Forced Vital Capacity (FEV1/FVC)
2.5. Forced Expiratory Flow at 50% (FEF50)
2.6. Forced Expiratory Flow at 25-75% (FEF2575)
2.7. SGaw ratio (the ratio of SGaw preceded by a deep inspiration and that without a prior deep inspiration)
3. CPAP (one hour)
4. Repeat lung function tests

For those with OSA (with or without asthma)
5. Home treatment with CPAP at night for one month. The average nightly CPAP compliance will be obtained from downloading a data card in the CPAP machine. Whilst patients are advised to aim for >4 hours a night, this may be less in the first month. Correlations of variables with CPAP compliance can be made.

One month later (only in those who have had Home CPAP). Repeat investigations
6. Assessment of reflux symptoms
6.1. Leicester cough questionnaire
6.2. Reflux Symptoms Index Questionnaire
6.3. Saliva pepsin test
7. Lung function tests:
Exhaled Nitric Oxide
7.1. Specific airway conductance (SGaw)
7.2. FEV1
7.3. FEV1/FVC
7.4. FEF50
7.5. FEF2575
7.6. SGaw ratio (the ratio of SGaw preceded by a deep inspiration and that without a prior deep inspiration)

Intervention Type
Other

Primary outcome measure
1. The number of patients who were eligible for the study
2. The number invited to take part in the study

3. The number that entered the study
4. The number that completed the study
5. The number of patients where all observations were obtained

This information is obtained and updated at each study visit up to the end of the study.

Secondary outcome measures
1. Change in Forced Expiratory Flow 25-75 (FEF 25-75) , Specific Airway Conductance (SGaW) post 1 hour Continuous Positive Airway Pressure (CPAP) in the patient groups. Spirometry done by body plethysmography is used to calculate FEF 25-75 and SGaW. • CPAP is administered by Resmed AirSense CPAP machine. Outcomes will be measured before and after 1 hour treatment with Continuous Positive Airway Pressure (CPAP) for all participants.
2. Change in Forced Expiratory Flow 25-75 (FEF 25-75), Specific Airway Conductance (SGaW) after one month treatment with Continuous Positive Airway Pressure (CPAP) in patients receiving CPAP. Spirometry done by body plethysmography is used to calculate FEF 25-75 and SGaW. • CPAP is done by Resmed AirSense CPAP machine. Outcomes will be measured before and after 1 month treatment with Continuous Positive Airway Pressure (CPAP) for patients who will have home CPAP (i.e., patients with Obstructive Sleep Apnea (OSA) with and without asthma).
3. The prevalence of reflux; salivary pepsin, Reflux Symptom Index (RSI) questionnaire and cough (Leicester cough questionnaire) in the patient groups. • Salivary pepsin is measured by a PEPTEST (a lateral flow, near patient measurement device that measures salivary pepsin). • Reflux Symptom Index is measured by the Reflux Symptom Index questionnaire. Cough is measured by the Leicester cough questionnaire. Outcomes will be measured at recruitment for all participants. For patients who have home CPAP (i.e. patients with Obstructive Sleep Apnea (OSA) with and without asthma). Outcomes will be measured after 1 month treatment with Continuous Positive Airway Pressure (CPAP)
4. Difference in Small airway function Forced Expiratory Flow 25-75 (FEF 25-75 (Specific Airway Conductance (SGaW) between the patient groups. Spirometry done by body plethysmography is used to calculate FEF 25-75 and SGaW. Outcomes will be measured at recruitments and after 1 hour Continuous Positive Airway Pressure (CPAP) treatments for all participants. Then, they will be measured after 1 month treatment with (CPAP) for patients who will have home CPAP (i.e., patients with Obstructive Sleep Apnea (OSA) with and without asthma).
5. Fraction Exhaled Nitric Oxide (FeNO) as an index of inflammation. FeNO (Fraction Exhaled Nitric Oxide) measurements are performed with an electrochemical analyser. Outcomes will be measured at recruitment and after 1 hour Continuous Positive Airway Pressure (CPAP) treatments for all participants. They will then be measured after 1 month treatment with (CPAP) for patients who will have home CPAP (i.e., patients with Obstructive Sleep Apnea (OSA) with and without asthma).

