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Description of cough headache in a cough unit

Submission date
07/02/2019

Recruitment status
No longer recruiting

Registration date
08/02/2019

Overall study status
Completed

Last Edited
11/05/2020

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
Cough headache is a very rare headache type that accounts for less than 1% of the diagnoses in specialised headache centres. By targeting a population from a cough clinic, this study aims to provide a better evidence on what the headache characteristics and other associated features are.

Who can participate?
Patients aged 18-80 with cough headache

What does the study involve?
The study consists of one visit. Participants go through a semi-structured interview in which general medical history and features of headache are assessed. A neurological examination is performed as well as modified Valsalva Test.

What are the possible benefits and risks of participating?
If the study were to find a likely diagnosis of cough headache, specific and more directed treatment could be recommended to the patient's GP if this has not been the case to date. The modified Valsalva test may cause or worsen headache for a brief period of time. Potentially, if performed in cough headache patients it could cause a similar headache to the one they would get when they cough, and it would presumably resolve within minutes. There are no other known risks of participating on this trial.

Where is the study run from?
King's College Hospital (UK)

When is the study starting and how long is it expected to run for?
February 2019 to February 2020

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Dr David Moreno Ajona
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
KCH19-021

Study information

Scientific Title
Description of primary cough headache in a cough unit: a prospective study

Acronym
PCH-CU

Study objectives
According to the current available data, primary cough headache (PCH) occurs mainly in subjects over the age of 40 years, being the mean age of onset 67 years. A male predominance has been pointed, although the male/female ratio changes dramatically among series. Furthermore, it seems to be an episodic disease as it normally lasts less than 2 years. Pain is usually localized bilaterally, with a major involvement of the occipital region. Pain quality, however, has been described as sharp, stabbing, splitting, explosive, electrical, pressing, dull or even pulsatile. Precipitants may include coughing, sneezing, nose blowing, laughing, crying, singing, lifting a weight, straining at stool, and stooping. Nevertheless, they should not include sustained physical exercise which would be typical of exertional headache. Regarding the headache associated features, nausea, dizziness and photo/photophobia have been documented in a very little proportion of patients, being these, vertigo, ataxia and syncope, red flags indicating a probable secondary origin.

In this context, differential diagnosis with secondary or symptomatic cough headache is crucial. The most common reported cause is Chiari type 1 malformation, although any posterior fossa lesion could cause the symptoms as well as syringomyelia, platybasia, obstructive

hydrocephalus, subdural hematoma, sphenoid sinusitis, spontaneous intracranial hypotension, brain aneurysm and even carotid artery disease. Overall, it is considered that almost 50% of cough headaches are symptomatic. However, the only published study in cough patients found 3 /32 (9%) secondary headaches (all of them due to Arnold Chiari malformation).

A 16-patient study showed that a modified Valsalva manoeuvre (exhalation into the spigot of an aneroid sphygmomanometer to a pressure of 60 mm Hg and maintain this for 10 seconds) was capable of distinguishing primary from secondary headache. According to this result, the authors hypothesized that a transient increase in intracranial pressure during exertion due to obstruction to normal CSF dynamics should explain secondary Cough headache. Conversely, they stated PCH could be caused through congestion of the orbital venous plexus in the presence of jugular venous incompetence and a reduced threshold for trigeminal sensory activation. On the other hand, it is argued that a relative obstruction of CSF flow could take place, following research by Chen et al., who described a more crowded posterior fossa in PCH patients.

PCH may respond to Indomethacin (50-150 mg daily) which has also been attributed to its carbonic anhydrase inhibitor property, leading to decreased intracranial pressure.

Knowledge on the clinical aspects of this disorder is a necessary step towards the understanding of the pathophysiology and subsequent development of targeted therapies, hence, a better description of PCH patients is required.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Scotland Research Ethics Committee 01, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, Tel: +44 (0)131 465 5473, Email: Sandra.Wyllie@nhslothian.scot.nhs.uk, 30 /01/2019, REC ref: 18/SS/0165, Protocol number: 1, IRAS project ID: 256341

Study design
Cross-sectional cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Primary cough headache

Interventions
The study consists of one visit. Previously, a pre-screening questionnaire performed at the cough clinic will determine potential eligibility. Study visit: consent will be sought and, after screening, eligible participants will go through a semi-structured interview in which general medical history and features of headache will be assessed. Neurological examination will be performed as well as a modified Valsalva Test.

Intervention Type
Other

Primary outcome(s)
The clinical features and prevalence of cough headache in patients attending a Cough Unit and the differences between primary and secondary cough headache, measured using questionnaire adapted from the usual headache clinic and cough clinic interviews at the single study visit.

Key secondary outcome(s))
Measured using questionnaire adapted from the usual headache clinic and cough clinic interviews at the single study visit:
1. Specific comorbidities related to cough headache
2. The use of opioids and other drugs in cough patients and possible relationship with the development of chronic headache
3. The utility of the modified Valsalva manoeuvre in these patients

Completion date
31/12/2020

Eligibility

Key inclusion criteria
1. Patients are capable of giving signed informed consent indicating that the subject has been informed of all pertinent aspects of the trial detailed in the patient information sheet (PIS), informed consent form (ICF), and in the protocol
2. Subjects must be willing to receive a telephone call or travel to and from King's College Hospital as preferred, during normal working hours
3. Diagnosis of Primary Cough Headache (PCH) using criteria previously published
4. Aged 18-80 years inclusive
5. Willing and able to comply with scheduled visits and study procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding from consent until the end of study involvement
2. History of psychosis, depression or psychological diseases either (a) requiring ongoing psychoactive drugs, or (b) that the Investigator has reason to believe will either affect the

patient’s neural pathways or hinder the performance of the patient with regard to ability to successfully complete the tasks required of them according to the protocol
3. History/presence of cerebral haemorrhage, brain tumour, brain aneurysm, cryptococosis or other brain mass lesion within the last 12 months
4. Any other medical condition that in the opinion of the Investigator would make the subject unsuitable for the study
5. Inclusion to another research study within the past 30 days

Date of first enrolment
11/02/2019

Date of final enrolment
01/12/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Organisation
King’s College Hospital NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name
NIHR BRC grant – Pain theme

Results and Publications

Individual participant data (IPD) sharing plan
Each patient will be assigned a study number. Personal Identifiable Information (PII) and medical records from participants recruited at the site (King's College Hospital) will be de-identified and recorded on source documents created specifically for the study. Source documents from participants recruited at the site (King's College Hospital) and consent forms will be stored in the Headache Group, Clinical Research Office, Welcome Foundation Building, Denmark Hill Campus, King's College London. Access to this office is restricted and paperwork is stored in locked filing cabinets.
Source documentation collected will be stored as per local data protection standard operating procedures.
Clinical data from source documents will be entered by an investigator into an Excel database in an anonymized format, locked with a password and kept on a KCH computer. PII will be kept on a different Excel file on a different KCH computer, also locked with a different password than the other file. KCH computers are located in the same office which is locked and accessible to the investigators only.
King's College Hospital will keep identifiable information about participants for 12 months after the study has finished.
During study conduct, data will be reviewed to ensure that the protocol and Good Clinical Practices are being followed. Source document may be reviewed to confirm that data recorded on the CTF is accurate. The site may be subject to review by the Independent Ethics Committee and/or to inspection by appropriate regulatory authorities. The investigator and relevant personnel will ensure that they will be available during monitoring and possible audits and inspections.
No identifiable information will be provided. For any other documents, please contact the Institute of Psychiatry, Psychology and Neuroscience (King's College London), Headache Group on:
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IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary	Participant information sheet		28/06/2023	No	No

Participant information sheet	version V2.2	11/11/2025	11/11/2025	No	Yes
Protocol file		28/01/2019	12/02/2019	No	No