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Evaluating the effectiveness of a legume-enriched nutritional intervention, in treatment of severe undernutrition in children

Submission date
18/05/2018

Recruitment status
No longer recruiting

Registration date
23/05/2018

Overall study status
Completed

Last Edited
04/06/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Severe acute malnutrition is a serious illness and a common problem. In malnutrition, the gut becomes damaged and does not function properly. This means a lot of the food is lost in the stool, sometimes as diarrhoea, and not enough food gets into the body. Healthy bacteria live in the gut and do not cause any illness, but the types of bacteria may change in malnutrition to ones that can cause serious infections. Good bacteria use food that the body cannot digest (fibre /roughage) and turn it into helpful products. The Uganda Ministry of Health, UNICEF and the WHO recommend special feeds (F75/F100) to treat children with malnutrition in order to increase the amount of energy and nutrients received. These feeds do not contain any fibre /roughage, so numbers of good bacteria may decrease. They also contain a common milk sugar called lactose, which normally does not cause any problems. However, due to damage to the gut, this may be poorly digested, making diarrhoea worse and making it more difficult for the child to recover. If bad bacteria are present, they could use this sugar, increasing the risk of infection. The aim of this study is to see whether giving children an altered nutritional feed helps repair the gut and encourage the good bacteria, which may reduce illness or improve recovery. In the study the standard nutritional feed that all children with severe malnutrition receive routinely is altered by removing the lactose and adding a chickpea flour. Chickpea flour contains fibre /roughage that can help good bacteria. The aim is to find the best nutritional treatment for children with severe malnutrition.

Who can participate?
Children aged 6 months to 5 years with severe acute malnutrition

What does the study involve?
Participants are randomly allocated to receive standard treatment (F75/F100) or the lactose-free, chickpea flour feed which provides similar amounts of energy and nutrients. Treatment is for 14 days, followed by standard treatment as required. This includes provision of ready to use therapeutic feeds until the child has recovered. Children are followed up for 90 days.

What are the possible benefits and risks of participating?
Benefits include closer observation during admission which consequently may allow the clinical team to make important changes to the child's treatment during in hospital stay. All routine non-study medications required by the hospital to treat the child will be made available. The parents or guardians for the children will be asked to return for follow up at 28 days after admission. This additional visit will include a clinical review thus an opportunity for medical treatment if required. Education regarding nutrition will also be readdressed at this time. Reimbursement will be made for transport cost for this follow-up visit plus any treatment costs required during the visits. There are very few risks involved in this study. The chickpea flour feeds are used within the local diets but have been milled/processed in such a way to maximise their ability to ferment within the bowel to create a favourable microbiome. Intolerance or allergy is rare. The G6PD variant in these populations retains >12% of its activity thus not rendering G6PD deficient patients to susceptibility to oxidant stress (as seen in Mediterranean variants rendering them susceptible to 'Favism'). Blood samples are required as part of this study; this includes routine bloods according national guidelines and an additional 12 ml over the whole duration of the study. Required volumes of blood will be minimized wherever possible and be within the locally agreed maximum. Urine and stool will be collected in a non-invasive manner thus should not cause any distress to the child or their family.

Where is the study run from?
Mbale Clinical Research Institute (Uganda)

When is the study starting and how long will it run for?
June 2018 to December 2019

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Mr Kevin Walsh

Contact information

Type(s)
Public

Contact name
Mr Kevin Walsh

Contact details
Division of Infectious Diseases
Department of Paediatrics
Faculty of Medicine
Imperial College London
3rd Floor SAF Building
South Kensington Campus
London
United Kingdom
SW7 2AZ

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
17IC4146

Study information

Scientific Title
Modifying Intestinal integrity and the MicroBiome in severely malnourished children with LEgume-based Feeds to improve outcome compared to standard treatment: a randomised controlled trial

Acronym
MIMBLE II

Study objectives
That legume-enriched, lactose-free nutrition support will improve outcomes in children with severe acute malnutrition, compared with standard nutritional rehabilitation milks as recommended by the World Health Organization

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Imperial College Research Ethics Committee, 23/04/2018, ref: 17IC41456
2. Mbale Regional Referral Hospital REC, 09/05/2018, ref: MRRH-REC In – COM 019/2018
3. Uganda National Council for Science and Technology: applied March 2018

Study design
Two-centre open-label randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions

Randomisation will be in permuted blocks. Cards with treatment allocation (standard or altered standard with chickpea flour) will be prepared in Kilifi and sent to Mbale. They will be kept in numbered, sealed opaque envelopes, each signed across the seal. The cards will be numbered consecutively and will be opened in numerical order.

Children will be randomised to a legume-enriched feed or standard treatment (WHO F75/F100) on a 1:1 basis:
Control arm: World Health Organisation recommended F75 (0.75kcal/ml) and F100 (1kcal/ml) feeds
Investigation arm: Lactose-free, chickpea enriched feed containing 2kcal/ml, provided in quantities to match energy provision in standard treatment.

Treatment with randomised intervention/control will be for 14 days duration, followed by standard treatment as required. This includes provision of ready to use therapeutic feeds until child has recovered, defined by weight-for-height z-score >-2. The duration of this is variable. Children will be followed up to 90 days post admission date.

