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The Antibiotics In Miscarriage Surgery (AIMS) trial

Submission date
26/03/2013

Recruitment status
No longer recruiting

Registration date
17/04/2013

Overall study status
Completed

Last Edited
14/08/2019

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
Infection following miscarriage surgery is a problem affecting over 33 million pregnancies each year. A majority of women will have their miscarriage managed with surgery to empty the womb. Infection can occur following this surgery and this is a particular problem in low income countries. In some low income countries the rates of infection following miscarriage surgery are as high as 30%. These infections can result in death, serious illness or long-term health problems. Currently international and national medical guidelines do not recommend antibiotics to be given routinely in miscarriage surgery, because there is no evidence that tells us that this works. If antibiotics are given just before the procedure of miscarriage surgery this may reduce the chance of infection occurring. The aim of this study is to test this in four low income countries.

Who can participate?
Women who have suffered a miscarriage and are scheduled to have their miscarriage managed surgically, through an operation to empty their uterus.

What does the study involve?
Participants are offered either a single dose of prophylactic antibiotics (doxycycline and metronidazole) or an identical looking dummy pill (placebo), to be taken by mouth before the surgery. Participants are followed for 2 weeks after surgery to see if there is any difference in the rate of women developing pelvic infection. If any women show signs of infection they are given full treatment as soon as it is detected. The study also assess whether using antibiotics before surgery is cost effective.

What are the possible benefits and risks of participating?
Those women taking part in the study may benefit by having their health followed very carefully after the surgery. The study team also facilitate these women receiving prompt treatment if there are any problems. Even if participants do not benefit personally they study may help improve care for women in the future. Risks of taking part include the small risk of side effects from doxycycline or metronidazole, but these medications have been selected because they have a low risk of serious side effects such as allergy.

Where is the study run from?
The study is being managed and sponsored by the University of Birmingham (UK). The study sites are:
1. Malawi: Queen Elizabeth Central Hospital, Zomba Central Hospital and Kamuzu Central Hospital
2. Uganda: Mbale Regional Referral Hospital and Soroti Regional Referral Hospital
3. Tanzania: St Francis Hospital, Mwananyamala Hospital and Bagamoyo District Hospital
4. Pakistan: Aga Khan University Main Hospital, Hyderabad Hospital, Garden Hospital, Kharader Hospital and Karimabad Hospital

When is the study starting and how long is it expected to run for?
September 2013 to May 2017

Who is funding the study?
The Medical Research Council, the Wellcome Trust and the Department for International Development (UK)

Who is the main contact?
Dr David Lissauer
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Study website
http://www.aimstrial.org/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RG_12-048

Study information

Scientific Title
Effectiveness of antibiotic prophylaxis during surgical evacuation of the uterus for miscarriage management in low income countries: a multinational, randomised, double-blind placebo-controlled trial

Acronym
AIMS

Study objectives
To test the hypothesis that in women having miscarriage surgery, pre-surgery prophylactic antibiotics (oral doxycycline 400 mg and oral metronidazole 400 mg) reduces the risk of pelvic infection within 14 days of surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. UK - Liverpool Ethics, 10/04/2013, protocol 13.15
2. Malawi - College of Medicine Research Ethics Committee, 11/10/2013, P.06/13/1393
3. Pakistan - Aga Khan University Research Ethics Committee, 11/11/2013, 2756-obs-erc-13
4. Pakistan - Drugs Regulatory Authority of Pakistan, 16/09/2014, F.6-1/2013
5. Tanzania - IHI IRB, 30/08/2013, IHI/IRB/no.25-2013
6. Tanzania - NIMRI, 01/11/2013, NIMRlHQ/R.8aJVol. IX/1652
7. Tanzania - TDFA, 04/08/2014, TFDAI4/CTR/001/03
8. Uganda - UNCST, 28/05/2014, HS 1400
9. Uganda - NDA, 06/12/2013, 347/ESR/NDA/DID-06/2013

Study design
Randomised double-blind placebo-controlled multi-national study with economic evaluation

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
http://www.aimstrial.org/patientinfo.aspx?lang=1

Health condition(s) or problem(s) studied
Infection, miscarriage, sepsis, antibiotic prophylaxis

Interventions
1. Doxycycline 400 mg oral and Metronidazole 400 mg oral, taken approximately 2 hours before the scheduled time of surgery
2. Placebo tablets of identical appearance and weight

Both the woman and health worker will not know which type of tablets they have been given. Participants are followed for 2 weeks after surgery to see if there is any difference in the rate of women developing pelvic infection. If any women show signs of infection they will be given full treatment as soon as it is detected. The study will also determine whether using antibiotics before surgery is cost effective.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Doxycycline, metronidazole

Primary outcome measure
Current primary outcome measures as of 27/01/2017:
Pelvic infection within 14* days of surgery, defined as two or more of:
1. Purulent vaginal discharge - on vaginal examination
2. Pyrexia >38.0°C - using a standardised tympanic thermometer
3. Tenderness on clinical examination
4. A white cell count >12x109/l , with no other recognised cause of infection
5. Or one of the above features, with the clinically identified need (following clinical assessment) to administer antibiotics for the treatment of presumed pelvic infection.
*In cases where participants do not return for follow up within this period, follow up until 28 days will be acceptable

