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Do phosphodiesterase-5 inhibitors improve exercise capacity in COPD patients with pulmonary hypertension?

Submission date
31/08/2010

Recruitment status
No longer recruiting

Registration date
19/10/2010

Overall study status
Completed

Last Edited
03/05/2016

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
Lung disease often causes high pressure in the blood vessels in the lung (pulmonary hypertension). It can put a strain on one side (the right side) of your heart and make your breathlessness worse. One possible new way to treat this is to use a drug which inhibits an enzyme in the lung blood vessels. (The enzyme is called Phosphodiesterase 5). This drug should dilate the lung blood vessels and relieve the strain on your heart. These drugs appear also to work well in other diseases where pulmonary hypertension occurs but they have never been assessed in patients with your type of lung disease (chronic obstructive pulmonary disease or COPD). The exact drug used here is Tadalafil. For your information, this drug is not that new as it has a separate use, which is to help patients with erectile dysfunction.

Who can participate?
You can participate if you are aged between 35 and 85 years, and have COPD. We will obtain written consent and assess your suitability for the trial by taking your blood, measuring your lung function by blowing into a machine and lastly by doing a simple heart scan called an echocardiogram.

What does the study involve?
The study takes 3 months to complete. The study is a randomised, double blind design. This means that you will take a tablet which will either be Tadalafil (the test drug) or a placebo (an inactive tablet). The tablet allocated to you is decided in a random way (like tossing a coin) such that neither you nor the research staff will know which tablet you are taking until after the study is completed. This enables the study results not to be influenced. After making sure you are suitable for the trial, we will arrange a repeat visit where we will ask you to walk along a level corridor for six minutes (the six minute walk test). We will also ask you to fill in three quality of life forms. Thereafter, you will be randomised to the active drug or placebo. In order to make sure you do not feel unwell on this drug, we would like to observe you in hospital for 3 hours after you take the first tablet. During this time we will perform lung function tests and in some cases a further echo test. The first tablet will be a shorter acting drug (Viagra) which is similar to the main test medication. In fact, all patients will receive the active drug for the first dose even if

they are randomised to receive the dummy tablet for the next 3 months. Thereafter, we will repeat the six minute walk test and the quality of life questionnaires twice and echocardiogram once. For the whole trial, there will be 6 hospital visits over 3 months and several telephone calls. Six Minute Walk test: This assesses your overall exercise ability. You will be asked to walk for 6 minutes along a level corridor at your own pace. You will be allowed to stop if you need to. Quality of Life Questionnaires: We will use three standard questionnaires which ask questions about your normal life focusing on how active you are able to be with your lung disease. Our hope will be that your ability to be active will improve with the active drug.

What are the possible benefits and risks of participating?
The study may not immediately benefit you, but if the results of the study are positive, this may change the practice of managing patients with lung disease like you and this potentially will have a great impact on thousands, even millions of patients in the future. If so, you may gain eventually from our discovering a new treatment for your condition. The main test medication is Tadalafil (Cialis) which is used routinely to treat erectile dysfunction in men. Side effects occasionally occur. The most common one is headache but it can rarely cause nausea, dizziness, visual disturbance, hearing upset and nasal congestion. In men who are sexually active it should be noted that erections do not occur unless Tadalafil is taken in combination with sexual stimulation. Very rarely priapism has been reported (painful prolonged erections). Allergic responses can occur very rarely. There is a theoretical risk that it might decrease oxygen in your body. Consequently, you will be monitored for 3 hours after the first dose to identify anyone who will develop the above effects, in which case you will not continue in the trial. It is also important that no-one gives you a nitrate tablet, as used in the treatment of angina, as this interacts badly with Tadalafil causing a marked fall in blood pressure. Theoretically another drug called nicorandil, also used in the treatment of angina, could have this effect. Doxazosin (an alpha-blocker), which is used in the treatment of high blood pressure, can also interact with Tadalafil resulting in a decrease in blood pressure. Recent literature suggests that Tamsulosin (another alpha-blocker used in the treatment of prostatic enlargement) and Tadalafil can safely be taken together. However, it would be sensible not to start this medication whilst participating in the trial. We will alert your GP to make sure you are not given these drugs for the duration of the study. Having blood taken can cause some mild bruising. The six minute walk test may make you feel breathless but you will be free to stop at any time.

