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Acipimox to improve muscle function

Submission date
10/06/2021

Recruitment status
No longer recruiting

Registration date
29/06/2021

Overall study status
Completed

Last Edited
19/03/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Sarcopenia is the loss of muscle size and strength that accompanies ageing. It is a major risk factor for falls, need for care, hospital admission, prolonged hospital stay, and earlier death. There are currently no approved drug treatments for this common and important clinical condition. Recent research suggests that levels of NAD, a molecule vital to energy generation, are low in the muscles of people with sarcopenia. Boosting NAD levels may therefore provide a way to improve muscle function. This feasibility study will test whether acipimox, a medicine already used to reduce cholesterol levels, can boost NAD levels in muscles in older people with muscle weakness.

Who can participate?
We will recruit 11 participants aged 65 and over (8 men and 8 women), all of whom have muscle weakness and slow walking speed.

What does the study involve?
Each participant will attend two visits at the start of the study, then take acipimox 250mg two or three times a day for two to three weeks, and then attend two further visits.
We will measure muscle strength and walking speed, take a blood sample, take a muscle biopsy (a small sample of muscle from the outside of the thigh), measure how active the participant is over a week using a body-worn activity tracker, and perform an MRI scan of the lower leg before and after exercise to test how well the leg muscle recovers from exercise. These tests will be spread across the two visits at the start and then repeated at the two visits at the end.
The results from this study will tell us whether acipimox can increase NAD levels in muscle, whether we can also detect these changes through blood tests and MRI scans, and which participants are most likely to benefit from acipimox. The results will help us to design a future, larger, randomised controlled trial of acipimox.

What are the possible benefits and risks of participating?
We cannot promise the study will help you directly. However, the information we collect from this study may help to improve the treatment for older people with muscle weakness.
Risks:
As with any medicine, the medicine used in this study (acipimox) may cause side effects in some people. Doctors around the world have used acipimox for nearly 40 years and the side effects are well understood. If you do get a side effect from the study medicine, your doctor can stop

your medicine. The side effects should disappear rapidly.
In some people, acipimox can cause flushing (redness of the face) and headache. This side effect usually affects people for the first few doses but then gets better. To minimise this side effect, we will give you a low dose of aspirin to take once a day (if you already take aspirin, you will just keep taking your normal dose of aspirin). Less commonly, acipimox can cause nausea or indigestion. To help prevent this, we will ask you to take your study medicine during or just after meals.
Aspirin can cause inflammation of the stomach lining, and in rare cases can cause stomach ulcers. We are using a low dose of aspirin over a short period of time to minimise side effects, but if you have indigestion, stomach ulcers or are prone to bleeding, we will not include you in the study.
The muscle biopsy will be taken after your skin and surrounding area is numbed by injecting local anaesthetic. The injection and biopsy may cause some minor discomfort and bruising after biopsy and may be uncomfortable for a few days. Muscle biopsy is a simple procedure removing only a small amount of muscle with a low risk of complications. In very rare cases permanent muscle weakness, infection or a patch of numbness might occur.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2021 to March 2024

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof Miles Witham, Miles.Witham@newcastle.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Miles Witham

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000993-28

Integrated Research Application System (IRAS)
293565

Protocol serial number
CPMS 49429, Grant Codes: MC_PC_19047, IRAS 293565

Study information

Scientific Title
Acipimox to improve muscle function and sarcopenia – a feasibility study

Study objectives
This feasibility study will test whether acipimox, a medicine already used to reduce cholesterol levels, can boost NAD levels in muscle in older people with muscle weakness.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/06/2021, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 2071048285; tyneandwearsouth.rec@hra.nhs.uk), ref: 21/NE/0100

Study design
Interventional non-randomized

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Sarcopenia, muscle weakness

Interventions
Current interventions as of 08/12/2023:
The trial is a before and after-comparison trial. All participants will receive the study medication (acipimox) and aspirin (some participants may be taking aspirin already, in which case they will continue to take this). There is no control group and no participant receives a placebo (dummy) tablet.

Prescreening:
Participants will be contacted through clinics, GP practices and the SarcNet registry of people who have already expressed an interest in joining studies for muscle weakness. Please see section 27 for details. Once participants have expressed interest in taking part, the study team will contact them by telephone, video link or in person to conduct a brief prescreen. The

prescreen will ask a series of questions about current medications and health problems and a series of five questions about daily function (the SARC-F questions). These questions will help to decide if the study is right for the participant. If it is, and the participant is still interested, the full study information will be posted to the participant and then a screening visit will be arranged once they have read the full information.

Screening visit:
The screening visit can take place at the Clinical Ageing Research Unit (CARU) in Newcastle or the participant's own home if they prefer. At the screening visit, consent will be obtained, handgrip, time taken to stand up and sit down 5 times and walk speed over a 4-metre course will be tested, and a blood sample taken.
If the results from the screening visit confirm that the participant is eligible to take part in the study, the baseline and follow-up visits will be arranged.

