ISRCTN81936667 https://doi.org/10.1186/ISRCTN81936667

Medium-chain fat supplementation and growth in infants with biliary atresia: a feasibility study

Submission date
11/01/2023

Recruitment status
No longer recruiting

Registration date
23/01/2023

Overall study status
Completed

Last Edited
13/08/2025

Condition category
Digestive System

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Biliary atresia (BA) is a rare liver disease of the bile ducts which results in many babies eventually needing a liver transplant. As bile from the bile ducts is needed to digest fat, babies with BA may not absorb enough fat and can become malnourished. Babies with biliary atresia are given medium-chain fat, a special fat made from coconut oil that can be absorbed even when there is no bile in the gut. Medium-chain fat is incorporated into specialist formula milk for children with liver disease. It can also be added separately to formula milk or to expressed breast milk as an oil. The aim of giving medium-chain fats is to provide an energy source so babies can grow. Even though medium-chain fats 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. The aim is to carry out a future trial comparing growth and outcomes in babies receiving different amounts of medium-chain fats. To prepare for this trial the researchers will first carry out this study to test whether a future trial would be possible.

Who can participate?
Infants with biliary atresia who have had a kasai portoenterostomy performed at King's College Hospital NHS Foundation Trust at or before 12 weeks of age will be invited to participate. Infants will not be included if they have had previous liver surgery, have a severe cardiac illness, were born before 32 weeks' gestation or have planned follow-up outside the United Kingdom.

What does the study involve?
In this feasibility study, 30 babies with biliary atresia will have either low or high amounts of medium-chain fat for 6 weeks. This will be achieved by adding different oils to their formula milk, oils commonly used in the diet and in the NHS. Information on weight, intake and tolerance will be recorded. Caregivers will be asked about their experiences of being in the study through a questionnaire and interview.

What are the possible benefits and risks of participating?
There may be no direct benefit to participants but the aim is to help babies who are diagnosed with biliary atresia in the future. Some participants might find it a benefit to have a dedicated

feeding diary for recording formula milk intake information. Participants might also find it a benefit to have regular contact with the researcher who is a dietitian and will provide additional support with feeding. There are no anticipated risks of participating.

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

When is the study starting and how long is it expected to run for?
December 2021 to April 2025

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

Who is the main contact?
Sara Mancell, sara.mancell@nhs.net

Contact information

Type(s)
Scientific

Contact name
Miss Sara Mancell

ORCID ID
https://orcid.org/0000-0002-6811-3461

Contact details
Department of Nutrition & Dietetics
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS
+44 (0)203 299 4434
sara.mancell@nhs.net

Additional identifiers

Integrated Research Application System (IRAS)
311670

Central Portfolio Management System (CPMS)
54463

Study information

Scientific Title

Medium-chain triglyceride supplementation and growth in infants with biliary atresia: a feasibility study

Study objectives
It is feasible to carry out a future randomised controlled trial investigating the impact of medium-chain triglyceride supplementation on growth and outcomes in infants with biliary atresia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/12/2022, London – Dulwich Research Ethics Committee (Health Research Authority, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JO, UK; +44 (0)207 104 8241, +44 (0)207 104 8274; Dulwich.rec@hura.nhs.uk), ref: 22/LO/0822

Primary study design
Interventional

Study design
Randomized; Interventional; Design type: Treatment, Dietary

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Biliary atresia

Interventions
Design
This study will be a feasibility study. The purpose will be to determine whether it would be acceptable and achievable to carry out a future study on how different amounts (concentrations) of medium-chain fats impact on growth and outcomes in babies with biliary atresia. Immediately after diagnosis, 30 babies with biliary atresia will be randomly allocated to have either low or high amounts of medium-chain fat for six weeks. The study will be double-blind. This means that neither the caregivers nor the researcher will know whether babies are having low or high amounts of medium-chain fats. To assess the acceptability of the study, caregivers will be invited to complete a brief questionnaire and take part in a 30-minute interview.

Participants
30 babies diagnosed with biliary atresia will be included in the study following kasai portoenterostomy surgery. Babies will be included who have had their surgery at or before 12 weeks of age. Babies will be excluded if they have had previous liver or bile duct surgery, have a severe cardiac illness, if they were born before a gestational age of 32 weeks or if it is anticipated that their follow-up care will be outside of the United Kingdom.

Recruitment
As it will not be possible to take consent from babies, their caregivers will be asked to provide consent on their behalf. The study will be explained to caregivers and they will have at least 24 hours to read the participant information and ask questions before providing consent. Those

caregivers who do not wish to take part will be invited to instead participate in a 10-minute interview exploring barriers to participation.

Medium-chain fat recipe
The different medium-chain fat amounts will be achieved by adding oils to babies' formula milk, oils commonly used in the diet and in the NHS. The oils will be safflower oil which contains 100% regular fat (long-chain fats) and refined coconut oil which contains 100% medium-chain fat. The oils were chosen as they are unflavoured and routinely available to the public. The labels will be removed so it will not be possible for caregivers to tell which oil is which. The formula milk that babies with biliary atresia are given after kasai portoenterostomy surgery contains some medium-chain fats already. Adding medium-chain fats to formula milk which already contains medium-chain fats increases the overall medium-chain fat concentration. Adding regular fats reduces the medium-chain fat concentration. Caregivers will be given instructions on how to add the oil to the formula milk in line with normal practice. This was considered acceptable to PPI members who said they were used to following formula milk recipes. The concentration for the low medium-chain fat group will be 30% (+/-3%) and for the high medium-chain fat group it will be 70% (+/-3%). These concentrations were chosen as they represent the lower and upper levels of what is used in practice. As these concentrations are in the range used nationally, both the low and high amounts of medium-chain fats will be considered 'treatment as usual'.

