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Muscle wasting in chronic obstructive pulmonary disease (COPD): the role of resistance training and protein supplementation

Submission date 21/10/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/12/2009	**Overall study status** Completed	
Last Edited 25/02/2015	**Condition category** Respiratory	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MRC ref: G0501985; UHL 10146

Study information

Scientific Title
Molecular approaches to reversing skeletal muscle wasting in chronic obstructive pulmonary disease (COPD): the role of resistance training and protein supplementation - a double-blind randomised placebo-controlled trial

Study objectives
This project will test the following principal hypotheses:
1. That muscle wasting in chronic obstructive pulmonary disease (COPD) is characterised by alterations in the expression of catabolic and anabolic genes (mRNA) and signalling pathways (protein and protein phosphorylation) that have been implicitly associated with the regulation of skeletal muscle protein degradation and synthesis when compared with non-wasted COPD patients, and similar aged healthy controls.
2. That a carefully controlled resistance training programme known to restore muscle mass in immobilised young healthy humans will have similar restorative effects in COPD patients and that these benefits will be mediated through changes in these candidate gene and signalling pathways. We will also determine how these effects differ between wasted and non wasted COPD patients and between patients and healthy controls.
3. That changes in the expression and activation of these regulatory pathways occurs early (within 24 hours) from the onset of rehabilitation as was seen following limb immobilisation in young healthy subjects.
4. That the positive effects of resistance training on skeletal muscle mass in COPD patients can be augmented when training is combined with dietary protein supplementation.

More details can be found at the following links:
UK Clinical Research Network Study Portfolio: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=4049
MRC research portfolio: http://www.mrc.ac.uk/ResearchPortfolio/Grant/Record.htm?GrantRef=G0501985&CaseId=6937

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1, 26/09/2006, ref: 06/Q2501/138
2. University Hospitals of Leicester (UHL) NHS Trust R&D, 05/01/2007, ref: 10146
3. Leicester City Primary Care Trust (PCT), 12/02/2008, ref: LNR PCRA 0696

Study design
Double-blind randomised placebo-controlled single-centre trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
1. Resistance training: The training programme will last 8 weeks and comprise three supervised half-hour lower limb resistance training sessions per week. Training will take place on an isokinetic dynamometer (Cybex II Norm: CSMi, USA). Subjects will perform 5 sets of 30 maximal knee extensions performed at 180 degrees/sec. Sets will be separated by 1 minute rest. Both legs will be trained.

2. Protein supplementation: COPD patients will be randomly allocated to receive a dietary protein (with carbohydrate) supplement or placebo throughout training. Healthy volunteers will receive a placebo. The supplement will contain 19 g protein and 49 g carbohydrate (Vitargo® Gainers Gold: Swecarb, Sweden) made up to 500 ml of water. The placebo will be an identical volume non-nutritive and non-caloric drink. Supplementation will take place immediately following each training session, as the timing of protein intake appears to be critical.

Intervention Type
Mixed

Primary outcome measure
Muscle gene and protein expression (vastus lateralis needle biopsy samples) at baseline, 24 hours, 4 weeks and 8 weeks.

Secondary outcome measures
1. Muscle strength (isometric and isokinetic quadriceps strength) at baseline, 4 weeks, 8 weeks and 6 months
2. Total body and quadriceps fat-free (muscle) mass (dual energy X-ray absorptiometry [DEXA]) at baseline, 4 weeks and 8 weeks
3. Circulating inflammatory cytokines (blood tests) at baseline, 24 hours, 4 weeks and 8 weeks
4. Whole-body exercise performance (incremental cycle ergometry test) at baseline and 8 weeks
5. Physical activity (questionnaire and activity monitor) at baseline and 8 weeks
6. Lung function and capillary blood gas tensions at baseline

Overall study start date
14/02/2007

Completion date
31/10/2010

Eligibility

Key inclusion criteria
For both COPD subjects and healthy control subjects:
1. Both males and females, aged between 50-85 years

COPD subjects:
1. Moderate-severe airflow obstruction (Forced expiratory volume in one second [FEV1] <50% predicted, FEV1/forced vital capacity [FVC] ratio <70%)
2. Reduced exercise tolerance (MRC grades III-V)
3. Stable
4. Able to carry out lower-limb resistance training

Healthy age-matched control subjects:
1. No evidence of airflow obstruction (FEV1 >80% predicted)
2. Able to carry out lower-limb resistance training

Participant type(s)
Mixed

Age group
Adult

Sex
Both

Target number of participants
120

Key exclusion criteria
COPD subjects:
1. Long-term oral corticosteriods
2. Anticoagulant therapy or disorders
3. long term oxygen therapy (LTOT)
4. Diabetes
5. Co-morbid conditions preventing exercise training
6. Subects who have completed pulmonary rehabilitation in the previous 12-months

Healthy age-matched controls:
Same as for COPD subjects, also those who meet the criteria for fat-free mass depletion are excluded.

Date of first enrolment
14/02/2007

Date of final enrolment
31/10/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Glenfield Hospital
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Sponsor information

Organisation
University Hospitals of Leicester NHS Trust (UK)

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Sponsor type
Hospital/treatment centre

Website
http://www.uhl-tr.nhs.uk

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Government

Funder Name

Medical Research Council (ref: G0501985; grant ID: 77170)

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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 (inflammatory and satellite cells in the quadriceps)	01/11/2012		Yes	No
Results article	results (ultrasound assessment of lower limb muscle mass)	28/12/2012		Yes	No
Results article	results (ventilatory requirements of quadriceps resistance training)	05/06/2014		Yes	No