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Hepcidin and Anaemia in Pregnancy (HAPn)

Submission date
19/03/2014

Recruitment status
No longer recruiting

Registration date
14/04/2014

Overall study status
Completed

Last Edited
15/10/2019

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Iron supplementation is recommended for all pregnant women in those places where anaemia (iron deficiency) rates exceed 40%. Recent studies show this can pose a risk to pregnant women. Therefore, there is a need to explore screen-and-treat options to minimise iron exposure during pregnancy. This can be done using an overall lower dosage of iron that would achieve similar results as the standard recommendation. However, we dont know how to best assess iron deficiency when infections are prevalent. The level of the hormone hepcidin is thought to indicate whether it is safe to receive iron. This initial study will lead to a larger study to find out if a screen-and-treat approach to iron supplementation using hepcidin levels will prevent anaemia at a lower iron dose, hence improving safety.

Who can participate?
Pregnant women, 14 22 weeks into pregnancy, coming to participating Reproductive and Child Health Clinics (RCH) can take part.

What does the study involve?
After taking an initial blood sample from the vein and assessing the age of their pregnancy, each participant is randomly allocated into one of the three study groups, to either receive: (a) UNICEF /WHO/UNU international multiple micronutrient preparation (UNIMMAP) containing 60 mg/day iron (reference group); (b) UNIMMAP containing 60 mg/day iron but based on a weekly hepcidin screening to tell if iron should be given for the next 7 days or not; (c) UNIMMAP containing 30 mg /day iron as in (b) for 12 weeks in rural Gambia. Each week, finger prick blood samples will be taken to find out the hepcidin level, haemoglobin (Hb) level and test for malaria. During the 12-week follow-up, additional blood samples are taken and side-effects and any other health issues are assessed. Although active participation finishes at the end of the supplementation period, a last investigation regarding pregnancy outcome will be made after delivery. This will include a postnatal check-up to monitor the mothers general condition after delivery and assessment of babies. All participants will be provided with long-lasting insecticide-treated nets (LLINs).

What are the possible benefits and risks of participating?
Benefits will include study participants having access to basic medical services for free. Participants will benefit from weekly monitoring by qualified field workers where anaemia can be detected. Malaria can also be diagnosed and managed. There are risks associated with a large intake of iron supplement. However, the reference group of this study takes iron as per standard

government practice and the other two groups take an overall lower dose of iron. This will decrease the risk of over dosage. If those in group (c) are moderately anaemic (borderline severe anaemia), they may be at risk of receiving too little iron but will be monitored every week and if seen to become severely anaemic, will be treated as per Gambia Government recommendation for management of severe anaemia. The UNIMMAP formulation has been used in other pregnancy studies in developing countries with good patient compliance and acceptability. No emergency is expected from taking this supplement. However, a study nurse will always be available who will decide whether to refer a participant to a health facility in case this is necessary.

Where is the study run from?
This study will be run from 12 communities in Jarra West and Kiang East of Rural Gambia.

When is the study starting and how long is it expected to run for?
The study starts in April 2014 and will finish enrolment within about 1 year.

Who is funding the study?
Medical Research Council (MRC) (UK) and the Bill & Melinda Gates Foundation (USA).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
SCC 1357v3

Study information

Scientific Title
A double-blind randomised controlled trial comparing standard dose of iron supplementation for pregnant women with two screen-and-treat approaches using hepcidin as a biomarker for ready and safe to receive iron

Acronym
HAPn

Study objectives
It is hypothesised that a screen-and-treat approach to iron supplementation will achieve similar efficacy in combating iron deficiency (ID) and iron deficiency anaemia (IDA) at a lower overall dosage of iron (with the assumption that this will improve safety and tolerability).

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Gambia Government/MRC Joint Ethics Committee, 19/12/2013, ref. SCC 1357v3

Study design
Proof-of-concept three-arm double-blind randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Anaemia in pregnancy

Interventions
This study will involve 462 pregnant women between 14 and 22 weeks gestation over a period of 12 weeks randomly assigned (1:1:1 ratio) to either receive:
1. UNIMMAP containing 60 mg/day iron
2. UNIMMAP containing 60 mg/day iron but based on a weekly hepcidin screening indicating if iron can be given for the next 7 days or not
3. UNIMMAP containing 30 mg/day iron

Intervention product
The nutritional supplement to be used in this trial is the UNICEF/WHO/UNU international multiple micronutrient preparation (UNIMMAP). All formulations also contain 400 ug folic acid and 14 other micronutrients. Three investigational products will be administered:

UNIMMAP with 60 mg iron
UNIMMAP with 30 mg iron
UNIMMAP with 0 mg iron (for when iron is not needed).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Hepcidin

Primary outcome measure
Haemoglobin - defined as pregnancy stage adjusted haemoglobin at day 84

Secondary outcome measures
1. Proportion of anaemia (Hb < 11 g/dl) at day 84
2. Iron deficiency prevalence at day 84
3. Iron deficiency anaemia (IDA) prevalence at day 84
4. Iron dosage
5. Beneficial and adverse events
6. Compliance

Overall study start date
21/04/2014

Completion date
21/03/2015

Eligibility

Key inclusion criteria
1. Pregnant (gestational age between 14 - 22 weeks)
2. Age: 18 to 45 years
3. Likely to be resident in study area for duration of trial
4. Written informed consent obtained

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Female

Target number of participants
462

Total final enrolment
498

Key exclusion criteria
1. Severely anaemic (< 7 g/dl)
2. Seriously ill (infectious disease of clinical significance) at recruitment
3. Chronic disease
4. Pregnancy complications (e.g. pre-eclampsia) at enrolment
5. Already part of another study

Date of first enrolment
21/04/2014

Date of final enrolment
21/03/2015

Locations

Countries of recruitment
Gambia

Study participating centre
MRC International Nutrition Group
Banjul
Gambia
POBOX 273

Sponsor information

Organisation
The Medical Research Council (MRC) (UK)

Sponsor details
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Sponsor type
Research council

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) - International Nutrition Group

Funder Name
Bill & Melinda Gates Foundation (USA)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	13/07/2016		Yes	No
Results article	results	01/11/2019	15/10/2019	Yes	No