The half-lives of neutrophils in the blood and lungs of patients with cystic fibrosis

Published: 04-12-2012
Last updated: 26-04-2024

Objective of the study:The results of this study will lead to an improved insight in the lifecycle of these cells in health and diseases, and our results will be of importance for more insight in chronic inflammatory diseases particularly CF. For...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON37320

Source
ToetsingOnline

Brief title
HANCO

Condition

- Respiratory disorders congenital

Synonym
cysteuze fibrose (CF) chronische ontsteking van de longen

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Nederlandse CF stichting en Else-Kröner-Fresenius Stiftung

Intervention

Keyword: Cystic fibrosis, Innate immunity, lifespan, neutrophil

Outcome measures

Primary outcome

Primary study parameters/outcome of the study:

Granulocyte post-mitotic pool transit times and lifespans in blood and sputum

in normal healthy volunteers and CF patients

Secondary outcome

Secundary study parameters/outcome of the study (if applicable):

None

Study description

Background summary

Remarkably little is known about the lifecycle of neutrophils while this cell type is important in the pathogenesis in CF. Knowledge about this lifecycle is important for both for fundamental insights in the immune system under homeostatic conditions, but also under conditions of systemic inflammation. This will lead to an important increase in the understanding of the pathogenesis of CF but also for other chronic inflammatory diseases of the lung such as COPD. An important difficulty is the development of new medications is is the lack of knowledge on the basal characteristics of neutrophils under conditions of health and chronic inflammation: how fast they are produced, how long they remain in the blood and tissues and where they are cleared. Little is described in literature regarding these topics. In the 60's and 70's studies were performed on the lifespans of neutrophils, but with inadequate techniques. These data probably underestimate the lifespans of these cells, but they are still mentioned in modern tekst books.

Study objective

Objective of the study:
The results of this study will lead to an improved insight in the lifecycle of these cells in health and diseases, and our results will be of importance for

more insight in chronic inflammatory diseases particularly CF. For example, it will improve our ability to interpret the results from previous and future intervention studies that block survival and production of leukocytes.

Study design

Study design:
On day one the volunteers or patients will come to the clinic with an empty stomach.
First we will withdraw 20ml of blood for baseline measurements of glucose levels and DNA deuterium enrichment.
After that, the volunteers/patients will be orally administered 1g of deuterated glucose per kilogram bodyweight in 12 doses over a period of 6 hours. Also, after 1, 3 and 6 hours after the first administration we will withdraw two drops of blood by skinprick to determine the amount of deuterated glucose in the blood of the volunteer. During this day, the volunteer will receive low-carb breakfast and lunch.
At 5 more timepoints, the volunteer will come to the clinic to donate 20ml of blood. The exact days after intake of glucose differ for each volunteer but will not be in weekends or more than two days in a row. (A clear scheme of the withdrawals can be found in the "onderzoeksprotocol", paragraph 3.2.). On 2 days (7 days apart see table 2 page 13/25 of protocol) sputum will be collected.
From the collected blood and sputum white blood cell populations will be separated using high performance FACS sorting. DNA from these cells will be isolated and analysed for deuterium enrichment using a combination of gas chromatography and mass-spectometry.
These data will be fed to a mathematical model, which can calculate the half-lives of the cells.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness (if applicable):
Risks:
The deuteriated glucose used and sputum induction procedure are considered safe, so risks are negligible
Burden:
Subject will pay five visits to the clinic for blood withdrawl. Each visit, 20ml of blood will be withdrawn, which can be easily missed by adults. Besides, subjects will spend one day in hospital for one blood withdrawal and the intake of 1g/kg bodyweight of glucose

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
UTRECHT 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
UTRECHT 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Controls:
Age > 18 years and younger than 50 years
Healthy without indications of any inflammatory disease
Written informed consent;CF patients without treatment wtih corticosteroids
Age > 18 and younger than 50 years
Diagnosis of CF by clinical symptoms and positive sweat tests (sweat Cl- concentration > 60 mmol/l) and/or disease causing mutation(s) in the CFTR gene
Being clinically stable and on steady concomitant therapy at least four weeks prior to the study
FEV1 > 30% of predicted
written informed consent;CF patients on treatment wtih corticosteroids
Diagnosis of CF by clinical symptoms and positive sweat tests (sweat Cl- concentration > 60 mmol/l) and/or disease causing mutation(s) in the CFTR gene
Being clinically stable and on steady concomitant therapy at least four weeks prior to the study

FEV1 > 30% of predicted
inhalation of fluticasone proprionate (or equivalent) >400 microg total daily for at least 2 weeks prior to the study.
written informed consent

Exclusion criteria

Any infection
Smoking
Auto-immune disease
Use of medication, excluding: anticonceptives and pain killers (used less than once a week)
exuberant alcohol consumption (for males > 36 glasses per week, for females > 24 glasses per week)
drugs abuse
History of cancer

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:	Recruitment stopped
Start date (anticipated):	06-05-2014
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	04-12-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL40962.041.12