Immunological Defects in Chronic Pulmonary Aspergillosis

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In this study, we aim to characterize the immunological defect in patients with CPA as compared to patients with chronic obstructive pulmonary disease (COPD) without CPA on a functional, genetic, transcriptional and metabolic level.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Fungal infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON48258

Source
ToetsingOnline

Brief title
Immunological Defects in CPA

Condition

- Fungal infectious disorders
- Respiratory tract infections

Synonym
Chronic Pulmonary Aspergillosis (CPA); Chronic lung infection with Aspergillus

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ERC-grant: Identifying novel immunotherapeutic treatment strategies in chronic pulmonary aspergillosis in patients with COPD

Intervention

Keyword: Aspergillus, Chronic Pulmonary Aspergillosis, Immunology

Outcome measures

Primary outcome

The main study parameters / endpoints are the differences between patients with CPA and patients with COPD without CPA with regard to:

1. Cytokine production by peripheral blood mononuclear cells (PBMCs) in response to different stimuli

2. Aspergillus fumigatus conidia killing capacity of polymorphonuclear neutrophils (PMNs)

3. Single nucleotide polymorphisms (SNPs) in relevant genes involved in immune recognition and / or immune response

4. RNA expression of relevant genes involved in immune recognition and / or response in PBMCs

5. Metabolome pathways in macrophages (derived from CD14+ monocytes from peripheral blood)

6. LC3-associated phagocytosis (LAP) by CD14+ monocytes

Depending on interim results, the investigators would like to retain the possibility to decide to change the exact stimuli and read-out parameters during the course of this research project, not leading to any changes in the amount of blood drawn or burden in any other way for the patients.

To be able to correlate experimental results to clinical characteristics,

several clinical characteristics will be collected about the patients in coded

form (coded according to patient number in the electronic patient file),

including:

- Age

- Sex

- CPA subgroup (aspergilloma, Aspergillus nodule, CCPA, CFPA)

- Medication used

- HIV status, if known

Secondary outcome

Not applicable.

Study description

Background summary

Aspergillus species can cause a spectrum of disease in human hosts, ranging from invasive infections to allergic disease (e.g., allergic bronchopulmonary aspergillosis or ABPA). Which disease the host develops is largely dependent on the immune response he or she mounts against this ubiquitous fungus. On the one hand, invasive pulmonary aspergillosis (IPA) develops in (severely) immunocompromised patients, whereas allergic bronchopulmonary aspergillosis (ABPA) can develop in patients with underlying allergic disease. However, chronic pulmonary aspergillosis (CPA) develops in apparently immunocompetent patients or those with underlying anatomical/structural lung disease, raising the question why some patients develop CPA, whereas others do not.

Study objective

In this study, we aim to characterize the immunological defect in patients with CPA as compared to patients with chronic obstructive pulmonary disease (COPD) without CPA on a functional, genetic, transcriptional and metabolic level.

Study design

Comparative in vitro / ex vivo functional, genetic, transcriptional and

metabolomics study.

Study burden and risks

Patients will be asked to donate 60 ml of peripheral venous blood once. The risk and burden of this intervention is considered to be minimal, potentially consisting of pain during collection of blood, vasovagal syncope during collection of blood, possible haematoma formation after blood donation and the slight risk of local infection of the puncture site.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Adult patient (> 18 years of age)
2. Patient is able to give written informed consent
3. Diagnosis of CPA is established in the patient based on the diagnostic criteria according to the ESCMID/ERS guidelines

Exclusion criteria

Known active infection with HIV

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:	Recruiting
Start date (anticipated):	22-08-2019
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	17-06-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-08-2019

Application type:	Amendment
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	NL69716.091.19