Supplementary material: PIL

Procedural Pain
in Premature Infants

poppi

Parent Information Leaflet

We would like to tell you about a study this hospital is carrying out for babies who have been born early. Before you decide, it is important for you to understand why the research study is being done and what it will involve. Please read the following information carefully. Please ask us if there is anything that is not clear or if you would like more information.

Study title

Poppi: Procedural pain in premature infants.

Short title: Is morphine an effective analgesic for procedural pain in infants?

What is the purpose of the study?

The overall aim of our research is to find an effective way of treating pain in babies. Babies who are born prematurely are exposed to many painful procedures as part of their essential medical care. As they are unable to tell us when they are in pain, it is difficult to know when they need pain medication or to determine if the pain medication is working. We are looking at whether using a pain relieving medication (morphine) reduces the pain and discomfort caused by routine eye examinations and blood tests. To help us assess this we have developed a way of detecting pain in babies by non-invasively measuring brain activity.

You have been invited to take part in this study because your baby was born prematurely. As part of your baby's routine clinical care your baby will need regular eye tests from 32 weeks gestation to look for retinopathy of prematurity – this is an eye disease related to prematurity. Routinely your baby will be given anaesthetic eye drops for this test as it is considered to be painful and stressful to your baby. They would not be given any additional pain relief (other than standard comfort techniques such as swaddling or use of a dummy), even though the anaesthetic eye drops are not thought to be completely effective. Morphine is a medication we use routinely in the neonatal unit. Your baby will probably have received morphine to make them more comfortable if he or she has been ventilated. We want to find out whether a single dose of morphine given orally can relieve the pain caused by the eye exam and by a routine blood test which will be performed at the same time.

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If your baby is due to have an eye exam and blood test we will randomly assign him or her to receive either an oral dose of morphine or a placebo (a harmless inactive solution that does not contain morphine). After your baby receives the medication we will monitor him or her to see if the medication causes any reduction in pain. We will do this by videoing his or her facial expressions, and by gently placing monitoring leads on your baby's body to record oxygen saturations, heart rate, muscle activity and brain activity during the routine blood test and eye exam. Your baby will probably already be monitored for some of these measures as part of their normal care.

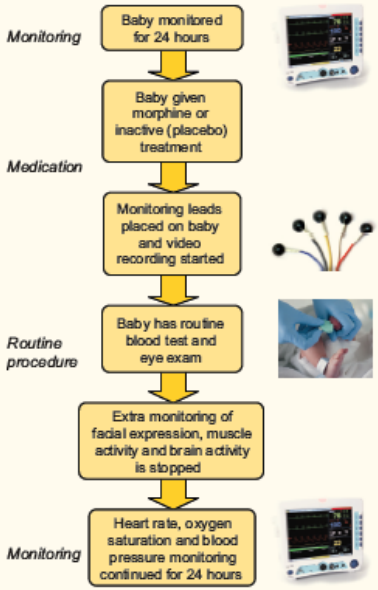
We also want to find out if the pain medication can help make your baby more stable and comfortable for the rest of the day following the examination. In order to determine this, we will record his or her heart rate and oxygen saturations and blood pressure for the 24 hours before and 24 hours after the eye test so that we can identify whether the pain medication has helped make your baby more comfortable.

Does my baby have to take part?

No, it is up to you to decide whether or not your baby will take part. If you agree to your baby taking part, we will ask you to sign a consent form. If you decide you do not want your baby to take part, we fully understand and assure you that this will have no adverse effect on your baby's normal clinical care.

What is involved in the study?

Babies who are included in the study will have their blood tests and eye tests completed in the routine way. No extra painful procedures or extra blood tests will be done for the purpose of this study. The study will not interfere with your baby's clinical care, nor will there be any delay if an emergency procedure is required.



