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Role of hypovolaemia in the acidosis of severe malaria

Submission date
12/09/2005

Recruitment status
No longer recruiting

Registration date
14/10/2005

Overall study status
Completed

Last Edited
23/05/2014

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Shock is a medical emergency which occurs when there is not enough blood flow around the body. As a result of tissues not receiving enough oxygen, too much acid builds up in the body (metabolic acidosis). Children with severe malaria often have metabolic acidosis as a complication of shock. The usual treatment for shock is to replenish lost fluid (fluid resuscitation). We have shown previously that human albumin solution (HAS: a by-product of blood transfusion) safely corrects this acidosis and improves the outcome of children with severe malaria complicated by acidosis. HAS is currently expensive and not widely available in Africa. This study aims to examine the safety and dose required for the correction of acidosis of lower cost infusions called colloids: Gelofusine, Dextran 70 and Hetastarch. These will be compared to a control group of children receiving HAS. The results of this study will form the basis for the future larger trials comparing colloidal solutions with saline or maintenance alone, which are required before specific treatment recommendations can be made.

Who can participate?
Children aged over 3 months, either sex, who have severe falciparum malaria (impaired consciousness and or deep breathing) and metabolic acidosis.

What does the study involve?
Children will be randomly allocated to undergo fluid resuscitation with either HAS, Gelofusine, Dextran 70 or Hetastarch.

What are the possible benefits and risks of participating?
Children will be closely monitored and fluid will be administered cautiously.

Where is the study run from?
The study will be based at the KEMRI Centre for Geographic Medicine Research (Coast) at Kilifi District Hospital (KDH), Kenya.

When is the study starting and how long is it expected to run for?
The study started in December 2004 and ended in December 2008.

Who is funding the study?
The Wellcome Trust (UK).

Who is the main contact?
Professor Kathryn Maitland
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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
062258

Study information

Scientific Title
Role of hypovolaemia in the acidosis of severe malaria: a randomised controlled trial

Study objectives
This study adds to and extends the original aims of previous studies. In those we provided new, clear evidence for the presence of hypovolaemia in severe malaria and showed that this could be safely corrected by volume resuscitation with either 0.9% saline or 4.5% human albumin solution (HAS). In a formal randomised controlled trial we showed that volume expansion with albumin was associated with a significantly lower mortality in children with severe malaria acidosis, especially those admitted in coma. As HAS is costly and not available in Africa in this current study we aim to examine the safety and dose required (efficacy) for the correction of hypovolaemia of lower cost colloids: Gelofusine, Dextran 70 and Hetastarch. These will be compared to a control group of children receiving HAS. In this prospective study we aim to enrol

children and randomised them to either Gelofusin, Dextran 70, Hetastarch or HAS. The results of this study will form the basis for the future design of multicentre trials comparing colloidal solutions with saline or maintenance alone, which are required before specific treatment recommendations can be made.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Kenya Medical Research Institute (KEMRI) National Scientific Steering Committee and Ethics Review Board, July/August 2004, ref: 864

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Severe falciparum malaria

Interventions
Fluid resuscitation with either:
1. Human albumin solution
2. Gelofusine
3. Dextran 70
4. Hetastarch

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Human albumin solution, gelofusine, Dextran 70, Hetastarch

Primary outcome measure
The resolution of clinical features of shock and case fatality

Secondary outcome measures
Development of major side effects or complications of volume resusciation:
1. Abnormal clotting indices
2. Pulmonary oedema
3. Raised intracranial pressure

Overall study start date
01/11/2004

Completion date
31/10/2006

Eligibility

Key inclusion criteria
1. Kenyan children aged more than three months, either sex
2. Clinical features of severe falciparum malaria (impaired consciousness and or deep breathing)
3. Metabolic acidosis (base deficit more than or equal to eight)

Participant type(s)
Patient

Age group
Child

Lower age limit
3 Months

Sex
Both

Target number of participants
40 in each group (160 in total)

Key exclusion criteria
1. Children of families who decline consent
2. Children with:
2.1. Severe anaemia (haemoglobin less than 5 g/dl)
2.2. Cerebrospinal fluid (CSF) changes consistent with meningitis
2.3. Clinical features of pulmonary oedema (defined as clinical evidence presence of fine crepitations in both lungs plus oxygen saturations less than 95%)
2.4. Evidence of raised intracranial pressure (brain stem features of coning, systolic blood pressure more than 90% centile for age plus falling heart rate and/or papilloedema)
2.5. Any conditions that may contraindicate the use of volume replacement, e.g. established renal failure or known congenital heart disease

Date of first enrolment
01/11/2004

Date of final enrolment

31/10/2006

Locations

Countries of recruitment
Kenya

Study participating centre
Wellcome Trust Research Unit
Kilifi
Kenya
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Sponsor information

Organisation
Imperial College London (UK)

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Sponsor type
University/education

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ROR
https://ror.org/041kmwe10

Funder(s)

Funder type

Charity

Funder Name
The Wellcome Trust (UK) (grant ref: 062258)

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?
Other publications	retrospective review	01/06/2003		Yes	No
Results article	preliminary results	15/02/2005		Yes	No
Results article	results	15/09/2006		Yes	No
Results article	results	01/08/2010		Yes	No