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Transfusion and treatment of severe anaemia in African children trial

Submission date
25/01/2013

Recruitment status
No longer recruiting

Registration date
11/02/2013

Overall study status
Completed

Last Edited
14/02/2022

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
In sub-Saharan Africa severe anaemia in children is a leading cause of hospital admission, a major cause of direct mortality. Guidelines developed by the World Health Organization (WHO) encourage the rational use of blood transfusion to preserve this scarce resource and to reduce the risk of transfusion-transmitted infections. The evidence base for the paediatric guidelines is weak and thus adherence is poor. Outcome of severe anaemia is unsatisfactory with high rates of in-hospital (9-10%) and 6-month (12%) case fatality, and relapse or re-hospitalisation (6%), indicating that the current recommendations and management strategies are not working in practice. At the moment it is not known whether a blood transfusion is the best way to treat this and then how to treat or prevent the underlying illnesses, which may have caused the child to have severe anaemia.
The aim of this study is to:
1. Find out whether or not giving a blood transfusion is the best treatment. For children getting a blood transfusion we also do not know how much to give either the standard volume (dose) recommended in the current guidelines or a slightly higher volume (dose). We also want to find out whether or not giving extra treatments during the first three months after this hospital admission will prevent some of them from dying or becoming sick again. We will be looking at whether:
2. A multi vitamin multi mineral (MVMM) treatment called Sprinkles containing 15 different chemicals/vitamins is better than then usual recommended treatment of folate and iron.
3. Whether a single pill containing an antibiotic, cotrimoxazole, will fight infections and stop them from getting sick in the next 3 months.

Who can participate?
Children between the ages of 2 months to 12 years at the point of hospital admission. The blood test to check whether the child has anaemia is called a haemoglobin level. Children with a haemoglobin (Hb) less that 6g/dl will be included in the study.

What does the study involve?
Children will be treated according to standard Ministry of Health guidelines for severe illness and /or severe malaria.
1. Transfusion:

Children with a Hb below 4g/dl and those with Hb 4-6 g/dl with additional complications will all receive a transfusion. Half will receive the standard volume (dose) 20mg/kg of whole blood (as currently recommended) and the other half will receive a higher volume 30mg/kg.
Children with a Hb 4-6 g/dl haemoglobin without complications will be randomly allocated either receiving no transfusion (current WHO recommendations) or to receiving 20mg/kg of whole blood (as currently recommended) or 30mg/kg.
2. Vitamin treatments
Half the children will get iron and folate for 3 months (this is the current recommendation) while the other half will get a different MVMM medicine which is sprinkled onto their food every day for 3 months (or if the child is still breast feeding, mum will receive this medicine instead) to make the childs blood stronger.
3. Infection prevention
Often children with severe anaemia come back to hospital with another illness in the 6 months after this current admission. In order to try to prevent this, we will give half of the children a antibiotic tablet called cotrimoxazole for 3 months and the other half will not get this tablet. All children will have to come back after one month, three months and six months. We will check the health of your child at this visit, find out what food they have eaten on the day before they came to the clinic, find out whether they have been ill or to hospital since the last visit and check on whether they have been able to take the treatments and if they are causing any problem and then given them more treatments at the one month visit. When they come for these visits we will check on the strength of the blood (Hb level) and do a malaria test.

What are the possible benefits and risks of participating?
The direct benefits to the child and/or family include closer observation during the first 48 hours of admission, which, as a result, allows doctors and nurses to make important changes to the childs treatment during in-hospital admission, as well as being able to detect and treat any complications as they arise. All routine non-trial medications prescribed to treat the child will be made available. The parents or guardians for the children will be asked to return for follow up at the clinic 28, 90 and 180 days after admission. Reimbursement for transport cost after discharge and for follow up visits plus any treatment costs required during the visits will be made. Risks are minimal. Both MVMM and cotrimoxazole prophylaxis have been widely used in children with minimal risk. Although substantial efforts have been made to ensure the safety of blood, failure to correctly cross-match and/or infected blood have the potential to cause harm. The study will directly evaluate whether these potential risks are outweighed by improved survival. TRACT teams will work closely with the local blood transfusion services (BTS) to ensure that recommended safety and quality control practices are being maintained.

Where is the study run from?
The study is being run from KEMRI Wellcome Trust Programme, P.O Box 230-80108, Kilifi, Kenya. It is being conducted at three hospitals in Uganda (Mulago National Referral Hospital, Kampala Mbale and Soroti Regional Referral Hospitals, Eastern Uganda) and Queen Elizabeth Hospital, Blantyre, Malawi.

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

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

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
P39233, 203077/Z/16/Z

Study information

Scientific Title
TRansfusion and TReatment of severe Anaemia in African Children: a randomised controlled Trial

Acronym
TRACT

Study objectives
1. A liberal rather than a conservative blood transfusion policy will decrease mortality (cumulative to 4 weeks) in children admitted to hospital with severe anaemia (haemoglobin (Hb) <6g/dl).
2. Supplementary multi-vitamin multi-mineral treatments or cotrimoxazole prophylaxis or both for 3 months post discharge will reduce rates of readmission, severe anaemia relapse, re-transfusion or death (cumulative to 6 months) compared to current recommendations (iron and folate).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Imperial College Research Ethics Committee (ICREC) 13/01/2011
2. Makerere University School of Medicine research ethics committee (SOMREC), 27/03/2013, #REC ref: 2013-050
3. University of Malawi College of Medicine research and ethics committee (COMREC), 08/08/2013, ref: P.03/13/1365

Study design
Randomised controlled factorial trial with a 3x2x2 design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Severe anaemia

Interventions
The trial will have a factorial design with 3 randomisations, each to address one of the potential approaches to reducing mortality and morbidity in children with SA:

R1: Immediate liberal transfusion (30ml/kg) versus conservative transfusion (20ml/kg) versus no transfusion (last strategy only for children with uncomplicated SA and a Hb 4-6 g/dl).

