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Early compared to delayed umbilical cord clamping in very small prematurely born babies: A study to know which one is better for infant health

Submission date
30/03/2017

Recruitment status
No longer recruiting

Registration date
11/04/2017

Overall study status
Completed

Last Edited
21/11/2017

Condition category
Pregnancy and Childbirth

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Premature birth is the leading cause of neonatal (post birth) and infant death in Argentina and worldwide. Preterm infants (weighing less than 1500 grams) are very vulnerable as they have higher risk of short and long-term health issues. Preterm infants have a higher risk of getting sepsis (a complication from illness that makes the body's organs shut down) especially while they are hospitalised post birth. After the birth of a baby, the umbilical cord (a cord that connects a baby in the womb to the mother) needs to be clamped and cut. It is usually recommended that this is not done any earlier than one minute after birth in order to improve the health of the baby and the mother. Delaying the clamping of the umbilical cord can allow for more blood to be transferred to the baby. When babies born are born early, there is some research showing that delayed umbilical cord clamping can reduce neonatal mortality (death) and morbidity (diseases/illness). However, as there are only a small amount of studies supporting these benefits, there is an urgent need to conduct a larger and well-designed study to confirm or deny these results. The aim of this study is to assess the effect of delayed umbilical cord clamping in very low birth weight premature infants on the rate of sepsis during hospitalization and to see if it improved other health outcomes without posing any harmful effects to the baby or to the mother.

Who can participate?
Women aged 14 and older who are 24 to 30 weeks pregnant.

What does the study involve?
Participating are randomly allocated to one of two groups. All participants receive the standard care while giving birth. Those in the first group receive an early umbilical cord clamping around 30 seconds after giving birth. Those in the second group receive delayed umbilical cord clamping done 90 seconds after birth. The mothers are followed up for blood loss during labour and until they are discharged from the hospital. The babies are followed up for sepsis and other illnesses after they are born and until they are discharged from the hospital.

What are the possible benefits and risks of participating?
Participants may benefit from delayed umbilical cord clamping as they may have higher hemoglobin (blood iron) levels, less need for blood transfusions, a lower incidence of hemorrhage (blood loss) and a lower rate of sepsis. There are no direct risks with delayed umbilical cord clamping however it should not be done in an emergency situation or if it could delay other medical needs.

Where is the study run from?
Centro Rosarino de Estudios Perinatales (lead centre) and seven other hospitals in Argentina

When is the study starting and how long is it expected to run for?
June 2015 to December 2020

Who is funding the study?
1. Pan American Health Organisation (PAHO) (USA)
2. Paediatric Hospital Foundation- The Garrahan Foundation (Argentina)

Who is the main contact?
Dr Guillermo Carroli

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
2/16

Study information

Scientific Title
Early versus delayed umbilical cord clamping in preterm infants born at less than 31 weeks of gestational age: A multicenter randomized controlled trial

Study objectives

Umbilical cord clamping at 90 seconds after birth reduces hospital-acquired or late-onset sepsis rate in very small preterm infants and improves other clinical end-points without posing any harmful effects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethics Committee of Research Protocols of the Hospital Italiano de Buenos Aires, 20/04/2006, ref: 960.
2. Ethics committee of Research Protocols Hospital Italiano de Buenos Aires,13/10/2016, ref: 960.
3. CREP Independent Ethics Committee, 25/10/2016. Ref: 2/16

Primary study design
Interventional

Study design
Multi-centre randomised controlled clinical trial

Study type(s)
Prevention

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

Interventions
Participants are randomly allocated to one of two groups. Randomisation is done using a random generator by a statistical software. Randomisation is performed centrally and is stratified for each of the participating centres. Allocation concealment is ensured by using sequentially numbered, sealed and opaque envelopes containing the assigned intervention. All participants receive the standard care while giving birth (either vaginally or through a caesarean section).

Group 1: This group receives early umbilical cord clamping 30 seconds after birth. The clamping is done the standard level of care.

Group 2: This group receives delayed umbilical cord clamping 90 seconds after birth. The clamping is done to the standard level of care.

The timing of the umbilical cord clamping is measured using a stopwatch by an independent observer who is not in charge of any specific task of care at the time of birth.