Baseline visit 1 (day 0):
This visit will be performed at CARU. At this visit, the following will be done:
- Measure weight and height.
- Balance test, stand from a chair five times, walk speed over a 4-metre course.
- Test handgrip strength.
- Ask questions about activity level, weight change and levels of tiredness
- Take a blood sample
- Magnetic resonance imaging (MRI) scan of the leg muscle. For this scan, the participant will lie with their legs in the scanner. After a first scan at rest, they will then exercise one leg by repeatedly pressing on a pedal for several minutes until they are not able to do more. A series of leg scans will then be done whilst the muscle recovers.
- Accelerometer. This will be attached to the lower back of the participant at the end of the visit to be worn for seven days until the next study visit.

Baseline visit 2 (day 7):
This visit will be performed at CARU. At this visit, the accelerometer will be removed and the muscle biopsy will be done. To do this, local anaesthetic will be used to numb a patch over the side of the thigh. A small cut will be made down to the muscle, and several samples of muscle will be taken from the thigh using forceps. Steristrips and a dressing will then be applied. Stitches are not required. The participant will rest for an hour after the procedure, and we will telephone twice after the biopsy (2 days after and 5-7 days after) to check that everything is healing. Participants will be asked not to take aspirin on the day of the biopsy, and not to restart aspirin or anti-inflammatories for 48 hours after the biopsy.

Medication:
At the end of the baseline visit, the study medication (acipimox) and the aspirin will be given to the participant. They will be asked NOT to start taking either until we telephone them two days later. They will take acipimox one tablet two or three times a day (depending on their kidney function), and aspirin one tablet once a day until the end of the follow-up visit 2.

Follow-up visit 1 (day 21):
This visit will be performed at CARU. It will be the same as baseline visit 1 except that we will not repeat the height and weight.

Follow-up visit 2 (day 28):
This visit will be performed at CARU. It will be the same as baseline visit 2, except that at the end

of the visit, we will collect the study medications and no further study medications will be taken. If the participant usually takes aspirin, we will ask them NOT to take this until we have telephoned them two days after this final visit.

Previous Interventions:
The trial is a before and after-comparison trial. All participants will receive the study medication (acipimox) and aspirin (some participants may be taking aspirin already, in which case they will continue to take this). There is no control group and no participant receives a placebo (dummy) tablet.

Prescreening:
Participants will be contacted through clinics, GP practices and the SarcNet registry of people who have already expressed an interest in joining studies for muscle weakness. Please see section 27 for details. Once participants have expressed interest in taking part, the study team will contact them by telephone, video link or in person to conduct a brief prescreen. The prescreen will ask a series of questions about current medications and health problems and a series of five questions about daily function (the SARC-F questions). These questions will help to decide if the study is right for the participant. If it is, and the participant is still interested, the full study information will be posted to the participant and then a screening visit will be arranged once they have read the full information.

Screening visit:
The screening visit can take place at the Clinical Ageing Research Unit (CARU) in Newcastle or the participant's own home if they prefer. At the screening visit, consent will be obtained, handgrip and walk speed over a 4-metre course will be tested, and a blood sample taken.
If the results from the screening visit confirm that the participant is eligible to take part in the study, the baseline and follow-up visits will be arranged.

Baseline visit 1 (day 0):
This visit will be performed at CARU. At this visit, the following will be done:
- Measure weight and height.
- Balance test, stand from a chair five times, walk speed over a 4-metre course.
- Test handgrip strength.
- Ask questions about activity level, weight change and levels of tiredness
- Take a blood sample
- Magnetic resonance imaging (MRI) scan of the leg muscle. For this scan, the participant will lie with their legs in the scanner. After a first scan at rest, they will then exercise one leg by repeatedly pressing on a pedal for several minutes until they are not able to do more. A series of leg scans will then be done whilst the muscle recovers.
- Accelerometer. This will be attached to the lower back of the participant at the end of the visit to be worn for seven days until the next study visit.

Baseline visit 2 (day 7):
This visit will be performed at CARU. At this visit, the accelerometer will be removed and the muscle biopsy will be done. To do this, local anaesthetic will be used to numb a patch over the side of the thigh. A small cut will be made down to the muscle, and several samples of muscle will be taken from the thigh using forceps. Steristrips and a dressing will then be applied. Stitches are not required. The participant will rest for an hour after the procedure, and we will telephone twice after the biopsy (2 days after and 5-7 days after) to check that everything is healing. Participants will be asked not to take aspirin on the day of the biopsy, and not to restart aspirin or anti-inflammatories for 48 hours after the biopsy.

