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Intravenous and oral rehydration of children with severe malnutrition and gastroenteritis

Submission date
23/07/2018

Recruitment status
No longer recruiting

Registration date
08/08/2018

Overall study status
Completed

Last Edited
16/06/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Severe acute malnutrition (SAM) is a severe problem for African children. It can lead to the development of gastroenteritis, diarrhoea and dehydration, which leads to hospitalisation. However, on the current treatment recommended by the World Health Organization (WHO), the outcome is poor, with 20% of children dying during hospital admission.
A standard treatment for gastroenteritis, which leads to dehydration, is rehydration therapy, given by either an IV drip, which is used for more severe cases, or oral salt solutions, which is used for less severe cases or as a follow-on treatment after using a drip. The WHO guidelines for children with dehydration as a result of diarrhoea (which can be a complication of SAM, but also a result of bacterial or viral infections) recommend using oral salt solutions, with restricted use of intravenous drip therapy; however, this is controversial, as these recommendations are not based on results from clinical trials.
The aim of this study is to compare the recommended treatments for the rehydration of children with SAM with the standard treatments for the rehydration of children without SAM, to determine if these can be safely used for and improve the outcome of children with SAM.

Who can participate?
African children aged 6 months to 12 years who are hospitalised with SAM and have gastroenteritis leading to dehydration

What does the study involve?
For children with severe dehydration, we will compare the effects of giving them fluid via a drip, either quickly or slowly, with giving them the WHO SAM recommended regime, which involves using oral rehydration salts (ORS) and only starting drip treatment if the child goes into shock.
For children with less severe dehydration, we will compare the effects of using standard ORS treatment, which has a higher amount of sodium, with an ORS called ReSoMal (designed specifically for SAM), which has a lower sodium content.

What are the possible benefits and risks of participating?
The benefit of participating is that the children will be closely monitored throughout, so that any clinical deterioration can be identified at the earliest opportunity and appropriate therapy initiated. The possible risks of participating are:

1. Drip insertion and taking blood for laboratory tests may lead to pain, swelling or infection at the site of the drip; however, this will be minimised by careful technique and regular inspection
2. Liberal intravenous rehydration and salt-rich solution has the potential to cause malnourished hearts to go into pump failure or lead to harmful fluid accumulation
To minimise these risks, the nurses and doctors will monitor children very closely to look for side effects and if detected the treatments may be stopped. The trial sites in Africa have considerable experience with management of very ill children and this will serve minimise the risks to the patients in the trial

Where is the study run from?
KEMRI Wellcome Trust Research Programme (Kenya)

When is the study starting and how long is it expected to run for?
October 2018 to October 2024

Who is funding the study?
Medical Research Council (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
MRC Grant Refrence: MR/R018502/1

Study information

Scientific Title
GASTROenteritis: Intravenous and oral rehydration of children with Severe Acute Malnutrition

Acronym
GASTROSAM

Study objectives
For children with severe acute malnutrition (SAM) with severe dehydration due to diarrhoea, we hypothesize that standard intravenous regime WHO Plan C (100 ml/kg over 3-5 hours) used for non-SAM gastroenteritis with severe dehydration will result in better outcomes than the current very conservative SAM rehydration recommendations.
In addition, we propose that the rate of rehydration may be critical and hypothesize that 100 ml /kg over 8 hours in SAM children will result in fewer fluid related adverse effects than rapid World Health Organization (WHO) Plan C guideline.
We also propose that standard oral rehydration solutions (ORS) may be equally as effective with fewer side effects than low salt ReSoMal ORS recommended by WHO.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Imperial College Research Ethics committee (ICREC), 20/03/2018, 18IC4427
Mbale Regional Referral Hospital Research Ethics Committee, submitted for approval 17/07 /2018

Study design
Interventional open multi-centre phase II randomised controlled trial with a factorial design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Severe acute malnutrition

Interventions
Randomisation lists are generated and kept at the MRC CTU at UCL, London. The randomisation envelopes are prepared before the trial at the Clinical trials facility, KWTRP, Kilifi. These contain the actual allocation visible only once opened. The cards will be numbered consecutively and opened in numerical order.
The trial includes 2 strata:
Stratum A includes children with severe dehydration only. Children will be randomised in a 1:1:2 ratio to compare:
1. WHO Plan C arm: Rapid intravenous (IV) rehydration as per WHO Plan C (usually for non-SAM) children (100 ml/kg Ringers Lactate (RL) over 3-6 hours according to age including boluses (20 ml /kg) for those with shock (experimental))
2. Slow Rehydration arm: A slower IV rehydration regimen (100 ml/kg RL given over 8 hours and no boluses (experimental)).
3. WHO SAM arm: rehydration regime involves no intravenous rehydration and rehydration with ReSomMal Oral rehydration solution (ORS) with IV boluses of RL only for children with shock (standard of care)
Stratum B includes all children with some dehydration and all those with severe dehydration post IV rehydration, randomised in a 1:1 ratio to compare:
1. Standard WHO ORS given for non-SAM (experimental) versus
2. WHO SAM-recommended low-sodium ReSomMal
The trial will run for a total of 18 months for both strata.

