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Clamping the umbilical cord in premature deliveries (CUPID)

Submission date
25/01/2016

Recruitment status
No longer recruiting

Registration date
05/02/2016

Overall study status
Completed

Last Edited
30/11/2020

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
About 11% of all babies born worldwide are preterm (premature) meaning that they are born more than three weeks before their due date. Premature babies have had less time to develop in the womb, and so often have a low birth weight. It has been found that around one in 70 babies (1.4%) are born more than eight weeks prematurely, and around 51% of all infant deaths occur in this group. Surviving infants are much more likely to develop serious disabilities such as cerebral palsy (a condition caused by injury to the parts of the brain responsible for controlling muscles before or shortly after birth), as well as developmental and behavioural problems. After a baby is born, the umbilical cord may be clamped immediately (within 20 seconds of birth, later (deferred cord clamping) at around 60 seconds after birth or by using a technique called milking, in which blood is “pushed” through the umbilical cord to the baby by hand. Studies have shown that in premature infants, cord milking and deferred clamping appear to be more beneficial than the usual practice of immediate clamping, lowering the risk of intraventricular haemorrhage (bleeding in the brain), which is a major cause of disability in children, although to date, these techniques have not shown to affect general brain development. The aim of this study is to find out whether the technique used to cut the umbilical cord is related to brain activity in newborns.

Who can participate?
Babies born at Cork University Maternity Hospital at least 8 weeks prematurely and their mothers.

What does the study involve?
Participants are randomly allocated to one of three groups. For those in the first group, the infants cord is clamped within 20 seconds of delivery around 6cm from the belly button. For those in the second group, the infants cord is clamped 60 seconds after delivery around 6cm from the belly button. For those in the third group, infants receive umbilical cord milking before the cord is clamped. This involves the placenta being held in line with or above the infant following delivery, and using the hand to gently squeeze along the length of the umbilical cord (20cm) towards the infant. This action is repeated every 2 seconds. The umbilical cord is then clamped around 6cm from the belly button. All infants then have sticky pads (electrodes) which are connected to specialised machines attached to their heads at 6 and 12 hours after birth, so that the electrical activity in their brains (brain function) can be measured. Mothers also have a

sample of blood taken between 24 and 36 hours after birth in order to measure their red blood cells.

What are the possible benefits and risks of participating?
There are no direct benefits or risks to participants taking part in this study.

Where is the study run from?
Cork University Maternity Hospital (Ireland)

When is the study starting and how long is it expected to run for?
July 2015 to July 2017

Who is funding the study?
Science Foundation Ireland (Ireland)

Who is the main contact?
Professor Eugene Dempsey

Contact information

Type(s)
Scientific

Contact name
Prof Eugene Dempsey

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Additional identifiers

Protocol serial number
2.0

Study information

Scientific Title
Clamping the Umbilical cord In Premature Deliveries (CUPID): A randomised controlled pilot trial

Acronym
CUPID

Study objectives
Preterm infants who have delayed cord clamping with assisted ventilation at the bedside have healthier brain oxygenation and electrocortical activity in the first day of life compared to preterm infants who have had immediate cord clamping or umbilical cord milking.

Ethics approval required
Old ethics approval format

Ethics approval(s)
University College Cork Clinical Research Ethics Committee, 19/08/2015

Study design
Single-centre randomised controlled pilot trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Prematurity

Interventions
Participants are randomly allocated using computer generated envelope randomisation to one of three study arms. Allocations will be stratified by gestation (23+0-27+7 weeks, and 28+0-31+6 weeks gestational age).

Arm 1: Immediate Cord Clamping (ICC)- active comparator
The infants cord will be clamped approximately 6 cm from the infants' umbilicus within 20 seconds of delivery. Routine neonatal care will commence immediately. A designated fellow will start a timer at the time of delivery and record the time of cord clamping.

Arm 2: Deferred cord clamping (DCC)- experimental
Following delivery the infant will be placed on a mobile resuscitation trolley (the Lifestart) with the cord in tact, and at or below the level of the placenta. Routine neonatal care will commence immediately at the bedside. The cord will be clamped approximately 6 cm from the infants' umbilicus at 60 seconds following delivery. A designated fellow will start a timer at the time of delivery and record the time of cord clamping. Respiratory support will be provided with cord intact as is deemed necessary by the attending neonatologist.

Arm 3: Umbilical cord milking (UCM)- experimental
Following delivery, the obstetrician will hold the infant at or below the level of the placenta, and his/her assistant will strip the cord 3 times in the direction of the infant. Each stripping should cover 20 cm of cord, at a speed of 20cm/2seconds. 2 seconds will be allowed in between each milking to allow the cord to refill. The infants' cord will then be clamped approximately 6 cm from the infants' umbilicus and routine neonatal care will commence immediately. A designated fellow will start a timer at the time of delivery, count out loud during the milking of the cord, and record the time of cord clamping.

Intervention Type

Procedure/Surgery

Primary outcome(s)
Neonatal outcome measure:
Brain activity in the newborn infant is measured using electroencephalogram (EEG) and near-infrared spectroscopy (NIRS) 6 and 12 hours post-partum.

Maternal outcome measure:
Maternal hemoglobin is measured at 24-36 hours post-partum.

Key secondary outcome(s))
Maternal outcome measures:
1. Maternal Postpartum hemorrhage incidence is determined at 24 hours after delivery
2. Maternal estimated blood loss is determined up to 1 hour after delivery
3. Maternal blood transfusion is determined up to 5 days after delivery
4. Length of third stage of labor is determined up to 1 hour after birth
5. Use of uterotonic agents is determined up to 1 hour after birth
6. Manual removal of placenta is determined up to 1 hour after birth
7. Operating time for cesarean delivery is determined up to 3 hour after birth

Neonatal Outcome measures:
1. Neonatal Immediate Outcomes, measured by APGAR scores (1 and 5 minute) and Delivery Room interventions (oxygen concentration, intubation, cardiac compressions and medications)
2. Neonatal Admission Outcomes, measured by temperature, blood pressure, and blood sugar on admission
3. Neonatal haemodynamic outcome, measured by mean blood pressure, number of volume challenges, inotropic support and urinary output (ml/kg/day) over first 24 hours of life. All infants will also have measurements of systemic blood flow measured by echocardiography at 12 +/- 3 hours of life.
4. Neonatal CNS outcomes: Cerebral tissue oxygenation, measured by NIRS at 6, 12 and 24 hours. Cerebral activity measured by EEG at 6, 12 and 24 hours. Intravventricular hemorrhage or Periventricular leukomalacia measured by cranial ultrasound at days 1, 7 and 28 of life
5. Neonatal Haematological outcomes: Hemoglobin measured by blood sampling at 1 and 12 hours of life. Peak serum bilirubin over first 2 months of life. Number of blood transfusions required over first 2 months of life.
6. Neonatal Respiratory outcomes: Intubation, Surfactant, Mechanical ventilator days, Bronchopulmonary dysplasia (oxygen requirement at 36 weeks gestational age), use of postnatal steroids within first 2 months of life
7. Neonatal Sepsis, either clinical suspicion or blood culture positive over first 2 months of life
8. Neonatal Necrotising enterocolitis over first 2 months of life
9. Neonatal intensive care unit lenth of stay, measured in days
10. Neonatal death: yes or no

Completion date
01/07/2017

Eligibility

Key inclusion criteria
Neonatal inclusion criteria:
1. Infants born at less than 32 weeks gestational age (from 23+0 weeks' up to and including 31+6

weeks' gestational age)
2. Vaginal and Caesarean deliveries

Maternal inclusion criteria:
Informed antenatal consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
45

Key exclusion criteria
Neonatal Exclusion criteria:
1. Major congenital anomaly (defined as those that are at high risk of neonatal death or require postnatal surgery)
2. Monochorionic twins with known or suspected twin to twin transfusion syndrome (TTTS) +/- significant growth discordance (>10%)
3. Hydrops fetalis (any aetiology)
4. Known Rh sensitized pregnancy
5. Cord prolapse

Maternal Exclusion criteria:
1. Inability to obtain informed consent
2. Severe or multiple maternal illnesses, including bleeding from placenta praevia, clinical suspicion of placental abruption or accreta, uterine rupture and other causes of maternal coagulopathy

Date of first enrolment
01/12/2015

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
Ireland

Study participating centre

Cork University Maternity Hospital
Corcaigh
Wilton
Cork
Ireland
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Sponsor information

Organisation
Cork University Maternity Hospital

Organisation
University College Cork

ROR
https://ror.org/03265fv13

Funder(s)

Funder type
Research organisation

Funder Name
Science Foundation Ireland

Alternative Name(s)
SFI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

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	01/05/2019	30/11/2020	Yes	No