Medication:
At the end of the baseline visit, the study medication (acipimox) and the aspirin will be given to the participant. They will be asked NOT to start taking either until we telephone them two days later. They will take acipimox one tablet two or three times a day (depending on their kidney function), and aspirin one tablet once a day until the end of the follow-up visit 2.

Follow-up visit 1 (day 21):
This visit will be performed at CARU. It will be the same as baseline visit 1 except that we will not repeat the height and weight.

Follow-up visit 2 (day 28):
This visit will be performed at CARU. It will be the same as baseline visit 2, except that at the end of the visit, we will collect the study medications and no further study medications will be taken. If the participant usually takes aspirin, we will ask them NOT to take this until we have telephoned them two days after this final visit.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Acipimox

Primary outcome(s)
Skeletal muscle NAD concentration measured using a Jamar dynamometer. at baseline and follow up (2 - 3 weeks). Three readings per hand will be taken, with the maximum value used for analysis

Key secondary outcome(s))
Measured at baseline and follow up (2 - 3 weeks):
1. Mitochondrial Respiratory chain activity via immunohistochemistry and immunofluorescence
2. ATP/ADP concentrations and ratio measured using bioluminescence assays
3. Mitochondrial DNA copy number via quantitative PCR (as a measure of mitochondrial numbers)
4. Erythrocyte NAD concentration measured using bioluminescence assays
5. Peripheral blood white cell NAD concentration measured using bioluminescence assays
6. Phosphocreatine recovery rate measured via 31P magnetic resonance spectroscopy of the calf
7. NAD(P)H levels in skeletal muscle via 31P magnetic resonance spectroscopy of the calf
8. Short Physical Performance Battery
9. Maximal handgrip strength measured using Jamar dynamometer
10. Physical activity, gait speed, variability and postural control measured using triaxial accelerometry

Completion date
30/03/2024

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 08/12/2023:
1. Age 65 years and over
2. Low maximum handgrip strength (<16kg for women, <27kg for men) or 5 times sit to stand >15 seconds
3. Walk speed <=0.8 m/s on 4-metre walk test

Previous participant inclusion criteria:
1. Age 65 years or over
2. Low maximum handgrip strength (<16kg for women, <27kg for men)
3. Walk speed <=0.8 m/s on 4 metre walk test

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
65 years

Sex
All

Total final enrolment
11

Key exclusion criteria
1. General:
1.1. Allergy to acipimox or other niacin-related products
1.2. Allergy or intolerance of aspirin
1.3. Unable to give written informed consent
1.4. Currently enrolled in another intervention study (observational studies are permitted)
1.5. Currently participating in supervised exercise classes or physiotherapy
1.6. Any progressive neurological or malignant condition with life expectancy <6 months
2. Safety of Acipimox and Aspirin:
2.1. eGFR <45ml/min/1.73m² (a measure of kidney function)
2.2. Taking statin medication or fibrate medication
2.3. Active peptic ulcer disease or indigestion
3. Safety of muscle biopsy and MRI:
3.1. Platelets <100x10^9/L at screening (contraindication to muscle biopsy)
3.2. Presence of a bleeding tendency or use of oral or injectable anticoagulant medication
3.3. Antiplatelet agents other than low dose (75mg once daily) aspirin
3.4. Unable to feel quadriceps muscle in leg to locate where to biopsy
3.5. Contraindications to MRI scanning (mild claustrophobia is not a contraindication)
4. Other causes of skeletal myopathy:
4.1. Liver function tests (bilirubin, ALT, alkaline phosphatase) >3x upper limit of normal
4.2. Symptomatic (NYHA class II-IV) chronic heart failure (diagnosed according to European Society of Cardiology guidelines)

4.3. Severe Chronic obstructive pulmonary disease (GOLD stage IV)
4.4. Known myositis or other established myopathy (muscle disease)
4.5. Self-reported weight loss of >10% in last 6 months (to exclude significant cachexia)
4.6. Known uncontrolled thyrotoxicosis (overactive thyroid disease)
4.7. 7.5mg/day or greater prednisolone use (or equivalent) (steroid that can cause muscle weakness)

Date of first enrolment
01/08/2021

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Freeman Hospital
Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Road
High Heaton
Newcastle
United Kingdom
NE7 7DN

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

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
The datasets generated during the current study will be available upon request from Professor Miles Witham (Miles.Witham@newcastle.ac.uk). Anonymised, individual participant data may be made available as part of collaborative analyses with the study team and bona fide academic collaborators, subject to current data protection laws, agreement on an analysis and use plan and a data sharing agreement being put in place between Newcastle University and the collaborating institution. Data will be available from the end of 2022 onwards."

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		18/03/2025	19/03/2025	Yes	No
Protocol article		27/02/2024	05/03/2024	Yes	No
Basic results			14/10/2024	No	No
HRA research summary			26/07/2023	No	No