BronchoPulmonary Dysplasia: an inflammatory disorder in children? The BPD PINK study

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Ethical review	Approved WMO
Status	Pending
Health condition type	Neonatal respiratory disorders
Study type	Observational invasive

Summary

ID

NL-OMON57294

Source
ToetsingOnline

Brief title
BPD PINK study

Condition

- Neonatal respiratory disorders

Synonym
bronchopulmonary dysplasia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Stichting Astma Bestrijding

Intervention

Keyword: bronchopulmonary dysplasia, exhaled breath, inflammation, oxidative stress

Outcome measures

Primary outcome

Differences in markers of oxidative stress/ inflammation in exhaled breath

between children with BPD and healthy controls.

Secondary outcome

- Correlations between markers of oxidative stress/ inflammation in exhaled

breath and symptoms, lung function and chest CT scores.

Study description

Background summary

Bronchopulmonary dysplasia (BPD) is the most common complication of extremely preterm birth affecting 250-300 children in the Netherlands US every year. BPD is characterized by an arrest in lung and pulmonary vascular development and has lifelong consequences. Children with BPD have more respiratory symptoms and related hospital admissions compared to term or preterm born controls without BPD. A recent study showed that adults born before 28 weeks of gestation had an Odds ratio of 7.4 for the development of Chronic Obstructive Pulmonary Disease (COPD) and this OR was even higher in adults with BPD.
In addition to symptoms, the forced expiratory volume in 1 second (FEV1) in children with BPD is reduced with a 16% lower mean compared to healthy controls. More notable, this lung function deficit further deteriorates during childhood with as much as 0.1 Zscore FEV1 per year.
Unfortunately, the underlying pathophysiology of increased, progressive pulmonary morbidity is unclear.

Ongoing oxidative stress and/or neutrophilic inflammation have been suggested as mechanisms responsible for the decline in lung function in patients with BPD, although only few studies assessed inflammation in older children with BPD, and the potential relationship with pulmonary morbidity. One study in 52 school children with BPD showed higher levels of 8isoprostane, a biomarker of oxidative stress, in exhaled breath condensate (EBC). Another study in 36 preterm born school children found higher neutrophil and lymphocytes counts,

and higher interleukin (IL)8/protein values in sputum suggesting ongoing neutrophilic inflammation. In contrast, a third study did not show significant differences in markers of eosinophilic or neutrophilic inflammation, nor for oxidative stress between preterm born school children with or without BPD and controls. In a bronchoscopy study in young adults with BPD a T cell pattern as in COPD was found in bronchoalveloar lavage fluid. BPD subjects had a higher proportion of CD8+ T-cells, a lower proportion of CD4+ T-cells and a higher proportion of activated T-cells in patients, possibly leading to tissue remodelling and deterioration of lung function.

In summary, patients with BPD are at risk of long-term deterioration of pulmonary function. However, the pathophysiology of BPD after the neonatal period is unclear although inflammation and oxidative stress most likely play a role.

Study objective

The aim of this project is to unravel whether BPD after the neonatal period is a chronic inflammatory disease, and if markers of inflammation and/or oxidative stress are related to pulmonary morbidity in patients with BPD. Based on these findings, targeted, individualized specific care can be developed to improve pulmonary health in patients with BPD.

Primary Objective: to study if preterm born patients with BPD have signs of increased oxidative stress and/or inflammation as compared to matched healthy subjects.

Secondary Objective(s):
To study if:
- Markers of oxidative stress/ inflammation correlate with symptoms, lung function and CT scores in children with BPD.

Study design

This is an exploratory prospective pilot study with 1 study visit.
Patients will be recruited from the long-term BPD follow up clinic in Erasmus MC and Amsterdam UMC. During this follow up, all BPD patients perform routinely lung function tests (spirometry before and after a bronchodilator) at the age of 5 and 8 years. In Erasmus MC all children with BPD undergo chest CT scanning at the age of 8-10 years, in Amsterdam UMC CT scanning is performed in individual children on clinical indication.
We aim to include 36 patients with BPD and 36 healthy age-matched controls.
In all children we will sample exhaled breath (gas-chromatography-mass spectrometry analysis in Amsterdam UMC) at the study visit.
Children with BPD perform spirometry before and after a bronchodilator. Healthy children will only perform spriometry without bronchodilator reversibility

testing. Additionally, all children will perform analysis of nitric oxide in exhaled air (FeNO), as marker of eosinophilic inflammation, as study test.

Study burden and risks

The risks associated with participation are considered negligible and the burden minimal: study procedures will be performed during a routine clinic visit. Exhaled breath collection is non-invasive and the procedure to obtain exhaled breath takes few minutes.
Spirometry is routine care for the BPD patients but extra for the healthy controls. In general, children experience spirometry as *fun* as we use computer games to stimulate and motivate them. In many studies spirometry has been performed in healthy controls (e.g. Generation R) without any problems. This study cannot be performed in adults or other groups as we want to get insight in the pathophysiology of BPD in school children. It is important to identify potential therapeutic targets in childhood when lung growth and development take place, in order to improve respiratory health in children, which will also improve respiratory health during the life course.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

BPD patients:
- Diagnosis of severe BPD defined as oxygen need for >= 28 days from birth until 36 weeks postmenstrual age (PMA) AND need for >= 30% supplemental oxygen or dependence on continuous positive airway pressure, high flow nasal cannula or mechanical ventilation at 36 weeks PMA, following the 2001-National Institute of Health (NIH) definition.
- Visiting the BPD follow up clinic at 8-10 years of age
- Able to perform spirometry
-Chest CT scan performed for clinical reasons
- Written informed consent of both parent(s)/ caregiver(s)/ legal guardian as applicable

Healthy controls:
- Age 6-10 years
- Sibs of BPD patient that will be included
- Able to perform spirometry
- Informed consent of both parent(s)/ caregiver(s)/ legal guardian(s) as applicable

Exclusion criteria

BPD patients
- respiratory diseases other than BPD, in particular clinical suspicion of allergic asthma
Control patients:
- respiratory diseases, in particular clinical suspicion of allergic asthma
- born < 37 weeks of gestation

Study design

Design

Study type: Observational invasive

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	72
Type:	Anticipated

Ethics review

Approved WMO

Date:	10-02-2025
Application type:	First submission
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	NL87012.078.24