ISRCTN51426226 https://doi.org/10.1186/ISRCTN51426226

Treatment of Nigerian women with Iron by drip or iron tablets taken by mouth, for low blood level, hours after delivery

Submission date
22/09/2022

Recruitment status
No longer recruiting

Registration date
03/10/2022

Overall study status
Completed

Last Edited
04/04/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Iron deficiency anaemia is a condition where a lack of iron in the body leads to fewer red blood cells. Anaemia is a public health burden with a high incidence in Africa. Iron deficiency anaemia is often treated with high-dose iron tablets taken by mouth if it is mild or moderate in severity, while blood transfusion is give in severe cases of anaemia. Some women do not tolerate the tablets well as they may develop side effects like constipation, stomach pain, nausea or vomiting. Others forget to use the oral iron tablets and hence the blood levels still remain low. There are iron preparations in existence that can be given in infusion (drip) form and have been found to be safe, and their use for the treatment of iron deficiency anaemia after delivery is currently being studied. The aim of this study is to compare the effectiveness of ferric carboxymaltose (FCM) given as an infusion through a vein and oral ferrous sulphate (FS) taken by mouth for treating iron-deficiency anaemia in women after delivery, and to compare the acceptability of these two forms of iron preparation in Nigerian women with moderate or severe iron deficiency anaemia after delivery.

Who can participate?
Women aged between 15 and 49 who are anaemic (haemoglobin concentration <10 g/dL), and within 6-48 hours of delivery.

What does the study involve?
Information will be collected about the participants' health and delivery, after which blood samples will be taken for some tests which include iron studies, serum phosphate, and complete blood count. Participants will be randomly allocated to one of two drug treatment arms (FCM or FS group). Women in the FCM arm will be given ferric carboxymaltose in 200 ml of normal saline infusion (drip) and this will be given through the woman's vein over 20 minutes. Women in the FS arm will be started on ferrous sulphate tablets which will be given as one 200 mg tablet (containing 65 mg of elemental iron) twice a day until 6 weeks after delivery. They will be checked on the postnatal wards until discharge from hospital, and then followed up at the hospital or home at 2 weeks, 6 weeks, 3 months, and 6 months after delivery. During the follow-ups, questions about her health and that of their newborn will be asked, vital signs will be

checked, specimens will be collected for investigation, and they will be assessed for depression, fatigue, maternal-to-infant bonding and quality of life at various intervals.

What are the possible benefits and risks of participating?
The study drugs to be used have been found to be safe in women after delivery and while breastfeeding. They may reduce the need for blood transfusion in women with low blood levels. Although, it is still possible to suffer some side effects from any of the medications like nausea, vomiting, and diarrhoea to any of the two study drugs. Participants will be monitored closely to identify any side effects and will be treated at no cost. All the study drugs will be given free of charge and all the tests relating to this research will also be done for free. Participants will be given contacts of their caregivers and will be sent regular reminders about their appointments. The findings of this study will improve the knowledge about the treatment of anaemia in women after delivery. This is planned to lead to the possible change of existing treatments, with improvement in the well-being of women after delivery and their newborns.

Where is the study run from?
University of Lagos (Nigeria)

When is the study starting and how long is it expected to run for?
February 2022 to December 2024

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Prof. Bosede B. Afolabi, bbafolabi@unilag.edu.ng

Study website
http://www.ivonpptrial.com

Contact information

Type(s)
Scientific

Contact name
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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2021-002867-23

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
01/2.0

Study information

Scientific Title
Intravenous ferric carboxymaltose versus oral ferrous sulphate for the treatment of moderate to severe postpartum anaemia in Nigerian women

