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Mechanisms affecting the gut of preterm infants

Submission date	Recruitment status	[_] Prospectively registered
18/05/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/08/2016	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/09/2024	Digestive System	

Plain English summary of protocol

Background and study aims
About 11% of all babies born worldwide are preterm (premature), meaning that they are born more than three weeks before their due date. The earlier babies are born, the more likely they are to die or develop long-term complications, particularly those born before 32 weeks. Over the last 20 years, breathing support has improved significantly, meaning that more babies now service. Currently, the most common cause of serious illness after the first week are due to complications or infections in the gut (digestive system). About 20-25% of very preterm infants (born before 32 weeks) develop a serious infection (sepsis) or a bowel complication called necrotising enterocolitis (NEC). Infants who get sepsis or NEC have a much higher risk of dying or being disabled. Better methods of preventing these complications in very preterm infants are needed. The ELFIN study started recruiting infants in 2015, and will test whether giving them supplemental lactoferrin (a natural antibiotic protein from cow's milk) reduces the number of serious infections, and also whether it affects rates of gut complications. Regardless of the results of the ELFIN study, the way that the extract lactoferrin works on the gut will still be unknown. It is thought that lactoferrin will work by changing the pattern of bacteria in the gut, and that in turn this will reduce the number of harmful bacteria that might cause sepsis. Increasing the number of healthy bacteria in the gut may allow the infant to better tolerate milk feeds, and less likely to develop gut complications such as NEC. The aim of this study is to find out how lactoferrin supplements work by looking at changes to the gut bacteria.

Who can participate?
Premature babies who are taking part in the ELFIN study of lactoferrin.

What does the study involve?
Details about the ELFIN trial are available at: http://www.isrctn.com/ISRCTN88261002.
For all participants, a sample of stool is collected from the nappy, and a urine sample (collected using cotton wool balls) each day the baby is in the hospital until they are close to going home. These samples are then stored at the local hospital before being transferred to central laboratories in Newcastle. The samples are analysed for the overall patterns of gut bacteria, as well as the presence of specific species that may be harmful or associated with improved recovery.

What are the possible benefits and risks of participating?
There are no direct benefits or risks involved for participants taking part in this study.

Where is the study run from?
The Neonatal Unit at Royal Victoria Infirmary (lead centre) and ten other neonatal units in NHS hospitals in the north of England (UK)

When is the study starting and how long is it expected to run for?
February 2016 to June 2019

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

Who is the main contact?
Dr Nicholas Embleton

Study website
http://www.neonatalresearch.net/magpie.html

Contact information

Type(s)
Public

Contact name
Dr Nicholas Embleton

Contact details
The Royal Victoria Infirmary
Ward 35 RVI
Newcastle Hospitals NHS Foundation Trust
Newcastle Upon Tyne
United Kingdom
NE1 4LP

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CPMS 30750

Study information

Scientific Title
Mechanisms Affecting the Gut of Preterm Infants in Enteral feeding trials (MAGPIE)

Acronym
MAGPIE

Study objectives
The aim of this study is to determine, in preterm infants, whether the mechanism of action of enteral lactoferrin supplementation in reducing infections or gut complications involves changes in the pattern of gut bacteria.

This study is linked to the ELFIN – Enteral Lactoferrin in Neonates study (available via http://www.isrctn.com/ISRCTN88261002)

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Nottingham 2 Research Ethics Committee, 16/03/2016, ref: 16/EM/0042

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Specialty: Children, Primary sub-specialty: Neonatal; UKCRC code/ Disease: Oral & Gastro/ Other diseases of the digestive system

Interventions
Infants who join the trial will all have been enrolled in the ELFIN study, and are anticipated to be recruited to MAGPIE at the same time in most cases i.e. within the first few days after delivery. We will collect a daily stool and urine sample from the infants from recruitment until hospital discharge (average 6 weeks, range 3-12 weeks in total duration). These samples will be collected at the cot-side and then placed in a freezer on the neonatal intensive care unit (NICU). Samples will be transferred to central laboratories and the most informative samples chosen for analysis of gut microbiota (16s next generation sequencing) and metabolomic analysis (stool and urine).

Intervention Type

Other

Primary outcome measure
Gut microbial diversity (Shannon Diversity Index) and differences in the proportions of key bacterial taxa measured using 16s next generation sequencing in stool samples collected after enrolment on days 1-3, 7, 10-14, and 21 (+/- 1) days.

Secondary outcome measures
1. The association between the pattern of gut microbiota and the stool metabolome using mixed effect models, structural equation modelling and ordination analyses. Stool metabolome is measured using Gas Chromatography and/or Liquid Chromatography in samples collected on days 1-3, 7, 10-14, and 21 (+/- 1) days.
2. Pattern of gut microbiota prior to the onset of NEC or sepsis (diagnosed according to criteria used in the ELFIN trial) is measured using up to 7 daily stool samples in the period immediately prior to disease compared to samples from control cases who do not develop disease
3. The gut tissue inflammatory response in surgically resected gut tissue affected by NEC and in control tissue (either non-affected tissue from the same infant, or tissue from an infant requiring gut resection who does not have disease), is determined by immune-histochemistry using paraffin blocks cut into small sections for staining, a digital slide scanner and white cell infiltrates identified using antibodies. This is measured after trial completion by retrieving samples from hospital pathology archives.

Overall study start date
01/02/2016

Completion date
30/06/2019

Eligibility

Key inclusion criteria
Preterm infants <32 weeks gestation who have been enrolled into the ELFIN study of lactoferrin

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
Planned Sample Size: 480; UK Sample Size: 480

Total final enrolment
479

Key exclusion criteria
Lack of informed consent

Date of first enrolment
01/07/2016

Date of final enrolment
30/06/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Victoria Infirmary
Neonatal Unit
Richardson Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Sunderland Royal Hospital
Neonatal Unit
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
University Hospital of North Tees
Neonatal Unit
Hardwick Road
Stockton
United Kingdom
TS19 8PE

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Leeds General Infirmary
Neonatal Unit
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Birmingham Women's Hospital
Neonatal Unit
Queen Elizabeth Medical Centre
Mindelsohn Way
Birmingham
United Kingdom
B15 2TG

Study participating centre
Nottingham City Hospital
Neonatal Unit
Hucknall Road
Nottingham
United Kingdom
NG5 1PW

Study participating centre
Nottingham University Hospital
Neonatal Unit
Queen's Medical Centre Campus
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Sheffield Teaching Hospital
Neonatal Unit
Jessop Wing
Tree Root Walk
Sheffield
United Kingdom
S10 2SF

Sponsor information

Organisation
The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Sponsor details
Newcastle Joint Research Office
1st Floor Regent Point
Regent Farm Road
Gosforth
Newcastle-Upon-Tyne
England
United Kingdom
NE3 3HD

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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 of a protocol in 2017 and the first stage analysis (effects on gut microbiota) in 2019 in a relevant peer reviewed journal. Metabolomic and integrative analysis, and tissue analysis publication will be in 2019-2020. It is anticipated that the preliminary results will be presented at international conferences. However, because this is an embedded mechanistic study, no key (un-blinded) data collected as part of MAGPIE will be presented or published until the primary results of the ELFIN trial have been accepted for publication.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	08/05/2017		Yes	No
Results article		01/09/2021	26/10/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		17/11/2022	12/09/2024	Yes	No