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Leucine and ACEi to treat sarcopenia

Submission date
18/02/2015

Recruitment status
No longer recruiting

Registration date
18/02/2015

Overall study status
Completed

Last Edited
10/03/2023

Condition category
Musculoskeletal Diseases

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

Plain English Summary

Background and study aims
Sarcopenia is the term used to describe the loss of muscle, leading to muscle weakness, that happens as we age. Muscle weakness can cause a number of problems, such as in getting about (mobility problems) and doing day-to-day tasks. It can also result in an increase in the number of falls, leading to fractures, hospital admissions and even death. It is therefore very important to find ways to strengthen these muscles. Exercise is the only treatment known to work but not everyone wants to do exercise, and some people are unable to. Other ways of strengthening muscle therefore have to be found and two potential medical treatments are showing promise. One is leucine, a food supplement which is naturally found in proteins and the other is perindopril, which is an angiotensin converting enzyme inhibitor (ACEi) drug. Older people need larger amounts of leucine before they can build up protein in muscles. Increasing leucine intake increases muscle protein build up even when less protein is being consumed. Therefore leucine may lead to the development of stronger muscles in older people. Perindopril is a commonly used medicine for managing heart trouble. Our previous research showed that use of perindopril in older people with mobility problems improved their ability to exercise just as much as 6 months of exercise training would have done. We now want to know how well leucine and perindopril do in terms of improving muscle strength and physical activity of older people with sarcopenia.

Who can participate?
Adults aged 70 or over and diagnosed with sarcopenia.

What does the study involve?
All participants visit their local hospital for a screening visit where researchers note down medications the participant takes, checks their blood pressure, height and weight, measures the participants muscle size and take blood samples. Each participant is then asked to walk a few yards, do a grip strength test and undergo a test of their balance. If the screening test confirms that the participant is eligible to take part in the trial, they are asked to attend a second hospital visit where they are asked to walk as far as they can up and down a corridor for six minutes, undergo a leg strength test, answer questionnaires on their quality of life and daily activities, give blood samples and have a scan of their muscles and bones. They are then given another questionnaire to fill in about their diet, are given a diary to record any falls they might have over the next 3 months and also a pedometer to wear every day for a week. Participants are then randomly allocated into one of four groups. Those in group 1 are given perindopril and leucine.

Those in group 2 are given perindopril and a placebo (dummy drug). Those in group 3 are given leucine and a placebo. Those in group 4 are given two placebos. The perindopril or matching placebo is a single capsule taken once a day (usually in the morning). The leucine or matching placebo comes as a tub of powder taken mixed with meals three times a day. Two weeks later, and again at five weeks, a study nurse visits each participants home to check their blood pressure, take a blood sample and adjust the dose of perindopril (if applicable). At 3, 6, 9 and 12 months, participants are asked to attend their hospital again where they will undergo a combination of the tests that they had at earlier hospital visits.

What are the possible benefits and risks of participating?
Participants are monitored closely during the study by the study team. The tests give information on each participants kidney function, fitness and general wellbeing. If any of these investigations reveal any new abnormality, this will be discussed with the participants GP (with the participants consent) or the participant will be referred to a specialist clinic (whichever seems most appropriate.) The study may not immediately benefit the participants, but might make them feel stronger. If the results of the study are positive this may change how people with sarcopenia are treated in the future. Perindopril can cause a cough, which affects about one in ten people. Uncommonly, it can cause dizziness or kidney problems with increases in blood levels of potassium. Participants are monitored via blood tests and blood pressure to catch any problems that might occur. Leucine is used as food supplement and is not known to cause any medical problems. Having blood taken may cause minor bruising and discomfort. Participants are allowed plenty of rest in between the walking and strength tests.

Where is the study run from?
Ninewells Hospital and Medical School (lead centre) and 13 after NHS hospitals in the UK.

