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Impact of intravenous iron injections on musculoskeletal function in older adults

Submission date 25/01/2021	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 28/01/2021	**Overall study status** Stopped	
Last Edited 04/03/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Anaemia is caused by a lack of iron, often because of blood loss or pregnancy. Anaemia is a risk factor for functional decline and frailty in older adults including decreased physical performance and muscle strength, increased hospitalisation risk and mortality, falls, and poorer recovery from activities of daily living. Iron deficiency and associated anaemia is a frequent accompanier of debilitating chronic diseases such as heart failure and chronic lung diseases.
These conditions, more commonly seen in older patients, are strongly linked to deterioration in physical function, reduced skeletal muscle mass and quality, frailty, and poor quality of life. Exercise intolerance is also a common feature of these conditions as iron deficiency impairs the capacity of carrying oxygen leading to inability to sustain physical activities. Furthermore, the age-related decline in the muscle mass and quality (so-called sarcopenia) and associated frailty has rapidly become a major health concern in the older adults, particularly when accompanied by other chronic diseases. Recently, there has been an increasing interest in exploring the role of iron as a causative factor in the development of sarcopenia and related frailty.
In summary, it is not clear whether Iron repletion leads to meaningful enhancements in the skeletal muscle function and physical performance in older adults suffering from iron deficiency anaemia. This study will investigate the impact of a standard care intervention (intravenous iron therapy) on muscular function and physical performance in older patients through a range of laboratory assessments.

Who can participate?
Patients aged 60 - 85 years, who have iron deficiency anaemia.

What does the study involve?
Participants will be randomly allocated to receive either intravenous iron therapy or oral ferrous sulphate. Each participant will require to attend the School of Health Sciences' laboratories (Liverpool Hope University) on four different occasions (once before intervention and three times after receiving the iron therapy) throughout a 3-year period to complete multiple assessments in relation to basic blood tests and musculoskeletal function and physical performance. In addition to this, participants in the first group will require to attend the Aintree Hospital NHS Trust clinics on one occasion to receive a single-dose intravenous iron.
The study will broadly investigate musculoskeletal function (health) and physical performance

by means of muscle quality, muscle mass, muscle strength, muscle activation and fatigue levels, gait quality, muscle physiology (level of oxygen carried into the muscles), and functional questionnaires prior to, during, and after iron therapy. In addition to this, changes in patients' quality of life in each group will be assessed through administration of validated questionnaires.

What are the possible benefits and risks of participating?
Benefits: We cannot promise that this study will help you directly but the information we get from this study might help improve the treatment of older people suffering from iron deficiency anaemia.
Risks: Generally intravenous iron is very safe and well tolerated. However, there are known side effects including nausea, headaches, dizziness, high blood pressure, injection site reactions, increased liver enzymes. and allergic reaction.

Where is the study run from?
Liverpool Hope University (UK)

When is the study starting and how long is it expected to run for?
April 2019 to October 2025

Who is funding the study?
Vifor Pharma UK Limited

Who is the main contact?
Prof. Omid Khaiyat, alizado@hope.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2020-000056-35

IRAS number
253852

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 44977, IRAS 253852

Study information

Scientific Title
Impact of intravenous iron (Ferinject) on musculoskeletal function profiles in older adults with Iron Deficiency Anaemia (IDA)

Study objectives
Anaemia is a risk factor for functional decline and frailty in older adults including decreased physical performance and muscle strength, increased hospitalisation risk and mortality, falls, and poorer recovery from activities of daily living. Despite a major gap in human studies, research in animals has demonstrated an interrelationship between iron deficiency anaemia and deteriorated functional capacity and physical performance particularly in older adults. Iron deficiency and associated anaemia is a frequent accompanier of debilitating chronic diseases such as heart failure and chronic lung diseases. These conditions, more commonly seen in older patients, are strongly linked to deterioration in physical function, reduced skeletal muscle mass and quality, frailty, and poor quality of life. Exercise intolerance is also a common feature of these conditions as iron deficiency impairs the capacity of carrying oxygen leading to inability to sustain physical activities. Furthermore, the age-related decline in the muscle mass and quality (so called sarcopenia) and associated frailty has rapidly become a major health concern in the older adults particularly when accompanied by other chronic diseases. Recently, there has been an increasing interest in exploring the role of iron as a causative factor in the development of sarcopenia and related frailty.
In summary, there is a substantial gap of evidence whether Iron repletion leads to meaningful enhancements in the skeletal muscle function and physical performance in older adults suffering from iron deficiency anaemia. This study will investigate the impact of a standard care intervention (intravenous iron therapy) on muscular function and physical performance in older patients through a range of laboratory assessments.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/09/2020, North West - Liverpool Central Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44(0)207 1048387; liverpoolcentral.rec@hra.nhs.uk), ref: 20/NW/0090

Study design
Interventional randomized 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 to request a patient information sheet.

