ISRCTN13007439 https://doi.org/10.1186/ISRCTN13007439

Treatment of iron deficiency anaemia in pregnancy study

Submission date	Recruitment status	[ ] Prospectively registered
20/02/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
25/06/2019	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
12/09/2023	Haematological Disorders	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Over a third of pregnant women are anaemic by their third trimester of pregnancy. The most common cause is iron deficiency (low iron in the blood). The main reason is rising iron requirements throughout pregnancy. Anaemia can make pregnant women feel tired and unwell. There is some evidence that anaemia may also increases the risk of babies being born prematurely and/or underweight. The evidence shows that anaemia could also be a risk factor for stillbirth and neonatal death. It can also be a real problem around the time of delivery if a mother bleeds when she is already anaemic. This increases the chance of her anaemia carrying on after pregnancy leading to more risk of infections and problems with breast feeding. Also, in more severe cases there will be more need for a blood transfusion.

Although we know how to treat this type of anaemia we don't know how effective the treatment is, or how severe the side effects are for pregnant women. In fact, we know that many pregnant women are troubled by these side effects and thus don't take the iron in the recommended way. This study aims to better understand anaemia and how to use oral iron therapy for iron deficiency anaemia in pregnant women. This includes recording the effect of treatment on anaemia symptoms, side effects, and the level of success of iron therapy using several blood tests.

Who can participate?
Anaemic pregnant women and those anaemic up to 6 weeks postpartum are invited to participate in this study and treated using an iron treatment schedule as described in national guidelines.

What does the study involve?
Blood samples for routine care and research will be taken at each clinic visit and tested to better understand iron metabolism and to better predict the response to oral iron therapy during pregnancy. Women will be asked to complete three short questionnaires at each visit and complete a symptoms diary for 2-4 weeks whilst taking iron tablets.

What are the possible benefits and risks of participating?
There is no risk to women and their fetus in taking part in this study as we are following routine

standard care and treatment of anaemia. There may be some inconvenience in completing the study diary and questionnaires. Some women might suffer side effects from the iron tablets, but they will be closely monitored by the research doctor who will give further advice on what to do.

Where is the study run from?
This study is run from the Royal Wolverhampton NHS Trust .

When is the study starting and how long is it expected to run for?
June 2018 to March 2020

Who is funding the study?
Rotha Abraham Trust

Who is the main contact?
Mr David Churchill
david.churchill1@nhs.net

Prof Simon Stanworth
simon.stanworth@nhsbt.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Mr David Churchill

ORCID ID
http://orcid.org/0000-0003-0548-2953

Contact details
The Royal Wolverhampton NHS Trust, New Cross Hospital,
Wolverhampton,
United Kingdom
WV10 0QP
01902 695153
david.churchill1@nhs.net

Type(s)
Scientific

Contact name
Prof Simon Stanworth

ORCID ID
http://orcid.org/0000-0002-7414-4950

Contact details
Department of Haematology,
Consultant Haematologist,

Oxford University Hospitals NHS Foundation Trust/NHSBT,
Level 2, John Radcliffe Hospital,
Headley Way,
Headington
Oxford
United Kingdom
OX3 9BQ
+44 (0)1865
simon.stanworth@nhsbt.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03725150

Secondary identifying numbers
2018OBS100

Study information

Scientific Title
Iron deficiency anaemia in pregnancy: an observational study of tolerability, compliance with oral iron therapy and effects on haematological/biochemical markers

Acronym
TIAP

Study objectives
To better define the natural history and understand how to use oral iron therapy for iron deficiency anaemia in pregnant women. Specifically, the study will document the impact of treatment on symptomatology, the induction of side effects, and the utility of several haematological indices; haemoglobin, ferritin, transferrin saturation, reticulocyte haemoglobin concentration, alongside changes in new markers of iron homeostasis (hepcidin), which may better predict the success of treatment with iron.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/04/2018, the West Midlands - Black Country Research Ethics Committee (West Midlands - Black Country Research Ethics Committee, The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; 0207 1048106, 0207 104 8102; nrescommittee.westmidlands-blackcountry@nhs.net), ref: 18/WM/0090.

Study design

Prospective cohort study.

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
See study outputs table

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

Interventions
This study is an observational study of practice.

