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Investigating Neuronal responses by assessing Cough in Asthma

Submission date	Recruitment status	[X] Prospectively registered
05/10/2015	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
09/11/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
01/06/2020	Respiratory	

Plain English summary of protocol

Background and study aims
Coughing is very common and troublesome in asthma. We don't fully understand what makes asthmatics cough and whether the nerves that trigger cough are abnormal. The aim of this study is to find out how nerves are affected in asthma by measuring cough responses to capsaicin, an extract of chilli peppers known to cause cough.

Who can participate?
Patients aged over 18 with mild asthma.

What does the study involve?
The study involves measuring how much asthmatics cough in response to capsaicin when they are exposed to something they are allergic to. To do this study we need to do skin prick tests to check for a small skin reactions to air allergens such as grass or pollen which some people have a reaction to. We also need to do blowing tests and a test for asthma by getting patients to breath in a chemical called methacholine that can cause the airways to become a little tighter, and we also take some sputum samples. In participants with mild allergic asthma we need to do further blowing tests, and participants are asked to breathe in a substance which they are sensitive to in order to provoke mild asthma symptoms (allergen challenge). At the start and end of this we will ask participants to breathe in capsaicin, which will make them cough slightly and may sometimes a brief hot sensation in the throat.

What are the possible benefits and risks of participating?
This results of this study may lead to the development of new treatments for asthma. The tests in this study may trigger asthma symptoms. Sputum induction may cause an unpleasant taste at the back of the throat and there is a small risk of narrowing of the airways. There is a small risk of a serious allergic reaction with the allergen challenge and allergy skin test. Capsaicin can cause a burning/hot sensation at the back of the throat when inhaled but this wears off quickly. Capsaicin also makes people cough several times at the highest doses.

Where is the study run from?
NIHR South Manchester Clinical Research Facility, NIHR/Wellcome Trust Central Manchester Clinical Research Facility (UK) and McMaster University Medical Centre (Canada).

When is the study starting and how long is it expected to run for?
January 2016 to January 2017.

Who is funding the study?
British Medical Association (UK).

Who is the main contact?
Dr Imran Satia

Contact information

Type(s)
Public

Contact name
Dr Imran Satia

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1

Study information

Scientific Title
Investigating neuronal responses by assessing capsaicin evoked cough responses in an allergen challenge model of asthma: a randomised cross-over study

Acronym
INCA

Study objectives

The interaction between airway inflammation and capsaicin-evoked coughing is unclear. Our previous CoAst study suggested that cough responses to capsaicin were independent of airway inflammation; however, that was in an observational study in stable subjects with asthma. Our follow up study suggested that airflow obstruction increases neuronal responses to inhaled capsaicin. Hence, this study aims to investigate whether an increase in both airway inflammation and bronchial hyper-responsiveness (BHR) affects neuronal activation via TRPV1 on vagal C-fibres. Based on my studies so far, I hypothesise that neuronal dysfunction is an important contributor to clinical symptoms in asthma, but this is dependent of the degree of airflow obstruction but independent of airway inflammation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West Haydock Park Ethics Committee, 02/11/2015, ref: NW/NW/0787

Study design
Randomised single-blind placebo-controlled two-way cross-over study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Subjects with mild asthma, i.e. steroid naive

Interventions
This is an eight-visit randomised, single-blind, placebo-controlled, two-way cross-over study comparing cough responses to inhaled capsaicin in allergic asthma patients during and 24 hours after exposure to allergen compared with diluent (saline) control.

Fifteen mild atopic asthmatics will undergo full dose allergen/diluent (saline) challenge in a cross-over study. Early asthmatic responses (fall in FEV1>20% at 30 minutes) and late asthmatic responses (fall in FEV1>15% at 3-7 hours) will be documented. Full dose capsaicin challenge will be performed once in the screening visit followed by 4 inhalation of a single dose of capsaicin at 30 mins and 24 hours after inhaled allergen/diluent challenge. Cough counts will be measured throughout, along with methacholine challenge and induced sputum before and after allergen challenge.