PPI members viewed the concentrations as acceptable as they are routinely used in practice. They felt that if babies were given no medium-chain fats as part of the study, caregivers might not want to participate due to concerns about growth. The interviews for this study will help to explore the acceptability of also including 0% medium-chain fats or 50% medium-chain fats in the future study.

Outcomes
Clinical outcomes of growth, formula milk intake and formula milk tolerance will be assessed in this study in order to determine whether it would be feasible to include these outcomes in the future trial. Growth will be measured following kasai portoenterostomy and at the six-week appointment in line with normal practice. Caregivers will be asked to record the amount of milk that is consumed each day in a formula milk intake diary. The researcher will ask questions relating to feeding tolerance (stools, vomiting, flatulence, crying, fussiness) in weeks 2 and 6 using a questionnaire called the Infant Gastrointestinal Symptom Questionnaire. This tool has proven reliability and validity (Riley et al, 2015).

Recruitment and retention
The researcher will record the number of eligible patients, the number who agree to take part, the number of patients recruited per month and the number who complete the study. For those who drop out of the study, the reason for dropping out (if known) will be recorded.

Fidelity
The feeding diary will include a daily tick box so that caregivers can indicate whether the recipe for making the formula milk was followed. The researcher will contact caregivers weekly (by telephone, email or video call depending on caregiver preference) to ask the number of days they followed the recipe correctly in the previous week. This will be done in case of missing data on the feeding diary and was supported by PPI members. Reasons for not giving the formula milk as per protocol will be explored to inform the future trial.

Acceptability
Caregivers will be asked to complete a short questionnaire on the study’s acceptability at their six-week appointment. The questions have been developed with help from PPI members.

Caregivers will also be invited to take part in a one-to-one 30-minute recorded interview at the appointment or within seven days of their 6-week appointment. It will be carried out by telephone or in-person according to participant preference and any specific COVID restrictions.

Sample size
A sample of 30 babies with BA will be included in this study. This is the lower end of the sample size used for feasibility studies and is acceptable given this very rare disease. Preparatory work suggests that there would be 20-25 potentially eligible patients annually, so over 24 months there would be 40-50 potential patients. It is expected that patients are very likely to take part in and complete the study based on PPI members' feedback and a previous study (Jain et al, 2017). The researchers will be able to estimate the expected rate of recruitment and retention for the future study using this sample. All participants will be invited to take part in the interviews with a target sample of at least 15 participants which should be enough participants to assess acceptability (O'Cathain et al, 2015).

Data analysis
Descriptive data for outcomes will be presented as averages and percentages depending on the type of data. For the interviews the recorded sessions will be transcribed word for word. The transcripts will be analysed to categorise common themes related to the acceptability of the study. Discussion with the PPI panel will help to ensure that the findings are relevant and credible.

Public and patient involvement (PPI)
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

Primary outcome(s)
1. Recruitment is assessed by reporting the proportion of eligible patients recruited overall and the flow of participants over time
2. Retention rate is the proportion of randomised participants retained for the study’s duration
3. Fidelity is measured using the daily feeding diary where caregivers indicate whether the formula milk was given as per protocol
4. Acceptability is measured using an acceptability questionnaire and interview at 6 weeks post kasai portoenterostomy

Key secondary outcome(s)
1. Weight is measured in kg using class III clinical electronic scales at baseline and 1, 2, 3, 4, 5 and 6 weeks post kasai portoenterostomy and converted to age- and sex-adjusted z-scores (WHO, 2009)
2. Length is measured in cm using a recumbent length board at baseline and 6 weeks and converted to age- and sex-adjusted z-scores (WHO, 2009)
3. Head circumference is measured in cm using a disposable paper tape measure at baseline and 6 weeks and converted to age- and sex-adjusted z-scores (WHO, 2009)
4. Mid upper arm circumference is measured in cm using a disposable paper tape measure at baseline and 6 weeks
5. Formula milk intake (ml/kg/day) is measured using the feeding diary over the 6-week period
6. Medium-chain triglyceride intake (g/kg/day) is measured using the feeding diary over the 6-week period

7. Feeding tolerance is measured using the Infant Gastrointestinal Symptom Questionnaire (IGSQ) at baseline and 6 weeks
8. Stool is assessed using 16S rRNA/metagenomic sequencing and metabolome analysis at baseline and 6 weeks
9. Liver function is assessed using serum measurements of aspartate aminotransferase, alanine aminotransferase, total bilirubin, conjugated bilirubin, gamma-glutamyl transferase and international normalised ratio at baseline and 6 weeks

Completion date
09/04/2025

Eligibility

Key inclusion criteria
1. Biliary atresia diagnosis
2. Kasai portoenterostomy procedure performed at King's College Hospital at or before 12 weeks of age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
30

Key exclusion criteria
1. Previous hepatobiliary surgery
2. Severe cardiac illness
3. Born before a gestational age of 32 weeks
4. Not for follow-up in the United Kingdom

Date of first enrolment
30/01/2023

Date of final enrolment
04/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: NIHR302152

Results and Publications

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			28/06	No	No

summary			/2023		
Other publications	Digital animation as a tool to enhance informed consent when recruiting infants with biliary atresia to a clinical trial	12/08 /2025	13/08 /2025	Yes	No