Anaemic pregnant women will be invited to participate in a study aiming to assess response and tolerability to current doses and schedules for oral iron, as recommended in national (BSH) guidelines. At follow-up clinic visits a full blood count will be performed as per standard care. The following assessment/tests will also be performed as part of this study:
1. Blood samples will be taken for subsequent detailed analysis of pathways of iron metabolism.
2. Participants will be asked to complete Quality of Life questionnaires (The World Health Organisation- Five Well-Being Index (WHO-5), and the Well-being in Pregnancy (WiP) questionnaire.)
3. An additional Questionnaire to investigate the barriers and enablers to taking oral iron therapy
4. Participants will be asked to complete a tolerability and symptom diary

Pregnancy and fetal outcome data will also be collected 8 weeks after birth. These data are collected routinely for this group of women.

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ferrous sulphate

Primary outcome measure

The proportion of pregnant women who meet the criteria for a clinical response, defined as an increase in haemoglobin concentration of 10g/l measured using serum haemoglobin concentration at baseline and 2-4 weeks after the onset of iron therapy.

Secondary outcome measures
1. The change in frequency and severity of symptoms associated with anaemia in pregnancy measured using The 'Anaemia in Pregnancy Assessment Questionnaire' at baseline and any subsequent visit/s (depending on how many visits required but a minimum of one visit measurement is required at 2-4 weeks after the onset of iron therapy).
2. The frequency and severity of side effects induced by iron therapy to treat anaemia measured using tolerability and symptom diary at baseline and any subsequent visit/s (depending on how many visits required but a minimum of one visit measurement is required at 2-4 weeks after the onset of iron therapy).
3. A measurement of compliance with currently recommended oral iron regimens prescribed in pregnancy measured using tolerability and symptom diary and the need for dose adjustments in line with BSCH guidelines at baseline and any subsequent visit/s (depending on how many visits required but a minimum of one visit measurement is required at 2-4 weeks after the onset of iron therapy)
4. To document the longitudinal changes in haemoglobin, red cell indices, iron, transferrin, ferritin, CRP, during a treatment course of oral iron measured using serum haemoglobin, red cell indices, iron, transferrin, ferritin, CRP concentration at baseline and any subsequent visit/s (depending on how many visits required but a minimum of one visit measurement is required at 2-4 weeks after the onset of iron therapy).
5. To investigate the changes in research biomarker serum hepcidin, and whether it can predict the response to oral iron measured by serum hepcidin at baseline and any subsequent visit/s (depending on how many visits required but a minimum of one visit measurement is required at 2-4 weeks after the onset of iron therapy).

Overall study start date
01/12/2017

Completion date
01/03/2020

Eligibility

Key inclusion criteria
1. Pregnant women (any stage during pregnancy up to 36 weeks) and women in the puerperium (within 6 weeks post-delivery)
2. Anaemia as defined by WHO criteria and described in British Society Haematology (BSH)/ British Committee for standards in Haematology (BCSH) guidelines.
2.1. First trimester < 110g/l
2.2. Second and third trimester < 105g/l
2.3. Puerperium < 100g/l
3. Age: 18-45 years

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants
120

Total final enrolment
111

Key exclusion criteria
1. Presenting at or after 36 weeks
2. Affected by a (major) haemoglobinopathy e.g. B thalassaemia major sickle cell disease
3. Overt clinical signs of sepsis
4. Allergies to iron
5. Hyperemesis Gravidarum / persistent vomiting
6. Inflammatory conditions such as Crohns, ulcerative colitis, Systemic lupus erythematosus, Rheumatoid arthritis.
7. Chronic renal failure

Date of first enrolment
01/06/2018

Date of final enrolment
01/12/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Wolverhampton Hospitals NHS Trust
New Cross Hospital,
Wolverhampton,
United Kingdom
WV10 0QP

Sponsor information

Organisation
The Royal Wolverhampton NHS Trust,

Sponsor details
Research & Development, The Chestnuts (Building 9), New Cross Hospital,
Wolverhampton,
England
United Kingdom
WV10 0QP
01902 695065
sarah.glover7@nhs.net

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05pjd0m90

Funder(s)

Funder type
Charity

Funder Name
Rotha Abraham Trust

Results and Publications

Publication and dissemination plan
The main report of this trial and any associated papers will be submitted for publication in high impact peer review journals within a year of study completion. In addition, results will be presented at national and international meetings/conferences.

Intention to publish date
31/10/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Mr David Churchill (david.churchill1@nhs.net) once the study write up and publications have been completed. The data will become available in 2021 once all the analyses and publications have been completed. It will be available for individual patient systematic

reviews. Consent was not obtained from the participants who would need to be contacted by those wishing to utilise the data. These data are anonymised.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V1.2	24/05/2018	25/06/2019	No	Yes
Protocol file	version 1.2	04/05/2018	25/10/2022	No	No
HRA research summary			28/06/2023	No	No