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STOPMiP: Intermittent Screening and Treatment Or intermittent Preventive therapy for the control of Malaria in Pregnancy in Indonesia

Submission date
29/04/2013

Recruitment status
No longer recruiting

Registration date
08/05/2013

Overall study status
Completed

Last Edited
30/07/2019

Condition category
Infections and Infestations

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Malaria in Indonesia is a substantial problem with approximately 35% of the population at risk and 10-14% of pregnant women being infected with malaria at any time. Pregnant women are a vulnerable group and both P.falciparum and P.vivax infections contribute to adverse effects of malaria in pregnancy. If you contract malaria during your pregnancy you can have devastating consequences resulting in fever which may trigger preterm labour or pregnancy loss. It is also possible for you to be infected without showing any outward signs or symptoms of malaria, yet if these infections are undetected and left untreated, they can cause anaemia in the mother and can interfere with the growth of the fetus leading to low birth weight, which increases the risk of babies dying during infancy.

Who can participate?
Women between 16-30 weeks of gestation with a viable pregnancy at antenatal visit and residing in the study area will be eligible to join the study.

What does the study involve?
The study will use three intervention methods to assess whether malaria infections in pregnancy and adverse effects associated with it can be reduced. One intervention will provide malaria testing to women with or without the symptoms of malaria at every scheduled antenatal visit. A rapid diagnostic test (RDT) will be used. The RDT is simple to perform, uses a single drop of blood and gives results within 15 minutes. If you test positive for malaria you will be treated with an artemisinin combination drug called dihydroartemisinin-piperaquine (DHP), which is the treatment of choice in the 2nd and 3rd trimester of pregnancy in Indonesia. This method is called intermittent screening and treatment for prevention of malaria in pregnancy (ISTp). A second method called intermittent preventive treatment (IPTp), which is used in most countries in Africa but not yet in Asia, will also be tested. With this method pregnant women regardless of malaria symptoms will be selected to receive the same drug but without prior blood testing. These new methods will be compared with the existing policy in Indonesia, where all pregnant

women are tested for malaria at the first antenatal visit only, and those with a positive result are treated with DHP in second and third trimester and with quinine in first trimester. During subsequent antenatal visits, women are tested only if they have symptoms of malaria such as fever. This means that some infections will go undetected. It is anticipated that the two new methods will either detect infections much earlier than the current approach, or prevent malaria altogether.

What are the possible benefits and risks of participating?
DHP is a very effective treatment for malaria in pregnancy. Experience in previous studies of more than 1200 pregnancies treated with DHP in second and third trimester found it a safe drug for the baby. However we will carefully monitor all babies born to the women in the study to see if the drug has any adverse effect on the pregnant or her baby. The findings of this study, together with an assessment of feasibility and cost effectiveness of each of the method stated above, will be used to inform malaria prevention policy for pregnant women in Indonesia and other parts of South East Asia. Those participating in the study will be tested for anaemia and malaria and receive free treatment for these conditions. Transport cost to attend antenatal care will be provided and every woman will receive a long lasting insecticide treated bed net at the time of enrolment. Participants will be followed from recruitment until 8 weeks after delivery.

Where is the study run from?
Women attending routine antenatal care in the community health facilities (Puskesmas) and community integrated health services (Posyandu) under the selected health facilities in SW Sumba and Timika in eastern Indonesia will be recruited. The Eijkman Institute for Molecular Biology (EI) in Jakarta will coordinate the trial and Liverpool School of Tropical Medicine (LSTM) is the Sponsor.

When is the study starting and how long is it expected to run for?
May 2013 to December 2016

Who is funding the study?
The trial is funded by the Medical Research Council (MRC)/Wellcome Trust/Department for International Development (DFID), under the Global Trial Health Schemes, UK

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Protocol serial number
Version 1.0

Study information

Scientific Title
Intermittent Screening and Treatment Or intermittent Preventing therapy for the control of Malaria in Pregnancy in Indonesia: an open label cluster randomised controlled superiority trial

Acronym
STOPMiP

Study objectives
Among pregnant women protected with long lasting insecticide treated bed nets (LLITNs), intermittent screening with rapid diagnostic tests (RDTs) at Antenatal care (ANC) visits provided at least 3 or more times during pregnancy and treatment of RDT positive women with dihydroartemisinin-piperaquine (ISTp-DHP), or intermittent preventive treatment with dihydroartemisinin-piperaquine (IPTp-DHP) is more efficacious than single screening and treatment (SSTp-DHP) in preventing malaria in pregnancy in an area of relatively low prevalence of P. falciparum and P. vivax.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Liverpool School of Tropical Medicine, 16/10/2012, Research Protocol ref: 12.28
2. London School of Hygiene and Tropical Medicine, 03/01/2013, ref: 6325
3. Eijkman Institute for Molecular Biology, Jakarta, 20/02/2013, ref: Project N: 57
4. Litbangkes, Ministry of Health, Jakarta (NIH), 01/03/2013, ref: LB02.01/5.2/KE059/2013

