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A study looking at how effective and safe a very low dose of dexamethasone is in helping ventilator-dependent preterm babies who are at high risk of bronchopulmonary dysplasia (a serious lung condition that affects infants) get off the ventilator more quickly and effectively

Submission date
01/08/2016

Recruitment status
No longer recruiting

Registration date
01/08/2016

Overall study status
Completed

Last Edited
19/12/2019

Condition category
Respiratory

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Many premature babies are at risk of developing breathing problems because their lungs are not fully matured when they are born, and may require breathing support through a breathing tube (ventilation) at the start of life. Babies who receive prolonged breathing support are at risk of developing a lung condition called bronchopulmonary dysplasia (BPD, sometimes called chronic lung disease). This is caused, in part, by inflammation (swelling) of the baby's developing lungs, which is likely made worse by the ventilator. When this happens, the baby needs more oxygen and may have difficulty breathing, which can take some time to improve. Babies with BPD generally stay in hospital longer and are more likely to have issues with their brain development, which affects them as they grow up. Currently, many babies who require prolonged ventilation and are at high risk of developing BPD are treated with dexamethasone, a steroid that is used in many conditions to reduce inflammation in the body. In the past, doctors used to use high doses of dexamethasone to get babies off ventilators. These high doses did work, as the babies came off the ventilators earlier and had fewer lung problems, but there were side effects. The dose being used in this study is ten times lower than the usual dose of dexamethasone. This dose appears to be effective and seems to cause fewer side effects. The aim of this study is to find out if this reduced dose, 'minidex', is helpful, harmful or makes no difference to the outcomes of these babies.

Who can participate?
Babies who were born more than 10 weeks early, who require prolonged ventilation and are aged between 10 and 24 days old.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive dexamethasone through a drip everyday for ten days and then every other day for a further six days. The dose given is calculated using the weight of the infants at the start of the study. Those in the second group receive a placebo (dummy), which is made up of saline (salt water) everyday for ten days and then every other day for a further six days. Participants in both groups are closely monitored and the length of time until the breathing tube is removed (extubation) is recorded.

What are the possible benefits and risks of participating?
All babies will benefit from being monitored very closely throughout the study by the staff on the Neonatal Intensive Care or Special Care Unit. There are no notable risks involved with participating in this study, as the dose of dexamethasone used is ten times lower than the standard dose and so it is unlikely that babies will suffer any side effects.

Where is the study run from?
Leeds General Infirmary (lead centre) and nine other neonatal units across the Midlands and North of England (UK)

When is study starting and how long is it expected to run for?
November 2015 to November 2018

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

Who is the main contact?
Ms Vaneesha Short
minidex@npeu.ox.ac.uk

Study website
http://www.npeu.ox.ac.uk/minidex

Contact information

Type(s)
Public

Contact name
Miss Vaneesha Short

Contact details
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Additional identifiers

EudraCT/CTIS number
2015-005342-63

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
31350

Study information

Scientific Title
Minidex: The efficacy and safety of very low dose dexamethasone used to facilitate the extubation of ventilator dependent preterm babies who are at high risk of bronchopulmonary dysplasia

Acronym
Minidex

Study objectives
The aim of this study is to determine if treatment with very low dose dexamethasone facilitates the extubation of ventilator dependent preterm babies of less than 30 weeks' gestation who are at high risk of developing bronchopulmonary dysplasia (BPD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West – Liverpool Central Research Ethics Committee, 21/06/2016, ref: 16/NW/0396

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

https://www.npeu.ox.ac.uk/minidex/parent-resources

Health condition(s) or problem(s) studied
Specialty: Children, Primary sub-specialty: Neonatal; UKCRC code/ Disease: Reproductive Health and Childbirth/ Other disorders originating in the perinatal period

Interventions
Babies will be randomised in the ratio 1:1 to receive either very low dose dexamethasone or a matched placebo. Randomisation will be managed via a secure web-based randomisation facility hosted by the NPEU CTU, University of Oxford, with telephone backup available at all times (24 /7, 365 days a year). The randomisation program will use a minimisation algorithm to ensure balance between the groups with respect to collaborating hospital, sex, multiple births, gestational age at birth and existing diuretic therapy for the 24 hours prior to randomisation.

Intervention arm: Participants receive daily intravenous infusions of 50 mcg/kg Dexamethasone for 10 days then alternate days for 6 days. Dose to be calculated on working weight at trial entry; can be increased in line with working weight as per local practice.

Control arm: Participants receive daily intravenous infusions of 50 mcg/kg placebo (0.9% saline solution) for 10 days then alternate days for 6 days. Dose to be calculated on working weight at trial entry; can be increased in line with working weight as per local practice.

All participants will be followed up for safety outcomes and other outcomes until 36 weeks postmenstrual age (PMA) or discharge if sooner.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Dexamethasone

Primary outcome measure
Time to first extubation after randomisation when the baby remains extubated for more than 24 hours is determined using an intubation log recording times of extubations and re-intubations which will be maintained throughout the intervention period (16 days).