Medication

When investigating if a treatment works it is necessary to compare it to an inactive (placebo) treatment so we can be sure any differences are due to the treatment. We allocate babies randomly to each group so that the groups are equal in number. This is called a 'blinded' trial which means that neither you, your doctor or the research team will know which treatment group your baby has been allocated to (although if your doctor needs to find out he/she can do so). It is only at the end of the trial when results are being analysed that we will find out which group your baby was in.

Your baby's details will be entered into a computer programme that will randomly select whether your baby will receive morphine or an inactive solution that looks the same (a placebo). This will be given to your baby (in their mouth) one hour before their eye examination. Your baby will have a 50% chance of receiving morphine and a 50% chance of receiving the inactive placebo.

Monitoring for pain

Your baby's reaction to the blood test and eye exam will be recorded on a video camera, and extra monitoring will be used to see if the medication is effectively reducing the discomfort caused by the procedures.

1. We will video your babies face and calculate a pain score based on how much they change their facial expression during and after the procedures. Pain scores are often used on the neonatal unit to measure infant pain.
   Video footage or photographs will not be used for public use and only for study data analysis.
2. We will measure your baby's brain waves using a technique called EEG (electroencephalography). EEG is routinely used on the neonatal unit, on children's wards and in clinics to look at infant brain activity. Monitoring leads (silver discs) will be gently placed on your baby's head to measure the brain waves. This is not painful or harmful to your baby.
3. We will measure how much your baby moves during the eye test and blood test by measuring their muscle activity. We will put two EMG (Electromyography) discs on your baby's thigh muscle to measure their reaction to the tests. EMG is a safe non-invasive technique used to record muscle activity.

4. Your baby will probably already have their heart rate and oxygen saturation monitored for clinical reasons but if these monitors are not in place then a small probe will be wrapped around your baby's wrist to record these measures.

What are the known risks of the study?

Obtaining video footage of your baby is non-invasive and does not present any risk to your baby. EEG, EMG and ECG have been used on the neonatal unit, wards and clinics for almost 20 years without adverse effects.

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 your baby will experience these side effects and your baby will be monitored very closely by the staff on the neonatal unit .

What are the possible benefits of taking part?

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.

What information will be collected about my baby?

We will collect basic clinical information about your baby's delivery, condition at birth and their progress and medical treatment while they were in the neonatal unit. For example, their gestational age at birth and on the day of the study, their need for support with breathing or any medication they are or were receiving. We require this information as these factors may influence the way a baby copes with pain.

All information and videos that are collected about your baby during the course of the research will be kept strictly confidential.

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Who is organising and funding the research?

The study is sponsored and run by researchers at the University of Oxford and NPEU, Clinical Trials Unit and is funded by the Wellcome Trust and National Institute of Health Research, EME Programme. None of your doctors will be paid for enrolling your baby onto the study.

Withdrawal from the project

You are free to withdraw your baby from the study at any time without having to give a reason. The clinically required procedures will go ahead subject to a review by a suitably qualified clinician. We will ask you whether data already collected may be retained and used for the purposes of the trial.

Who has reviewed the study?

All research that involves NHS patients has been approved by an NHS Research Ethics Committee before it goes ahead. Approval means that the Committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given sufficient information on which to make an informed decision to take part or not. The Northampton Research Ethics Committee has reviewed and approved this study. This study has also been approved by the Medicines and Healthcare products Regulatory Authority (MHRA) who oversee the safety of new and existing drugs.

What will happen to the results of the research study?

At the end of the study, the results will be analysed and published in a medical journal. We will send you a summary of the final results of the study. A copy of the full journal article can be requested from the NPEU. Your baby will not be identified in any report or publication about the study.

Contact for further information:

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If you would like to contact an independent organisation to discuss the inclusion of babies in research studies generally we suggest that you contact Bliss, a special care baby charity. Bliss contact details are:

Bliss
for babies born too soon, too small, too sick

Chapter House, 18-20 Crucifix Lane, London SE1 3JW

Freephone Family Support Helpline: 0500 618 140

Thank you for reading this information sheet

The POPPI trial is funded by the National Institute for Health's EME Programme and The Wellcome Trust

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