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Optimising newborn nutrition during therapeutic hypothermia

Submission date
20/07/2017

Recruitment status
No longer recruiting

Registration date
24/07/2017

Overall study status
Completed

Last Edited
06/09/2023

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
Every year about 1200 babies in England, Wales and Scotland suffer from a lack of oxygen around birth which can lead to long-term brain injury or death. This is called Hypoxic Ischaemic Encephalopathy (HIE). Research has shown that cooling babies with HIE by a few degrees for the first 3 days protects the brain therefore all babies with moderate or severe HIE in the UK are treated with therapeutic hypothermia (cooling). Doctors do not know how best to care for babies while they are cooled. A key question is “how to provide nutrition to babies during cooling”. There are two main parts to this question, milk feeds (“enteral” nutrition) and intravenous nutrition (“parenteral” nutrition). - Some neonatal units in the UK carefully feed babies (usually with maternal breast milk) while they are cooled. This avoids intravenous lines and is believed to help them feed and go home earlier. Other neonatal units do not feed cooled babies because they worry about a condition called necrotising enterocolitis (a devastating and often fatal disease that causes inflammation of the digestive system) which might be more common with feeding. All cooled babies need intravenous fluid (even when milk feeds are given it takes several days before enough fluid can be given this way). Some neonatal units give babies intravenous nutrition (which contains fat, protein, carbohydrate, vitamins and minerals) as this may improve growth and recovery. Other neonatal units only give intravenous dextrose with simple salts because of concerns that intravenous nutrition leads to more infections. It is not known how best to provide either milk or intravenous nutrition to cooled babies. This study compares these different ways of providing nutrition using a research database called the National Neonatal Research Database (NNRD). In England, Scotland and Wales doctors and nurses looking after babies in neonatal care (including all cooled babies) use an Electronic Health Record system. Data from this system are anonymised (no baby can be identified) and form the NNRD, so the NNRD holds data from all babies who have been looked after on NHS neonatal units. This has been developed closely with parents and charities. The aim of this study is to determine the best enteral and parenteral nutrition strategy for newborns with HIR during and after therapeutic hypothermia.

Who can participate?
Infants born at 36 gestational weeks or later who received therapeutic hypothermia for at least 72 hours

What does the study involve?
This study collects data in the NNRD about babies and their nutrition during therapeutic hypothermia. Babies who were fed milk while cooled are compared to those who were not fed any milk by collecting rates of necrotising enterocolitis. Babies who get intravenous nutrition are compared to those who get intravenous dextrose. The rate of infection, the amount of babies who died, how long they stayed in neonatal care, how soon they were able to breastfeed and how many who were breastfeed when they go home is collected from the NNRD. This is done to find the optimum nutrition strategy for newborns.

What are the possible benefits and risks of participating?
There are no direct benefits or risks with participating.

Where is the study run from?
This study is taking place at the Chelsea and Westminster Hospital (UK) and includes data from 200 NHS neonatal units in England, Scotland and Wales (UK).

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

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

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
17IC4064

Study information

Scientific Title
Optimising newborn nutrition during therapeutic hypothermia: An observational study using routinely collected data

Study objectives
The overarching aim of this project is to determine the optimum enteral and parenteral nutrition strategy for newborns with Hypoxic Ischaemic Encephalopathy (HIE) during and after therapeutic hypothermia. To do this we will perform two primary comparisons:

Enteral: To determine whether any enteral (milk) feeding, when compared to withholding enteral feeding (no milk), during therapeutic hypothermia, is associated with a difference in the incidence of necrotising enterocolitis.
Parenteral: To determine whether provision of intravenous dextrose, when compared to provision of parenteral nutrition, during therapeutic hypothermia, is associated with a difference in the incidence of blood stream infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)

East Midlands-Leicester Central Research Ethics Commitee, ref: 17/EM/0307

Study design
Retrospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
There is no participant information sheet for this study

Health condition(s) or problem(s) studied
Hypoxic-ischaemic encephalopathy requiring therapeutic hypothermia

Interventions
This study collects existing data help in the National Neonatal Research Database (NNRD). The analysis will apply the potential outcomes framework using propensity score matching. The data was collected from January 2008 to December 2016.

All analysis uses anonymised data held in an approved research database, the NNRD. No patient identifiable information is used in this study.

The data is collected in order to compare the milk feeding and intravenous nutrition that babies receive during therapeutic hypothermia.

