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Saline hypertonic in preschoolers with cystic fibrosis and lung structure as measured by computed tomography (CT)

Submission date
15/10/2015

Recruitment status
No longer recruiting

Registration date
05/11/2015

Overall study status
Completed

Last Edited
13/05/2022

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
People with cystic fibrosis (CF) often have thick mucus in the airways of the lungs that is hard to cough up. The mucus builds up and eventually leads to chronic cough and lung infections. Research has shown that even young children with CF may have thickened mucus in the lungs. Inhaling a concentrated salt solution, called hypertonic saline (HS), may help thin the mucus in the lungs. HS is about 7-8 times as salty as the fluid in the body. Thinning the mucus can make it easier to cough up. This helps to clear the lungs and improve lung health. Research studies about the safety and effectiveness of inhaled HS have been done in adults and children with CF 6 years of age and older. Patients in these studies took HS for up to a year. HS appears to be a safe treatment in these age groups. The use of HS in older children and adults decreased the need for antibiotics for acute respiratory infections. It also improved lung function and quality of life. HS is now routinely used by many CF patients over 6 years of age. Because HS treats a very early step in the chain of events that leads to chronic lung problems in people with CF, it may be particularly helpful when started early in life. Based on several studies, HS appears to be safe in children less than 6 years of age, but its effectiveness has been difficult to measure. In a previous study, children less than 6 years old receiving HS had the same number of lung infections as children receiving normal saline. However, we think that children this young need a more sensitive test to see if HS works in preventing lung damage, with a CT-scan of the lungs. The goal of this study is to see if the inhalation of HS improves lung function by comparison with normal or isotonic saline (IS), which contains the same salt concentration as the fluid in the body, by means of CT images.

Who can participate?
Patients with CF who are 3-6 years old

What does the study involve?
Each child is randomly allocated to one of two groups. Those in group 1 are given 7% HS to inhale twice a day for a year. Those in group 2 are given 0.9% IS twice a day for about one year. A medicine called a B” bronchodilator is used to help open up the airways before treatment with HS or IS. The child then attends 6 study visits and has 6 phone calls over the next 53 weeks.

Procedures done during the study visits include a physical exam, height and weight measurements, measurements of vital signs, oximetry (a method of measuring the amount of oxygen in the blood), breathing exercises for the CT scan, CT scan, spirometry (a test that tests how well the lung is functioning) and the collection of a health diary, filled in by the parents at home.

What are the possible benefits and risks of participating?
The child may benefit from taking part in this study if the hypertonic saline or isotonic saline helps to clear mucus from the lungs. Potential risks include side effects of the HF or IS (such as cough, wheezing, shortness of breath, and a salty taste in the mouth). The short acting B2 bronchodilator may lead to a short term increase in heart rate and feelings of anxiety and being shaky. The project also involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation. The risk is believed to be low and is theoretically similar to 3 to 6 months exposure to normal background radiation.

Where is the study run from?
Erasmus MC Rotterdam (Netherlands), University Hospitals Gasthuisberg (Belgium), Vall d'Hebron University Hospital (Spain), Hospices Civils de Lyon (France), Pitié-Salpêtrière Hospital (France), Copenhagen University Hospital, Rigshospitalet (Denmark), UZ Brussel (Belgium), Azienda Ospedaliera Universitaria Integrata Verona (Italy), Bambino Gesù Children's Hospital (Italy).

When is the study starting and how long is it expected to run for?
August 2016 to November 2020

Who is funding the study?
Cystic Fibrosis Foundation Therapeutics (USA)

Who is the main contact?
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Contact information

Type(s)
Public

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Clinical Trials Information System (CTIS)
2015-004143-39

Protocol serial number
1.1 10 FEB 2016

Study information

Scientific Title
A phase 3 randomised, double-blind, controlled trial of inhaled 7% hypertonic saline versus 0.9% isotonic saline for 48 weeks in patients with cystic fibrosis at 3-6 years of age in parallel with the North American SHIP clinical trial

Acronym
SHIP-CT

Study objectives
The primary hypothesis of the SHIP study (SHIP001) which runs in North America, is that compared to 0.9% Isotonic Saline (IS), HS will improve the LCI, a measure of ventilation heterogeneity, during the 48 week treatment period among preschool children with CF. The SHIP-CT study will use a near identical study design as the SHIP study, with similar eligibility criteria and treatment arms, to determine whether HS reduces structural lung disease as measured by chest computed tomography (CT), in addition to stabilizing or improving functional outcomes as measured by LCI. Thus, we aim to conduct a randomised, double-blind, controlled trial of inhaled HS vs. IS for 48 weeks in patients with CF 3-6 years of age in parallel with the North American SHIP clinical trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics committee of Erasmus University Medical Center, 09/08/2016

Study design
Multicentre randomised double-blind controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cystic fibrosis

Interventions
The child receives one of two treatments. The treatment group will be decided by a process called randomization, which is similar to flipping a coin. The child will be given either 7% HS or 0.9% IS twice a day for about one year. IS is the same salt concentration as the fluid in your body (0.9%). HS is about 7-8 times as salty as the fluid in your body. There is a 50% chance that the

child will be assigned to the group receiving HS and a 50% chance that the child will be assigned to the group receiving IS. The child will have 6 study visits and 6 phone calls over approximately 53 weeks.

