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Remifentanil intravenous patient controlled analgesia (PCA) versus intramuscular pethidine for pain relief in labour

Submission date
08/08/2013

Recruitment status
No longer recruiting

Registration date
08/08/2013

Overall study status
Completed

Last Edited
05/11/2020

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Childbirth can be a painful experience. Providing women with prompt pain relief is a priority for the midwives and doctors who care for them in labour. There are several forms of pain relief available to women, including gas-and-air (Entonox), strong pain relieving drugs, such as Pethidine and epidurals. Pethidine is the standard drug given in the UK, usually by injection into the thigh or arm. It is effective, but can cause side effects such as drowsiness and sickness. In recent years, some labour wards have begun to offer a different drug called Remifentanil for pain relief to some women. Remifentanil is given through a drip. By pressing a hand-held button, women give themselves a small dose of drug whilst having a contraction. Research done so far shows that Remifentinail is safe for women, and their babies, and provides effective pain relief. However, it is not yet offered as standard care. As with Pethidine, women can experience drowsiness and sickness. Epidurals provide excellent pain relief but can increase the chance of forceps or suction delivery. We do not know yet which of Remifentanil or Pethidine is better at helping women avoid the need for an epidural and experience a more straightforward birth. This study will find this out.

Who can participate?
Women at the participating hospitals who are expecting to have a vaginal birth and request pain relief will be considered for the study. We hope that 400 women will agree to take part.

What does the study involve?
If happy to take part in the study, women will be asked to sign a consent form. The person who takes consent will then enter their details into a computer. This will randomly allocate the woman to either the Pethidine or Remifentanil group. This decision will be made by chance, rather like the toss of a coin. This is important because it ensures that the two forms of pain relief can be tested fairly against each other. Information about the woman's labour will be then be collected by the midwife until they give birth and be kept confidentially. During labour, women will be asked how effective their pain relief is. We will record details of when the woman and baby are discharged from hospital, and details of any treatments received whilst in hospital. Participants will also be asked to fill in a short questionnaire to find out what they thought of

the care they received during labour and the birth of the baby. There are no further tests or hospital visits connected with this study. No payments are available for taking part in this study.

What are the possible benefits and risks of taking part?
Women will be offered pain relief in labour whether they participate in the study or not. We cannot promise the study will help individuals involved, but the answers we get from this study will help improve the care provided to women in labour in the future. Both pethidine and remifentanil are strong drugs related to morphine. Women can experience side effects such as drowsiness, dizziness or sickness with both. All women taking part will be monitored constantly by their midwife for drowsiness and anti-sickness medication given promptly if required. There are no known differences in risks to mother and baby for either type of pain relief. There are no restrictions on having an epidural if needed.

Where is the study run from?
The lead centre for the study is the Birmingham Women's Hospital (UK).

When is the study starting and how long is it expected to run for?
It is hoped that recruitment will begin in the Autumn of 2013 and run for 20 months.

Who is funding the study?
National Institute of Health Research (NIHR) (UK)

Who is the main contact?
Leanne Beeson
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Study website
http://www.birmingham.ac.uk/respite

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2012-005257-22

IRAS number

ClinicalTrials.gov number
NCT02179294

Secondary identifying numbers
14923

Study information

Scientific Title
Remifentanil intravenous patient controlled analgesia (PCA) versus intramuscular pethidine for pain relief in labour: a randomised controlled trial

Acronym
RESPITE

Study objectives
Childbirth can be extremely painful and the provision of pain relief during labour is a vital component of a positive maternal experience. The majority of women who deliver in modern obstetric units choose a pharmacological method of pain relief, including Entonox, the injection of opioids or epidural placement. The commonest opioid used in labour is pethidine administered by intramuscular (im) injection. The effectiveness of pain relief provided by pethidine has long been challenged. Its shortcomings are more serious when set against known side effects including maternal sedation, nausea and potential transfer across the placenta to the foetus. More than a third of women who receive pethidine subsequently require an epidural due to inadequate pain relief. Epidurals provide highly effective pain relief, but increase the risk of a forceps or suction delivery resulting in prolonged hospital stay. Therefore, there is a clear need for a safe, effective, easy to administer analgesic alternative. Patient Controlled Analgesia (PCA) comprises drug administration into an intravenous drip with a small dose given each time a woman presses a button, giving her control over her own pain relief. The pump is programmed to ensure that the maximum dose allowable is within the safe range. This form of delivery of pain relief matches the drug dose to pain sensation within the relevant time frame, which is not possible using a single dose intramuscular injection. Whilst PCA is in widespread use for acute pain relief it has only a limited role in obstetrics. The most common drug given by PCA is morphine, however, since it has a long duration of action and crosses the placenta, the potential for accumulation in the foetus and consequent neonatal sedation at delivery restricts its utility (within obstetrics) to contexts where neonatal status is not relevant, such as intrauterine foetal death or foetal abnormality incompatible with survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Nottingham 2 MREC, 01/08/2013, ref: 13/EM0239

