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Intravenous iron in chronic obstructive pulmonary disease (COPD)

Submission date 13/03/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/06/2013	**Overall study status** Completed	
Last Edited 23/06/2020	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a progressive condition characterised by irreversible airway narrowing, usually caused by smoking. It is very common, with a prevalence of 4-10% and accounts for 27,000 deaths per year in the UK. Current therapies have little impact on symptom and disease progression. Iron is essential for many processes in the body, including carrying and using oxygen. We think that raising iron levels may be beneficial for several reasons. Patients who have COPD may be vulnerable to low iron levels. The aim of this study is to find out more about how a solution of iron into a vein compared to a drip of inactive saline control helps to improve well being in people with chronic obstructive pulmonary disease (COPD) and how quickly any benefits are seen.

Who can participate?
Patients who take part in this study must have COPD.

What does the study involve?
The patients are randomly allocated to receive either an iron or saline solution. The study involves four visits to the study site. Patients complete questionnaires and undergo a series of tests (pulse oximetry, spirometry, blood test, capillary blood gas, ECG, echocardiogram, walk test) at each visit.

What are the possible benefits and risks of participating in this study?
For patients with low iron levels and who are randomly allocated to have iron solution, their iron levels will be restored to normal very quickly. This may lead to an improvement in energy levels and other symptoms much more quickly than simply by taking iron tablets. The risks to participants are few as the procedures are safe and well-tolerated. Possible side effects are that the patients may experience shortness of breath, headache and nausea. From the iron solution they may have allergic reaction or experience a bitter taste in the mouth.

Where is the study run from?
Churchill Hospital, Oxford, UK.

When is the study starting and how long is it expected to run for?
This study runs from March 2015 onwards for 2 years.

Who is funding the study?
The Oxford Biomedical Research Centre (BRC), UK.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-002952-17

Protocol serial number
IronCOPD

Study information

Scientific Title
Effects of intravenous iron in COPD

Study objectives
Current hypothesis as of 28/09/2015:
To determine whether intravenous iron improves arterial oxygen saturation in patients with COPD at one week following an infusion of iron compared to saline control (primary endpoint).

Previous hypothesis:
To determine whether intravenous iron attenuates the pulmonary arterial systolic pressure rise (PASP) with a long (6-hour) hypoxic exposure in COPD immediately following an infusion of iron compared to saline control (primary endpoint), as we have previously demonstrated to be the case in normal, healthy volunteers.

On 28/09/2015 the following changes were made to the trial record:
1. The overall trial start date was changed from 25/03/2013 to 01/03/2015.
2. The overall trial end date was changed from 30/06/2016 to 31/03/2017.
3. The target number of participants was changed from 24 to 48.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central Berkshire, 01/10/2012, REC ref: 12/SC/0539

Study design
Randomised single-blind study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Current interventions as of 28/09/2015:
Iron or saline infusion at baseline visit via a drip over 15 minutes. The dose is dependent on the patient’s weight.

Dose: 15 mg/kg up to 1000 mg ferric carboxymaltose (Ferinject®) in 250 ml saline or 250 ml saline

Previous interventions:
Iron or saline infusion at day 1 via a drip over 15 minutes and at weeks 1 & 4 via a slow injection. The dose is dependent on the patient's weight.

The hypoxic exposure: patients will have a practice hypoxic exposure at the screening visit. At baseline a short hypoxic exposure of 10-20 minutes and a long hypoxic exposure of 8 hours. They will also have a long hypoxic exposure at day 1 and at week 8.

Dose: 15 mg/kg up to 1000 mg fcm on day 1, then 200 mg bolus top ups up to x2. saline in analogy

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measures as of 28/09/2015:
Peripheral arterial oxygen saturation at one week at rest using pulse oximetry

Previous primary outcome measures:
Change in PASP from baseline to day 1 (immediately post infusion) in the iron group compared to the saline group

