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Angiotensin converting enzyme (ACE) inhibition and mechanisms of skeletal muscle weakness in chronic obstructive pulmonary disease (COPD)

Submission date
26/06/2008

Recruitment status
No longer recruiting

Registration date
31/10/2008

Overall study status
Completed

Last Edited
13/02/2020

Condition category
Respiratory

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Nicholas Hopkinson

Contact details
Royal Brompton Hospital
Fulham Road
London
United Kingdom
SW3 6NP
+44 (0)20 7349 7775
n.hopkinson@ic.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01014338

Protocol serial number
MRC ref: G0701628; IC-DHTAX_P15099

Study information

Scientific Title
Angiotensin converting enzyme (ACE) inhibition and mechanisms of skeletal muscle weakness in chronic obstructive pulmonary disease (COPD): a double-blind, randomised, placebo-controlled, parallel trial

Study objectives
That angiotensin converting enzyme (ACE) inhibition will improve muscle function in patients with chronic obstructive pulmonary disease (COPD) who have leg weakness. Muscle function will be assessed in terms of strength and endurance. Changes in muscle function (strength and endurance) will be related to changes in the molecular pathways which are thought to be involved in muscle wasting in COPD.

As of 17/02/2009 this record was updated to include a change to the ACE-I drug used. more details of this can be found in the interventions section. At this time, the anticipated trial dates were also updated; the initial trial dates at the time of registration were:
Initial anticipated start date: 01/10/2008
initial anticipated end date: 30/09/2011

Ethics approval required
Old ethics approval format

Ethics approval(s)
The study has been approved by the Joint UCL/UCLH Committees on the Ethics of Human Research Committee Alpha on the 2nd October 2008 (ref: 08/H0715/90)

Study design
A double-blind, randomised, placebo-controlled, parallel trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Amended as of 17/02/2009:
10 or 20 mg of fosinopril per day for three months, versus placebo on same administrative routine.

Initial information at time of registration:
Imidapril tablets (ACE-I) up to 20 mg per day for three months, versus placebo on same administrative routine.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Angiotensin converting enzyme inhibitor (ACE-I) (Imidapril)

Primary outcome(s)
Primary analysis will focus on the activity of the insulin-like growth factor-1 (IGF-1) Akt pathways controlling muscle catabolism and anabolism assessed in muscle biopsies. Measurements will include phosphorylated and non-phosphorylated Akt and mammalian target of rapamycin (mTOR) as well as myogenic differentiation factor (MyoD), muscle-specific RING-finger protein (MuRF) and atrogin-1 messenger ribonucleic acid (mRNA) and protein levels. Changes in these pathways will be related to changes in muscle phenotype. These measurements will be made in muscle biopsies taken at baseline and after three months of treatment.

Key secondary outcome(s))
The following will be assessed in muscle biopsies taken at baseline and after three months of treatment:
1. Effect of ACE-I on quadriceps maximum voluntary contraction force
2. Effect of ACE-I on quadriceps endurance: T80 Time for force output in response to stimulation
3. Effect of ACE-I on quadriceps bulk (cross-sectional area)
4. Effect of ACE-I on systemic inflammation and serum IGF-1

At the initial screening assessment patients biopsies will have been obtained from patients who are not weak and therefore ineligible for this trial. Data from these patients will be compared cross-sectionally with the weaker patients to compare activity of the molecular pathways mentioned above and related to muscle phenotype.

Completion date
01/05/2012

Eligibility

Key inclusion criteria
Adult patients (greater than 18 years, either sex) with COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Only patients with quadriceps weakness will be enrolled into this randomised controlled trial (RCT).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Clinically unstable patients (within one month of exacerbation)
2. Those with a permanent pacemaker (which is a contraindication to magnetic stimulation), or significant co-morbidity
3. Patients with an accepted indication for ACE inhibition (left ventricular dysfunction, diabetes) or a contraindication such as renovascular disease
4. Creatinine clearance (estimated) less than 50 ml/min
5. Hypotension
6. Use of anticoagulants (contraindication to biopsy) or angiotensin converting enzyme inhibitor (ACE-I) or angiotensin II (ATII) receptor antagonists
7. Allergy to ACE-I
8. Pregnancy
9. Patients who have participated in a pulmonary rehabilitation programme within the past three months

Date of first enrolment
01/06/2009

Date of final enrolment
01/05/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Brompton Hospital
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
Imperial College London (UK)

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) (ref: G0701628)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National 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	01/10/2014		Yes	No
HRA research summary			28/06/2023	No	No