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Is cows' "first milk" an acceptable and effective way of improving gut health and nutrition in children with Crohn's disease?

Submission date
01/07/2019

Recruitment status
No longer recruiting

Registration date
08/07/2019

Overall study status
Completed

Last Edited
02/12/2022

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Crohn's disease (CD) is an incurable, long-lasting, inflammatory bowel disease that causes pain, diarrhoea and reduced growth. CD can result in poor quality of life, illness and high treatment costs. The first recommended treatment in young people is exclusive enteral nutrition (EEN). This is when a special milk feed is given as the sole source of food for 6-8 weeks. Over 85% of children with active CD stop experiencing symptoms or show improvement of symptoms during EEN. The problem is that disease flares often occur after the young person's usual diet is re-introduced. Continuing some of a special milk every day may help to maintain gut health and nutrition and reduce the risk of disease flares. However, many young people dislike the special milks and are not able to take them long-term. There is a need for dietary therapy that is effective but also acceptable for longer-term use.
This study aims to investigate whether "First Milk" taken daily alongside a young person's usual diet is acceptable for long-term use and whether it may improve gut health and nutrition. First Milk or pre-milk is produced by cows after giving birth and is also called bovine colostrum. It contains high levels of naturally occurring substances that may reduce inflammation and help to repair and reduce the leakiness of the intestinal lining in CD. First Milk also improves defenses against infection. Only a small amount of First Milk may be needed every day to improve gut health and nutrition in CD. First Milk is tasteless and many different flavourings can be used to make a milkshake which may improve acceptability for long-term use.

Who can participate?
50 young people aged 8-18 years with stable mild or moderate CD. Young people who are allergic to, or intolerant to, cow's milk and those already taking a dietary supplement will not be able to participate.

What does the study involve?
Participants will be allocated randomly to receive either First Milk or a normal cow's milk powder every day for 6 weeks and will not know which milk they are receiving. This is the "blinded" phase of the study. From weeks 7 to 12, all participants will receive daily First Milk in the "open" phase. How young people manage with the supplement will be recorded in a daily diary. They

can also provide blood and stool samples and do sugar absorption tests that will require them to provide urine samples to monitor gut leakiness. These samples will be collected at the beginning of the study and at weeks 6 and 12.
20 young people and their families who are taking part in the study will be interviewed to assess their perceptions and opinions of dietary therapy, First Milk and the research methods.
All of the information collected will help to assess whether or not First Milk might have a useful role in managing CD. If so, the information from this initial study will allow a larger study to be designed to assess the effects of First Milk on important clinical outcomes such as the prevention of disease flares.

What are the possible benefits and risks of participating?
All of the young people in the study will take the First Milk daily for either 6 or 12 weeks. This may improve their gut health and nutritional status. It is unlikely that taking the comparison milk would result in any benefits. First Milk has been taken by over 2000 people in research studies for many different illnesses. No serious side effects have been reported. Some people have reported feeling nauseous, flatulence, diarrhoea, skin rash, and unspecified tummy discomfort; however, these possible side effects have been mild. Therefore, we do not anticipate that either of the milks will cause any harm in young people who are not allergic to, or intolerant to, cow's milk. The clinical and laboratory measurements being done in the study are for research and will not help the treatment of individual young people. Taking part in the study will require providing information and samples, but these are not considered to pose any risk.

Where is the study run from?
Alder Hey Children's Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2018 to July 2021 (updated 11/06/2021, previously: June 2021; updated 08/03/2021, previously: March 2021)

Who is funding the study?
The NIHR Research for Patient Benefit Scheme (UK)

Who is the main contact?
Prof. Stephen Allen
Stephen.allen@lstmed.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Stephen Allen

ORCID ID
http://orcid.org/0000-0001-6675-249X

Contact details
Clinical Sciences Department
Liverpool School of Tropical Medicine
Pembroke Place

Liverpool
United Kingdom
L3 5QA
+44 (0)151 705 3752
stephen.allen@lstmed.ac.uk

Type(s)
Scientific

Contact name
Mrs Janet Clark

Contact details
Gastroenterology Department 2A
Alder Hey Children’s NHS Foundation Trust
Eaton Road
Liverpool
United Kingdom
L12 2AP
+44 (0)1512284811 ext. 4041
Janet.clark@alderhey.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
246070; CPMS: 39688

Study information

Scientific Title
Dietary therapy with bovine colostrum to improve nutrition and gut health in paediatric Crohn’s disease; a feasibility study

Study objectives
1. First Milk is acceptable to children and their parents/carers for long-term use (3 months) and free of significant adverse effects
2. Children/young people with Crohn's disease (CD) and their parents/carers are interested in participating in research of dietary therapy as a possible safe, acceptable and long-term means of controlling intestinal disease
3. It is possible to perform additional sample collection and procedures alongside usual clinical care to enable assessment of novel dietary interventions
4. First Milk improves biomarkers of nutrition and gut health in paediatric CD

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/11/2018, North West - Liverpool East Research Ethics Committee (Barlow House, 3rd Floor,
4 Minshull Street, Manchester, M1 3DZ; nrescommittee.northwest-liverpooleast@nhs.net), ref: 18/NW/0637

Study design
Prospective qualitative trial and randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Crohn's disease in children

Interventions
Young people will be randomised 1:1 to the two study arms (weeks 1-6) using a computer-generated random allocation sequence with blocks of varied size generated and held by the CTU at LSTM. A Research Nurse will allocate children at baseline to the next unique research number in the allocation sequence. Plain bags of the appropriate milk powder, identified only by the unique research number, will be prepared in advance according to the random sequence. The Research Nurse will provide the young person/family with the appropriate milk powder.

First Milk study arm: 20 g/day of First Milk tasteless powder.
Comparator study arm: 20 g/day of a mix of skimmed milk powder (70%) and milk protein concentrate (30%) to make a matched comparator with equivalent protein and lactose content.

Both milks can be made up with about 150 ml semi-skimmed milk, full cream milk, water or other fluids. In both study arms, the dose could be reduced to 10 g/day if a larger volume is not tolerated and a range of flavourings can be added according to personal preference to make a palatable milkshake.

Either First Milk or the comparator milk are given for the first 6 weeks of the study (blinded phase). For weeks 7-12, all young people will receive First Milk (open phase).

Intervention Type
Supplement

Primary outcome measure
Compliance with dietary supplement recorded in a daily diary collected during weeks 2, 6 and 12 and during weekly phone calls

Secondary outcome measures
1. Young people's and parent's/carers' perceptions and views regarding dietary therapy and on participating in research on dietary therapy assessed using interviews conducted at the end of the first week, end of week 6 and after completion of the intervention by week 13-14
2. Recruitment rate assessed using the number of screened young people who participate in the study
3. Retention rate assessed using the number of screened young people who complete the study
4. Acceptability and feasibility of the sugar permeability test and collection of stool, urine and blood samples assessed using the number of participating young people who provide samples of blood, stool and urine at baseline and 6 and 12 weeks
5. Intestinal inflammation assessed using calprotectin level in stool samples measured using ELISA at baseline, 6 and 12 weeks
6. Intestinal permeability assessed using urinary concentrations of lactulose, rhamnose and mannitol following oral administration, blood concentrations of endotoxin antibodies and intestinal fatty acid binding protein and faecal α1-antitrypsin measured using ELISA at baseline, 6 and 12 weeks
7. Systemic inflammation assessed using serum C-reactive protein level, erythrocyte sedimentation rate, α-1 acid glycoprotein level, cytokine assay (multiplex method) and blood platelets measured by haematology analyser at baseline, 6 and 12 weeks
8. Serum levels of growth factors, including insulin-like growth factor (IGF)-1 and IGF binding protein-3, measured using ELISA at baseline, 6 and 12 weeks
9. Disease activity measured using the weighted paediatric Crohn's Disease Activity Index at baseline, 6 and 12 weeks
10. Quality of life assessed using a paediatric inflammatory bowel disease disease-specific health-related quality of life instrument - the IMPACT III questionnaire - at baseline, 6 and 12 weeks

Overall study start date
01/04/2018

Completion date
26/07/2021

Eligibility

Key inclusion criteria
1. Aged 8 years and above
2. CD in clinical remission or mild/moderate disease severity (weighted pCD Activity Index [wPCDAI] ≤57.5)
3. Stable clinical condition defined as either receiving no treatment or maintenance therapy that has been unchanged for at least the last 2 months with no intention to change therapy at the time of recruitment

4. Willing for clinical information to be used for the purposes of the trial
5. Willing to partake in the study procedures
6. Able to complete the daily diary in English

Participant type(s)
Patient

Age group
Child

Lower age limit
8 Years

Sex
Both

Target number of participants
50

Total final enrolment
23

Key exclusion criteria
1. Severe CD (wPCDAI >57.5)
2. Intolerance of dairy products
3. Receiving dietary therapy for the management of Crohn's disease (e.g. Modulen IBD)
4. Already taking BC regularly
5. Established diagnosis of a significant gut disorder other than CD (e.g. short bowel syndrome)
6. Failure to obtain informed consent from the patient and/or parent/guardian

Date of first enrolment
18/02/2019

Date of final enrolment
08/04/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Alder Hey Children's Hospital
E Prescot Rd
Liverpool
United Kingdom
L14 5AB

Sponsor information

Organisation
Alder Hey Children's NHS Foundation Trust

Sponsor details
E Prescot Rd
Liverpool
England
United Kingdom
L14 5AB
+44 (0)151 228 4811
richard.kirk@alderhey.nhs.uk

Sponsor type
Hospital/treatment centre

Website
https://alderhey.nhs.uk/

ROR
https://ror.org/00p18zw56

Funder(s)

Funder type
Government

Funder Name
Research for Patient Benefit Programme

Alternative Name(s)
NIHR Research for Patient Benefit Programme, RfPB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Results of the research will not be available to individual patients but participants will be able to access a summary of the study findings written in lay language.
Our findings will be of interest to clinicians, allied health professionals and researchers working in IBD. We will publish the study protocol and share our findings at specialist society meetings and key scientific conferences.
The study database of the quantitative data will be publicly accessible through a central data management system at the Liverpool School of Tropical Medicine or available on request.
Dissemination of results to clinicians, allied health professionals and academics will be facilitated by membership of the investigators on specialist society groups and charity boards. We will use these channels to encourage further research in dietary management of paediatric CD.

Intention to publish date

30/12/2022

Individual participant data (IPD) sharing plan

Informed consent has been secured for the anonymised demographic, clinical and laboratory datasets generated during the current study to be publicly accessible through a central data management system at the Liverpool School of Tropical Medicine or available on request from Prof Stephen Allen; Stephen.allen@lstmed.ac.uk). Data will be available for a minimum of 5 years after publication of the study results.

IPD sharing plan summary

Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v0.7	15/10/2018	05/07/2021	No	No
Results article		01/11/2022	02/12/2022	Yes	No
HRA research summary			28/06/2023	No	No