Supplemental oxygen strategies in children with bronchopulmonary dysplasia (BPD) after the neonatal intensive care unit: the SOS BPD study.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neonatal respiratory disorders
Study type	Interventional

Summary

ID

NL-OMON54694

Source
ToetsingOnline

Brief title
SOS BPD study

Condition

- Neonatal respiratory disorders

Synonym
bronchopulmonary dysplasia, chronic lung disease of prematurity

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Zon MW,Longfonds

Intervention

Keyword: bronchopulmonary dysplasia, growth, oxygen saturation target, supplemental oxygen

Outcome measures

Primary outcome

The primary objective of this study is to investigate if targeting a higher

SpO2 (i.e. 95% lower limit) leads to superior growth of normal lung tissue

(assessed indirectly by body weight) at 6 months corrected age as compared to

targeting a lower SpO2 (90% lower limit) in children with moderate-severe BPD

from 36 weeks PMA and onwards.

Secondary outcome

Secondary outcomes are:

- body weight and height at 12 months corrected age

- health care consumption (visits to helath care professionals, admissions)

- quality of life of the parents or caregivers.

In a subgroup of children:

- lung function (lung clearance index)

- chest CT scores

- pulmonary hypertension and/or right ventricle systolic function.

Study description

Background summary

Extreme preterm birth leads to an arrest in lung and pulmonary vascular development which may result in bronchopulmonary dysplasia (BPD). BPD is a chronic lung disease that leads not only to life-long respiratory issues, but also to adverse cardiovascular and neurodevelopmental outcomes. Moreover, the impact on parents of taking care of a child with BPD can be significant,with increased stress, low sleep quality and depressive symptoms, all having an impact on their quality of life. In the Netherlands, BPD affects approximately 500 infants each year, of whom two thirds have the moderate to severe form of the disease, which means that they are still oxygen-dependent at 36 weeks postmenstrual age (PMA).

The main treatment for BPD is supplemental oxygen. Several randomised controlled trials have assessed a liberal versus a restricted use of supplemental oxygen in extreme preterm infants in the first weeks of life on major outcomes such as death, development of BPD or retinopathy of prematurity, and neurodevelopment. However, no study has ever examined the optimal oxygen saturation (SpO2) target that should be obtained by supplemental oxygen in children with established BPD after 36 weeks PMA. This target may be different from the established SpO2 targets in the first weeks of life, as at 36 weeks PMA vulnerability to oxidative stress (and e.g. development of retinopathy of prematurity) has most probably decreased. Moreover, alveolar growth only starts from approximately 34 weeks of gestation, announcing a new era in lung growth.

Due to the lack of studies, the Dutch BPD guideline refrains from any recommendations on SpO2 targets in children with established BPD. This has resulted in wide practice variability between hospitals in lower SpO2 targets, with most hospitals accepting a lower SpO2 limit of 90%. However, this limit may be too low, because, according to a number of observational studies, supplemental oxygen may decrease respiratory symptoms, prevent pulmonary hypertension, be beneficial for neurodevelopment and improve weight gain if BPD is present. Importantly, in children with BPD, body weight during infancy has been positively associated with the amount of normal lung tissue as assessed with CT scans, and better lung growth is related to increased lung function in later life. Furthermore, poor weight gain is associated with increased vulnerability to infections and supplementary oxygen may reduce the risk for nosocomial infections and consequently for re-hospitalisation. On the other hand, hyperoxia (e.g. too much oxygen) may result in increased levels of reactive oxygen species and subsequent oxidative damage. This may negatively influence lung development but also the development of other organs such as the eyes and the brain. In short, too little oxygen may have detrimental effects on preterm children with BPD, while too much oxygen should also be avoided, and it

is unknown where this balance lies between too little and too much oxygen.

Study objective

The objective of this study is to determine the optimal lower oxygen saturation target in children with moderate-severe BPD, i.e. children who are oxygen-dependent at 36 weeks PMA.

Study design

This is a multi-centre randomised controlled, open study in children with moderate-severe BPD from 36 weeks PMA onwards with two parallel arms:
1. weaning of supplemental oxygen based on SpO2 lower limit >= 95%
2. weaning of supplemental oxygen based on SpO2 lower limit >= 90%.

This is a non-blinded study because we considered it not feasible to blind parents and treating physicians for SpO2, as supplemental oxygen will be weaned based on SpO2. Study duration for each patient will be one year with three visits: at inclusion and at 6 and 12 months corrected age.
Setting of the study: patients will be included between 36 and 38 weeks PMA, when they are still admitted on the NICU or post-IC-high care units. Follow up will be alongside neonatal follow up pathways at outpatient clinics.

Intervention

Besides from the two saturation targets, there are no other interventions.

Study burden and risks

The burden associated with participation is minimal. As long as the children are on respiratory support, we ask the parents or physician to download a saturation profile from the pulse oximeter (which is already used for the child because of the respiratory support) and send it to us. This saturation profile will be done once a week when at home or twice a week when admitted. Children will attend their regular check-ups in the outpatient clinic. We ask the parents to fill in a questionnaire a few times.
Only if it is part of routine follow up, we will look at CT-scans, echocardiography or multiple breath wash-out (MBW).

The risk associated with participation is minimal. The intervention (= higher oxygen saturation target) will probably lead to better outcomes. Hyperoxia can potentially lead to lung damage and retinopathy of prematurity. However, the risk of these morbidities is considerably lower for children at the age of 36 weeks postmenstrual age than before this age. Potentially, the children in de controle group (i.e. lower oxygen saturation target) will grow less and show

more work of breathing.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

- born < 32 weeks of gestational age - oxygen need for >= 28 days from birth until 36 weeks of PMA - moderate or severe BPD at 36 weeks postmenstrual age

Exclusion criteria

- Significant congenital heart disease (not being persisting ductus arteriosus, small atrial septal defect, ventricular septal defect)
- pulmonary hypertension treated with sildenafil or bosentan

- retinopathy of prematurity for which the ophthalmologist recommended a patient specific SpO2 target
- congenital malformations of the lung or airways
- severe acquired upper airway abnormalities like subglottic stenosis necessitating endotracheal intubation
- interstitial lung disease

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-01-2020
Enrollment:	198
Type:	Actual

Ethics review

Approved WMO Date:	13-03-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-10-2019
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-09-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-01-2025
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	NL66087.078.18