Intervention Type
Mixed

Primary outcome measure
Current primary outcome measures as of 07/08/2023:
1. For the intravenous rehydration strategy, mortality at 96 h after enrolment
2. For the oral rehydration strategy, change in plasma sodium levels, measured by standard laboratory clinical chemistry analyser from baseline (time of enrolment) to 24 h after enrolment

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Previous primary outcome measures:
1. For intravenous rehydration, urine output (ml/kg/hour) will be assessed as a surrogate marker of rehydration efficacy 8 hours after treatment
2. Change in plasma sodium levels, measured by standard laboratory clinical chemistry analyser at the baseline (time of enrolment) and after 24 hours

Secondary outcome measures
1. Evidence of pulmonary oedema or heart failure during period of hospital admission:
1.1. Pulmonary oedema defined as developed of bilateral bi-basal crepitations of lungs on clinical examination
1.2. Heart failure defined as development of signs of severe tachycardia, elevated jugular venous pressure and de novo or increasing hepatomegaly
2. Changes in sodium from post-IV levels for those in Stratum A, measured using standard laboratory clinical chemistry analyser at the baseline and after intravenous rehydration is completed
3. Perturbations of electrolyte abnormalities (severe hyponatraemia < 125 mmol/l or hypokalaemia < 2.5 mol/l), measured by standard laboratory clinical chemistry analyser at the baseline and at any time during admission
4. Mid-upper arm circumference (MUAC) change, measured using MUAC tape (supplied by UNICEF) at the baseline and day 7
5. Survival at day 28 (child is confirmed to be alive at day 28)

Overall study start date
20/07/2017

Completion date
31/10/2024

Eligibility

Key inclusion criteria
Severe dehydration - Stratum A:
1. Aged 60 days to 12 years
2. Severe malnutrition defined as any of the following: Mid-upper arm circumference (MUAC) <11.5 cm, weight for height Zscore (< -3SD), or signs of kwashiorkor
3. Gastroenteritis, defined as > 3 loose stools per day
4. Signs of severe dehydration, defined (as per WHO definition) as at least one of the following: unable to drink, Alert Voice Pain Unresponsive scale (AVPU) < A, sunken eyes, reduced skin pinch (>2 seconds) or inability to take or retain oral fluids, and/or shock (defined as patient with cold peripheries, weak and fast pulse and capillary refill time > 3 seconds)

Moderate/some dehydration - Stratum B:
1. Aged 60 days to 12 years
2. Severe acute malnutrition criteria, complicated by dehydrating diarrhoea (defined as > 3 loose stools per day)
3. Some to moderate dehydration or completing management of severe dehydration. Some to moderate dehydration defined as two of the following: restlessness, irritability, thirst, sunken eyes or skin pinch goes back slowly

Participant type(s)
Patient

Age group
Child

Lower age limit
60 Days

Upper age limit
12 Years

Sex
Both

Target number of participants
Children aged 272 children in the stratum with severe dehydration and an additional 64 children with some dehydration; overall 336 children

Total final enrolment
272

Key exclusion criteria
1. Diarrhoea lasting more than 14 days
2. Known congenital or rheumatic heart disease
3. Refusal of consent

Date of first enrolment
02/09/2019

Date of final enrolment
30/08/2024

Locations

Countries of recruitment
Kenya

Niger

Nigeria

Uganda

Study participating centre
Mbale Regional Referral Hospital
Pallisa Road Zone
P.O. Box 921
Mbale
Uganda
-

Study participating centre
Soroti Regional Referral Hospital
Department of Paediatrics

P.O. Box 289
Soroti
Uganda
-

Study participating centre
Kilifi County Hospital
Hospital Road
PO Box 230
Kilifi
Kenya
-

Study participating centre
Coast General Teaching Hospital
Madakara Road
Mombasa
Kenya
-

Study participating centre
Nilefa Kiji MSF Hospital
Behind CBN Quarters
Kushari
Damboa Road
Maiduguri
Nigeria
-

Study participating centre
Hôpital du district du Magaria
Région de Zinder
Département de Magaria
Magaria
Niger
-

Study participating centre
Hôpital de district de Madarounfa
Region de Maradi
Département de Madarounfa

Maradi
Niger
-

Sponsor information

Organisation
Imperial College, London

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

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

Results and Publications

Publication and dissemination plan

Results will be published in peer review open access journals. The results from this trial will be disseminated locally through community meetings and national meetings with the wider healthcare professional community. These systems have been developed for dissemination of MRC FEAST trial results, and we plan to extend these with the ongoing TRACT trial and to this proposed trial (GASTROSAM).
The lead investigators in Uganda will discuss with their Ministry of Health about the proposed trial. A summary or evidence brief will be produced to highlight the trial results and next steps required to inform rationale evidence-based guidelines. At that stage since the data generated from the study will not be immediate able to inform treatment guidelines rather it will generate new data, which will help inform the design of a larger Phase III trial.

We have already had teleconferences with members of the epidemic consortium and WHO GOARN (Global Outbreak Alert and Response Network). We have shared systematic reviews we undertook in preparation of this trial. The current rehydration management guidelines for children with severe malnutrition are under intense speculation currently as a potential reason for the poor outcome in the current cholera epidemics. Through these connections will seek meetings with WHO, MSF and UNICEF and other international policy makers to discuss the results and subsequent trial plans.

Intention to publish date

30/04/2025

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 3.0	21/10/2022	15/04/2024	No	Yes
Protocol file	version 3.0	19/10/2022	15/04/2024	No	No
Statistical Analysis Plan	version 3.0	19/10/2022	15/04/2024	No	No
Statistical Analysis Plan	version 4.0	17/12/2024	16/01/2025	No	No
Results article		13/06/2025	16/06/2025	Yes	No