MULTICENTRE RANDOMISED CONTROLLED TRIAL OF MINIMALLY-INVASIVE SURFACTANT THERAPY IN PRETERM INFANTS 25-28 WEEKS GESTATION ON CONTINUOUS POSITIVE AIRWAY PRESSURE

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To determine whether administration of exogenous surfactant using a minimally-invasive technique improves outcome in preterm infants 25-28 weeks gestation treated with continuous positive airway pressure (CPAP).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neonatal and perinatal conditions
Study type	Interventional

Summary

ID

NL-OMON44166

Source
ToetsingOnline

Brief title
OPTIMIST-A TRIAL

Condition

- Neonatal and perinatal conditions
- Neonatal respiratory disorders

Synonym
respiratoire insufficientie, respiratory distress syndrome (RDS)

Research involving
Human

Sponsors and support

Primary sponsor: Menzies Research Institute Tasmania, University of Tasmania
Source(s) of monetary or material Support: National Health and Medical Research Council (NHMRC) in Australie

Intervention

Keyword: Continuous positive airway pressure, Preterm infants, Respiratory Distress Syndrome, Surfactant

Outcome measures

Primary outcome

Primary outcome: Incidence of composite outcome of death or physiological

bronchopulmonary dysplasia (BPD).

Secondary outcome

Secondary outcomes: Incidence of death, major neonatal morbidities (BPD,

intraventricular haemorrhage, periventricular leukomalacia, retinopathy of

prematurity, necrotising enterocolitis), pneumothorax and patent ductus

arteriosus; need for intubation and surfactant therapy; durations of mechanical

respiratory support, intubation, CPAP, intubation and CPAP, high flow nasal

cannula, oxygen therapy, intensive care stay and hospitalisation;

hospitalisation cost; applicability and safety of the MIST procedure; and

outcome at 2 years.

Study description

Background summary

Nasal CPAP is often very effective in preterm infants as the initial means of respiratory support, but a sub-group of infants, most with features of respiratory distress syndrome, fail on CPAP and require intubation and ventilation in the first 72 hours. When compared to those in whom CPAP is successful, infants failing CPAP have a substantially longer duration of respiratory support, and a higher risk of adverse outcomes. Decreasing the risk of CPAP failure would thus seem advantageous, and may be achievable with minimally invasive surfactant therapy (MIST), in which surfactant is administered to a spontaneously breathing infant who then remains on CPAP. A technique of MIST (the *Hobart method*) using a semi-rigid surfactant instillation catheter has been shown to be feasible in preterm infants on CPAP, and appears to have the potential to alter respiratory course and outcome. This method of MIST now requires evaluation in randomised controlled trials.

Study objective

To determine whether administration of exogenous surfactant using a minimally-invasive technique improves outcome in preterm infants 25-28 weeks gestation treated with continuous positive airway pressure (CPAP).

Study design

Multicentre, randomised, masked, controlled trial. With parental consent, eligible infants will be randomly allocated using a web-based randomisation server, with stratification by study centre, to receive exogenous surfactant via the Hobart MIST technique, or to continue on CPAP.
Once consent has been obtained, the infant will be randomised by the OPTIMIST Treatment Team, after handover of care from the treating clinicians. Enrolled infants will be randomised into surfactant via MIST* and *standard care* groups, with an allocation ratio of 1:1, using a webbased randomisation procedure that will require confirmation of eligibility criteria and consent before revealing the randomly determined allocation. The randomisation schedule and web-based OPTIMIST-A trial protocol will be provided by the Clinical Epidemiology and Biostatistics Unit at the Murdoch Childrens Research Institute. The randomisation will be in randomly permuted blocks of variable length, stratified by study centre, and by gestational age. For the OPTIMIST-A trial there will be two gestational age strata (25-26 weeks and 27-28 weeks). Twins and higher order multiples will be randomised independently. Infants who are unstable and in need of intubation should not be randomised, even if consent has been obtained; such infants will not be considered to have been enrolled.

Intervention

Infants randomised to surfactant treatment will receive a dose of poractant alfa (Curosurf) administered under direct laryngoscopy using a surfactant instillation catheter, at a dosage of 200 mg/kg. CPAP will thereafter be reinstituted. Controls will continue on CPAP (after a sham intervention procedure). The intervention will be masked from the clinical team.

Study burden and risks

Burden and risks:
Direct laryngoscopy for tracheal catheterisation will be performed with risks of bradycardia and desaturation. Athough usually self resolving, premedication with sucrose (buccal) will be given as well as atropine (intravenous and at the discretion of the OPTIMIST Treatment Team). In addition tot CPAP positive pressure inflations can be given to restore saturation.

Benefit and group relatedness:
In view of the difficulties associated with intubation for surfactant delivery, this less invasive mean of delivering surfactant has been pursued.
In addition it is expected in line with other data that respiratory course and outcomes in infants treated with MIST will be better, i.e., more rapidly weaning of FiO2, reduced intubation rate < 3 days, and a shorter duration of oxygen therapy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Preterm infants 25-28 weeks gestation
2. Requiring CPAP or nasal IPPV because of respiratory distress.
3. CPAP pressure of 5-8 cm H2O and Fi (fractional inspiratory) O2 * 0.30.
4. Less than 6 hours of age.
5. Agreement of the Treating Physician in charge of the infant*s care.
6. Signed parental consent.

Exclusion criteria

1. Previously intubated, or in imminent need of intubation because of respiratory distress, apnoea
or persistent acidosis.
2. Congenital anomaly or condition that might adversely affect breathing.
3. Identifiable alternative cause for respiratory distress (e.g. congenital pneumonia or pulmonary
hypoplasia).
4. Lack of availability of an OPTIMIST treatment team.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-07-2016
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Curosurf
Generic name:	poractant alfa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-04-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-11-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
Other	ACTRN126111000916943
EudraCT	EUCTR2013-005429-21-NL
CCMO	NL47763.042.15