R2: Post-discharge multi-vitamin multi-mineral (MVMM) supplementation (which includes folate and iron) versus routine care (folate and iron) for 3 months.

R3: Post-discharge cotrimoxazole prophylaxis versus no prophylaxis for 3 months.

R1 addresses both conservative aspects of current guidelines: "whether to give" in uncomplicated SA (4-6g/dl without complications), and "how much to give" in all children with SA. The transfusion and post-discharge interventions (R2 and R3) will be open-label for reasons of practicality and compliance.

Intervention Type
Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)
Cotrimoxazole, Nutrimix (Multivitamin Multimineral mix) 'Sprinkles'

Primary outcome measure
Cumulative mortality to 4 weeks for the transfusion strategy comparison, and to 6 months for the nutritional support/antibiotic prophylaxis comparison

Secondary outcome measures
1. Mortality at 48 hours, 28 days, 90 day and 180 days (cumulative) (where not the primary outcome).
2. Morbidity: endpoints relating to the specific mechanisms of action of each intervention:
2.1. Re-admission to hospital
2.2. Proportion achieving correction of anaemia (defined by WHO as Hb>9g/dl) at 48 hours, 28 days, 90 day and 180 days
2.3. Development of new profound anaemia (Hb<4g/dl) during acute admission or development of severe anaemia (Hb<6g/dl) post discharge
3. Nutrition: changes in weight and MUAC at 90 day and 180 days
4. Anti-infection: changes in inflammatory markers (CRP, PCT), incidence of bacterial infections and malaria at 28 days, 90 day and 180 days

Overall study start date
01/01/2013

Completion date
30/12/2019

Eligibility

Key inclusion criteria
Children will be recruited at the point of hospital admission
1. Aged 2 months to 12 years
2. Severe anaemia (SA) (Hb<6g/dl) within 2h of admission to hospital
3. Carer willing/able to provide consent

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Months

Upper age limit
12 Years

Sex
Both

Target number of participants
3954 including at least 1950 complicated severe anaemia and no more than 2000 uncomplicated severe anaemia.

Total final enrolment
1565

Key exclusion criteria
1. Malignancy
2. Surgery
3. Acute trauma
4. Signs of bi-ventricular heart failure

Date of first enrolment
01/09/2014

Date of final enrolment
14/05/2017

Locations

Countries of recruitment
Malawi

Uganda

Study participating centre
Mulago Hospital
Department of Paediatrics
PO Box 7072
Makerere University
Kampala
Uganda
-

Study participating centre
Mbale Regional Referral Hospital
Department of Paediatrics
Pallisa Road Zone
PO Box 921
Mbale
Uganda
-

Study participating centre

Soroti Regional Referral Hospital
Department of Paediatrics
PO Box 289
Soroti
Uganda
-

Study participating centre
University of Malawi
College of Medicine
Department of Paediatrics and Child Health
P/Bag 360
Chichiri
Blantyre
Malawi
-

Sponsor information

Organisation
Imperial College London (UK)

Sponsor details
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Sir Alexander Fleming Building
Imperial College
Exhibition Road
London
England
United Kingdom
SW7 2AZ
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Sponsor type
University/education

Website
http://http://www1.imperial.ac.uk/medicine/research/researchsupport/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) and Department for International Development (through a concordat with MRC), United Kingdom Grant Number MR/J012483/1

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trial results will be made available in a number of different formats and fora, in order to be appropriate for and accessible to different audiences. The trialists will use face-to-face meetings; workshops; open access peer-reviewed publication; policy briefs; presentation at international conferences; press releases; lay summaries; and websites. Depending on the results the trialists may also develop and distribute films and radio programmes; and will consult with members of the intended audiences to assess what other opportunities and tools for communicating they should use.

Intention to publish date
01/09/2018

Individual participant data (IPD) sharing plan
The TRACT trial will follow a controlled access approach as per guidance from the MRC Methodology Hubs for Trials Methodology research (Tudor Smith et al, BMC Medicine 2016 PubMed ID 26675031). The ownership of the TRACT dataset will lie with the Trial Steering Committee (TSC), who will approve all requests for use of trial data before and after the trial ends (also to be approved by the TRACT Data Monitoring Committee before the trial ends). The dataset will be held electronically for at least 20 years after the end of the trial in accordance

with local and MRC policies. The Data Sharing Policy will state that proposals to use TRACT data and samples will be welcomed, and supported widely where this does not conflict with existing plans within the trial team. Independent oversight of the data access process will be provided by TSC independent members and Imperial College, London (the trial sponsors).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	29/12/2015		Yes	No
Results article	results	01/08/2019	01/08/2019	Yes	No
Results article	results	01/08/2019	01/08/2019	Yes	No
Results article	results	01/10/2019	23/09/2019	Yes	No
Results article	Secondary analysis	29/07/2021	02/08/2021	Yes	No
Results article		11/02/2022	14/02/2022	Yes	No