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Early antibiotic use and intestinal disease (necrotising enterocolitis) in premature babies

Submission date
09/06/2022

Recruitment status
No longer recruiting

Registration date
13/07/2022

Overall study status
Completed

Last Edited
07/12/2022

Condition category
Neonatal Diseases

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

Plain English summary of protocol

Background and study aims
Necrotising enterocolitis (NEC) is a key cause of death and disease in preterm infants. Early antibiotic use has been shown to impact on rates of NEC, with data suggesting that receipt in the first days after birth is protective, but long duration has adverse impact on NEC rates. We aim to use the large UK dataset of preterm births known as The National Neonatal Research Database (NNRD) to further delineate this relationship. The NNRD holds data on 'every' preterm neonate admitted in the United Kingdom in a link anonymised fashion, allowing exploration of the role of antibiotics in NEC development in a much bigger population than previously explored.

Who can participate?
Premature babies born at <32 weeks gestation with data entered into The National Neonatal Research Database

What does the study involve?
Analysis of data already collected in the National Neonatal Research Database exploring impact of antibiotics on NEC

What are the possible benefits and risks of participating?
There are no benefits or risks to individuals as this is a database analysis of existing data

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2020 to December 2023

Who is funding the study?
1. Investigator initiated and funded
2. Novo Nordisk Fonden

Who is the main contact?
Dr Janet Berrington
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Contact information

Type(s)
Principal investigator

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
312574

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 312574

Study information

Scientific Title
Early antibiotic use and incidence of necrotising enterocolitis in very preterm infants: A UK based observational study using routinely recorded data

Study objectives

Early antibiotic timing and duration impacts incidence of necrotising enterocolitis (NEC) in preterm infants

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, Ref: 22/NE/0113

Study design
Analysis of data already collected in the National Neonatal Research Database exploring impact of antibiotics on NEC

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Preterm infant

Interventions
We will access and extract details about infants with gestation <32 completed weeks, and the primary outcome measure of developing necrotising enterocolitis. We will also extract data on antibiotic exposure in the first 2 days to compare NEC incidence in those on antibiotics in the first 2 days with those without. We will collect additional data to allow for the effects of confounding factors as determined by the directed acyclic graph of other essential factors to consider in this analysis, including the availability of these items within the National Neonatal Research Database (NNRD), which holds this data routinely. There is no patient intervention, all data already exists.

Intervention Type
Drug

Phase
Not Applicable

Primary outcome(s)
Incidence of severe necrotising enterocolitis resulting in death or surgery developed before discharge from neonatal care as measured by the 'Battersby' definition and collected from the National Neonatal Research Database (NNRD)

Key secondary outcome(s))
All are measured before discharge from the neonatal unit and collected from the NNRD between 01/07/2022 and 31/12/2022:
1. Late onset sepsis (bloodstream or CSF confirmed pure growth in culture (NNAP definition) after the first 3 days and/or treatment with 5 days of antibiotics and a concurrent diagnosis of infection after the first 3 days)
2. Total antibiotic use (number of days with any treatment of antibiotics during admission)

3. Length of stay (postnatal age at discharge or death)
4. Time to reach full feeding (first day of 3 consecutive days where parenteral nutrition or intravenous fluid are not recorded)
5. Growth (change in standard deviation score (SDS) between birth and 36 weeks and discharge)
6. Total pre-discharge mortality
7. Further, we will analyse effects on some relevant adverse outcomes:
7.1 Total pre-discharge mortality
7.2. Death prior to day 7, day 14, day 28
7.3 Bronchopulmonary dysplasia (BPD; respiratory support given at 36 weeks)
7.4. Retinopathy of prematurity (ROP; in receipt of treatment, according to NNRD standard operating procedure)
7.5. Brain injury (intraventricular hemorrhage grade 3 or above or periventricular leukomalacia diagnoses recorded)
7.6. Need for surgical procedures

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Preterm infant born at <32 weeks gestation
2. Data entered into the The National Neonatal Research Database

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Key exclusion criteria
Death before 3 days

Date of first enrolment
01/07/2022

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Royal Victoria Infirmary
Neonatal Unit
(Ward 35)
Richardson Road
Newcastle
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Funder Name
Novo Nordisk Fonden (postdoctoral fellowship to René Shen, BRIDGE Translational Excellence Programme, grant no. NNF18SA0034956)

Alternative Name(s)
Novo Nordisk Foundation, Novo Nordic Foundation, NNF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Denmark

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Janet Berrington janet.berrington1@nhs.net

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		15/11/2022	23/11/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes