Multiple Breath Washout to measure lung function in Congenital Diaphragmatic Herniation survivors between 5 and 18 years old

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital respiratory tract disorders
Study type	Observational non invasive

Summary

ID

NL-OMON48533

Source
ToetsingOnline

Brief title
MBW in CHD

Condition

- Congenital respiratory tract disorders

Synonym
congenital diaphragmatic hernia

Research involving
Human

Sponsors and support

Primary sponsor: Kindergeneeskunde

Source(s) of monetary or material Support: Stichting kindergeneeskunde

Intervention

Keyword: CDH, congenital diaphragmatic hernia, MBW, multiple breath washout

Outcome measures

Primary outcome

We intend to perform an observational cross-sectional pilot study, thus no formal power calculation is performed. We aim to included 32 patients between 5 and 18 years old who have a regular follow-up visit during our study period. The main goal of this pilot study is to describe the first-ever outcomes of using MBW in CDH follow-up care. The amount of patients we aim to include should be sufficient to reach this goal and to further explore associations between MBW outcomes, age and prognostic factors present at birth.

Secondary outcome

n/a

Study description

Background summary

Children with congenital diaphragmatic herniations (CDH) are born with life threatening pulmonary hypertension and hyperplasia.1 Postnatally, these children require immediate artificial ventilation and other medical interventions.1 Unfortunately, even with the current advances in medical treatment, the mortality of neonates with CDH remains high.1 Of those infants who survive these crucial interventions, the lung parenchyma and function will gradually recover to near-normal with age.1 However, pulmonary problems usually persist even beyond adolescent age. Especially pulmonary obstruction, bronchial hyperreactivity and pulmonary hypertension are often reported.1-3 For these reasons are survivors of CDH asked to regularly visit their pediatric pulmonologist.4

During these visits, pulmonary function is usually measured by spirometry and body-plethysmography.4 These pulmonary function tests are especially useful in measuring lung volumes and pulmonary obstruction. However, due to our advances in postnatal and long-term CDH care, the lung volumes of CDH survivors have often recovered to near-normal values at pubescent age.1-4 This results in a mismatch between pulmonary function values and reported symptoms, making these tests less effective in the pulmonary care of this population.1-4

During recent years an interest has developed for a new pulmonary function test called Multiple Breath Washout (MBW). During MBW an inert tracer gas, usually nitrogen, is washed out during tidal breathing of 100% oxygen until 1/40th (2.5%) of the starting concentration has been reached.5-6 The amount of functional residual capacity (FRC) turnovers needed to reach this concentration gives a measure of ventilation inhomogeneity (VI).5-6 VI is mostly affected by peripheral airway damage, which is in many pulmonary diseases the main location for mild or early lung disease.5-8 Therefore, the more peripheral airway damage is present, the longer it will take to wash out an inert tracer gas and the higher (i.e. worse) the measured VI will be.5-6 In contrast, pulmonary function tests that focus on lung volumes mainly reflect damage of the larger airways, which represents more developed lung disease.

Additionally, because a MBW test only requires a tidal breathing pattern, is non-invasive and requires less cooperation than conventional pulmonary function tests, it is feasible to perform in all age groups.9-10 For example, spirometry is challenging for young children to perform, because it involves a forced expiration maneuver, which requires a certain level of coordination. During a MBW test children are distracted by watching TV and only have to calmly breathe through a snorkel-like tube. In short, MBW is more sensitive to mild and early lung disease than spirometry and body-plethysmography, and is also more feasible to perform in young children.5-10

MBW has been studied extensively in children with cystic fibrosis, asthma and primary ciliary dyskinesia.7-8,11 In these studies MBW has found to be more sensitive in detecting and monitoring children with early or mild lung disease than other pulmonary function tests.7,8-11 In the field of CDH care where current pulmonary function tests are becoming less effective in older children, MBW could be a useful tool in disease monitoring. Unfortunately, few studies have been carried out in this population.

We intend to perform a cross-sectional pilot study in which we carry out MBW measurements in 32 children aged 5 to 18. The outcomes will be compared to both normal values and outcomes of regular spirometry and body-plethysmography tests. Furthermore will the relation between MBW outcomes and age in our population be studied in more detail. Prognostic factors of the herniation present at the birth of our participants, such as liver herniation and lung-to-head ratio, will be collected and compared to MBW outcomes. Seeing that one MBW test will be the only additional task for the participants, and that

MBW tests are safe and non-invasive, the burden of participation will be low.

Study objective

Our research project aims to answer 3 key questions:

1. How do MBW, spirometry and body-plethysmography outcomes compare in survivors of CDH?

2. What is the relation between MBW outcomes in survivors of CDH and age?

3. Are prognostic factors of the herniation present at birth (e.g. location of herniation, lung-to-head ratio, liver herniation) associated with increased (i.e. worse) MBW outcomes in survivors of CDH?

