

Is morphine an effective analgesic for procedural pain in infants?

Submission date 29/07/2015	Recruitment status Stopped	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 29/07/2015	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 18/08/2023	Condition category Signs and Symptoms	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 Rebecca Slater

Contact information

Type(s)

Public

Contact name

Dr Rebecca Slater

Contact details

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

Additional identifiers

EudraCT/CTIS number

2014-003237-25

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Study design

Blinded placebo-controlled parallel-group randomized clinical trial

Primary study design

Interventional

Secondary study design

Clinical trial of an investigational medicinal product (CTIMP)

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

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 measure

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

Secondary outcome measures

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 the 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

Overall study start date

01/01/2015

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

Age group

Child

Lower age limit

34 Weeks

Upper age limit

42 Weeks

Sex

Both

Target number of participants

Planned Sample Size: 156; UK Sample Size: 156

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

England

United Kingdom

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

Sponsor details

Joint Research Office

Churchill Hospital

Oxford

England

United Kingdom

OX3 7LE

Sponsor type

Hospital/treatment centre

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

Publication and dissemination plan

The plan to publish the results of the study in a peer-reviewed medical journal after we have acquired and analysed the data.

Intention to publish date

01/11/2019

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?
Protocol article	protocol	15/11/2016		Yes	No
Results article	results	15/12/2018		Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/08/2019	18/08/2023	Yes	No