Milk feeding: Data is collected about babies who are fed milk while cooled with those that are not fed any milk. This is to establish whether there is any difference in rates of necrotising enterocolitis.

Intravenous Nutrition: Data is collected to compare babies who get intravenous nutrition with those that only get intravenous dextrose. The main data collected is the rate of infection. The amount of babies who die, how long they stay in neonatal care, how soon breastfeeding starts and many are breastfed when they go home is also collected.

De-identified data held in the NNRD and the potential outcomes framework with application of propensity scoring is used to define matched subgroups for comparison.

Intervention Type
Mixed

Primary outcome measure

1. Necrotising enterocolitis is defined using the case definition (Battersby et al 2017) between birth and final neonatal unit discharge, and is collected and analysed using the data from the NNRD
2. Blood stream infection defined as pure growth of a recognised pathogen from a normally sterile site between birth and final neonatal unit discharge, and is collected and analysed using the data NNRD

Secondary outcome measures
1. Survival is measured using the NNRD data between birth and neonatal unit discharge
2. Length of stay is measured using the number of days between first neonatal unit admission and final neonatal unit discharge for surviving infants using the NNRD data between birth and final neonatal unit discharge
3. Breastfeeding at discharge is measured using any breastfeeding using NNRD discharge at time of final neonatal unit discharge
4. Hypoglycaemia is measured as any diagnosis of hypoglycaemia recorded during therapeutic hypothermia and is collected and analysed using the data from the NNRD
5. Time to full feed is measured as the number of days until an infant is recorded as not requiring any parenteral nutrition or intravenous fluid between birth and final neonatal unit discharge and is collected and analysed using the data from the NNRD
6. Growth, weight and head circumference for post-menstrual age standard deviation score at final neonatal unit discharge is measured using the data from the NNRD at final neonatal unit discharge

Overall study start date
15/09/2016

Completion date
09/01/2019

Eligibility

Key inclusion criteria
1. Infants born at 36 gestational weeks or later
3. Received therapeutic hypothermia for Hypoxic Ischaemic Encephalopathy (HIE) for at least 72 hours
3. Died during therapeutic hypothermia

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
We estimate that the National Neonatal Research Database (NNRD) holds data on approximately 7200 eligible infants

Total final enrolment
6030

Key exclusion criteria
Infants with missing data for principal background and outcome variables. Missing values for other variables will be dealt with using multiple imputation.

Date of first enrolment
01/10/2017

Date of final enrolment
01/10/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Chelsea and Westminster NHS Foundation Trust
369 Fulham Road
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Sponsor information

Organisation
Imperial College London

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Sponsor type
University/education

Website
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ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Not defined

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Final study report and academic publication
• This will describe the work undertaken, research, conclusions and recommendations from both parent and health professional perspectives
• The parent perspective will be publicised through social media, websites and other materials to highlight the value of such involvement

Scientific presentations
• These will be at neonatal and perinatal conferences and will describe clinical outcomes of different nutritional strategies
• We plan for parent and/or patient co-applicants to deliver presentations at these meetings to highlight the value of such involvement

Scientific publications
• Clinical results will be published in peer reviewed neonatal/paediatric journals to maximise impact within the UK and internationally

Social media
• Personal, charity and research group Twitter, Facebook and related social media resources will link to scientific publications and plain English summaries (produced by parent and parent representative co-applicants)

Websites
• Charity (Bliss) and professional (United Kingdom Neonatal Collaborative: UKNC, Imperial College London and University of Nottingham) websites will publicise the results of this work and highlight the value added by parent involvement

Professional communications
• UKNC and University of Nottingham newsletters and other communications will publicise results and link to scientific publications

Intention to publish date
01/03/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository called the National Neonatal Research Database (NNRD) http://www.imperial.ac.uk/neonatal-data-analysis-unit/neonatal-data/utilising-the-nnrd/ The data stored here will be de-identified paraticipant level data that is updated quarterly. All parents are informed and have the opportunity to opt out of their baby's data from being included in the NNRD. To access the database, ethical as well as other approvals are required, which is outlined here: http://www.imperial.ac.uk/neonatal-data-analysis-unit/neonatal-data /utilising-the-nnrd/

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	23/10/2018	26/11/2020	Yes	No
Results article		01/06/2021	08/06/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article	Feeding during therapeutic hypothermia	30/06/2021	06/09/2023	Yes	No
Results article	Parenteral nutrition during therapeutic hypothermia association with higher late-onset infection but lower mortality	05/05/2021	06/09/2023	Yes	No