ISRCTN82342359 https://doi.org/10.1186/ISRCTN82342359

Is morphine an effective analgesic for procedural pain in infants?

Submission date
29/07/2015

Recruitment status
Stopped

Registration date
29/07/2015

Overall study status
Stopped

Last Edited
18/08/2023

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
Pain in babies has negative consequences, both immediately and in the longer term. As babies cannot describe their pain the measurement and treatment of pain is difficult and, compared to adults and older children, pain is undertreated in this group. Given that a baby requiring intensive care will experience an average of 12 painful procedures per day and, the youngest and sickest babies may experience 50 procedures per day, this is a serious clinical issue that urgently needs to be addressed. The aim of this study is to test whether morphine can provide effective pain relief in babies during invasive medical procedures. While morphine is frequently given to adults when they experience pain, it is not known whether morphine provides effective pain relief for acute pain in babies. An example of a painful procedure that is frequently and regularly performed on premature babies is an eye exam that tests for Retinopathy of Prematurity – this is a disease which if untreated can lead to permanent blindness. Although the exam is considered to be painful and can result in unstable breathing and heartbeat for up to 24 hours after the exam, the pain relief currently provided during this procedure has limited efficacy. Here, we want to see if morphine can provide effective pain relief for babies undergoing this exam.

Who can participate?
Infants that were born at less than 32 weeks gestation or with a birth weight or less than 1501g. They must be in-patients at the John Radcliffe Hospital in Oxford and be between 34-42 weeks gestational age when undergoing the test.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given morphine during an eye exam testing for Retinopathy of Prematurity. Those in group 2 are given a placebo during the same procedure. Clinical pain assessment tools are used to measure pain experienced. Newly developed brain imaging techniques are also used to see how morphine can affect pain related brain activity.

What are the possible benefits and risks of participating?
We cannot guarantee any direct benefits. At present we don’t know whether giving a pain relieving medication (morphine) reduces the pain and discomfort caused by eye exams and

blood tests. We are carrying out this study to help doctors make the right decisions about the care of preterm babies in the future. Morphine is a pain-relieving drug that is routinely used in children and adults to treat acute pain. Morphine is routinely used in the neonatal unit to sedate babies when they are ventilated, although to-date few studies have been carried out where morphine has been administered to babies to provide pain relief prior to invasive procedures. The dose of morphine (100 µg/kg) will be administered by mouth and has been approved by the neonatal pharmacist. Although morphine can have effects on breathing rate and blood pressure, a study that used twice this dose did not report any adverse side effects. We do not anticipate that the babies will experience these side effects and they will be monitored very closely by the staff on the neonatal unit

Where is the study run from?
John Radcliffe Hospital, Department of Paediatrics (UK)

When is the study starting and how long is it expected to run for?
January 2015 to March 2018

Who is funding the study?
1. National Institute for Health Research, EME (UK)
2. Wellcome Trust (UK)

Who is the main contact?
Dr Rebeccah Slater

Contact information

Type(s)
Public

Contact name
Dr Rebeccah Slater

Contact details
John Radcliffe Hospital
Department of Paediatrics
University of Oxford
Level 2, Children's Hospital
Oxford
United Kingdom
OX3 9DU

Additional identifiers

Clinical Trials Information System (CTIS)
2014-003237-25

Protocol serial number
19317

Study information

Scientific Title
A blinded randomised placebo controlled trial investigating the efficacy of morphine analgesia for procedural pain in infants

Acronym
POPPI: procedural pain in premature infants

Study objectives
The aim of this study is to test whether morphine can provide effective pain relief in babies during invasive medical procedures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Northampton Research Ethics Committee, 23/07/2015, ref.: 15/EM/0310

Primary study design
Interventional

Study design
Blinded placebo-controlled parallel-group randomized clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Children; Subtopic: Pain

