ISRCTN72413202 https://doi.org/10.1186/ISRCTN72413202

The POPS trial (PICC Out Parenteral nutrition Stopped): In preterm infants less than 1500grams, does stopping intravenous nutrition and removing Peripherally Inserted Central Venous Catheters (PICC lines) at 100mls /kg/day of oral feeds compared to 140mls/kg /day (full oral feeds) significantly increase time to regain birth-weight?

Submission date
10/06/2013

Recruitment status
No longer recruiting

Registration date
20/06/2013

Overall study status
Completed

Last Edited
03/11/2020

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Very low birth weight infants (infants less than 1500grams) can initially only tolerate small amounts of oral feeds due to their immature digestive systems. Feeds (breast milk or formula) are given through a tube (passed from the nose down into the stomach) and are slowly increased over the first weeks of life until full feeds are reached. Adequate nutrition during this time is important for growth and can affect important outcomes such as development. For this reason babies are given intravenous nutrition while feeds are being increased. This is called parenteral nutrition and is best given through a central line [Central Venous Catheter (CVC)]. A CVC is inserted in the first few days of life and delivers this nutritional fluid into a large vein near the heart. If parenteral nutrition leaks out of small veins it can damage the delicate surrounding tissue. Larger veins are better able to tolerate this concentrated fluid. CVCs also last much longer than peripheral lines and venous access is usually limited in these tiny infants. Peripherally Inserted Central Venous Catheters (PICC lines) are central lines inserted into a large blood vessel through the skin and are the preferred type of CVC in many neonatal units. All babies lose some weight in the first week of life and the time to regain birth-weight is a good marker of early post-natal (after birth) nutrition. Birth-weight is normally regained after about 11 days. The main outcome in this study will be to see if there is a significant difference, approximately 2 days, in the time it takes to regain birth weight between the babies who have their PICC line removed and parenteral nutrition stopped at 100mls/kg/day versus 140mls/kg /day (i.e. full feeds). If we show that there is no significant difference in nutritional outcomes

between babies in both groups, then removing PICC lines earlier should help to reduce the risk of infection without negatively affecting nutrition.

Who can participate?
All babies less than 1500grams who have a PICC line inserted and are initiating oral feeding can participate.

What does the study involve?
Babies in this study will be randomly allocated to have their PICC line removed and parenteral nutrition stopped at either 100mls/kg/day (intervention group) or 140mls/kg/day (control group). Their treatment and care will otherwise be the same. No one will know which group a baby is in until an envelope, telling the doctor at what feeding volume the PICC line is to be removed, is opened. Once babies have reached full feeds, there will be no difference in the treatment they receive.A doctor will assess each baby prior to the PICC line being removed. If there is some medical reason why intravenous access is required then the PICC line will not be removed. Babies in the study will not have any extra tests or treatments compared to babies who do not participate in the study.

What are the possible benefits and risks of participating?
The benefit of continuing parenteral nutrition until full oral feeding (140mls/kg/day) is achieved is that maximal nutrition for growth is delivered. However, the longer the PICC line is in place and parenteral nutrition is delivered, the greater the risk of infection and other PICC line complications. There is no evidence to suggest that stopping parenteral nutrition at 100mls/kg /day oral feeds negatively affect sugar levels or hydration status. However, babies will be monitored for these complications and can be quickly managed if they occur.

Where is the study run from?
The study is run from two tertiary level neonatal centres in Dublin, Ireland. These are the Coombe Women and Infants University Hospital (CWIUH) and the National Maternity Hospital (NMH), Holles Street. The CWIUH is the lead centre. We plan to enrol 70 babies from each centre, 140 babies in total.

When is the study starting and how long is it expected to run?
This study plans to start in June 2013 and will continue until 140 babies are recruited. This will take approximately one year.

Who is funding the study?
Coombe Women and Infant's University Hospital

Who is the main contact?
Dr. Lucy Perrem: lucy.perrem@hertford.ox.ac.uk, lucyperrem@yahoo.com
Dr. Jan Miletin, is the Clinical Director of Newborn Medicine in the CWIUH and is the lead supervisor: miletinj@hertford.ox.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Study number 9 - 2013 (CWIUH)

Study information

Scientific Title
In preterm infants less than 1500g, does PICC line removal and parenteral nutrition discontinuation at 100mls/kg/day enteral feed volume compared to 140mls/kg/day (full enteral feeds) significantly increase mean time to regain birth-weight: A randomised controlled trial

Acronym
POPS

Study objectives
The Very Low Birth Weight (VLBW) infant is often slow to tolerate the introduction and advancement of enteral feeds because of delayed gastric emptying and intestinal peristalsis.

Early postnatal nutrition may have a significant impact on important outcomes, including long-term neurodevelopment (Ehrenkranz et al., 2006) so these infants receive intravenous parenteral nutrition while enteral feeds, given via a nasogastric tube, are being established (Wilson et al., 1997).

Peripheral intravenous (IV) cannulas (lines) are easily inserted but infiltrate quickly (hours to days), requiring frequent replacement (Ainsworth et al., 2007). Parenteral nutrition is a hypertonic and irritating solution to peripheral veins and can result in extravasation injury with local skin ulceration, secondary infection and scaring. Central Venous Catheters (CVC) are placed in larger veins closer to the heart and can tolerate more concentrated solutions. They provide long-term venous access (days to weeks), and are a solution to minimal vascular access in these infants. The most commonly used CVCs in newborns are umbilical venous catheters (UVCs) and peripherally inserted central catheters (PICC lines). PICC lines are inserted percutaneously into a large vessel in the arm or leg and are the preferred CVC for PN administration in many units.

However, PICC lines are not without their hazards and along with parenteral nutrition (PN) are independent risk factors for nosocomial infection (Olsen et al., 2009, Moro et al., 1996, Stoll et al., 2002). Other complications of PICC lines include venous thrombosis, embolism (air or thrombus), extravasation and rarely cardiac tamponade (Camara, 2001, Darling et al., 2001). Stoll et al (2002) showed that infants with prolonged duration of central catheters and parenteral nutrition, those with delayed initiation of enteral feeds and those with a prolonged period to reach full enteral feeds or to regain birth weight were all at substantially increased risk of late-onset sepsis. These data suggest that efforts to initiate enteral feedings as early as possible, to minimize the use of PICC lines and to reduce the number of catheter days and/or days on parenteral nutrition would not only improve nutritional status but also decrease the risk of infection.

Recommendations exist to remove PICC lines in Very Low Birth Weight (VLBW) infants at 75% full enteral feeds (Bedford M, 2007). Currently there are no randomized trials to support this recommendation and uncertainty remains regarding the impact of the nutritional and fluid deficit accrued before full feeds are attained.

We speculate that there will be no significant difference (≥2 days) in the primary outcome, time to regain birth-weight, between the infants who have parenteral nutrition discontinued at 100mls/kg/day (intervention group) versus 140mls/kg/day (100% enteral feeds, control group). Time to regain birthweight is used as a surrogate marker for early nutrition in the Very Low Birth Weight (VLBW) infant. We also propose that the secondary outcomes including hypoglycaemia, hydration status and discharge weight will also fail to show a significant difference. The main reason for removing PICC lines as soon as possible is to reduce their associated complications, most notably infection. The incidence of late onset sepsis (LOS) increases with increasing length of time the PICC is in situ and parenteral nutrition administered. This study will not be powered to detect a significant difference in catheter associated blood stream infections but it will be an important secondary outcome. We anticipate that this study will provide evidence regarding the safety of removing PICC lines at 100mls/kg/day enteral feed volume. However, if significant differences in our endpoints exist, guidelines regarding the removal of PICC lines will need to be reassessed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
CWIUH ethics board, approved 17th March 2013. Ref: study 9-2013

Study design
Two-centre parallel group randomised controlled trial

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Very Low Birth Weight / extremely premature infants: Nutrition and Late onset sepsis (LOS), CVC /PICC complications

Interventions
Removal of PICC line at 100mls/kg/day of enteral feeds compared to 140mls/kg/day (full feeds).

Participants will be followed until their discharge from hospital.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
To compare the two allocation groups with respect to the time taken to regain birth weight. This will be calculated in days from birth. Infants are weighed daily.

Secondary outcome measures
To compare the two allocation groups with respect to the following:
1. Episodes of CVC associated blood stream infection/Late onset infection (>72hours)
2. PICC complications (thrombosis, infiltration, leaking, thrombophlebitis, superficial skin infection at site)
3. Hypoglycaemia Point Of Care Testing (POCT) glucose ≤2.6mmol/L within 24 hours of PICC line removal
4. Peripheral IV inserted within 24hours of PICC removal for the purpose of IV hydration
5. Discharge weight (kg), occipital-frontal circumference (OFC) (cm) and length (cm) and centiles (WHO centile chart)
6. The mean difference in calorie, carbohydrate, lipid and protein intake between between removal of PICC line and 140mls/kg/day
7. Mean duration PICC line in situ, calculated in hours

Overall study start date
16/06/2013

Completion date
16/10/2013

Eligibility

Key inclusion criteria
1. Very Low Birth Weight Infants (less than 1500g) who are initiating enteral feeding
2. Peripherally inserted central catheter (PICC) in situ

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
140 total (70 per centre)

Total final enrolment
139

Key exclusion criteria
1. Infants diagnosed with a major congenital or chromosomal abnormality which will affect growth parameters and time to full feeds
2. Death/transfer out of unit likely before primary outcome (i.e return to birth-weight)
3. Enteral feed volume of 100mls/kg/day achieved prior to randomisation

Date of first enrolment
16/06/2013

Date of final enrolment
16/10/2013

Locations

Countries of recruitment
Ireland

Study participating centre
Coombe Women and Infants University Hospital (Ireland)
Dublin
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8

Sponsor information

Organisation
Coombe Women and Infants University Hospital (Ireland)

Sponsor details

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Sponsor type
Hospital/treatment centre

Website
http://www.coombe.ie/

ROR
https://ror.org/00bx71042

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Coombe Women and Infant's University Hospital (Ireland)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2019	03/11/2020	Yes	No