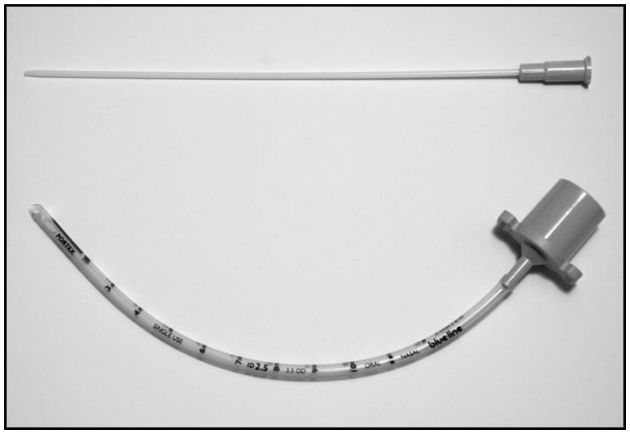

Surfactant instillation catheter (above) compared with 2.5 mm endotracheal tube

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OPTIMIST TRIALS MANAGEMENT

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NHMRC

Optimist
cOllaborative Paired Trials Investigating Minimally Invasive Surfactant Therapy

OPTIMIST-A TRIAL

Multicentre randomised controlled trial of surfactant administration via tracheal catheterisation in preterm infants 25-28 weeks gestation on continuous positive airway pressure

RHH ROYAL HOBART HOSPITAL

UNIVERSITY of TASMANIA
MENZIES

Murdoch Childrens Research Institute

the women's the royal women's hospital

Research question

Does administration of exogenous surfactant using a minimally-invasive technique **improve outcome** in preterm infants 25-28 weeks gestation treated with continuous positive airway pressure (CPAP)?

Background

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.[1-3] 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"), in which the trachea is catheterised using a semi-rigid surfactant instillation catheter, has been shown to be feasible in preterm infants on CPAP,[4,5] and appears to have the potential to alter respiratory course and outcome. This method of MIST now requires evaluation in a randomised controlled trial.

The OPTIMIST-A trial

The OPTIMIST-A trial is a randomised controlled trial of surfactant administration via MIST in preterm infants at 25 to 28 week gestation. The intervention will be masked from treating clinicians. The trial will give definitive information about the place of MIST in preterm infants on CPAP.

Trial overview

Study participants

Preterm infants 25-28^{+6} weeks gestation, aged less than 6 hours.

Inclusion criteria

- Need for CPAP or NIPPV because of respiratory distress syndrome
- FiO_2 ≥0.30

Exclusion criteria

- Imminent need of intubation
- Presence of a congenital anomaly
- Alternative cause for respiratory distress.

Randomisation

With parental consent, eligible infants will be randomly allocated to receive exogenous surfactant via MIST, or to continue on CPAP.

Intervention

Infants randomised to surfactant treatment will receive a dose of surfactant (Curosurf™, Chiesi Farmaceutici) administered via the Hobart method of MIST at a dosage of 200 mg/kg. CPAP will thereafter be continued. Controls will remain on CPAP. The intervention will be masked from the clinical team.

Post-intervention management

Other than the requirement to adhere to intubation criteria, management after intervention will be at the discretion of the clinical team. Enrolled infants on CPAP will be intubated if FiO_2 ≥0.45, or if there is unremitting apnoea or persistent acidosis. A room air trial will be conducted in selected infants at 36 weeks corrected gestational age.

Primary outcome

Incidence of composite outcome of death or bronchopulmonary dysplasia (BPD)

Secondary outcomes

Incidence of death, major neonatal morbidities (CLD, intraventricular haemorrhage, periventricular leukomalacia, retinopathy of prematurity, necrotising enterocolitis), pneumothorax and patent ductus arteriosus; need for intubation and surfactant therapy; durations of each form of mechanical respiratory support, intensive care stay and hospitalisation; hospitalisation cost; applicability and safety of the MIST procedure; and outcome at 2 years.

Sample size

606 infants (303 per group), giving 90% power to detect a 33% reduction in death or BPD from the anticipated rate of 38% in the control arm, $\alpha = 0.05$.

Trial plan

The trial has commenced at 9 centres and it is expected that >30 Units worldwide will ultimately participate. It is anticipated that trial enrolment will be completed by end-2017.

Outcome and significance

MIST therapy appears to have the potential to ease the burden of respiratory morbidity in preterm infants starting life on CPAP, to reduce time on respiratory support, and, as a result, to save money. The trial will give a definitive picture of the place of MIST in the care of preterm infants.