High frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international randomized controlled trial

Published: 24-09-2008
Last updated: 06-05-2024

Primary objective: -to determine if there is a significant difference in the incidence of oxygen dependency at day 28 and/or death within the first 28 days of life between newborns with congenital diaphragmatic hernia treated with high frequency...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders congenital
Study type	Interventional

Summary

ID

NL-OMON36937

Source
ToetsingOnline

Brief title
the VICI-trial

Condition

- Respiratory disorders congenital
- Neonatal respiratory disorders

Synonym
CDH, congenital diaphragmatic hernia

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Kröger Stichting;SSWO

Intervention

Keyword: bronchopulmonary dysplasia, congenital diaphragmatic hernia, conventional ventilation, high frequency oscillatory ventilation

Outcome measures

Primary outcome

Oxygen dependency at day 28 and/or death within the first 28 days of life.

Secondary outcome

•Overall mortality in the first year of life

•Number of treatment failures, see paragraph 6.5 failure criteria and switching

•Severity of chronic lung disease using the Bancalari definition (see Appendix V).

•Number of days on a ventilator

•Severity of pulmonary hypertension according to echocardiographic parameters

•Medical treatment for pulmonary hypertension during the hospital admission

•The level of specific laboratory markers, urine desmosine and proteomic analysis of tracheal aspirates, up to day 28, to describe the severity of ventilator-induced lung injury

•Requirement of pulmonary and/or cardiac medication at discharge and/or during the first year of life

•Long-term pulmonary outcome, described as pulmonary function at the age of 6 and 12 months, diary card documented respiratory morbidity and healthcare utilisation

•Requirement of ECMO (only described for ECMO-centres)

(see also paragraph 6.1)

Study description

Background summary

A congenital diaphragmatic hernia is a congenital defect of the diaphragm, mostly unilateral, which allows abdominal organs to herniate into the chest cavity. This results in pulmonary hypoplasia. As a consequence, mechanical ventilation is needed directly after birth in most cases. Ventilator-induced lung injury, resulting from prolonged mechanical ventilation, may lead to bronchopulmonary dysplasia and pulmonary hypertension. This may lead to prolonged oxygen dependency, use of medication and even death. 33% of patients with congenital diaphragmatic hernia have bronchopulmonary dysplasia, resulting from prolonged mechanical ventilation.
There are two ventilation strategies used in newborns having a congenital diaphragmatic hernia. First, conventional ventilation, may be given. Second, high frequency oscillatory ventilation may be given. In high frequency oscillatory ventilation, oxygen is provided by high frequencies, small tidal volumes and a continuous mean airway pressure. In comparison to conventional ventilation, fewer fluctuations in pressure exist.
Observational en retrospective studies have suggested high frequency oscillatory ventilation to reduce barotrauma, to improve survival and to lower the incidence of chronic lung disease. Still, no prospective randomized controlled trials have been carried out to compare hogh frequency oscillatory ventilation and conventional ventilation in children with congenital diaphragmatic hernia. A prospective randomized controlled trial is needed to achieve a better understanding of an optimal ventilation strategy to reduce long-term pulmonary damage in children with congenital diaphragmatic hernia.
(see also paragraph 1, Background)

Study objective

Primary objective:

-to determine if there is a significant difference in the incidence of oxygen dependency at day 28 and/or death within the first 28 days of life between newborns with congenital diaphragmatic hernia treated with high frequency oscillatory ventilation (HFO) and those treated with conventional mechanical ventilation (CMV) as initial ventilation mode.

The secondary objectives are:

-To compare overall mortality
-To compare the number of treatment failures (see paragraph 6.5 failure criteria and switching)
-To compare the number of days on the ventilator
-To compare the severity of chronic lung disease according to the Bancalari definition (see Appendix V)
-To compare the severity of ventilator-induced lung injury by using laboratory markers for pulmonary vascular endothelial damage and pulmonary hypertension (see paragraph 6.3)
-To compare the severity of pulmonary hypertension according to echocardiographic parameters
-To compare the use of medication given for pulmonary hypertension
-To compare the use of pulmonary and/or cardiac medication after discharge
-To compare long-term pulmonary function by using lungfucntion tests at the age of 6 and 12 months, a patient diary and healthcare questionnaires
-To compare the need for ECMO (only applicable for ECMO-centres)

Study design

This study is designed as a prospective, randomized, multicenter, international, controlled trial. Within two hours after birth, inborn infants with an antenatal diagnosis of congenital diaphragmatic hernia will be randomized to receive either high frequency oscillatory ventilation or conventional ventilation.
Before birth, parental informed consent will be obtained. Postnatally, infants will be treated according to standard practice, which is implemented in all participating centres. Of all patients, demographic and neonatal characteristics, as well as data on the clinical course and treatment will be collected in a central database in Rotterdam. An intention-to-treat analysis will be performed.
(See also paragraph 3, Study design)

Intervention

Conventional mechanical ventilation (CMV) will be provided by a neonatal ventilator capable of positive pressure ventilation or triggered modes.
High frequency oscillatory ventilation (HFO) will be provided by a high frequency oscillatory ventilator. HFO is based on high frequencies and small tidal volumes, together with a continuous mean airway pressure.

Study burden and risks

The purpose of the study is to achieve a better view of optimal ventilation strategies in children having congenital diaphragmatic hernia in future. If one

of the two ventilation strategies appears to give a better outcome, this may be of benefit for the children who received this ventilation strategy.
Procedures for the purpose of the study, are of minimal burden for the patient. Study-related procedures are part of standard care for a newborn with a congenital diaphragmatic hernia. During the follow-up period, lung function measurements will be done. Furthermore, parents have to fill in questionaires and a patient diary.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

•Antenatal diagnosis of congenital diaphragmatic hernia
•Prenatal informed consent
•The children are born in one of the participating centres
•The children are born at or after a gestational age of 34 weeks

•Infants who received a foetal intervention may be included

Exclusion criteria

•Infants with a severe chromosomal anomaly, like trisomy 18 or trisomy 13, which may imply a decision to stop further life-saving medical treatment
•Infants born with a severe cardiac anomaly, expected to need corrective surgery in the first 60 days of life (such as transposition of the great arteries or double outlet right ventricle)
•Infants born with renal anomalies associated with oligohydramnios
•Infants born with severe orthopaedic and skeletal deformities which are likely to influence thoracic and / or lung development (such as chest wall deformities and spine anomalies)
•Infants born with severe anomalies of the central nervous system

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2008
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO

Date:	24-09-2008
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL23374.078.08