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Comparison of two modes of non-invasive ventilation in preterm babies

Submission date	Recruitment status	[_] Prospectively registered
03/02/2015	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/02/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
18/11/2015	Respiratory	

Plain English summary of protocol

Background and study aims
The study compares two non-invasive ventilation modes in premature babies (born before 37 weeks). The organs of premature babies, including the lungs, can be immature and not function correctly. Lungs are essential to breath and to live. Therefore, these babies may need external support to help them breath. This support can be invasive (a tube in the mouth to deliver air to the lungs) or non-invasive (a small support in the nose). Non-invasive ventilation is increasingly being used immediately after birth to prevent aggressive ventilation (invasive ventilation). Continuous positive airway pressure (CPAP) works by using mild air pressure to keep the airways open. Bilevel continuous positive airway pressure (BiPAP) works by varying the pressure used to keep airways open depending on whether the person is breathing in or out. BiPAP seems to open up the airways more than CPAP and, in particular, works to keep the small part of the lungs (the alveoli) more open. This may be due to the different pressures favouring gas exchange (entry of oxygen in the lungs and blood and exit of carbon dioxide of the blood and lungs). There are few studies published comparing CPAP and BiPAP but no conclusions as to whether one is better than the other. We want to know if one type of non-invasive ventilation is better than the other applied immediately after birth in order to choose the most beneficial treatment.

Who can participate?
Small babies born between 27 weeks and 32 weeks and 6 days of gestation breathing spontaneously.

What does the study involve?
The babies are randomly allocated into one of two groups. Those in group 1 are given CPAP support immediately after birth. Those in group 2 are given BiPAP support immediately after birth. All other care given is the same for both groups.

What are the possible benefits and risks of participating?
The possible benefit is being able to avoid intubation and invasive ventilation which contribute to respiratory problems in infancy. The risks include the need of invasive ventilation, nasal bleeding and rupture of alveoli.

Where is the study run from?
1. Hospital Prof Dr Fernando Fonseca (Portugal)
2. Maternidade Dr Alfredo da Costa (Alfredo da Costa Maternity) (Portugal)

When is study starting and how long is it expected to run for?
May 2011 to May 2013

Who is funding the study?
Section of Neonatology of the Portuguese Society of Pediatrics (Portugal)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Randomized controlled trial comparing nasal bilevel and continuous positive airway pressure in preterm infants born 27 to 32 weeks and 6 days of gestation regarding the need of intubation within the first 120 hours

Study objectives

Continuous positive airway pressure (CPAP) as a first mode of ventilation is being increasingly used in preterms with spontaneous breath. It allows a better alveolar recruitment with less need for invasive ventilation. Bilevel CPAP (BiPAP) provides two levels of positive end expiratory pressure (PEEP) during the respiratory cycle of the patient with a frequency and a duration determined by the physician. Theoretically, BiPAP should allow a higher alveolar recruitment, a higher residual function capacity and a reduction in breath working when compared to nCPAP. Nevertheless, it hasn't yet been proven in clinical studies. The main purpose of this study is to compare nCPAP and BiPAP as a first intention mode of non-invasive ventilation in a sample of preterms with gestational age between 27 weeks and 32 weeks and 6 days.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Hospital Prof Dr Fernando Fonseca-Amadora, 21/1/2011
2. Maternidade Dr Alfredo da Costa, 21/1/2011

Study design
The study is an interventional randomised controlled multicentre trial enrolling preterm infants born 27 to 32 weeks and 6 days of gestation.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Respiratory distress syndrome at birth

Interventions
The study included the inborn infants with gestational age (GA) between 27 weeks and 32 weeks + 6 days, whose parents had signed an informed consent before delivery. At birth, delayed cord clamping was made. Babies who showed an effective respiratory drive in the delivery room were immediately connected to an Infant Flow device for non-invasive ventilation (nCPAP -PEEP of 6 cm H2O) and transferred to the NICU. To those who hadn´t well succeeded breathing movements, positive pressure ventilation with silicone mask was applied. If an effective breath was achieved in 30 seconds, the previous procedure was followed.
At NICU admission, enrolled infants were randomly assigned to nCPAP or BiPAP using sequentially numbered sealed opaque envelopes. Randomization by variable 2-4 blocks was stratified in two GA categories: 27 weeks to 29 weeks + 6 days of GA and 30 weeks to 32 weeks + 6 days. In this study Infant Flow® devices were used- Infant Flow® Nasal CPAP System (IF; Care

