Inflammatory markers in Broncho-alveolar Lavage fluid as risk factors for Lung disease in infants with Cystic Fibrosis: the I-BALL study

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To better understand the progression of early CF lung disease we aim to study lipid profiles and PMN dysfunction in relation to the severity of early lung disease in infants with CF, using BALF samples and peripheral blood. To optimally study these...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON47114

Source
ToetsingOnline

Brief title
I-BALL study

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
CF, Cystic fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: nieuwe NIH grant aanvraag wordt ingediend voor PMN deel. Lipidomics deel is geld voor van ZonMW;kan al uitgevoerd worden.

Intervention

Keyword: bronchiectasis, bronchoalveolar fluid, cystic fibrosis, inflammatory markers

Outcome measures

Primary outcome

1. Correlation of lipid profiles with early lung disease in CF:

Lipidomics endpoints. The primary end-points are the different bioactive lipid

levels in BALF of infants with CF using liquid chromatography (LC) coupled to

Mass spectrometry (MS). Lipid profiles will be derived of the BALF supernatant

2. Association early lung disease in CF with airway neutrophils reprogramming:

PMN endpoints. The primary endpoint for BALF cells flow cytometry analysis is

surface CD63 on airway PMNs (exocytosis of NE-rich granules), which was shown

to correlate with lung function in chronic CF disease

Secondary outcome

Other study parameters: We will assess various correlations, between:

* Bioactive lipid levels and chest CT score

* Bioactive lipid levels and past exacerbations / past antibiotic courses

* Bioactive lipid levels and future (after moment of samples) exacerbations /

future antibiotic courses (Bioactive lipid levels as riskfactors for later

problems)

* Bioactive lipid levels and microbiome (microorganisms from BALF / nasopharynx)

* PMN endpoints and chest CT score

* PMN endpoints and past exacerbations / past antibiotic courses

* PMN endpoints and future exacerbations / future antibiotic courses (PMN

endpoints as risk factors for later problems)

* PMN endpoints and microbiome

* PMN endpoints and bioactive lipid levels

Study description

Background summary

Airway disease, featuring early and intense inflammation and leading to progressive lung damage, is the main cause of morbidity and mortality in cystic fibrosis (CF). Mechanisms of CF airway inflammation remain unclear, hampering development of better treatments. Recent introduction of heel-prick screening for CF provides a unique longitudinal cohort of CF infants, in which the early phase of airway disease can be assessed. In our hospital we set up a clinical protocol for monitoring these infants in a structured way, using chest computed tomography (CT) and bronchoscopies with collection of broncho-alveolar lavage fluid (BALF) to assess early lung damage. Our protocol is designed according to the protocol used by the Australian AREST-CF consortium. Preliminary data from Dr Scholte's group show that lipid profiles differ in BALF from CF infants with a high score for lung damage, compared with a low score (minimal lung damage). Some of these lipids are products of activated polymorphonuclear neutrophils (PMN*s). Others are receptor-activating molecules involved in the resolution of inflammation and tissue injury. Also, in a pilot study by Dr Tirouvanziam's group, it was shown that CF airway PMNs are differently programmed than in normal airways, which leads to increased release of inflammatory factors and toxic enzymes. We hypothesize that CFTR deficiency causes abnormal inflammatory signaling in the lung of CF infants, resulting in abnormal programming of infiltrating PMNs, and subsequently excessive and chronic lung disease.

Study objective

To better understand the progression of early CF lung disease we aim to study lipid profiles and PMN dysfunction in relation to the severity of early lung disease in infants with CF, using BALF samples and peripheral blood. To optimally study these very precious samples, we will make use of state-of-the-art technologies for in vivo profiling and in vitro testing of PMN

function, including lipidomics and innovative cell- and fluid-based tools. Understanding the mechanisms at play in CF airway inflammation as it occurs in infants may lead to new paths for early intervention

Study design

This is an observational, exploratory study aimed at lipid and PMN biomarker evaluation in excess BALF samples from CF infants, the outcomes of which will be correlated with clinical outcomes, primarily the presence of bronchiectasis on chest CT

Study burden and risks

In most patients no additional burden, risks or benefits are associated with this study. The material used will be leftover material (not used for clinical studies) of BALF from patients that is collected in the context of the current AREST-CF program. However, in some patients 1 or 2 extra aliquots of saline may be necessary to obtain enough material. This adds a minimal additional burden to the patients, with no extra risk. Also as standard procedure several blood samples are taken during anaesthesia for routine investigations for the annual check. During this blood sampling, an extra vial EDTA blood will be taken for this study, and there will be no extra puncture for that.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Subjects are eligible for this study when:
- They are diagnosed with CF, confirmed with 2 mutations found by genetic analysis, either from heel prick screening or diagnosed later in life.
- Aged 1, 3 or 5 years, when they will undergo bronchoscopy and chest CT scan as part of the routine monitoring program for CF.
- Authorized by an informed consent from parents to undergo a possible extra rinse during bronchoscopy to retrieve sufficient BALF, an extra blood sample of 2 ml during the routine venous puncture, and permission to use excess biomaterials and coded clinical data for research.

Exclusion criteria

Absence of previously given informed consent for use of encoded clinical data for scientific purposes

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	18-05-2015
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	16-04-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-11-2018
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	NL49725.078.14