Acronym
IVON-PP

Study objectives
Hypothesis 1: Intravenous ferric carboxymaltose is effective, tolerable and safe in treating iron deficiency anaemia in postpartum women compared with oral ferrous sulphate.
Hypothesis 2: Intravenous ferric carboxymaltose is acceptable and feasible for use in treating postpartum iron deficiency anaemia in Nigeria compared with oral ferrous sulphate.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 01/03/2022, Lagos University Teaching Hospital Health Research and Ethics Committee (Room 107, 1st Floor, LUTH administrative block, Surulere, Lagos, Nigeria; +234 (0) 15850737, +234 (0)15852187, +234(0)15852209, +234(0) 15852158, +234(0)15852111; luthethics@yahoo.com), ref: ADM/DCST/HREC/APP/4908
2. Approved 07/09/2022, National Health Research and Ethics Committee (11th Floor, Federal Secretariat Complex Phase III, Amadu Bello Way, Abuja, Nigeria; +234 (0)9 523-8367; chairman@nhrec.net), ref: NHREC/01/01/2007
3. Approved 08/09/2022, National Agency for Food Drug Administration and Control (NAFDAC)(Plot 1, Isolo Industrial Scheme, Oshodi-Apapa Expressway, Isolo, Lagos, Nigeria; +234 (0)9 523-8367; der.headquarters@nafdac.gov.ng), ref: NAFDAC/DER/VCTD/IVON-PP/2022/01
4. Approved 26/07/2022, Lagos State Ministry of Health (LSMH) (Block 4, The Secretariat, Alausa, Ikeja, P.M.B 21007, Ikeja; no telephone number provided; health.lagosstate.gov.ng) ref: LSMH /6649/I/120
5. Approved 30/06/2022, Rivers State Health Research Ethics Committee (26 Okoroma street, Port Harcourt, Nigeria; +234 (0)84230828; rshmbph@yahoo.com), ref: RSHMB/RSHREC/2022/021
6. Approved 08/07/2022, Kano State of Nigeria Ministry of Health, Health Research Ethics Committee (2nd & 3rd floor, Post Office road, Kano State, Nigeria; +234 (0)8039472476; moh. kano2019@gmail.com), ref: NHREC/17/03//2018
7. Approved 20/07/2022, University of Port Harcourt Teaching Hospital Research Ethics Committee (P.M.B 6176, Port Harcourt, Nigeria; no telephone number provided; no email provided), ref: UPTH/ADM/90/S.II/VOL.XI/1394)
8. Approved 04/08/2022, Kwara State Ministry of Health Ethical Research Committee (ERC) (P.M. B 1386, Fate road, Ilorin, Kwara state, Nigeria; no telephone number provided; no email provided) ref: ERC/MOH/2022/08/068

Study design
Multicenter interventional parallel open-label individually randomized controlled trial with an implementation study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

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

Interventions
Postpartum women during 6-48 hours of delivery will be screened. Eligible women on the ward will be individually randomized in a 1:1 ratio to receive either intravenous ferric carboxymaltose or oral iron. The baseline biodata of the participant will be entered into "REDCap" and "Sealed envelope" will generate the randomisation code for each participant. The drugs have been pre-supplied and stored according to the manufacturer's standard on site. Research staff depending on the arm the participant is randomised into will administer the drug. The intervention group will receive ferric carboxymaltose, a single dose of 20 mg/kg up to a maximum of 1000 mg. This dose will be administered as an infusion in 200 ml 0.9% sodium chloride and infused over a minimum of 15 - 20 minutes. Thereafter, they will be observed closely for a minimum of 30 minutes after infusion. The control group will receive oral ferrous sulphate 200 mg (65 mg elemental iron), to be taken two times daily; 1 hour before meals or 2 hours after meals with a full glass of water till 6 weeks postpartum. All participants will be followed up subsequently till 6 months postpartum.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Current primary outcome measure as of 31/07/2024:

Proportion of participants who are anemic at six weeks postpartum. An anemic state is defined as hemoglobin level of < 11.0 g/dL, measured using haemoglobin levels at 6weeks postpartum

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Previous primary outcome measure:

Proportion of participants who are non-anaemic at six weeks postpartum. Non-anaemic state is defined as haemoglobin level ≥ 11.0g/dl, measured using haemoglobin levels at 6weeks postpartum