During the study visits the following procedures will be done:
1. Physical exam
2. Height and weight
3. Vital signs
4. Oximetry
5. Breathing exercises for the CT scan
6. CT scan
7. Spirometry
8. Health diary, filled in by the parents at home

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Hypertonic saline

Primary outcome(s)
The difference in PRAGMA-CF %Dis between HS and IS study arm at end of study (48 weeks), measured from standardized chest CT.

Key secondary outcome(s))
1. Longitudinal change in airway disease (%Dis), bronchiectasis (%Bx) trapped air (%TA), and airway dimensions, as well as the proportion of patients with bronchiectasis progression established by %BX and AA-system, airway wall thickness established by the AA-system, from baseline to end of study as established by PRAGMA-CF and the AA-system, on chest CTs
2. Longitudinal change in LCI from baseline to 48 weeks measured by N2 MBW
3. Protocol defined pulmonary exacerbation rate
4. Health-related quality of life as measured by the modified parent-reported CFQ-R for preschoolers (excluding European sites)

Completion date
01/11/2020

Eligibility

Key inclusion criteria
1. Diagnosis of CF as evidenced by one or more clinical features consistent with the CF phenotype or positive CF newborn screen AND one or more of the following criteria:
1.1. A documented sweat chloride ≥ 60 mEq/L by quantitative pilocarpine iontophoresis (QPIT)
1.2. A documented genotype with two disease-causing mutations in the CFTR gene
2. Informed consent by parent or legal guardian
3. Age ≥ 36 months and ≤72 months at screening visit
4. Ability to comply with medication use, study visits and study procedures as judged by the site investigator

5. Ability to cooperate with chest CT at the enrolment visit as determined by the lung function technician

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
36 months

Upper age limit
72 months

Sex
All

Total final enrolment
120

Key exclusion criteria
1. Chest CT within 8 months prior to the Screening visit
2. Acute intercurrent respiratory infection, defined as an increase in cough, wheezing, or respiratory rate with onset within 3 weeks preceding screening or enrolment visit
3. Acute wheezing at screening or enrolment visit
4. Oxygen saturation < 95% (<90% in centres located above 4000 feet elevation) at screening or enrolment visit
5. Other major organ dysfunction, excluding pancreatic dysfunction
6. Physical findings that would compromise the safety of the participant or the quality of the study data as determined by site investigator
7. Investigational drug use within 30 days prior to screening or enrolment visit
8. Treatment with inhaled HS at any concentration within 30 days prior to screening or enrolment visit
9. Start of any additional inhaled saline solution at any concentration, or other hydrating agent such as mannitol or mucolytic drug such as dornase alpha within 30 days prior or following the Screening or Enrolment visit
10. Chronic lung disease not related to CF
11. Inability to tolerate first dose of study treatment at the enrolment visit

Date of first enrolment
01/08/2016

Date of final enrolment
31/10/2019

Locations

Countries of recruitment
Belgium

Denmark

France

Italy

Netherlands

Spain

Study participating centre
Erasmus MC
's-Gravendijkwal 230
Rotterdam
Netherlands
3015 CN

Study participating centre
University Hospitals Gasthuisberg (Gasthuisberg ZH)
Herestraat 49
Leuven
Belgium
3000

Study participating centre
Vall d'Hebron University Hospital
Paseo de la Vall d'Hebron
Barcelona
Spain
119-129 (08035)

Study participating centre
Hospices Civils de Lyon
France
69002

Study participating centre

Pitié-Salpêtrière Hospital
47-83 Boulevard de l'Hôpital
Paris
France
75013

Study participating centre
Copenhagen University Hospital, Rigshospitalet
Afsnit 5003
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Copenhagen
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2100

Study participating centre
UZ Brussel
Laarbeeklaan 101
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1090

Study participating centre
Azienda Ospedaliera Universitaria Integrata Verona
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Study participating centre
Bambino Gesù Children’s Hospital
Cystic Fibrosis Unit
Piazza S. Onofrio 4
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Sponsor information

Organisation

Cystic Fibrosis Foundation Therapeutics

ROR
https://ror.org/00ax59295

Funder(s)

Funder type
Charity

Funder Name
Cystic Fibrosis Foundation Therapeutics

Alternative Name(s)
Cystic Fibrosis Foundation Therapeutics, Inc., CFFT

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from shipCTstudy@erasmusmc.nl.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/03/2022	13/05/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes