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Medium-chain fat supplementation in children with biliary atresia: a retrospective review

Submission date	Recruitment status	[_] Prospectively registered
03/04/2023	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/06/2023	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/12/2024	Digestive System	

Plain English summary of protocol

Background and study aims
Biliary atresia is a rare disease of the bile ducts that carry bile from the liver to the intestine. Surgery called a kasai portoenterostomy is needed in the first 12 weeks of life to restore the flow of bile. Despite this surgery, half of the babies with biliary atresia will eventually need a liver transplant. Babies with biliary atresia are given medium-chain fat (also known as medium-chain triglycerides or MCT), a special fat made from coconut oil that can be absorbed even when there is no bile in the gut. The aim of giving MCT is to provide an energy source so babies can grow. Even though MCTs are used widely in the NHS there is no agreement on how much to give. Babies are given anywhere from 30% to 75% of their total fat intake as medium-chain fat with the remainder being regular fat. Our aim is to investigate how MCT supplementation and the amount that is given impact growth, nutritional status and clinical outcomes in biliary atresia.

Who can participate?
Children with biliary atresia who had a kasai portoenterostomy at King's College Hospital NHS Foundation Trust in 2020 or earlier and were followed up for two years.

What does the study involve?
The study will examine the medical records of 200 children with biliary atresia that were previously looked after, many of whom received different amounts of MCTs. The study will investigate whether the amount of MCT that was given was associated with growth, nutritional status and outcomes in the two years after diagnosis.

What are the possible benefits and risks of participating?
The potential benefit to patients is that an understanding of MCT supplementation can improve the growth and nutritional status of children with biliary atresia and avoid later medical complications. As this study will be done retrospectively, there is no risk that the participation of patients will impact previous clinical care.

Where is the study run from?
The research is being carried out at King's College Hospital NHS Foundation Trust (UK) and is being sponsored by King's College London (UK) and co-sponsored by King's College Hospital NHS Foundation Trust.

When is the study starting and how long is it expected to run for?
December 2021 to December 2023

Who is funding the study?
National Institute for Health and Care Research (NIHR)

Who is the main contact?
Sara Mancell, a doctoral researcher and specialist children's liver dietitian, sara.mancell@nhs.net

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
312042

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 55111, IRAS 312042

Study information

Scientific Title
Retrospective medical records review to investigate the association between medium-chain triglyceride supplementation with growth, nutritional status and clinical outcomes in children with biliary atresia

Study objectives
There is an association between medium-chain triglyceride (MCT) supplementation and growth, nutritional status and clinical outcomes in infants with biliary atresia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/01/2023, North of Scotland Research Ethics Committee (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, UK; +44 (0)1224 558458; gram.nosres@nhs.scot), ref: 23/NS/0009

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Medical and other records

Study type(s)
Screening

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

Health condition(s) or problem(s) studied
Pediatric gastroenterology, hepatology and nutrition

Interventions

Design and aim

The study will examine the medical records of 200 children with biliary atresia that were previously looked after in the Trust, many of whom received different amounts of medium-chain fats. The study will investigate the association between medium-chain fat supplementation with growth, nutritional status, and clinical outcomes in the two years after kasai portoenterostomy surgery. This design will enable us to review the data for a large sample- a challenge when studying rare diseases such as biliary atresia. Two years follow-up was chosen to incorporate the period when transplantation is most likely. This is because transplantation is an important outcome impacting the variables that are being investigated.

Sample

Children with biliary atresia who had kasai portoenterostomy surgery at King's College Hospital and were followed up for at least two years (or until transplant/death) will be included in the study with a target sample of 200. Eligible patients will be included in reverse chronological order from 2020 until the target sample is reached. Patients will be excluded if they have a serious comorbidity or disease (e.g. cardiac illness, chromosomal abnormalities, congenital malformations).

Data collection

Data will be extracted by the researcher (a direct member of the care team) from electronic medical records. This will include medical record entries and letters written by members of the care team. Electronic flowsheets or forms will also be examined to extract data such as weight measurements and blood results. To help to reduce bias, a pre-agreed form will be used with precise definitions of the data to be extracted. For example, for weight measurements collected three months following surgery, the definition on the extraction form will state that it should be a weight done as close to three months as possible with a maximum range of +/- one month. Consultation with the PPI Panel will help ensure that all relevant variables are included in the extraction form. In addition, a second reviewer (also a member of the direct care team) who is unaware of the aims of the study will extract data from 20 medical records. The agreement between the researcher and the second reviewer will be compared. If there are major differences in the data collected, the extraction form will be revised.

The following information will be collected:

-Patient characteristics e.g. sex, date of birth, gestation, age at the time of kasai portoenterostomy surgery

-Outcomes: morbidity (e.g. ascites, gastrointestinal bleeding, cholangitis, intensive care admissions, rejection of the transplanted liver for those who have a transplant); two-year outcome (good = survival with the patient's own liver or poor = transplant or death), six-month post-transplant outcome (good = survival, poor = re-transplant or death).

Additionally, the following will be collected at six-time points: kasai portoenterostomy surgery, the six-week review and after 3, 6, 12 and 24 months or most recent contact if transplanted/died:

- Medium-chain fat supplementation levels: e.g. the prescribed medium-chain fat concentration (%), amount consumed and duration of time given

-Growth and nutritional status: weight-for-age, length-for-age, weight-for-length, head circumference-for-age, mid upper arm circumference-for-age z-scores

-Laboratory data: e.g. bilirubin, liver function tests

-Paediatric end-stage liver disease (PELD) score Data analysis: Data will be presented as

averages or % depending on the type of data. The data will be analysed to see if the amount of medium-chain fat that was given in the first six months was associated with growth measurements, nutritional status or outcomes.

Public and patient involvement:
Caregivers of children with biliary atresia have helped to shape this proposal and a panel of five caregivers will be formed and consulted on every aspect of the study.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
The following outcomes including medium-chain triglyceride (MCT) supplementation, growth and nutritional status and clinical outcomes are measured using patient medical records:

MCT supplementation
MCT intake (g/kg/day) prescription (% MCT) and duration of supplementation (months) determined based on caregiver-reported nutritional intake obtained at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy

Growth and nutritional status
1. Growth measurements (weight, length, head circumference, mid-upper arms circumference) obtained at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy and converted to age- and sex-adjusted z-scores.
2. Fat-soluble vitamin status (serum concentrations of vitamin A, vitamin D and vitamin E) at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy

Clinical outcomes
1. Two-year outcome is classed as good (survival with native liver) or poor (transplant/listed for transplant/death) at two years post kasai portoenterostomy
2. Post-transplant outcome for those who are transplanted is determined at six months post-transplant and is classed as good (survival) or poor (re-transplant/listed for re-transplant/death)
3. Morbidity at the time of the analysis
4. Paediatric End-Stage Liver Disease score measured at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy
5. The presence of ascites confirmed on abdominal ultrasound at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy
6. Number of episodes of gastrointestinal bleeding and cholangitis recorded in the two years following kasai portoenterostomy
7. Liver function (serum albumin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, gamma-glutamyl transferase and INR) obtained at baseline, 6 weeks, 3 months, 6 months, 12 months and 24 months post kasai portoenterostomy

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
21/12/2021

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Biliary atresia diagnosis
2. Kasai portoenterostomy procedure performed at King’s College Hospital
3. Followed up at King's College Hospital for two years or until liver transplant or death if this occurred before two years

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
Planned Sample Size: 200; UK Sample Size: 200

Key exclusion criteria
Serious comorbidities/ diseases (e.g. cardiac illness, chromosomal abnormalities, congenital malformations)

Date of first enrolment
01/04/2023

Date of final enrolment
31/07/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College Hospital NHS Foundation Trust
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
https://www.kch.nhs.uk/

ROR
https://ror.org/01n0k5m85

Organisation
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Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

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

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact, peer-reviewed journal

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as ethical approval was not sought for sharing of raw data.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Results article		02/12/2024	04/12/2024	Yes	No