Intervention Type
Supplement

Primary outcome(s)
1. Mid-upper arm circumference in centimeters and millimeters measured using measuring tape supplied by UNICEF designed for this purpose on admission (at trial recruitment), day 7, day 28 and day 90
2. Survival recorded by incidence of death up to day 90

Key secondary outcome(s))
Current secondary outcome measures as of 16/09/2021:
1. Weight measured daily from admission to discharge, then at day 28 and day 90, by clinical weighing scales. Daily weight (in grams and kilograms) change is calculated from this to assess response to the intervention, and moderate weight gain defined as being >5g/kg/day
2. Development of diarrhoea assessed by daily recording of stool passed during inpatient stay, and diagnosed if >3 watery stools are passed in any one day. Inpatient stay is variable, but likely to be minimum of 14 days. Children/parents are asked about number and consistency of stool passed at day 28 and day 90 reviews
3. Time to resolution of diarrhoea assessed in patients who presented with diarrhoea on admission (>3 watery stools in one day) during inpatient stay. Daily inpatient monitoring of stool passed is undertaken, and resolution defined as cessation of passing >3 watery stools in one day. Children/parents are asked about number and consistency of stool passed at day 28 and day 90 reviews
4. Presence of oedema recorded on admission assessed visually and severity recorded as affecting pretibial only (mild), involving hands/feet (moderate), or generalised (severe). Oedema monitored daily during inpatient admission, and at time to resolution noted. Presence of oedema assessed at day 28 and day 90 reviews also
5. Faecal calprotectin (by ELISA) used to assess inflammation in the gut, analysed on collected faecal samples at admission, day 7, day 28 and day 90
6. Safety assessed by reports of serious adverse events to include any untoward medical occurrence or effect that is 1) fatal, 2) life threatening, 3) permanently or temporarily disabling or incapacitating, 4) causes prolongation of hospital stay, or 5) any other event deemed to have

a real risk of resulting in one of the previous outcomes. Allergic reactions will be considered SAEs. SAEs reported immediately to the on-site PI, and captured in a dedicated form at the time of event or the next clinical review.

Previous secondary outcome measures:
1. Weight measured daily from admission to discharge, then at day 28 and day 90, by clinical weighing scales. Daily weight (in grams and kilograms) change is calculated from this to assess response to the intervention, and moderate weight gain defined as being >5g/kg/day
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5. Faecal calprotectin (by ELISA) used to assess inflammation in the gut, analysed on collected faecal samples at admission, day 7, day 28 and day 90

Completion date
01/09/2019

Eligibility

Key inclusion criteria
1. Marasmus defined by mid-upper arm circumference < 11.5cm
2. Kwashiorkor defined as symmetrical pitting oedema involving at least the feet irrespective of WHZ score or MUAC
3. Guardian/parent willing and able to provide consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
160

Key exclusion criteria

Children with severe acute malnutrition with very high risk of death due to comorbidity, e.g. malignant disease or terminal illness

Date of first enrolment
05/07/2018

Date of final enrolment
28/08/2019

Locations

Countries of recruitment
Uganda

Study participating centre
Mbale Clinical Research Institute
Mbale Regional Referral Hospital, Plot 29-33 Pallisa Road
Mbale
Uganda
-

Study participating centre
Soroti Regional Referral Hospital
Hospital Road
PO Box 289
Soroti
United Kingdom
-

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

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

Funder Name
Wellcome Trust Institutional Strategic Support Fund

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Funder Name
National Institute for Health Research (NIHR) - Research Imperial Biomedical Research Centre (BRC)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Engineering and Physical Sciences Research Council (ESPRC) Impact Acceleration Account

Alternative Name(s)
EPSRC Engineering & Physical Sciences Research Council, UKRI Engineering and Physical Sciences Research Council, Engineering and Physical Sciences Research Council - UKRI, Engineering & Physical Sciences Research Council, The Engineering and Physical Sciences Research Council (EPSRC), EPSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Royal Marsden NHS Foundation Trust

Alternative Name(s)
Royal Marsden, The Royal Marsden NHS Foundation Trust, The Royal Marsden, The Cancer Hospital (Free)

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Funder Name
UK Research and Innovation - Global Challenges Research Fund

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Gary Frost (gary.frost@imperial.ac.uk). Anonymised data including

clinical and anthropometric data will be made available, including results of any experimental analysis completed including faecal calprotectin, metataxonomic data, and metabolomic data. Data will be made available by reasonable request following the publication of the trial results (anticipated 01/09/2020), and following subsequent publication metataxonomic data, and metabolomic data so long as this does not conflict with planned ongoing analysis or sub-analyses and for 10 years following this date. The data used in this research was collected subject to the informed consent of the participants. Access to the data will only be granted in line with that consent, subject to approval by the project ethics board and under a formal Data Sharing Agreement.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/01/2023	07/03/2023	Yes	No
Results article		04/06/2024	04/06/2024	Yes	No
Protocol article	protocol	02/08/2018		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 3.1	06/10/2018	15/08/2023	No	No