ISRCTN98371961 https://doi.org/10.1186/ISRCTN98371961

Oral iron, intravenous iron or discontinuation of therapy for older adults with treatment unresponsive iron deficiency anaemia

Submission date
04/08/2017

Recruitment status
No longer recruiting

Registration date
16/08/2017

Overall study status
Completed

Last Edited
06/10/2022

Condition category
Haematological Disorders

[X] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Anaemia due to low iron levels is common in older people and can cause tiredness and breathlessness. It is commonly treated with iron tablets. However, iron tablets do not improve anaemia in many people and they have side effects. It is not known what strategy of care is best for patients who do not respond to iron tablets: should treatment stop, continue with tablets (which is current practice), or switch to iron given by a drip (intravenous iron)? Before a large study is run to find the answers to these questions, a smaller study is needed to make sure that the study processes can be run properly, to test that people can be recruited to the large study, and to work out how many people must be recruited to the large study. This is why this smaller study is being run first.

Who can participate?
Patients aged 65 and over with anaemia due to low iron levels who have not improved after at least 8 weeks of iron tablets

What does the study involve?
Participants are randomly allocated to either continue the iron tablets they are already taking, stop their iron tablets and receive iron in a drip on one or two occasions, or to stop their iron tablets and have no further iron. Before the start and 3 months later, all participants are asked a series of questions about how tired or breathless they feel; undergo a walking test and other measures of fitness and balance; and are asked questions about how well they are taking their medicines, their quality of life, and what contact they have had recently with health services. The trialists compare how easy it is to find eligible people through GP practices, adverts and hospital clinics, and measure levels of haemoglobin in the blood (a measure of anaemia) at the start and 3 months later.

What are the possible benefits and risks of participating?
If one treatment is better than another, participants may feel less tired and breathless, or not have the side effects that their usual iron tablets give them. Iron tablets can cause constipation and indigestion. These are the standard treatment that all participants will already be taking

before entering the study. Intravenous iron (through a drip) can rarely cause allergic reactions or damage skin if the drip leaks from the vein.

Where is the study run from?
The University of Aberdeen is leading the study, assisted by Tayside Clinical Trials Unit. Participants are recruited from Tayside, Grampian and Fife regions of Scotland, and through the Norfolk and Norwich NHS Trust area in England.

When is the study starting and how long is it expected to run for?
August 2017 to December 2019

Who is funding the study?
The Chief Scientist Office of the Scottish Government (UK)

Who is the main contact?
1. Prof. Phyo Myint
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2. Dr Miles Witham
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Study website
https://raindrop.org.uk/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Scientific title as of 21/09/2018:
RAndomised IroN Deficiency anaemia management Pilot

Previous scientific title:
Oral iron, intravenous iron or discontinuation of therapy for older adults with treatment unresponsive iron deficiency anaemia: a pilot randomised controlled trial

Acronym
RAINDroP

Study objectives
The primary objective of this pilot trial is to estimate the recruitment rates and examine recruitment strategies at pilot sites across different settings and different NHS providers.
The secondary objectives are to examine the change in a key surrogate outcome (haemoglobin levels) and to obtain preliminary data on the proposed patient outcomes (quality of life, symptoms and physical function) to inform the sample size calculation for a future definitive trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North of Scotland research ethics committee, approval date 05/06/2018, approval number 18/NS/0064

Study design
Three-arm parallel-group randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format; please use contact details to request a participant information sheet

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

Interventions
Participants will be randomised on a 1:1:1 allocation ratio via a web-based randomisation system run by a third party. A minimisation algorithm with a small random element will be used to ensure balance across recruitment centres and key baseline measures. Randomisation will be stratified by site, and further balanced using minimisation. Haemoglobin after minimum 8 weeks of oral iron (>=100g/L vs <100g/L), ferritin prior to commencement of oral iron (>=50ug/L vs <50ug/L) and six minute walk distance (>=300m vs <300m) will be the minimisation variables.

Participants are randomised to either:
1. Continue the iron tablets they are already taking
2. Stop their iron tablets and receive intravenous iron on one or two occasions
3. Stop their iron tablets and have no further iron

Before the start and 3 months later, participants are asked a series of questions about how tired or breathless they feel; undergo tests to see how quickly they can walk and other measures of fitness and balance; complete questionnaires about how well they are taking their medicines, their quality of life, and what contact they have had recently with health services. The trialists will compare how easy it is to find eligible people through GP practices, adverts and hospital clinics, and will measure haemoglobin in the blood (a measure of anaemia) at the start and 3 months later.

Intervention Type
Other

Primary outcome measure
Co-primary outcomes, measured from recruitment records at the end of recruitment:
1. The rate of randomisation per month across the pilot sites
2. The proportion recruited from each route of recruitment

Secondary outcome measures

Measured between baseline and 3 months:
1. Hemoglobin levels, measured by blood sample at baseline and 3 months
2. Eligible patients per site, measured from recruitment records at end of recruitment
3. Proportion of eligible patients agreeing to take part and passing screening, measured from recruitment records at end of recruitment
4. Feasibility of collecting primary (physical functioning and health-related and general quality of life) and secondary outcomes for main trial:
4.1. Six minute walk distance, measured by walk test at baseline and 3 months
4.2. Short physical performance battery (SPPB), measured at baseline and 3 months
4.3. Health-related quality of life, measured using EQ-5D, 15D
4.4. Anemia-related symptoms (e.g. breathlessness, tiredness, fatigue), measured by symptom questionnaire at baseline and 3 months
4.5. Healthcare useincluding use of blood transfusions and hospitalisation, measured by questionnaire at 3 months
4.6. Mortality, measured by death certificate records at 3 months
5. Dropout and crossover rate, measured from recruitment and follow up records at 3 months
6. Side effects and adverse events (GI symptoms, headache, dizziness, rash), measured from case record form at 3 months
7. Functional limitation, measured using six-minute walk (<400m) or short physical performance battery(≤10) at baseline and 3 months
8. Fatigue, measured using validated Fatigue Severity Scale at baseline and 3 months

Overall study start date
01/08/2017

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Age 65 years or over
2. Haemoglobin of >=85g/L and <=110g/L prior to commencing oral iron
3. Ferritin <100µg/L prior to commencing oral iron
4. Currently taking oral iron at any dose with a minimum of 8 weeks therapy
5. Insufficient response to oral iron therapy (sufficient response defined as improvement in Hb of 20g/L after a minimum of 8 weeks of oral iron therapy)
6. Relevant investigations (including upper and lower GI endoscopies) either already conducted, offered but declined by the patient, or deemed not appropriate by the treating clinician

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants

84

Total final enrolment
5

Key exclusion criteria
1. Active GI cancers
2. Active (unhealed) peptic ulcer disease
3. No ferritin level performed prior to commencing oral iron
3. Bleeding disorders (including being on oral anticoagulants; antiplatelet agents are permitted)
4. Weight loss of >5Kg in the last 3 months (as a possible marker of occult cancer)
5. Estimated GFR of <30ml/min/1.73m2 by CKD-EPI equation
6. Symptomatic chronic heart failure (defined according to the European Society of Cardiology guidelines; note asymptomatic left ventricular systolic dysfunction is not classed as heart failure)
7. Terminal illness (with life expectancy less than 3 months as deemed by the local investigator)
8. Severe cognitive impairment precluding written informed consent
9. Unable to mobilise without human assistance (walking aids are allowed)
10. Previous reaction to intravenous iron
11. Currently participating in, or within 30 days of completion of, another clinical trial

Date of first enrolment
01/09/2018

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
NHS Tayside
United Kingdom
DD2 1SP

Sponsor information

Organisation
University of Aberdeen

Sponsor details

Research and Innovation
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Sponsor type
University/education

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

ROR
https://ror.org/016476m91

Organisation
NHS Grampian

Sponsor details
R&D dept
Aberdeen Royal Infirmary
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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Results will be posted on ISRCTN, published in peer-reviewed journals and presented to both participants and scientific conferences after the end of 2019.

Intention to publish date
01/10/2022

Individual participant data (IPD) sharing plan
At the end of the trial, deidentified trial data will be made available on request to other bona fide academic investigators via data sharing agreements overseen by the University of Aberdeen.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2	14/06/2018	06/10/2022	No	No
HRA research summary			28/06/2023	No	No