Study design
Randomised; Interventional; Design type: Treatment

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Reproductive Health and Childbirth; Subtopic: Reproductive Health and Childbirth (all Subtopics); Disease: Reproductive Health & Childbirth

Interventions
Women will be randomly allocated to either:
1. Intervention group: Remifentanil via PCA pump (PCA bolus remifentanil 40 µg) administered intravenously
PCA pump programming will be pre-set by anaesthetic staff in accordance to the single protocol indicated above. This dose regime is based on sample guidelines adapted from those used in the introduction of Remifentanil PCA into clinical practice in the applicant's own labour ward and reflect those used in the largest study to date. In the event of excess sedation being recorded by regular observation of respiratory function, the regimen will be altered by reduction of the remifentanil bolus dose to 30 µg with a lock-out interval of 2 minutes.
2. Control group: Intramuscular injection of pethidine (100 mg) up to 4 hourly in frequency (up to a maximum of 4 doses). The maximum dose being 400mg in 24 hours.

After the administration of analgesia, a trial participant will receive the following standards of care independent of group allocation:
1. One-to-one midwifery care
2. 30-minute observations including
2.1. Respiratory rate and oxygen saturation by pulse oximetry
2.2. Sedation score
2.3. Visual analogue pain score
Indications for contacting an anaesthesia provider
1. Excessive Sedation Score (not rousable to voice)
2. Respiratory rate <8 breaths/minute
3. Oxygen Saturation <94% whilst breathing room air

There will be no follow-up of patients after discharge from labour ward.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Remifentanil, Pethidine

Primary outcome measure
The proportion of women who have an epidural placed for pain relief in labour, in each group

Secondary outcome measures
Secondary outcome measures as of 21/12/2015:
1. The effectiveness of pain relief provided by each technique, quantified by Visual Analogue Scale taken every 30 minutes after time zero, until delivery or transfer to theatre.
2. The incidence of maternal side effects, up to the end of 3rd stage, including:
2.1. Excessive sedation score
2.2. Oxygen Saturation <94% whilst breathing room air
2.3. Nausea requiring anti-emetic administration
2.4. Requirement and indication for supplemental oxygen
2.5. Respiratory depression (respiratory rate < 8 breaths/minute)
3. Delivery mode (Spontaneous, Instrumental Vaginal, Caesarean Section)
4. Incidence of foetal distress requiring delivery
5. Neonatal status at delivery:
5.1. APGAR score at 5 minutes
5.2. Incidence of foetal acidosis determined by umbilical cord gas analysis
5.3. Requirement for neonatal resuscitation
5.4. Incidence of and indication for admission to neonatal care
6. Rate of initiation of breastfeeding within the first hour of birth
7. Maternal satisfaction with childbirth experience determined by postpartum questionnaire prior to discharge from the delivery ward
8. Explore and compare women's birth experiences, perceptions of pain relief and infant feeding behaviours up to six weeks postpartum (RESPITE Post-Natal Sub-Study)

Previous secondary outcome measures:
1. The effectiveness of pain relief provided by each technique, quantified by Visual Analogue Scale taken every 30 minutes after time zero, until delivery or transfer to theatre.
2. The incidence of maternal side effects, up to the end of 3rd stage, including:
2.1. Excessive sedation score
2.2. Oxygen Saturation <94% whilst breathing room air
2.3. Nausea requiring anti-emetic administration
2.4. Requirement for supplemental oxygen
2.5. Respiratory depression (respiratory rate < 8 breaths/minute)
3. Delivery mode (Spontaneous, Instrumental Vaginal, Caesarean Section)
4. Incidence of foetal distress requiring delivery
5. Neonatal status at delivery:
5.1. Apgar score at 5 minutes
5.2. Incidence of foetal acidosis determined by umbilical cord gas analysis
5.3. Requirement for neonatal resuscitation
5.4. Incidence of admission to Special Care Baby Unit
6. Rate of initiation of breastfeeding within the first hour of birth
7. Maternal satisfaction with childbirth experience determined by postpartum questionnaire prior to discharge from the delivery ward
8. Resources used intra- and post-operatively, including PCA consumables, anaesthetist attendance
9. Costs of staff training, service procurement and provision of care will be collected alongside

clinical outcomes
10. Explore and compare women’s birth experiences, perceptions of pain relief and infant feeding behaviours up to six weeks postpartum (RESPITE Post-Natal Sub-Study)

Overall study start date
01/09/2013

Completion date
18/10/2017

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/04/2015:
1. Requesting systemic opioid analgesia
2. 16 years of age or older
3. Beyond 37+0 weeks' gestation
4. In established labour (defined as regular painful contractions, irrespective of cervical dilatation) with vaginal birth intended
5. Able to understand all information (written and oral) presented (using an interpreter if necessary) and provide signed consent
6. Not participating in any other clinical trial of a medicinal product
7. Live, singleton pregnancy with cephalic presentation

Previous inclusion criteria:
1. Requesting systemic opioid analgesia
2. 16 years of age or older
3. Beyond 30+0 weeks' gestation
4. In established labour with vaginal birth intended
5. Able to understand all information (written and oral) presented (using an interpreter if necessary) and provide signed consent
6. Not participating in any other clinical trial of a medicinal product
7. Singleton pregnancy with cephalic presentation

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Key exclusion criteria
Exclusion criteria as of 21/12/2015:
1. Contraindication to epidural analgesia
2. Contraindication to intramuscular injection

3. History of a previous adverse reaction to pethidine or remifentanil
4. Patients taking any long-term opioid drug therapy including Methadone
5. Systemic opioid pain relief in last 4 hours administered by intravenous or intramuscular injection. (Oral medications comprising opioids alone or in combination preparations, administered in this 4 hour period, are permitted).

Previous exclusion criteria as of 23/04/2015:
1. Contraindication to epidural analgesia
2. Contraindication to intramuscular injection
3. History of drug sensitivity to pethidine or remifentanil
4. Patients taking any long-term opioid drug therapy including Methadone
5. Systemic opioid pain relief in last 4 hours

Previous exclusion criteria:
1. Contraindication to epidural analgesia
2. Contraindication to intramuscular injection
3. History of drug sensitivity to pethidine or remifentanil
4. Patients taking any long-term opioid drug therapy including Methadone

Date of first enrolment
01/05/2014

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Birmingham Women's Hospital
United Kingdom
B15 2TG

Study participating centre
University Hospital of North Midlands
United Kingdom
ST4 6QG

Study participating centre

York Hospital
United Kingdom
YO31 8HE

Study participating centre
Bradford Royal Infirmary
United Kingdom
BD9 6RJ

Study participating centre
Frimley Park Hospital
United Kingdom
GU16 7UJ

Study participating centre
Stoke Mandeville Hospital
United Kingdom
HP21 8AL

Study participating centre
Northwick Park Hospital
United Kingdom
HA1 3UJ

Study participating centre
Birmingham Heartlands Hospital
United Kingdom
B9 5SS

Study participating centre
Good Hope Hospital
United Kingdom
B75 7RR

Study participating centre
Northwick Park Hospital
Watford Road

Harrow
United Kingdom
HA1 3UJ

Study participating centre
Norfolk & Norwich University Hospital
United Kingdom
NR4 7UY

Study participating centre
Medway Maritime Hospital
United Kingdom
ME7 5NY

Study participating centre
Homerton University Hospital
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
City Hospital Birmingham
Dudley Road
Birmingham
United Kingdom
B18 7QH

Study participating centre
Warwick Hospital
Lakin Road
Warwick
United Kingdom
CV34 5BW

Study participating centre
University Hospital Coventry
Clifford Bridge Road
Coventry

United Kingdom
CV2 2DX

Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
Edgbaston
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Clinician Scientist Award Scheme, UK; Grant Codes: CS-11-030

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/06/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study may be available upon request from m.j.wilson@sheffield.ac.uk

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	12/12/2016		Yes	No
Results article	results	25/08/2018		Yes	No
Results article	qualitative sub-study results	23/12/2019	05/11/2020	Yes	No