The babies are followed up for incidence of illness and sepsis during hospitalisation with clinical exams, blood samples and x-rays up until they are discharged from the hospital. Mothers are followed up for blood loss during birth and until discharge from the hospital.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Proven sepsis rates in new born infants is measured on the basis of clinical condition compatible with positive blood and/or cerebrospinal fluid and/or urine cultures (urine must be obtained by urethral catheterization or bladder puncture) at three days after birth and up until discharge from the hospital
2. Very probable sepsis rates in new born infants is measured on the basis of clinical signs of sepsis, negative cultures, antibiotic treatment equal or greater than seven days and two or more of the following diagnostic test results: <5000 white blood cells/mm3, <1500 neutrophils/mm3, Immature-to-Total-Neutrophil (I/T) Ratio (IN/TN): 0.2, C-reactive protein >10mg/L, <100,000 platelets/mm3, at three days after birth and up until discharge from the hospital

Key secondary outcome(s)
Infant outcomes:
1. Health at birth is measured using the Apgar scale at one and five minutes after birth
2. Assistance at birth is measured using time of first breath and need for bag mask-ventilation at hospital discharge
3. Intracranial hemorrhage is measured using brain ultrasonography following Papille´s classification (grades 1-4) at 24-48 hours after birth
4. Respiratory distress syndrome (RDS) using clinical indicators and chest x-rays at any time before discharge from the hospital
5.Symptomatic patent ductus arteriosus (PDA) is measured using echocardiography at any time before discharge form the hospital
6. Necrotizing enterocolitis (NEC) is measured using clinical and radiological findings according to Bell´s staging criteria at any time before discharge from the hospital
7. Bronchopulmonary dysplasia (BPD) is measured using clinical and radiological findings at any time before discharge from the hospital
8. Retinopathy of prematurity (ROP) is measured using alterations compatible with retinal grades at any time before discharge from the hospital
9. Death is measured through patient records at occurrence moment
10. Neurodevelopment is measured using Bayley scales at 18-24 months of age
11. Central packed cell volume are measured using blood samples at 6 and 24 hours after birth
12. Plasma bilirubin level are measured using blood samples at 24, 72 and 120 hours after birth
13. Plasma ferritin level are measured using blood samples at discharge from hospital
14. White blood cell count and C-reactive protein (CRP) in preterm infants with suspected sepsis are measured using blood samples at any time before discharge from the hospital
15. Blood pressure is measured using blood pressure cuffs at 2, 6,12 and 24 hours after birth

Maternal outcomes:
1. The proportion of women with blood loss of 500 mL or more is measured by collecting blood loss at one hour postpartum (or two hours postpartum if the bleeding continues beyond one hour)
2. The proportion of women with blood loss of 1000 mL or more is measured by collecting blood loss at one hour postpartum (or two hours postpartum if the bleeding continues beyond one hour)
3. Maternal blood loss in mL is measured by collecting blood loss at one hour postpartum (or two hours postpartum if the bleeding continues beyond one hour)

Completion date
30/12/2020

Eligibility

Key inclusion criteria
1. Singleton pregnant women
2. Aged 14 years and older
3. Vaginal or cesarean section delivery
4. Informed consent granted
5. Gestation period between 24 and 30 weeks and six days

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
Female

Key exclusion criteria
1. Congenital malformations or genetic syndrome (antenatal diagnosis or in the delivery room)
2. Rh-sensitized pregnant women

Date of first enrolment
19/08/2016

Date of final enrolment
30/06/2020

Locations

Countries of recruitment
Argentina

Study participating centre
Centro Rosarino de Estudios Perinatales
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Rosario
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2000

Study participating centre
Hospital Italiano de Buenos Aires
Juan D. Peron 4190

Buenos Aires
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Study participating centre
Hospital Fernandez
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Capital Federal
Argentina
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Study participating centre
Hospital Público Materno Infantil
Avenue Sarmiento 1301
Salta
Argentina
4400

Study participating centre
Hospital Nacional Profesor Alejandro Posadas
Av. Pres. Arturo U. Illia
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Buenos Aires
Argentina
1684

Study participating centre
Hospital Materno Infantil Ramón Sardá
Esteban de Luca
C1437 CABA
Buenos Aires
Argentina
1246

Study participating centre
Hospital Nuestra Señora de la Misericordia
Belgrano 1502
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Argentina
5000

Study participating centre
Hospital Escuela Eva Perón
Av. San Martín 1645
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Sponsor information

Organisation
Centro Rosarino de Estudios Perinatales

ROR
https://ror.org/01ag7n936

Funder(s)

Funder type
Government

Funder Name
Pan American Health Organisation (PAHO)

Funder Name
Paediatric Hospital Foundation- The Garrahan Foundation

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date