When is the study starting and how long is it expected to run for?
April 2015 to April 2020

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

Who is the main contact?
Dr Miles Witham

Study website
http://www.lacetrial.org.uk/

Contact information

Type(s)
Scientific

Contact name
Dr Miles D Witham

Contact details
Ninewells Hospital and Medical School
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
18290

Study information

Scientific Title
Perindopril and leucine to improve muscle function in older people (LACE study)

Acronym
LACE

Study hypothesis
To determine the efficacy of leucine and perindopril in improving physical function in older people with sarcopenia diagnosed using the EWGSOP (European Working Group on Sarcopenia) definition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Committee 2, 21/11/2014, ref: 14/ES/1099

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
See outputs table

Condition
Topic: Primary Care, Musculoskeletal disorders, Ageing; Subtopic: Musculoskeletal (all Subtopics), Ageing, Ageing; Disease: Musculoskeletal, All Diseases, All Ageing

Interventions
Oral perindopril 4mg once daily vs placebo, and oral leucine 2.5g three times per day with meals vs placebo

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Perindopril, leucine

Primary outcome measure
Between group difference in Short Physical Performance Battery (SPPB) score at 12 months

Secondary outcome measures
Between group differences in:
1. Appendicular muscle mass/height squared (measured by dual energy-X ray absorptiometry)
2. Grip strength
3. Quadriceps strength (handheld dynamometry)
4. 6 minute walk test
5. Gait speed (4m walk)
6. Chair stands (Sit to stand test x 10)
7. Activities of daily living (Nottingham extended ADL questionnaire) and quality of life (EuroQol 5D questionnaire).
8. HOMA IR (Homeostatic Index of insulin resistance; measured from glucose and insulin levels)
9. Falls frequency, collected by monthly falls diary
10. Biomarkers of muscle metabolism and predictors of response to treatment: baseline 3 and 12 months

Measured at baseline, 6 and 12 months, except for muscle mass, which is baseline and 12 months

Overall study start date
01/03/2015

Overall study end date
30/06/2020

Eligibility

Participant inclusion criteria

1. Age 70 and over
2. Sarcopenia criteria according to EWGSOP definition, based on:
2.1. Low total skeletal muscle mass on BioImpedance Assay (BIA) using the BIA 101 device (<13Kg for women, <20.5Kg for men)
2.2. Either low gait speed (<0.8 m/s on 4m walk) or low handgrip strength (<20Kg for women, <30Kg for men)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 352; UK Sample Size: 352

Total final enrolment
145

Participant exclusion criteria
1. Contraindications or existing indications to therapies or placebo
1.1. Known clinical diagnosis of chronic heart failure (by European Society of Cardiology criteria)
1.2. Confirmed LV systolic dysfunction on any imaging modality
1.3. Known aortic stenosis (peak gradient >30mmHg)
1.4. Systolic BP<90 mmHg (supine)
1.5. Dizziness on standing associated with a postural drop of >20/10mmHg (asymptomatic orthostatic hypotension will not be a contraindication)
1.6. Serum Creatinine >180 umol/L or eGFR<30ml/min by MDRD4 calculation
1.7. K>5.0 mmol/L; Na<130 mmol/L
1.8. Using ACEi, Angiotensin receptor blocker, aldosterone blocker or leucine already
1.9. Previous adverse reaction to ACEi or leucine
1.10. Current use of oral NSAIDs (aspirin is permitted, as are topical NSAIDs)
1.11. Lactose intolerance
2. Contraindications to consent or undertaking study outcomes
2.1. Peripheral oedema present above knee level
Unable to mobilise without human assistance (walking aids allowed)
2.2. Unable to give written informed consent
2.3. Currently enrolled in another research study, or less than 30 days since completing another research study
3. Overlap with other myopathic conditions or important confounders
3.1. Currently enrolled in a time-limited exercise-based rehabilitation programme
3.2. Any progressive neurological or malignant condition with life expectancy <6 months
3.3. Severe COPD (GOLD stage IV)
3.4. Known myositis
3.5. Self-reported weight loss of >10% in last 6 months (to exclude significant cachexia)
3.6. Known uncontrolled thyrotoxicosis
3.7. 7.5mg/day or greater prednisolone use (or equivalent)

Recruitment start date
01/05/2015

Recruitment end date
31/12/2018

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Ninewells Hospital and Medical School
Ageing and Health Division of Medicine and Therapeutics
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Sponsor information

Organisation
NHS Tayside

Sponsor details
R&D Office
Level 9
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/000ywep40

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Results will be published in peer-reviewed journals in early 2021.

Intention to publish date
30/09/2021

Individual participant data (IPD) sharing plan
The datasets generated during the study will be available upon request from the University of Dundee (contact tctu@dundee.ac.uk) following publication of the main trials results. Access will be available to bona fide non-commercial research teams, subject to submission of a proposal for use, approval by a data access committee, and involvement of the trial team.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	04/01/2018		Yes	No
Basic results		19/05/2021	19/05/2021	No	No
Participant information sheet			10/03/2023	No	Yes
Results article		01/08/2022	10/03/2023	Yes	No
HRA research summary			28/06/2023	No	No