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European study of neonatal excipient exposure: study of excipient kinetics in neonates

Submission date	Recruitment status	[_] Prospectively registered
06/03/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
28/05/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
14/02/2018	Other	

Plain English summary of protocol

Background and study aims
Medicines contain active pharmaceutical ingredients along with a range of other chemicals, collectively known as excipients. These excipients are required to overcome the chemical, physical and microbiological issues that occur when developing formulations that are of good quality to be used in clinical practice. Extensive work is done by pharmaceutical companies to ensure that excipients are safe, which requires knowledge about exposure and outcomes. Premature babies are a vulnerable group as they are not yet suited to life outside of the uterus and can become seriously ill as they adapt to birth, therefore they are often given multiple medications to help them. This may also be the case for full-term babies who are seriously unwell, for example with infections. Nobody has measured the levels of excipients used in medicines for babies and although we are happy with those currently used in clinical practice, it would help to know more about how the body handles the excipients currently used. It would also help pharmacists when developing new medicines for use in babies to ensure that only chemicals that are necessary are included in the formulations. The main aim of the study is to measure the concentration of selected excipient in blood samples taken from newborn babies.

Who can participate?
Treatment, or likely treatment, of neonates with a drug prescribed containing any of the following excipients; Propylene Glycol, Ethanol and metabolites (Fatty acid ethyl esters are no-oxidative ehtanol metabolities), Propylhydroxybenzoate and other parabens, sodium benzoate /benzoic acid/benzyl alcohol, Polysorbate 80, Sorbitol. Each neonatal unit will develop a list of medicines containing the excipient which will trigger eligibility to the study.

What does the study involve?
This is an observational study of routine clinical practice in which clinical data will be supplemented by information from blood samples taken opportunistically or during specific sampling periods.

What are the possible benefits and risks of participating?
There is no expected direct benefit to participants and no risks.

Where is the study run from?
Liverpool Women's NHS Foundation Trust

When is the study starting and how long is it expected to run for?
October 2011 to December 2012

Who is funding the study?
Medical Research Council (MRC), UK

Who is the main contact?
Ms Susan Graham
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11663

Study information

Scientific Title
European Study of Neonatal Excipient Exposure (ESNEE): an observational study of excipient kinetics in neonates

Acronym
ESNEE

Study objectives
Medicines contain drugs (active pharmaceutical ingredients) along with a range of other chemicals, collectively known as excipients. These excipients are required to overcome the chemical, physical and microbiological issues that occur when developing formulations that are of good enough quality to be used in clinical practice.

Extensive work is done by pharmaceutical companies to ensure that excipients are safe in adults. Nobody has measured the levels of excipients used in medicines for babies so that it is not possible at present to make robust evaluations of excipient safety, particularly in newborn babies. Although clinicians are happy with those currently used in clinical practice, it would help to know more about how the body handles the excipients currently used. It would also help pharmacists when developing new medicines for use in babies to know how the body deals with excipients.

This study will look at a selection of excipients and measure how much of these excipients get into the blood stream and how long those excipients stay in the blood stream of newborn babies. The selected excipients will serve as case studies to describe what happens to important excipients and to define the best ways to measure excipients in newborn babies.

More details can be found at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=11663

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Greater Manchester, 14/10/2011, ref: 11/NW/0665

Study design
Observational case-controlled study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please contact susan.graham@lwh.nhs.uk to request a patient information sheet

Health condition(s) or problem(s) studied
Medicines for neonates

Interventions

Parents will be asked to consent to allow their baby to participate in the study in advance of them being prescribed one of the medicines that contain the excipient of interest.

Where parents have consented to allow extra blood samples to be taken from their child, a maximum of 10 extra samples will be taken at specific time points.

Where parents consent to only allow for blood to be taken as part of routine clinical practice, any excess blood will be used instead of being discarded. The day of the last sample will be when 10 extra samples have been obtained or when the baby is transferred to a unit which is not collecting samples for the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
To develop pilot excipient kinetic models to indicate how much of each selected excipient is in the bloodstream of babies who have been given medicines containing those excipients

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/11/2011

Completion date
31/12/2012

Eligibility

Key inclusion criteria
Treatment, or likely treatment, of neonates with a drug prescribed containing any of the following excipients:
1. Propylene glycol
2. Ethanol and metabolites [Fatty acid ethyl esters (FAEEs) are nonoxidative ethanol metabolites]
3. Propylhydroxybenzoate and other parabens
4. Sodium benzoate/benzoic acid/ benzyl alcohol
5. Polysorbate 80
6. Sorbitol

Each neonatal unit will develop a list of medicines containing the excipient which will trigger eligibility to the study.

An example list of the drugs prescribed in the lead UK neonatal unit which contain the excipients can be provided on request to the study coordinator.

Participant type(s)
Patient

Age group

Neonate

Sex
Both

Target number of participants
Planned Sample Size: 1300; UK Sample Size: 500

Key exclusion criteria
1. Babies whose mothers refuse to give consent
2. Babies whose mothers are deemed too poorly or not competent to give valid consent

Date of first enrolment
01/11/2011

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
England

Estonia

France

United Kingdom

Study participating centre
Liverpool Women's Hospital
Liverpool
United Kingdom
L8 7SS

Sponsor information

Organisation
Liverpool Women's NHS Foundation Trust (UK)

Sponsor details
Neonatal Unit
Liverpool Womens Hospital
Crown Street
Liverpool

England
United Kingdom
L8 7SS

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04q5r0746

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) ref: G1100158 - Lifelong Health and Wellbeing

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	01/06/2016	Yes	No