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Evaluation of early and combined treatment with surfactant and inhaled nitric oxide in newborns with respiratory failure and pulmonary hypertension

Submission date
03/09/2019

Recruitment status
No longer recruiting

Registration date
06/09/2019

Overall study status
Completed

Last Edited
26/08/2020

Condition category
Neonatal Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Hypoxemic respiratory failure (HRF) is a leading cause of illness and death among term and near term newborns. Few studies have tested surfactant treatment in these patients with conflicting results. The aim of this study is to test whether early use of surfactant in combination with inhaled nitric oxide (iNO) will prevent newborns with moderate hypoxemic respiratory failure from developing severe HRF.

Who can participate?
Term and near-term newborns (35 weeks gestational ages and over) with acute HRF

What does the study involve?
Participants are randomly allocated to one of two groups. The surfactant-iNO group receive the combined treatment of surfactant plus inhaled Nitric Oxide (iNO). The control group receive standard treatment with iNO. Infants of both groups receive standard intensive care, which includes high frequency or conventional mechanical ventilation, inotropic support and sedation. ECMO was considered in patients with a persistent OI>40.

What are the possible benefits and risks of participating?
It is expected that the combined treatment of inhaled Nitric Oxide and surfactant will help to improve oxygenation and prevent the progression to severe HRF. This may reduce mortality and the need for ECMO treatment. Surfactant is a usual therapy for preterms with respiratory distress, occasionally its administration is associated with oxygen desaturation and bleeding, but the incidence of these complications is minimized with careful application and monitoring.

Where is the study run from?
Five level III Neonatal Intensive Care Units in five hospitals in Chile

When is the study starting and how long is it expected to run for?
August 2008 to July 2015

Who is funding the study?
Chilean National Fund for Research in Health (FONIS)

Who is the main contact?
Dr Alvaro González
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
FONIS SA07I20035

Study information

Scientific Title
Randomized controlled trial to assess the early addition of exogenous surfactant to inhaled nitric oxide in the treatment of newborns with respiratory failure and pulmonary hypertension

Acronym
Surfactant plus Nitric Oxide in Neonatal Hypoxic Respiratory Failure

Study objectives
The early addition of exogenous surfactant to the treatment with inhaled Nitric Oxide of newborns with respiratory failure (OI>20) and pulmonary hypertension will improve oxygenation and prevent them from developing severe hypoxemic respiratory failure (OI > 40).

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 08/07/2007, Research Ethics Committee of Medicine School Pontificia Universidad Catolica de Chile (Comité Etico Científico Facultad de Medicina, Pontificia Universidad Católica de Chile, Diagonal Paraguay 383, Torre 11, Local 4, Santiago, Chile 8330077; Tel: +56 (0)2 23548173; Email: cecmeduc@med.puc.cl), CE# 027807

Study design
Prospective randomized double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neonatal hypoxic respiratory failure and pulmonary hypertension

Interventions
Enrolled infants were randomized into one of the two study groups using sequential sealed opaque envelopes from a computer-generated randomization list. This allocation sequence was generated centrally by an independent statistician, and sequentially sealed envelopes were sent to each center.

Surfactant-iNO group: received treatment with 20 ppm of inhaled Nitric Oxide (INOmax, INO Therapeutics, USA) with up to 2 doses of 100 mg/kg of poractant alfa (Curocerf; Chiesi Farmaceutici, Italy)

Control group: received treatment with 20 ppm iNO + placebo (air) and standard intensive care, which in both groups includes high frequency or conventional mechanical ventilation with 100% FiO2., inotropic support and sedation

Infants in both groups could receive open-label surfactant if they developed an OI>40 within the first 48 hrs of study. ECMO was considered in patients with a persistent OI>40.

Study surfactant combined with iNitric Oxide treatment were used within first 48 hours after study entry, but infants continue receiving standard intensive care later according to local and physician in charge guidelines. Patients were strictly monitored and followed during their whole hospital stay until discharge home.

Intervention Type
Mixed

Primary outcome(s)
The proportion of infants developing treatment failure during the first 48 hours of study treatment, defined as an oxygenation index (OI) ≥ 40

Key secondary outcome(s))

1. Proportion of infants requiring ECMO or death recorded during hospital stay
2. Oxygen and ventilatory requirements recorded during hospital stay

Completion date
31/07/2015

Eligibility

Key inclusion criteria
1. Near term infants (35 weeks gestation) with birth weights > 2000 g and who are less than 72 hours old
2. Infants requiring mechanical ventilation with hypoxemic respiratory failure with an OI > 20, calculated on two consecutive measurements of post ductal arterial blood gases without acidosis (pH > 7.25) and efforts will be done to adjust ventilatory support to reach a PCO2 < 60
3. A previous echocardiogram will be performed to rule out a cardiac anomaly and evaluate the presence of pulmonary hypertension (a tricuspid insufficiency jet with an estimated systolic pulmonary artery pressure ≥ 2/3 of systemic systolic arterial blood pressure and/or evidence of right-to-left shunting through foramen ovale or ductus arteriosus)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
100

Key exclusion criteria
1. Life-threatening congenital anomalies
2. Congenital heart disease
3. Congenital diaphragmatic hernia
4. Other forms of lung hypoplasia syndromes
5. Suspected or confirmed chromosomal abnormality
6. Postnatal age > 72 hours

Date of first enrolment
01/03/2009

Date of final enrolment
30/04/2014

Locations

Countries of recruitment
Chile

Study participating centre
Hospital Clinico Pontificia Universidad Catolica de Chile
Marcoleta 367
Santiago
Chile
8330077

Study participating centre
Hospital Regional Guillermo Grant Benavente, Concepción
San Martin 1436
Concepción
Chile
4070038

Study participating centre
Hospital Dr Luis Tisné
Avenida Las Torres 5150
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Study participating centre
Hosptal Dr Sóteo del Río
Avenida Concha y Toro 3459
Puente Alto
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Study participating centre
Hospital San José
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Sponsor information

Organisation
Pontificia Universidad Católica de Chile

ROR
https://ror.org/04teye511

Funder(s)

Funder type
Government

Funder Name
Chilean Fund for Health Research (FONIS): SA07I20035

Results and Publications

Individual participant data (IPD) sharing plan
Deidentified individual participant data will be made available, in addition to study protocols, the statistical analysis plan, and the informed consent form. The data will be made available upon publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to alvgonza@med.puc.cl

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	13/08/2020	26/08/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes