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Allopurinol in Functional Impairment (ALFIE) trial: improving muscle strength

Submission date
07/03/2012

Recruitment status
No longer recruiting

Registration date
17/04/2012

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Muscle weakness that occurs as we get older can lead to a gradual slowing down of activity and increased difficulty in functioning independently. It may also lead to an increased risk of falls and can have a significant impact on social and healthcare costs. Exercise has been shown to improve muscle strength but many older people are unable to exercise due to underlying health problems so research into alternative treatments to improve muscle weakness are needed. There is now strong and compelling reasons from recent experimental studies both in animals and humans to show that an established drug used to treat gout called allopurinol may also have beneficial effects on muscles. It does this by reducing harmful molecules in muscle called free radicals that reduce the ability of the muscle to make use of oxygen and therefore make them tire more easily. Allopurinol has also been shown to improve blood flow to the muscles, again improving oxygen availability in them, and makes muscles more elastic so they are more efficient. This study will examine the effects of allopurinol compared to a placebo (dummy) medicine on how well muscles function in older people and is designed to show if a 20-week course of allopurinol improves how well leg muscles work.

Who can participate?
People aged 65 and over who are unable to walk more than 400 m in 6 minutes.

What does the study involve?
The participants will undergo a full clinical examination and routine screening blood tests during the first (screening) visit. They will then be randomly assigned to take either allopurinol 300 mg twice a day or placebo (dummy) tablets twice a day for 20 weeks. There will be two monitoring visits and blood tests during that time just to make sure the participants are tolerating their medications without any difficulty.

What are the possible benefits and risks of participating?
There are no direct benefits to the patients participating as allopurinol is not currently licensed for this particular condition. If the results are positive, it may help future patients with sarcopenia. Just like any drug, some people may have an adverse reaction to allopurinol but

these are usually mild (rash, gastrointestinal upset). We will be monitoring patients during the trial and provide them with contact telephone numbers if they feel unwell on the trial medication.

Where is the study run from?
The study will be run from the University of Dundee Medical School (UK).

When is study starting and how long is it expected to run for?
The study ran from October 2012 to September 2014.

Who is funding the study?
Dunhill Medical Trust (UK).

Who is the main contact?
Dr Jacob George
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2014-004122-18

IRAS number

ClinicalTrials.gov number
NCT01550107

Secondary identifying numbers
GEO006

Study information

Scientific Title
A prospective study to evaluate the effect of allopurinol on muscle energetics in primary sarcopenia

Acronym
ALFIE

Study objectives
Sarcopenia is increasingly becoming a significant cause of frailty, loss of independence and physical disability in ageing western populations. Recent experimental evidence has revealed that skeletal muscle is particularly susceptible to oxidative stress and that oxidative stress plays a prominent role in the development and progression of sarcopenia. Our group have previously shown that the xanthine oxidase inhibitor allopurinol is able to abolish vascular oxidative stress and improve endothelial function in cohorts such as optimally treated chronic heart failure and chronic kidney disease. Recently, our group has also shown that allopurinol improves exercise tolerance and time to ST-depression in optimally treated coronary artery disease, suggesting that allopurinol could also exert its effects through ATP and/or oxygen sparing mechanisms.

Therefore, we propose a randomised double blind placebo-controlled parallel group trial of allopurinol in patients with primary sarcopenia using MR-spectroscopy and Flow Mediated Dilatation to investigate the possible mechanisms that underlie this possibility.

On 11/11/2014 the following changes were made to the trial record:
1. The public title was changed from 'Allopurinol in sarcopenia' to 'Allopurinol in Functional Impairment (ALFIE) trial: improving muscle strength'.
2. The acronym 'ALFIE' was added.
3. The target number of participants was changed from 70 to 124.
4. Dunhill Medical Trust (UK) was added to the sources of funding field.
5. The anticipated start date was changed from 01/10/2012 to 01/12/2014.
6. The anticipated end date was changed from 30/09/2014 to 30/11/2016 .

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Prospective randomised double blind placebo controlled 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
Primary Sarcopenia

Interventions
Allopurinol vs Placebo

Following a screening visit, participants will be randomised to either allopurinol 300mg twice daily or placebo twice daily in a randomised double blind fashion.

They will undergo screening blood tests, baseline non-invasive vascular function assessments and MR-spectroscopy. Following this they will attend two monitoring visits every 8 weeks. The total involvement per participant is 20 weeks. At the end of the study the participants, will undergo final blood tests, baseline non-invasive vascular function assessments and MR-spectroscopy. Transport will be provided for participants within Tayside.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Improvement in muscle energetics as measured by magnetic resonance (MR) spectroscopy

Secondary outcome measures
1. Change in muscle volume (as measured by cross-sectional area on MR obtained during perfusion mapping)
2. Short Performance Battery test
3. Change in Flow Mediated Dilatation
4. Markers of oxidative stress (F2-Isoprostanes)

Added 11/11/2014:
5. Six-Minute Walk test
6. Quality of Life measured by EuroQOL EQ5D questionnaire

Overall study start date
15/05/2014

Completion date
28/02/2018

Eligibility

Key inclusion criteria

Current inclusion criteria as of 11/11/2014:
1. Age 65 years and over
2. 6-Minute Walk Distance <400 m

Previous inclusion criteria:
1. Age 65 and over
2. Muscle strength (grip strength <20kg women;<30kg men) AND physical performance (Short Physical Performance Battery test score less than or equal to 8/12). This will ensure both that the study population have sarcopenia according to European consensus guidelines
3. Gait speed less than 0.8m/s

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
124

Total final enrolment
124

Key exclusion criteria
Current exclusion criteria as of 11/11/2014:
1. Documented history of peripheral arterial disease
2. Pre-existing diagnosis of severe heart failure (LVEF <35%)
3. Malignancy under active treatment (excluding basal cell carcinoma)
4. Severe COPD (physician diagnosis)
5. Intolerance to allopurinol
6. Individuals with Active Acute Gout currently taking allopurinol; or those who have stopped taking allopurinol ≤1 month previously for this condition.
7. On long-term high-dose steroids (eq. Prednisolone >10 mg/day due to risk of steroid-induced myopathy and osteoporosis)
8. Immobility that would render the patient incapable of doing the Short Physical Performance Battery Test (SPPB) or 6MWT
9. Patients who have participated in any other clinical drug trial within the previous 30 days will be excluded
10. Cognitive impairment precluding informed consent
11. Any other considered by a study physician to be inappropriate for inclusion

Previous exclusion criteria:
1. Previously enrolled into the study
2. Pre-existing diagnosis of heart failure or any malignancy (excluding basal cell carcinoma)
3. Documented intolerance to allopurinol
4. Immobility that would render the patient incapable of doing the Short performance Battery Test (SPBT)

Date of first enrolment
26/02/2015

Date of final enrolment
22/02/2017

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
University of Dundee
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
University of Dundee (UK)

Sponsor details
Tayside Academic Sciences Centre
Ninewells Hospital & Medical School
George Pirie Way
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Sponsor type
University/education

Website
http://www.dundee.ac.uk/

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Charity

Funder Name
Dunhill Medical Trust (UK)

Alternative Name(s)
The Dunhill Medical Trust, DMT

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
28/02/2019

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?
Basic results			28/05/2020	No	No