Secondary outcome measures
1. Time to first extubation (whether or not more than 24 hours) is measured using the intubation log maintained throughout the intervention period (16 days)
2. Extubation by day 7 after randomisation (where the baby has remained extubated for more than 24 hours) is measured using the intubation log maintained throughout the intervention period (16 days)
3. Extubation by day 7 after randomisation (whether or not for more than 24 hours) is measured using the intubation log maintained throughout the intervention period (16 days)
4. Survival to 36 weeks' postmenstrual age (or discharge if sooner) is measured using medical record review at 36 weeks' postmenstrual age
5. Respiratory morbidity to 36 weeks' postmenstrual age (or discharge home if sooner) is measured by medical record review at 36 weeks' postmenstrual age (or discharge if sooner)

6. Inflammatory cytokine profile in blood and endotracheal tube secretion fluid is measured from endotracheal tube secretions and blood samples taken at baseline, 4, 7, 10 and 14 days after randomisation
7. Parent/family experience is measured using a parent-completed Diary of Care at maintained throughout the intervention period (16 days)

Safety outcomes:
1. Hypertension is reported from medical record review at 36 weeks' postmenstrual age (or discharge if sooner)
2. Hyperglycaemia is reported from medical record review at 36 weeks' postmenstrual age (or discharge if sooner)
3. Confirmed/suspected sepsis is reported from medical record review at 36 weeks' postmenstrual age (or discharge if sooner)
4. Spontaneous gastrointestinal perforation or NEC is reported from medical record review at 36 weeks' postmenstrual age (or discharge if sooner)
5. Deterioration in cranial ultrasound findings (new finding of severe intraventricular haemorrhage or periventricular leukomalacia) between the cranial ultrasound scan performed prior to randomisation and cranial ultrasound scan performed at 36 weeks' postmenstrual age (or discharge if sooner)
6. Growth measured through change in weight standard deviation score between weight measured at trial entry and day 14
7. Growth measured through change in weight standard deviation score between weight measured at day 14 and medical record review at 36 weeks' postmenstrual age (or discharge if sooner)
8. Growth measured through change in head circumference standard deviation score between medical record review at trial entry and at 36 weeks' postmenstrual age (or discharge if sooner)

Overall study start date
01/11/2015

Completion date
30/11/2018

Eligibility

Key inclusion criteria
1. Born at <30 weeks' gestation
2. Aged between 10 and 24 postnatal days (≥10 and ≤24)
3. At high risk of developing BPD: receiving mechanical ventilation via endotracheal tube (ET) with at least 30% inspired oxygen when the positive end expiratory pressure (PEEP) is at least 4 cm water and, in the opinion of the treating physician, unlikely to be extubated within 48 hours
4. Receiving caffeine therapy
5. Written informed parental consent

Parents of babies recruited at Leeds Teaching Hospitals and Bradford Royal Infirmary will be asked to consent to their
baby having samples taken for cytokine estimation. This will allow modelling of their inflammatory networks

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
Planned Sample Size: 94; UK Sample Size: 94

Total final enrolment
22

Key exclusion criteria
1. Previously received postnatal steroid treatment for respiratory disease
2. No realistic prospect of survival
3. Severe congenital anomaly affecting the lungs, heart or central nervous system
4. Previous surgical abdominal procedure
5. Concurrent illness for which postnatal corticosteroid would be contra-indicated (e.g. active fungal infection, confirmed or suspected acute sepsis and acute NEC/focal intestinal perforation)
6. Participation in another trial that would preclude baby from inclusion in Minidex

Date of first enrolment
01/11/2016

Date of final enrolment
14/04/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Leeds General Infirmary
Leeds Teaching Hospitals NHS Trust
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Bradford Royal Infirmary
Bradford Teaching Hospitals NHS Foundation Trus
Duckworth Lane

Bradford
United Kingdom
BD9 6RJ

Study participating centre
University Hospital of North Tees
North Tees and Hartlepool NHS Foundation Trust
Hardwick Road
Stockton-on-Tees
United Kingdom
TS19 8PE

Study participating centre
Royal Preston Hospital
Lancashire Teaching Hospitals NHS Foundation Trust
Sharoe Green Lane North
Preston
United Kingdom
PR2 9HT

Study participating centre
Birmingham Women's Hospital
Birmingham Women's NHS Foundation Trust
Mindelsohn Way
Birmingham
United Kingdom
Birmingham

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Royal Victoria Infirmary
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Queen Victoria Road
City Newcastle upon Tyne

United Kingdom
NE1 4LP

Study participating centre
Royal Hallamshire Hospital
Sheffield Teaching Hospitals NHS Trust
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
Liverpool Women's and Children's Hospital
Liverpool Women's NHS Trust
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
University Hospital Coventry
University Hospital Coventry and Warwickshire NHS Trust
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Hull Royal Infirmary
Hull and East Yorkshire Hospitals NHS Trust
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Sponsor information

Organisation
University of Liverpool

Sponsor details
Research Support Office
2nd Floor Block D Waterhouse Building
3 Brownlow Street
Liverpool
England
United Kingdom
L69 3GL

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04xs57h96

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 study results in a high-impact peer reviewed journal.

Intention to publish date
30/11/2019

Individual participant data (IPD) sharing plan

Selected results are uploaded on to the EudraCT database as per CTIMP requirements. Datasets will be made available via NPEU data sharing agreement. Applications to be made to NPEU CTU, University of Oxford, Old Road Campus, Oxford, OX3 7LF, tel: 01865 289700, email ctu@npeu.ox.ac.uk. Aggregated results reported in results publication.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2019	19/12/2019	Yes	No
HRA research summary			28/06/2023	No	No