Interventions
As of 02/09/2016:
1: Morphine Sulphate: 10ml of the IMP will be supplied in amber glass bottle at a concentration of 200 µg/ml. This will provide a dose of 100 µg/kg which will be administered orally by sterile oral/enteral 3ml syringe.
2: Placebo (inactive solution): The placebo (inactive solution) will be supplied in identical packaging but will contain only the carrier solution.
Study Entry: Single Randomisation only

Initial:
1. Morphine Sulphate: 2 ml of the IMP will be supplied at a concentration of 200 µg/ml. This will provide a dose of 100 µg/kg which will be administered orally by syringe
2. Placebo (inactive solution): The placebo (inactive solution) will be supplied in identical syringes but will contain only the carrier solution
Study Entry : Single Randomisation only

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Current as of 04/02/2016:
1. Clinical pain score measured using the Premature Infant Pain Profile-revised (PIPP-R) 30 seconds after ROP screening
2. Magnitude of nociceptive-specific brain activity evoked by heel lance

Previous:
1. Clinical pain score measured using the Premature Infant Pain Profile (PIPP) 1 minute after ROP screening
2. Magnitude of nociceptive-specific brain activity evoked by heel lance

Key secondary outcome(s)
Current as of 04/02/2016:
1. Clinical stability in the 6-hour and 24-hour period following the start of the clinical intervention. The clinical intervention is defined as the heel lance followed by rhe ROP screening.
2. Premature infant pain profile-revised (PIPP-R) score and amplitude of nociceptive reflex withdrawal activity following heel lance
3. Drug safety will be assessed by calculating the number of incidences of apnoea that require intervention using NeoPuff or 'bag and mask' and the number of incidences of hypotension that require treatment with inotropes in the 24-hour period following the administration of the IMP or placebo.following ROP screening

Previous:
1. Clinical stability in the 6-hour and 24-hour period after ROP screening
2. Premature infant pain profile (PIPP) score and amplitude of nociceptive reflex withdrawal activity following heel lance
3. Drug safety will be assessed by calculating the number of incidences of apnoea that require intervention using NeoPuff or 'bag and mask' and the number of incidences of hypotension that require treatment with inotropes in the 24-hour period following ROP screening

Completion date
15/03/2018

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. Participants will be in-patients on the neonatal unit at the John Radcliffe Hospital, Oxford
2. Infants born less than 32 weeks' gestation or birth weight <1501 g
3. At the time of study, infants will be between 34 and 42 weeks gestational age (GA) and will be studied if they require a clinical heel lance and retinopathy of prematurity (ROP) screening on the same test occasion. We will study infants during a single ROP examination when they are greater than or equal to 34 weeks' gestation
4. Infants for whom parents/guardians have consented to inclusion in the trial.; Upper Age Limit 42 weeks
Lower Age Limit 34 weeks
5. Senior clinician considers inclusion in trial to be medically appropriate (added 04/02/2016)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
34 Weeks

Upper age limit
42 Weeks

Sex
All

Total final enrolment
31

Key exclusion criteria
1. Intraventricular haemorrhage > grade II
2. Short bowel syndrome
3. Receiving nil by mouth due to documented gut pathology
4. Received opiates in the last 72 hours
5. Received other analgesics or sedatives in the last 24 hours
6. Previously documented episode of morphine sensitivity
7. Congenital malformation or genetic condition known to affect neurological development
8. Senior clinician considers inclusion in trial to be medically appropriate
9. Born to mothers who regularly use opiates during pregnancy or while breastfeeding or expressing breast milk

Date of first enrolment
01/09/2016

Date of final enrolment
13/12/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hospital
Department of Paediatrics

University of Oxford
Level 2, Children's Hospital
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
Research Services, University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research, EME

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

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/12/2018		Yes	No
Results article		01/08/2019	18/08/2023	Yes	No
Protocol article	protocol	15/11/2016		Yes	No
HRA research summary			28/06/2023	No	No