Key secondary outcome(s))
Current secondary outcome measures as of 28/09/2015:
Change in oxygenation, patient-orientated outcome measures, haematinics and physiological parameters from baseline to weeks 1 and 8 in the iron compared to the saline group:
1. Peripheral arterial oxygen saturation at rest at 8 weeks using pulse oximetry
2. Patient's daily home arterial oxygen saturation
3. Capillary or arterial blood gas oxygen saturation at rest
4. Peripheral arterial oxygen saturation at beginning and end exercise (6MWT)
5. Overnight peripheral arterial oxygen saturation with continuous pulse oximetry
6. Distance walked during the 6-minute walk test (6MWT)
7. Quality of life
8. Dyspnoea indices
9. Echocardiography measures – includes pulmonary arterial systolic pressure if measurable
10. Laboratory tests - haematinics, hepcidin, erythropoietin, haemoglobin and inflammatory markers such as C-reactive protein and interleukin-6
11. Forced expiratory volume in one second (FEV1)
12. Time to first exacerbation from daily diary cards
13. Observation of change in sputum microbiology, differential cell count and biomarkers

Previous secondary outcome measures:
Changes in cardiopulmonary factors during the long hypoxic exposure from baseline to day 1 and week 8, change in patient orientated outcome measures (exercise tolerance, quality of life, dyspnoea and time to infective exacerbation), blood parameters and physiological measures (forced expiratory volume in one second and blood gas parameters) from baseline to weeks 1, 4 and 8 in the iron group compared to the saline group.

Completion date
31/03/2017

Eligibility

Key inclusion criteria
Current inclusion criteria as of 28/09/2015:
1. Patients with a diagnosis of COPD, with at least mild disease (stage II – IV on GOLD criteria classification, FEV1 <80% predicted and FEV1/ FVC <70%)
2. Significant smoking history (>15 pack years, where a pack year is the product of [average number of cigarettes smoked per day] and [number of years smoked for] divided by 20) or other definite cause of COPD
3. Stable COPD for at least four weeks at study initiation
5. Able (in the Investigators opinion) and willing to comply with all study requirements.
5. Participant is willing and able to give informed consent for participation in the study.
6. Male or Female, aged 18 years or above.

Previous inclusion criteria:
1. Patients with a diagnosis of COPD, with at least mild disease (stage II - IV on GOLD criteria classification, FEV1 <80% predicted and FEV1/ FVC <70%)
2. Significant smoking history (>15 pack years, where a pack year is the product of [average number of cigarettes smoked per day] and [number of years smoked for] divided by 20) or other definite cause of COPD
3. Potential to have stable COPD at study initiation
4. Pulmonary arterial systolic pressure measurable on echocardiogram
5. Able (in the Investigators opinion) and willing to comply with all study requirements.
5. Participant is willing and able to give informed consent for participation in the study.
6. Male or Female, aged 18 years or above.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
48

Key exclusion criteria
Current exclusion criteria as of 28/09/2015:
The participant may not participate in the study if ANY of the following apply:
1. Female participants who are pregnant, lactating, planning pregnancy during the course of the study or of childbearing potential unless using effective contraception for the duration of the study.

2. Patients taking iron supplements (in the last six weeks) or who have had a blood transfusion in the last 6 months
3. Iron over-load, defined as ferritin >300mcg/ L
4. Hypersensitivity to previous iron infusion
5. Evidence of bacteraemia
6. Significant renal or liver disease (as judged by the investigator)

Previous exclusion criteria:
The participant may not participate in the study if ANY of the following apply:
1. Arterial oxygen saturations <90%
2. Unstable heart disease, or other contra-indication to hypoxic exposure
3. Female participants who are pregnant, lactating, planning pregnancy during the course of the study or of childbearing potential unless using effective contraception for the duration of the study
4. Oral iron, blood transfusion or altitude exposure within six weeks
5. Iron over-load, defined as ferritin >300mcg/ L
6. Hypersensitivity to previous iron infusion
7. Unable to tolerate exposure to hypoxia
8. Evidence of bacteraemia, such as fevers or systemic symptoms
9. Significant renal or liver disease

Date of first enrolment
01/03/2015

Date of final enrolment
31/03/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
University of Oxford (UK)

ROR

https://ror.org/052gg0110

Funder(s)

Funder type
Research organisation

Funder Name
Oxford Biomedical Research Centre (BRC) (UK) BRC reference A93127

Results and Publications

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?
Results article	results	01/06/2020	23/06/2020	Yes	No
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No