Question 1
We will include children aged 5-18 years with a history of CDH who have a regular follow-up visit scheduled during our study period. During these follow-up visits, spirometry and body-plethysmography measurements are standard of care. Children will be asked to perform a supplemental MBW test when they choose to participate. The MBW outcomes will be compared to the spirometry and plethysmography outcomes. Thus far, no studies have been performed on the use of MBW in children with CDH aged 5-18 years old.
Question 2
Our study population will consist of four age groups of 5, 8, 12 and 17 years old respectively, as routine follow-up takes place at these ages. We will try to include 8 children in each age group to reach a total study population of 32 children. Using these age groups, we will try to find an association between age and MBW outcomes. It is our hypothesis that younger participants will have higher (i.e. worse) MBW outcomes. Even though it may be unlikely that a significant relation can be found with the amount of children we aim to include in this pilot study, finding a trend would still be valuable for future research.
Question 3
Some characteristics of diaphragmatic herniations of neonates are related to prognosis. These factors include the side of the defect in the diaphragm, the lung-to-head ratio, the presence of liver herniation, the requirement of extracorporeal membrane oxygenation (ECMO) and whether the child was born prematurely. It is our hypothesis that presence of these prognostic factors at birth will be associated with (impairment of) lung development and therefore with a worse pulmonary function at later age and therefore worse MBW outcomes. Information about these prognostic factors has already been saved in the electronic patient files as part of standard care. Patients and their parents will be asked for their permission to extract these data and use them for this study. *

Study design

Patients with a history of CDH regularly visit the hospital for follow-up with, amongst others, their pediatric pulmonologist and surgeon. Patients with a history of Bochdalek-type CDH and/or their parents will receive a call from either their treating pediatric pulmonologist or surgeon. During this call, they will be asked whether they are interested in receiving the patient information file (PIF) of this study by mail. When patients and/or their parents agree to participate in this study, the participation forms will be signed at the next follow-up visit together with their treating pediatric pulmonologist or surgeon. Patients with a hernia-type other than Bochdalek, or patients who had any pulmonary surgery other than sequestration removal will not be asked to participate. Furthermore, children with a pulmonary infection requiring antibiotics within 4 weeks from the follow-up visit, or with a pulmonary infection not requiring antibiotics within 2 weeks from the follow-up visit are excluded from this study.
Only a MBW test will be scheduled in addition to the spirometry and body-plethysmography tests which are part of routine care. During the MBW test patients will be accompanied by a post-graduate medical student who has been trained and certified in performing MBW tests with children of the target age group. Before starting the test, the researcher will introduce and explain the procedure to the patient and parents. The researcher will also ask the patient to choose a program to watch on TV. Watching TV during the test helps to distract the children which stimulates a tidal breathing pattern. Maintaining a stable tidal breathing pattern is important for achieving a test result of good quality.
When the test starts the patient will breathe through a snorkel-like mouthpiece and wear a nose-clip. Therefore, a closed breathing circuit is created in which only 100% oxygen is delivered to the patient. By inhaling only oxygen, the subject will washout the resident nitrogen present in the lungs breath by breath until the target concentration of 1/40th (2.5%) of the starting nitrogen concentration has been reached. It is expected that in this population reaching the target concentration will take approximately 2-3 minutes. However, depending on the extent of peripheral airway damage this estimation could be increased. After reaching the target concentration, the researcher will stop the test which thereby completes one MBW trial. The patient can now remove his mouth from the mouthpiece and breathe normal room air. After every trial there is a waiting period of 1.5 times the trial time in order to wash the nitrogen present in room air back into the lungs. After this waiting period, another trial is started.
In order to successfully complete the MBW test occasion, at least two trials will have to be of good quality. Factors which can decrease the quality of trials are the opening of the closed circuit by a leak or unstable breathing patterns of the child. the researcher will try to prevent problems in acceptability by coaching and comforting the child to breathe calmly and to stimulate the patient to focus on watching TV. One test occasion typically

includes several MBW-trials to obtain at least two trials that are technically valid. The researcher will try to collect three successful trials, minimizing the chance of losing the test occasion when one of the trials still turns out to be unacceptable after post-test quality control. Dependent on the amount of trials needed to achieve three or more acceptable trials and the amount of peripheral airway damage present, total testing time will usually take 30 to 45 minutes including the introduction and explanation of the test to patient and parents. A maximum of two subjects per age-group will be replaced when subjects do not succeed in achieving two technically valid MBW-trials. MBW-test success rates will be reported in our study and will be compared to spirometry and body-box success rates.
In this study we will furthermore ask the patients and parents for permission to use the spirometry and body-plethysmography outcomes from the same follow-up visit for our study. These outcomes will be needed to answer our research questions. Furthermore, we will ask permission to use demographic data of the patients, and prognostic factors of the herniation present at birth. The prognostic factors will include the side of the herniation in the diaphragm, the lung-to-head ratio, the presence of liver herniation, the requirement of extracorporeal membrane oxygenation (ECMO) and whether the child was born prematurely including the gestational age at birth. These data will all be collected either during a regular follow-up visit, or retrospectively from the electronic patient file by a member of the research team. Collection of these data will therefore not pose any extra burden on the patient and his/her parents.

Study burden and risks

negligible burden, no risks

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- age 5, 8, 12 of 16-18 yr
- history of congenitale diaphragmatic hernia
- informed consent

Exclusion criteria

none

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting

Start date (anticipated):	30-01-2020
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO Date:	21-11-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL71947.091.19