Overall study start date
15/03/2015

Completion date
30/08/2017

Eligibility

Key inclusion criteria
1. Control group:
1.1. Normal males or females, who are 18 years or older.

1.2. No asthma on spirometry and no bronchodilator reversibility.
1.3. No OSA on sleep study and
1.4. No other known significant clinical condition according to the clinical assessment of Dr West /Dr Burns
2. OSA group:
2.1. Males or females, who are 18 years or older.
2.2. Significant OSA on sleep study,
2.3. having empirical CPAP clinically,
2.4. no asthma on spirometry and no bronchodilator reversibility.
2.5. No other known significant clinical condition according to the clinical assessment of Dr. West /Dr. Burns
3. Asthma group:
3.1. Males or females, who are 18 years or older who have a hospital corroborated clinical diagnosis of asthma.
4. Asthma with OSA group:
4.1. Males or females, who are 18 years or older
4.2. Confirmed asthma and confirmed OSA

Definitions:
1. “No asthma” means: no history of asthma, normal spirometry and no bronchodilator response
2. “Asthma” means: hospital specialist respiratory physician diagnosis, with history consistent with asthma, previous obstructive spirometry, ratio <70%, minimal smoking history or normal TLCO, (± bronchodilator response if documented previously) without evidence of chronic obstructive pulmonary disease (COPD) i.e. normal gas transfer
3. Significant OSA” means: oxygen desaturation index of >10 per hour or AHI of >15 per hour on overnight sleep study

Participant type(s)
Mixed

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40

Total final enrolment
42

Key exclusion criteria
For all groups
1. Inability to give written informed consent in English.
2. Where a participant is already involved in other research studies or medical intervention, which might have contraindications for this study.
3. Patients regarded unfit for any other clinical reason by their respiratory or sleep physician

4. As the study involve the use of a Pulmonary Function Test (PFT), some individuals with certain conditions should not take a PFT, as it can cause problems. These conditions include:
4.1. Recent heart attack
4.2. Heart disease
4.3. Recent eye surgery
4.4. Recent chest or abdominal surgery
4.5. Respiratory infections

Date of first enrolment
01/11/2016

Date of final enrolment
30/08/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Chest Unit- Royal Victoria Infirmary
Queen Victoria Rd
Newecastle upon tyne
United Kingdom
NE1 4LP

Study participating centre
Newcastle Regional Sleep Centre, Freeman Hospital
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
The Newcastle Upon Tyne Hospitals NHS Foundation Trusts.

Sponsor details
The Newcastle upon Tyne Hospitals NHS Foundation Trust Regents Point
Level 1
Gosforth

Newcastle upon Tyne
England
United Kingdom
NE3 3HD

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
The Newcastle Upon Tyne Hospitals NHS Foundation Trusts

Results and Publications

Publication and dissemination plan
Data and findings from this trial will be disseminated as widely as possible at the end of the trial. There are no plans for an interim analysis in this study.

Results will be presented in abstract form at national and international conferences to a respiratory audience e.g at the British Thoracic Society Conferences, European Respiratory Society Congress, and American Thoracic Society Conference. Following on from this we will seek to publish the research in peer reviewed medical journals. Where possible this will utilise Open Access publication strategies, to ensure a wide clinical and academic audience is reached to inform clinicians of the results and to inform future research.

Intention to publish date
28/01/2022

Individual participant data (IPD) sharing plan
Participant level data is available on request from Dr Graham Burns (graham.burns@nuth.nhs.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		21/11/2019	28/04/2021	No	No
HRA research summary			26/07/2023	No	No