

Hepcidin and Anaemia in Pregnancy (HAPn)

Submission date 19/03/2014	Recruitment status No longer recruiting	☒ Prospectively registered ☒ Protocol
Registration date 14/04/2014	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 15/10/2019	Condition category Pregnancy and Childbirth	☐ 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 don't 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

Protocol serial number

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

Primary study design

Interventional

Study design

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

Study type(s)

Prevention

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(s)

Haemoglobin - defined as pregnancy stage adjusted haemoglobin at day 84

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

Female

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)

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

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