Fusion) and Infant Flow® SiPAP System (Vyasis , Care Fusion) and the nasal interfaces were short binasal prongs. Infants were placed in bilevel CPAP or nasal CPAP according to the randomised envelope. If they belong to Bilevel CPAP group a positive end expiratory pressure (PEEP) 1of 6 cm H2O; PEEP2 of 8 cm H2O, inspiratory time (Ti) of 2 sec and a rate of 10 were applied. If they belong to CPAP group , a PEEP of 6 cm H2O was applied. Insertion of umbilical lines were performed. Blood sampling for hemogram, CPR (C protein reactive), culture, blood group and blood gas analysis were taken. Thoracic-abdominal X ray was done. All infants received caffeine citrate (loading dose 20 mg/Kg and maintenance dose 8 mg/Kg/day). At 30-45 minutes of life, a clinical reevaluation was made. If the infant was stable, the same parameters would be kept. If there was a sign of respiratory distress, parameters would be changed (In the CPAP group, PEEP was raised to 7-8 cm H2O; in the BiPAP group, if there was apnoea, rate would be raised to 15; if there was desaturation, Ti would be raised to 3 seconds). At 55 minutes of life, a clinical evaluation was made and a blood gas analysis was performed. If they were normal, the same parameters would be kept. If there was respiratory distress or the blood gas were not within the normal limits, administration of porcine surfactant (Curosurf) 200 mg/Kg would be performed by the technique of INSURE (intubation- surfactant administration and extubation to non-invasive ventilation). An arterial blood gas analysis was made every two hours in the first 6 hours and then at 12 hours of life. It was then done at least twice a day. Between the 24 to 72 hours of life, cardiac and transfontanellar ultrasound were performed. If significant patent ductus arteriosus was diagnosed, ibuprofen would be prescribed according to the National Neonatal Guidelines. The remaining diagnosis and treatment procedures were conducted according to the National Guidelines.

Intervention Type
Device

Primary outcome measure
The primary outcome of our study was the need of invasive ventilation within the first 120 hours of life. Intubation criteria were: pH <7.25, pCO2> 65 mmHg, SatO2 <88% with FiO2 ≥ 40%, one episode of apnoea requiring bag -and-mask ventilation, frequent episodes of bradycardia /apnoea (>2-3 per hour).

Secondary outcome measures
1. Duration of mechanical ventilation
2. Use of surfactant
3. Incidence of pneumothorax
4. Bronchopulmonary dysplasia (BPD- defined as need of oxygen supplementation at 36 weeks of gestation)
5. Peri and intraventricular haemorrhage (Volpe grades III/IV)
6. Necrotizing enterocolitis (Bell´s stage >2)
7. Severe retinopathy of prematurity (grade >2)
8. Patent ductus arteriosus (PDA)
9. Sepsis (defined as positive hemoculture
10. Clinical signs and intention to treat)
11. Length of stay and mortality

The outcomes were measured throughout the hospitalisation period.

Overall study start date
01/09/2010

Completion date
30/06/2014

Eligibility

Key inclusion criteria
1. Infants with gestational age (GA) between 27 weeks and 32 weeks + 6 days
2. Either gender
3. Parents had signed an informed consent before delivery
4. Don't need endotraqueal intubation at birth

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
A sample size of 200 patients was needed to show an absolute reduction in the need of ventilation from 35% to 15% (alpha 0,05; beta 0,80; 2 tailed test).

Key exclusion criteria
1. Need of endotraqueal intubation in the delivery room
2. Major congenital malformations
3. Neuromuscular diseases
4. Perinatal asphyxia (Apgar < 4 at 5 minutes and base excess of > -12 in the first hour)
5. Early onset sepsis

Date of first enrolment
15/05/2011

Date of final enrolment
21/05/2013

Locations

Countries of recruitment
Portugal

Study participating centre
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Study participating centre
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Sponsor information

Organisation
Section of Neonatology of the Portuguese Society of Paediatrics

Sponsor details
IC 19
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Sponsor type
Not defined

Funder(s)

Funder type
Government

Funder Name
Section of Neonatology of the Portuguese Society of Paediatrics (Portugal)

Results and Publications

Publication and dissemination plan
We intend to publicate the results of the study in 2015

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	10/04/2015		Yes	No