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Chronic cough treatment: the McGill experience

Submission date
26/11/2014

Recruitment status
Stopped

Registration date
06/01/2015

Overall study status
Stopped

Last Edited
29/10/2019

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
Having a chronic cough can strongly impact the quality of life of patients. One possible cause is post-viral vagal neuropathy, whereby a nerve (the vagus nerve) that provides sensation to the larynx (or voicebox) and triggers the cough reflex is damaged by a virus. This makes the nerve hyper-sensitive. The patient will react more than other people to irritants, such as allergens, smoke, cold air and perfumes, all of which trigger the cough reflex. This leads to a unrelenting chronic cough that does not seem to get better with time and can go in for many months, or even years. At the moment, the treatment we give to our patients is amitriptyline (Elavil©). We have noticed a great improvement of chronic cough in our patients when treated with this medication. Amitriptyline has been used for several years for the treatment of neuropathic pain (pain caused by damaged nerves). It is therefore thought to work in the same way in treating postviral vagal neuropathy leading to chronic cough. Another medication, gabapentin (Neurontin©) is also reported as a successful treatment for chronic cough. Just like amitriptyline, it has neuromodulator effects, which are used very commonly for neuropathic pain. Here, we want to look at two drugs, both of which have been proven to help with chronic cough and find out which one acts more quickly and has fewer side effects.

Who can participate?
Adults who have had cough symptoms for at least 3 months.

What does the study involve?
Patients are randomly allocated into one of two groups. Those in group 1 are given amitriptyline. Those in group 2 are given gabapentin. To understand if patients are showing responses to the medication, phone interviews are conducted 10 days and then 21 days after the treatment starts. For each of these two visits, each participant completes a questionnaire asking them about their chronic cough and are asked if they are experiencing side effects. 6 weeks after the treatment has started, patients are seen in clinic by a laryngologist. The questionnaire is filled in again and questions asked about side effects. The patient also undergoes a direct laryngoscopy to see how swollen (inflamed) their vocal cords are. The reflux finding score (a way of measuring the laryngopharyngeal reflux) is also completed.

What are the possible benefits and risks of participating?
Both amytriptyline and gabapentin have been shown to improve chronic cough. They have also both been used for many years in the treatment of other conditions, such as various

neuropathies. Both are extremely safe drugs, with few side effects. The most common side effects of amitriptyline are dry mouth and dizziness. With gabapentin, the most common side effect is low energy and muscle aches.

Where is the study run from?
1. Montreal General Hospital (Canada)
2. Royal Victoria Hospital, Montreal (Canada)

When is the study starting and how long is it expected to run for?
June 2013 to June 2016

Who is funding the study?
The Department of Otolaryngology - Head & Neck Surgery, McGill University Health Centre (Canada)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CC2014

Study information

Scientific Title
The McGill experience with Chronic Cough Treatment: A Phase 2 Pilot Study

Study objectives

Although both amitryptiline and gabapentin have been proven to improve chronic cough caused by post-viral neuropathy, we hypothesize that one agent has a more rapid onset of action and a better side effect profile.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. MUHC Ethics Committee, 26/06/2014, ref. 13-064 BMD
2. Health Canada, 15/01/2014, ref. 170996

Study design
Randomized controlled, non-inferiority trial.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet

Health condition(s) or problem(s) studied
Chronic cough secondary to irritable larynx and post-viral neuropathy

Interventions
Recruitment of patients (N=100) from our regular clinical activities, on 3 different sites: Montreal General hospital, Royal Victoria hospital, Jewish General hospital. Patients who meet the inclusion criteria will be randomized to treatment with either amitriptyline or gabapentin.
1. Gabapentin:
Day 1: 150 mg QHS
Day 2: 300 mg QHS
Day 3: 300 mg BID
We will conduct a phone interview after 10 days of treatment to assess for improvement and if there is none, we will increase to 300 mg TID. We will do another phone interview 3 weeks after initiation of treatment. We will also see the patient after 2 months of treatment commencement.
2. Amytriptyline
Starts at 10 mg qHS, followed by increases of 10 mg every 3 weeks depending on symptomatic relief, with a maximum of 50 mg qHS.

Intervention Type
Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
1. Amitriptyline 2. Gabapentin

Primary outcome measure
To observe the quality of life and symptomatic outcomes of chronic cough patients when treated with amitriptyline (Elavil) vs. gabapentin (Neurontin) therapy as measured by the Leicester cough questionnaire at 10 days, 3 weeks, 6 weeks and 4 months after initiation of treatment.

Secondary outcome measures
1. To evaluate the side effect profile of this medication when used to treat chronic cough
2. To understand the time line of symptom improvement with each of these agents

To understand if patients are showing responses to the medication, we will conduct phone interviews at days 10 and 21 after treatment initiation. At this time, we will repeat the Leicester Cough Questionnaire and patients will be asked about presence of different side effects. 6 weeks after the initiation of treatment, patients will be seen in clinic by the laryngologist. At this time, the questionnaire and side effect profile will be repeated for a third time, however the patient will also undergo direct laryngoscopy to assess changes in vocal cord inflammation. The reflux finding score will also be completed.

These will allow us to evaluate onset of action of each agent, side effect profile, and improvement in quality of life.

Overall study start date
01/12/2013

Completion date
01/06/2016

Reason abandoned (if study stopped)
Cancelled

Eligibility

Key inclusion criteria
Included patients will be patients having had cough symptoms for at least 3 months (chronic cough), and that have already been worked up by respirologists to rule out other etiologies of cough. These patients will have failed all other medical therapies: inhaled corticosteroids and single dose of antireflux medication.

Participant type(s)
Patient

Age group
Adult

Sex

Both

Target number of participants
100

Key exclusion criteria
1. Patients without cough symptoms for over 3 months
2. Patients that have not been worked up by a respirologist and who have not attempted inhaled corticosteroids or antireflux medication
3. Patients who have been taking over the counter (OTC) antitussives, or angiotensin converting enzymes inhibitors medication
4. Patients who have been taking antibiotics in the last month for a respiratory tract infection
5. Patients who are smokers (both smoking and recent respiratory tract infection could confound our results)
6. Patients who are pregnant or breast feeding
7. Patients with abnormal hepatic or kidney function tests (creatinine over 100, ALT over 36 U/L, AST over 35 U/L, total bilirubin over 26 mmol/L)
8. Patients with abnormalities on the electrocardiogram that have not been cleared by a cardiologist
9. Patients with significant cardiac, renal, hepatic, epileptic, hematologic antecedents
10. Patients taking anticholinergic or sympathomimetic medications
11. Patients above the age of 70

Date of first enrolment
01/12/2014

Date of final enrolment
01/12/2014

Locations

Countries of recruitment
Canada

Study participating centre
Montreal General Hospital
1650 Avenue Cedar
Montreal
Canada
H3G 1A4

Study participating centre
Royal Victoria Hospital
1001 Boulevard Décarie
Montreal
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H4A 3J1

Sponsor information

Organisation
McGill University Health Centre

Sponsor details
c/o Esther Boyle, Administrative Technician
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Sponsor type
University/education

ROR
https://ror.org/04cpxjv19

Funder(s)

Funder type
University/education

Funder Name
The Department of Otolaryngology - Head & Neck Surgery, McGill University Health Centre (Canada)

Results and Publications

Publication and dissemination plan
To be confirmed at a later date.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration