Physiological-based cord clamping for infants with congenital diaphragmatic hernia: a multicentre randomised controlled trial

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Primary Objective: To evaluate whether PBCC results in a reduced incidence of pulmonary hypertension in infants with CDH 24hrs after birth.Secondary Objectives: To measure and monitor physiological parameters during transition to provide information...

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Neonatal and perinatal conditions
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON54953

Source
ToetsingOnline

Brief title
PBCC in CDH (PinC study)

Condition

- Neonatal and perinatal conditions
- Congenital respiratory tract disorders
- Congenital and hereditary disorders NEC

Synonym
Congenital diaphragmatic hernia; stabilisation; pulmonary hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Collectebussenfonds

Intervention

- Other intervention

Keyword: Congenital Diaphragmatic Hernia, Physiological-based cord clamping, Pulmonary hypertension

Explanation

N.a.

Outcome measures

Primary outcome

Pulmonary hypertension diagnosed in the first 24hrs after birth via
echocardiography.

Secondary outcome

Treatment related
- Treatment failure defined as abortion of prescribed procedure and reasons why
- Time point of cord clamping

Neonatal
- Ventilator settings and circulatory support in first 72hrs
- Pulmonary hypertension: at 3 days of life and at discharge
- Use of inhaled nitric oxide (iNO) and the response to treatment
- Response to iNO treatment defined as follows: a decline of 10-20% in the
pre-postductal saturation difference, or an increase of 10-20% of PaO2, or
improvement in hemodynamic parameters meaning a 10% increase in mean blood
pressure, or a decrease in lactate levels
- Use of pulmonary vasodilators, such as sildenafil or prostaglandin E
- Cerebral oxygenation evaluated continuously with Near-infrared Spectroscopy
(NIRS) during the first 24 hours
- Broncho Pulmonary Dysplasia (oxygen dependence for at least 28 postnatal days)
- Need for extracorporeal membrane oxygenation (ECMO)
- Sepsis
- Intraventricular haemorrhage
- Number of days in intensive care unit
- Number of days ventilatory support (mechanical ventilation, CPAP, optiflow)
- Survival at discharge

- Oxygen dependency at discharge

Maternal
- Estimated blood loss at time of delivery (mL)
- Surgical site infection (caesarean section)
- Postpartum haemorrhage > 1000mL</p>

Study description

Background summary

Congenital diaphragmatic hernia is the result of a developmental defect in the diaphragm, enabling abdominal organs to migrate to the thoracic cavity thereby interfering with pulmonary development. This result in pulmonary hypoplasia. Immediately after birth, the lungs are stiff and small and vessels are underdeveloped, causing persistent pulmonary hypertension of the newborn (PPHN). The treatment of PPHN remains difficult and may not be successful. After umbilical cord clamping, changes in the cardiovascular system appear, especially the bloodflow towards the lungs is increased since the lungs need to take over oxygenation from the placenta. In most newborns, the transition from fetus to neonate happens quickly and without problemens. However, the lungs of children with pulmonary hypoplasia need a longer period of time to be aerated, leading to an instable circulation with low blood pressures and lower oxygenation rates.
Studies in preterm infants have revealed that the timing of cord clamping can make a difference, since delaying cord clamping until after lung aeration would be beneficial. Furthermore, ovine studies have revealed in CDH lambs, PPHN occurs less after delayed cord clamping in contrast to immediate cord clamping.

Study objective

Primary Objective: To evaluate whether PBCC results in a reduced incidence of pulmonary hypertension in infants with CDH 24hrs after birth.
Secondary Objectives: To measure and monitor physiological parameters during transition to provide information that improves our further understanding of the physiological changes occurring during transition for CDH infants.

Study design

This is a multicenter, non-blinded, randomized controlled trial in fetuses with an isolated CDH. The study will be initiated and coordinated by Sophia Children*s Hospital, Rotterdam. Additional participating centers that have agreed to collaborate and will join the trial after agreement of the local METC are: UMC Nijmegen. Patients will be randomized (1:1) between immediate cord

clamping versus PBCC. The infants will be managed using a consensus based postnatal management protocol after clamping of the cord.

Intervention

Physiological-based cord clamping (PBCC). For PBCC a new specially designed resuscitation table (the Concord) will be used. The table is fully equipped to perform everything that is needed for stabilisation of infants with CDH. All equipment needed for stabilisation that is attached to the table as well as the Concord are CE approved medical devices.

Study burden and risks

In this study, we explore the benefit of PBCC for infants with CDH. Delayed cord clamping has been incorporated in international guidelines for all infants, because of the proven beneficial effects. CDH infants need extensive support immediately after birth and we speculate that optimizing the timing of cord clamping provides an even greater benefit for these vulnerable infants.

In recent years, there have been several studies evaluating the use of commercially available resuscitation tables. So far, stabilisation with an intact cord has been considered a safe approach, both with vaginal delivery as well as during caesarean section. In addition, a recent feasibility study in CDH infants did not reveal any safety concerns.

The Concord is fully equipped for stabilisation and resuscitation and our feasibility study in preterm infants did not show any additional risks for the mother or the infant. Secondary outcomes include *safety parameters* for the mother and the infant. While the mother will benefit for having her baby close to her and able to touch her baby, there is a risk that it will cause anxiety as interventions take place close to the parents. We will minimize this by communicating to the parents antenatally what to expect and during the stabilisation the nurse will communicate what happens during the stabilisation.

The degree of respiratory insufficiency and pulmonary hypertension immediately after birth is specific for infants with CDH. Any intervention to improve outcomes in this patient group therefore needs to be studied in this specific population.

Contacts

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Trial sites

Trial sites in the Netherlands

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 60

Radboud Universitair Medisch Centrum
Target size: 50

Listed location countries

Belgium, Germany, Australia, Sweden, Italy, Austria, Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Newborns

Inclusion criteria

- Fetus/infant diagnosed with left sided CDH
- Isolated CDH: no associated structural or genetic abnormalities that are diagnosed before birth
- Gestational age at delivery >35wks

Exclusion criteria

- Right sided or bilateral CDH
- Major associated anomalies (structural and/or genetic)
- Maternal contraindications of PBCC: anterior placenta praevia, placental abruption
- High urgency caesarean section, with intended interval to delivery less than 15 min
- Cases that have undergone antenatal experimental medical therapy aiming to decrease the occurrence of pulmonary hypertension (such as sildenafil)
- A twin pregnancy with one of the fetuses diagnosed with CDH infant and that infant is first born either vaginally or via caesarean section
- Multiple birth > 2 (triplets or higher order)

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	No intervention
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	11-05-2020
Enrollment:	110
Duration:	6 months (per patient)
Type:	Actual

WORLD

Recruitment status:	Recruitment started
Start date (anticipated):	11-05-2020
Enrollment:	280
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	13-09-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-06-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-10-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-06-2025
Application type:	Amendment
Review commission:	METC Erasmus MC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04373902
CCMO	NL69575.078.19
Research portal	NL-008432