Health condition(s) or problem(s) studied
Iron deficiency anaemia

Interventions
The study will recruit two groups of stable patients (although likely with chronic diseases) with established iron deficiency anaemia through Aintree Hospital NHS Trust clinics. Fifty patients aged 60-85 years will be recruited into each group:
1. Intravenous iron therapy group: This group will receive intravenous iron calculated based on body weight and level of anaemia (hemoglobin concentration), as per the iron therapy's SPC
2. Active Control Group: This group will receive oral ferrous sulphate prescribed by their GP
Randmisation: Simple randomisation/parallel assignment/single-blinded

Identified patients with iron deficiency anaemia will receive an invitation to participate in the study together with a Patient Information Sheet clearly explaining different aspects of the research project. Each participant will require to attend the School of Health Sciences' laboratories (Liverpool Hope University) on four different occasions (once before the intervention and three times after receiving the iron therapy) throughout a 3-year period to complete multiple assessments in relation to basic blood tests and musculoskeletal function and physical performance. In addition to this, participants in the first group will require to attend the Aintree Hospital NHS Trust clinics on one occasion to receive a single-dose intravenous iron.

The study will broadly investigate musculoskeletal function (health) and physical performance by means of muscle quality, muscle mass, muscle strength, muscle activation and fatigue levels, gait quality, muscle physiology (level of oxygen carried into the muscles), and functional questionnaires prior to, during, and after iron therapy. In addition to this, changes in patients' quality of life in each group will be assessed through administration of validated questionnaires.

The data will be analysed at the end of the study to identify any significant and clinically meaningful changes in the musculoskeletal function, physical performance, and health-related quality of life resulted from the iron therapy in each group while also comparing such changes between the two study groups.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ferinject (ferric carboxymaltose), ferrous sulphate (oral)

Primary outcome measure
Muscle Quality Index (MQI) determined based on muscle strength relative to quantity/volume of the muscle mass generating the force. Muscle strength will be measured using various dynamometers designed for upper and lower extremities and muscle volume will be assessed using the Bioimpedance technique at screening, week 4, week 12 and week 24

Secondary outcome measures
1. History & Health Screening measured at screening:
1.1. Health-history measured using the Health-history Questionnaire
1.2. Resting Heart Rate
1.3. Blood Pressure (mmHg)
1.4. Height (cm), weight (kg), BMI (kg/m²), Waist Circumference (cm)
1.5. Physical activity measured using the International Physical Activity Questionnaire
2. Biochemical parameters: Blood count, Serum Iron, Serum Ferritin and Transferrin levels measured using blood test at screening, week 4, week 12 and week 24
3. Muscular Function Profile including strength Measurements of the key muscle groups essential for daily activities and independence including hand-grip, shoulder, knee at screening, week 4, week 12 and week 24
4. Skeletal Muscle Mass measured using Segmental Bio-Impedance at screening, week 4, week 12 and week 24
5. Fatigability and Activation Pattern of key lower & upper extremity muscle groups measured using electromyography and gait analysis at screening, week 4, week 12 and week 24
6. Mitochondrial Function measured using near-infrared spectroscopy atscreening, week 4, week 12 and week 24
7. Health-related Quality of Life: SF-12 Health Survey, The single-item 'Life Satisfaction and Personal Well-Being' question at screening, week 4, week 12 and week 24
8. Anxiety and depression measured using the Hospital Anxiety and Depression Scale at screening, week 4, week 12 and week 24
9. Mood measured using the Profile of Mood States – Short Form at screening, week 4, week 12 and week 24

Overall study start date
01/04/2019

Completion date
01/06/2026

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Anaemia attributable to iron deficiency
2. Haemoglobin <120 g/L in women, Hb <130 g/L in men
3. Ferritin <=100ng/mL or <=300ng/mL if transferrin saturation (TSAT) <=30%
4. Age >=60 to 85 years

5. Ambulatory individuals
6. BMI <=40 kg/m²
7. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
60 Years

Upper age limit
85 Years

Sex
Both

Target number of participants
Planned Sample Size: 100; UK Sample Size: 100

Key exclusion criteria
1. Uncontrolled hypertension/ diabetes
2. Potential medication interactions
3. Hemochromatosis or iron storage disorders
4. Recent treatment with IV antibiotics or red blood cell transfusion
5. Dialysis dependent
6. History of malignancy
7. Pregnant or lactating women
8. Severe hepatic and renal dysfunction
9. Advanced cardiovascular disease and COPD
10. Advanced Neuromuscular disorder
11. Obvious cognitive disability and psychological illness
12. Current treatment with systemic steroids or any other substantive medication
13. Alcohol or any other drug abuse

Date of first enrolment
20/02/2023

Date of final enrolment
30/12/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Liverpool Hope University
School of Health Sciences
Hope Park
Liverpool
United Kingdom
L16 9JD

Study participating centre
Aintree University Hospital
Aintree University Hospital NHS Foundation Trust
Lower Lane
Liverpool
United Kingdom
L9 7AL

Sponsor information

Organisation
Liverpool Hope University

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L16 9JD
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cooperc1@hope.ac.uk

Sponsor type
University/education

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

ROR
https://ror.org/03ctjbj91

Funder(s)

Funder type
Industry

Funder Name
Vifor Pharma UK Limited

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/09/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No