Secondary outcome measures
1. Proportion of women with postpartum depression, measured using the Edinburgh Postnatal Depression Scale at six weeks and six months postpartum.
2. Change in mean postpartum haemoglobin levels at two weeks and six weeks postpartum, measured using haemoglobin levels at two weeks and six weeks.
3. Achievement of a non-anaemic state (Hb≥11.0g/dl) at six months postpartum, measured using haemoglobin levels at six months.
4. Prevalence of moderate/severe anaemia at six weeks and six months postpartum, measured using haemoglobin levels at six weeks and six months. Moderate anaemia is defined as haemoglobin level 7.0-9.9 g/dl and severe anaemia as haemoglobin level
5. Change in mean serum ferritin, serum transferrin, serum iron and % transferrin saturation at two weeks and six weeks postpartum.
6. Need for blood transfusion after iron treatment during the first 6 weeks postpartum.

7. Prevalence of fatigue at six weeks and six months postpartum, measured using the Fatigue Severity Scale (revised FSS-5R version).
8. Proportion of women with secondary postpartum haemorrhage after treatment. This will be defined as excessive bleeding requiring surgical intervention or blood transfusion from 24 hours after delivery till 12 weeks postpartum.
9. Proportion of infants being breastfed (exclusive and any) at six weeks and six months postpartum.
10. Prevalence of impaired maternal-infant bonding at six weeks and six months postpartum measured using the Mother-to-Infant Bonding Scale at six weeks and six months postpartum.
11. Incidence confirmed or suspected maternal infection within 6 weeks of birth, as defined by a new prescription of antibiotics for presumed perineal wound-related infection, endometritis or uterine infection, urinary tract infection or other systemic infection (clinical sepsis).
12. Incidence of hypophosphatemia at two weeks and six weeks postpartum. Measurement of vitamin D, alkaline phosphatase, P1NP, FGF23, Ca, PO4, which are biomarkers of phosphorus homeostasis and bone turnover at two weeks and six weeks postpartum. Hypophosphatemia is defined as serum phosphate level < 1 mg/dL (0.32 mmol/L).
13. Incidence of early neonatal death, defined as death of new-born from enrolment of the mother to before 7 completed days.
14. Incidence of late neonatal death, defined as death of the new-born from enrolment of the mother to before 28 completed days.
15. Incidence of infant death, defined as death from enrolment before the age of six months.
16. Incidence of post-natal maternal death from enrolment up to 6 weeks and at 6 months postpartum.
17. Incidence of adverse drug events.
18. Quality of life measured using the WHOQOL BREF at enrolment, 6 weeks, and 6 months postpartum.

Overall study start date
01/02/2022

Completion date
18/12/2024

Eligibility

Key inclusion criteria
1. Women aged between 15 and 49 years
2. Between 6 and 48 hours after delivery
3. Baseline (enrollment) moderate or severe anemia (Hb ≤ 9.9g/dl), confirmed by Hemocue haemoglobinometer
4. Able and willing to give written informed consent

Participant type(s)
Patient

Age group
Mixed

Lower age limit
15 Years

Upper age limit
49 Years

Sex
Female

Target number of participants
1400

Total final enrolment
1400

Key exclusion criteria
1. Having received a blood transfusion, for any indication, within the last 3 months
2. Symptomatic anemia and a need for urgent correction
3. Known haemoglobinopathy such as sickle cell disease, HbCC disease
4. Clinically confirmed malabsorption syndrome
5. Known hypersensitivity or contraindication to any form of iron treatment, study drug or any of its excipients
6. Self-reported pre-existing maternal depression or other psychiatric illness and as evidenced by a YES response to any past history of psychiatry ward hospitalization, psychiatry medications, behavioral changes, or past consultation with psychiatry services
7. Severe allergic conditions such as severe asthma, eczema or other atopic condition
8. Known autoimmune conditions e.g., systemic lupus erythematosus, rheumatoid arthritis or known severe drug allergies.
9. Planning to move or reside outside the research area