Previous primary outcome measures:
Pelvic infection within 14 days of surgery, defined as two or more of:
1. Purulent vaginal discharge

2. Pyrexia >38.0°C
3. Uterine tenderness on examination and d) a white cell count >15x10^9 /l, with no other recognised cause of infection

Secondary outcome measures

Current secondary outcome measures as of 27/01/2017:
1. Secondary outcome measures:
Assessed at the follow-up appointment with a clinical assessment, history taking and reviewing available patient medical records:
1.1. Overall antibiotic use
1.2. Each component of the primary outcome
1.3. Death
1.4. Hospital admission
1.5. Unplanned consultations
1.6. Blood transfusion
1.7. Vomiting
1.8. Diarrhoea
1.9. Adverse events
1.10. Anaphylaxis and allergy
1.11. Duration of clinical symptoms (pain, additional analgesia, vaginal bleeding)
1.12. Days before return to usual daily activities
2. Outcomes for exploratory analyses:
2.1. Surgical complications
2.2. Full microbiological information, antibiotic sensitivities and any evidence of drug resistance will be collected where available
3. Resource use outcomes:
Resource use data will be prospectively collected to estimate the costs associated with the additional use of antibiotics in all participating centres in both arms of the trial. The main resources to be monitored include:
3.1. Additional staff time for explanation and dispensing of the medication
3.2. Type and grade of the health professional caring for each woman
3.3. Inpatient admissions and consultations (planned and unplanned)
3.4. Outpatient and emergency admissions and consultations
3.5. Unplanned further surgical interventions (e.g. curettage)
3.6. Additional investigation costs (e.g. ultrasounds)
3.7. Consumables (e.g. medication)
3.8. Resources used to manage surgery and treatment related complications (e.g. bleeding requiring transfusion)

Previous secondary outcome measures:
1. Secondary measures:
1.1. Death
1.2. Hospital admission
1.3. Unplanned consultations
1.4. Antibiotic use for presumed diagnosis of pelvic infection
1.5. Blood transfusion
1.6. Vomiting
1.7. Diarrhoea
1.8. Adverse events
1.9. Anaphylaxis and allergy
1.10. Duration of clinical symptoms (pain, additional analgesia, vaginal bleeding, days before

return to usual daily activities)
2. Outcomes for exploratory analyses:
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3.5. Unplanned further surgical interventions (e.g. curettage)
3.6. Additional investigation costs (e.g. ultrasounds)
3.7. Consumables (e.g. medication)
3.8. Resources used to manage surgery and treatment related complications (e.g. bleeding requiring transfusion)

Overall study start date
01/09/2013

Completion date
16/05/2017

Eligibility

Key inclusion criteria
1. Women with a spontaneous miscarriage (under 22 weeks gestation)
2. Women undergoing surgical evacuation of the uterus (by manual vacuum aspiration, suction curettage or sharp curettage)
3. Willing and able to give informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
3400

Total final enrolment
3412

Key exclusion criteria
1. Induced abortion of pregnancy
2. Septic miscarriage or evidence of infection
3. Allergy to either of the antibiotics
4. Current antibiotic use, or antibiotic use in the 7 days preceding surgical evacuation

5. Current febrile illness (temperature < 38oC)
7. Other contraindication to doxycycline or metronidazole use
8. Patient with condition requiring immediate care e.g. severe haemorrhage
9. Age less than 16 years

Date of first enrolment
02/06/2014

Date of final enrolment
26/04/2017

Locations

Countries of recruitment
Malawi

Pakistan

Tanzania

Uganda

Study participating centre
Queen Elizabeth Central Hospital
Malawi
-

Study participating centre
Zomba Central Hospital
Malawi
-

Study participating centre
Kamuzu Central Hospital
Malawi
-

Study participating centre
Mbale Regional Referral Hospital
Uganda
-

Study participating centre
Soroti Regional Referral Hospital
Uganda
-

Study participating centre
St Francis Hospital
Tanzania
-

Study participating centre
Mwananyamala Hospital
Tanzania
-

Study participating centre
Bagamoyo District Hospital
Tanzania
-

Study participating centre
Aga Khan University Main Hospital
Pakistan
-

Study participating centre
Hyderabad Hospital
Pakistan
-

Study participating centre
Garden Hospital
Pakistan
-

Study participating centre

Kharader Hospital
Pakistan
-

Study participating centre
Karimabad Hospital
Pakistan
-

Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
c/o Sean Jennings
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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Joint Global Health Trials Scheme

Funder Name

Medical Research Council (UK), grant ref: MR/J009792/1

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Wellcome Trust (UK), grant ref: 099943

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)

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

Publication and dissemination plan
Publication is planned in a high-impact peer reviewed journal within one year after the overall trial end date.

Intention to publish date

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	23/04/2018		Yes	No
Other publications	systematic review	08/05/2018		Yes	No
Results article	results	14/03/2019	14/03/2019	Yes	No
Other publications	cost-effectiveness analysis	01/09/2019	14/08/2019	Yes	No