Intervention Type
Other

Primary outcome measure
The number of coughs evoked by an ED50 dose of capsaicin 30 minutes and 24 hours after an allergen challenge compared with saline inhalation

Secondary outcome measures
1. 24-hour cough counts during allergen challenge compared with diluent
2. Correlations between changes in FEV1 and capsaicin cough responses
3. Correlations between changes in inflammation and capsaicin cough responses
4. Sputum cellular profile before and after allergen challenge compared with diluent
5. Changes in FEV1 before, during and after allergen challenge compared with diluent

Overall study start date
01/01/2016

Completion date
01/01/2017

Eligibility

Key inclusion criteria
1. Aged ≥18
2. Has a diagnosis of atopic asthma (based on at least one positive skin prick test)
3. The subject is treated with: Short acting Beta 2 Agonist PRN
4. Controlled or has partial asthma control according to GINA classification
5. The subject has an early and late response to an inhaled allergen to which they are sensitised (assess after visit 2)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
15

Total final enrolment
12

Key exclusion criteria
1. Subjects who have previously coughed less than a total of 4 coughs in one dose at the ED50 dose of capsaicin inhalation (assess after visit 1)
2. Subjects who bronchoconstrict by more than 10% at the end of the full dose capsaicin cough

challenge (assess after visit 1)
3. Subjects who do not display evidence of airway hyperresponsiveness (PC20>16mg/ml) (assess after visit 1)
4. Symptoms of upper respiratory tract infection (URTI) in the last 1 month which have not resolved
5. Lower respiratory tract infection or pneumonia in the last 6 weeks
6. Current smoker or exsmoker with ≥10 pack year smoking history and abstinence of ≤6 months
7. Asthma exacerbation in the previous month requiring an increase or start of an ICS or OCS
7. Asthma medication which include theophylline or anticholinergic drugs
8. Subject has changed asthma medication within the past 4 weeks prior to screening
9. A previous asthma exacerbation requiring Intensive Care Unit (ICU) admission
10. Significant other primary pulmonary disorders, in particular: pulmonary embolism, pulmonary hypertension, interstitial lung disease, lung cancer, cystic fibrosis, emphysema or bronchiectasis
11. Pregnancy or breastfeeding
12. Use of ACE inhibitors
13. Any centrally acting medication which in the view of the investigator could alter the sensitivity of the cough reflex*
14. History of psychiatric illness, drug or alcohol abuse which may interfere with participation in the trial
*Any participant who is taking tricyclic antidepressants, pregabalin, gabapentin or opioids will not be eligible to take part in this study unless they are willing and medically able to withdraw from such medication for the duration of the study. The reason for this is that centrally acting medications may alter the sensitivity of the cough reflex.

Date of first enrolment
01/01/2016

Date of final enrolment
01/01/2017

Locations

Countries of recruitment
Canada

England

United Kingdom

Study participating centre
NIHR South Manchester Clinical Research Facility
University Hospital of South Manchester
North West Lung Centre
Research and Allergy Clinical Research Facility
Manchester
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M23 9LT

Study participating centre
NIHR/Wellcome Trust Central Manchester Clinical Research Facility
Manchester Royal Infirmary
Grafton Street
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Study participating centre
McMaster University Medical Centre, McMaster University
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1280 Main Street West
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Sponsor information

Organisation
University Hospital of South Manchester (UK)

Sponsor details
Research and Development Directorate
Manchester
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Other

Funder Name
British Medical Association

Alternative Name(s)
BMA

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Part of PhD Thesis, National and Internation Conferences, and manuscript submission in a respiratory journal.

Intention to publish date
01/01/2018

Individual participant data (IPD) sharing plan

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?
Results article	results	01/09/2019	01/06/2020	Yes	No