Where is the study run from?
Centre for Cardiovascular and Lung Biology, Ninewells Hospital and Medical School (UK)

When is the study starting and how long is it expected to run for?
The study started in September 2010 and ended in September 2012

Who is funding the study?
Chief Scientist Office (UK)

Who is the main contact?
Prof. Allan D Struthers
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Contact information

Type(s)
Scientific

Contact name
Prof Allan Struthers

Contact details
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01197469

Protocol serial number
2008CV17

Study information

Scientific Title
Do phosphodiesterase-5 inhibitors improve exercise capacity in COPD patients with pulmonary hypertension?: a double-blind, randomised, placebo-controlled trial

Acronym
The 3P study

Study objectives
We hypothesise that Tadalafil, a phosphodiesterase type 5A (PDE5A) inhibitor, improves exercise capacity in those with chronic obstructive pulmonary disease (COPD) and secondary pulmonary hypertension (PH).

Ethics approval required
Old ethics approval format

Ethics approval(s)
The North of Scotland Research Ethics Committee, 09/07/2009, ref: 10/S0801/46

Study design
Double-blind randomised placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COPD with pulmonary hypertension

Interventions
We plan to do a stratified block randomisation based on their baseline Six minute walk distance (6MWD) test, the strata being <285 or ≥ 285m. They will then be randomly assigned placebo or Tadalafil 10mg once a day at for 3 months. Final follow up for all patients will be at 3 months.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Six-minute walk distance test (6WMD) performed at baseline, 2 and 3 months

Key secondary outcome(s))
Current secondary outcome measures as of 08/10/2012:
1. Quality of Life
1.1. St George's Respiratory Questionnaire (SGRQ)
1.2. SF-36
1.3. Minnesota Living with Heart Failure® questionnaire (MLHFQ)
2. Diffusing Capacity of the Lung for Carbon Monoxide (DLCO)
3. B-type Natriuretic Peptide
4. Echocardiogram Measurements
Outcomes assessed at baseline, 2 and 3 months with the exception of DLCO and echo which are performed at beginning and end only (protocol change approved 18/02/2011).

Previous secondary outcome measures until 08/10/2012:
Outcomes assessed at baseline, 2 and 3 months.

Completion date
30/09/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/10/2012:
1. Male or female participants, aged between 35 to 85 inclusive
2. COPD
3. Forced Expiratory Volume in one second (FEV1) <80% predicted (protocol change approved 18/02/2011)
4. Right Ventricular Systolic Pressure (RVSP) >30mmHg and/or pulmonary acceleration time <120 ms

Previous inclusion criteria until 08/10/2012:
1. Male or female participants, aged between 35 to 85 inclusive
2. Diagnosis of COPD or Emphysema (diagnosis of emphysema removed due to an error in the original application)
3. Forced Expiratory Volume in one second (FEV1) <50% predicted
4. Smoker or ex-smoker with a history ≥ 20 pack years (removed due to protocol change approved 23/01/2012)
5. Right Ventricular Systolic Pressure (RVSP) >30mmHg and/or pulmonary acceleration time

<120 ms
6. Plasma Brain Natriuretic Peptide (BNP) level >25 pg/ml (removed due to protocol change approved 18/02/2011)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pulmonary stenosis
2. Echo Left Ventricular (LV) outflow obstruction
3. LV systolic dysfunction (LVEF <45%)
4. Patients taking nitrates, nicorandil or doxazosin
5. Systolic blood pressure (BP) <90 mmHg, recent stroke, unstable angina, past history of non arteritic anterior ischaemic optic neuropathy

Date of first enrolment
04/09/2010

Date of final enrolment
30/09/2012

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
University of Dundee (UK)

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office (CSO) (UK) - CSO Grant (ref: CZB/4/666)

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

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	01/04/2014		Yes	No
HRA research summary			28/06/2023	No	No