Study design
Open-label three-arm parallel-group cluster randomised superiority trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
SSTp-DHP: (control group): Participants in the 2nd or 3rd trimester will be screened with HRP2-pLDH combination RDT (Pf/Pan First Response®, Premier Medical Corporation Ltd, India) at 1st antenatal visit (booking visit) and RDT-positive women will receive treatment with DHP. In subsequent visits only women with symptoms of malaria will be tested with RDT. This is the usual care in Indonesia.

ISTp-DHP: Women in their 2nd-3rd trimester attending scheduled antenatal care will receive screening at each visit regardless of malaria symptoms with the study RDT and RDT positive women will receive treatment with DHP.

IPTp-DHP: Intermittent preventive treatment with DHP provided at least one month apart in 2nd-3rd trimester women attending for scheduled antenatal care.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Dihydroartemisinin-piperaquine (ISTp-DHP), dihydroartemisinin-piperaquine

Primary outcome(s)
Malaria infection at delivery (peripheral and or placental) detected by RDT, microscopy or polymerase chain reaction (PCR), or placental Histology (active) measured at the time when women deliver, except incidence of malaria which will occur anytime between enrolment and delivery when and if they are positive for malaria.

Key secondary outcome(s))
Efficacy
Individual components of composite primary outcome
1. Incidence of malaria infection by species measured by PCR (using dried blood spots)
2. Congenital malaria, defined as parasitaemia in cord or newborn peripheral blood in the first seven days of life detected by smear, RDT or PCR.
3. Composite of spontaneous births resulting in either low birth weight, preterm birth
4. Mean and Low birth weight
5. Mean Gestational age at birth, Preterm delivery (< 37 weeks) measured by using Ballard score
6. Small for gestational age (<10th percentile of WHO recommended reference)
7. Mean maternal haemoglobin and anaemia at 36 weeks and at delivery measured using HemoCue reading
8. Incidence all-cause and malaria clinic visits

9. Cord haemoglobin (Hb) and newborn anaemia
10. Neonatal deaths
11. Perinatal death

Tolerability and safety
1. Serious adverse events & adverse events
2. Congenital malformations in the newborn identified at birth and by 6 weeks afterbirth.

Completion date
26/11/2016

Eligibility

Key inclusion criteria
Pregnant women of any age and gravidity with:
1. Gestational age 16 to 30 weeks (inclusive) by last menstrual period (LMP) (if available) or fundal height or after quickening
2. Viable pregnancy (fetal heart sound detected, or other signs of fetal life such as perceived motion of fetus)
3. Willing to participate and complete the study schedule
4. Has provided written informed consent
5. Resident of study area and intending to stay in the area for the duration of the follow-up
6. Willing to give birth in a study selected health facility (Puskesmas, Polindes or hospital)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
2279

Key exclusion criteria
1. Residence outside study area or planning to move out in the 6 months following enrolment
2. Pre-existing conditions likely to cause complication in the current pregnancy (e.g. hypertension, diabetes, asthma, renal disease, liver disease, any spinal deformity)
3. Known allergy or previous adverse reaction to any of the study drugs based on information provided by the participant such as development of skin rash, severe nausea and vomiting
4. Requires cotrimoxazole prophylaxis for opportunistic infection (e.g. for women known to be HIV positive)
5. Treatment with antimalarials in the last month (e.g mefloquine, halofantrine, lumafantrine, chloroquine) or last week (quinine)
6. Unable to give informed consent (for example due to mental disability)

7. Severe malaria according to WHO definition requiring parenteral treatment
8. Family history of sudden death or of congenital prolongation of QTc interval, or known congenital prolongation of the QTc-interval or any known cardiac condition, such as history of symptomatic cardiac arrhythmia, bradycardia or congestive heart failure
9. Taking medicinal products that are known to prolong QTc interval

Date of first enrolment
16/05/2013

Date of final enrolment
21/04/2016

Locations

Countries of recruitment
United Kingdom

England

Indonesia

Study participating centre
Liverpool School of Tropical Medicine
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Sponsor information

Organisation
Liverpool School of Tropical Medicine (UK)

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Charity

Funder Name
Medical Research Council (MRC) (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Wellcome Trust (UK), grant ref: : 096476

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Funder Name
Department for International Development (DFID) (UK), ref: JGHT 165

Alternative Name(s)
Department for International Development, UK, DFID

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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	01/09/2019	30/07/2019	Yes	No