

Optimising newborn nutrition during therapeutic hypothermia

Submission date 20/07/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 24/07/2017	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 06/09/2023	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> 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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Additional identifiers**Protocol serial number**

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 Committee, ref: 17/EM/0307

Study design

Retrospective cohort study

Primary study design

Observational

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Neonate

Sex

All

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

United Kingdom

England

Study participating centre
Chelsea and Westminster NHS Foundation Trust
369 Fulham Road
London
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SW10 9NH

Sponsor information

Organisation
Imperial College London

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, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository called the National Neonatal Research Database (NNRD)

<http://www.imperial.ac.uk/neonatal-data-analysis-unit/neonatal-data/utilising-the-nnr/>
 The data stored here will be de-identified participant 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-nnr/>

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/06/2021	08/06/2021	Yes	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
Protocol article	protocol	23/10/2018	26/11/2020	Yes	No
HRA research summary			28/06/2023	No	No