Date of first enrolment
28/11/2022

Date of final enrolment
03/07/2024

Locations

Countries of recruitment
Nigeria

Study participating centre
Lagos University Teaching Hospital
Idi-Araba
Lagos
Nigeria
100254

Study participating centre

Mother and Child Centre
1st Avenue 1st Gate
Festac Town
Amuwo-Odofin
Lagos
Nigeria
102102

Study participating centre
Mother and Child Centre
Gbaja St
Surulere
Lagos
Nigeria
101283

Study participating centre
General Hospital
14 College Road
Iju Road
Ifako-Ijaye
Lagos
Nigeria
101232

Study participating centre
Ipaja Primary Health Centre
Alimosho L.G.A.
Idimu
Lagos
Nigeria
100278

Study participating centre
University of Port Harcourt Teaching Hospital (UPTH)
East-West Rd
Port Harcourt
Rivers
Nigeria
500102

Study participating centre
Okrika General Hospital
Abuloma Port Harcourt
Rivers
Nigeria
501101

Study participating centre
Bori General Hospital
Hospital Road
Bori
Notem
Rivers
Nigeria
502101

Study participating centre
Ahoada General Hospital
Omoku-Obrikom Rd
Omoku
Rivers
Nigeria
510101

Study participating centre
Model Primary Health Centre
Ede Okia Community Road
Abuloma
Port Harcourt
Rivers
Nigeria
500102

Study participating centre
Aminu Kano Teaching Hospital
Zaria Road
Kano
Nigeria
700233

Study participating centre

Waziri Gidado General Hospital
Rijiyar Lemo
Kano,
Nigeria
700252

Study participating centre
Nuhu Bammali General Hospital
Emir Palace Rd
Kofar Nassarawa
Kano
Nigeria
700224

Study participating centre
Sheik Jeddah General Hospital
Murtala Mohammed Road
Kano
Nigeria
700271

Study participating centre
Kabuga Primary Health Care Center
Gwarzo Road
Kofar Dukayuwa
Kano
Nigeria
700282

Study participating centre
University of Ilorin Teaching Hospital (UITH)
Old Jebba Road
Oke Ose
Ilorin
Kwara
Nigeria
241102

Study participating centre
General Hospital Ilorin
5 Unity Rd

Ilorin
Kwara
Nigeria
240101

Study participating centre
Adewole Cottage Hospital
Adewole Road
Along Yebmot Hotel
Ilorin
Kwara
Nigeria
240101

Study participating centre
Civil Service Hospital
Ilofa Road GRA
Ilorin
Kwara
Nigeria
240101

Study participating centre
Okelele Health Center
Abayawo Road
Ilorin
Kwara
Nigeria
240101

Sponsor information

Organisation
University of Lagos

Sponsor details
College of Medicine
Lagos
Nigeria

12003
+234 (0)8023002960
provost@cmul.edu.ng

Sponsor type
University/education

Website
http://www.unilag.edu.ng/

ROR
https://ror.org/05rk03822

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Publication and dissemination plan
The study results will be used in preparing charts for health education and counselling of women at the antenatal clinics and postnatal wards. The findings of the study will be presented at conferences (both international and local) to disseminate them to a large body of professionals in the field of obstetrics and gynaecology, haematology, internal medicine, paediatrics, etc. The findings will also be published in high-impact peer-reviewed journals for wider dissemination of information. Press releases about the findings of the study will be issued.

Intention to publish date
30/12/2025

Individual participant data (IPD) sharing plan

The researchers will deposit the research data in the Open Science Framework. The data will be deidentified to maintain participants' confidentiality. The data will be shared at the time of publication of the first manuscript. This will likely be done within 6 months of study completion. The duration of IPD sharing will be 2 years.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1		03/10/2022	No	Yes
Protocol file	version 1.3	26/09/2022	03/10/2022	No	No
Protocol file	version 1.4	30/11/2022	09/02/2023	No	No
Protocol file	version 2.0	18/01/2024	12/03/2024	No	No
Statistical Analysis Plan		13/03/2025	04/04/2025	No	No