The Effect of Leukocyte DNA mEthylation and micRoBIOME diversity and function on host defense mechanisms during community-acquired pneumonia.

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Primary Objectives: 1.To obtain insight in the role of altered DNA methylation in blood leukocytes (monocytes and neutrophils) in innate immune responses and host defense in patients with CAP.2.To determine the composition and function of the gut...

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

Summary

ID

NL-OMON50274

Source
ToetsingOnline

Brief title
ELDER-BIOME study

Condition

- Bacterial infectious disorders
- Respiratory tract infections

Synonym
pneumonia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: community acquired pneumonia, intestinal microbiota, leukocyte DNA methylation

Outcome measures

Primary outcome

The main parameters of this study will be the alterations in leukocyte DNA methylation and the composition and function of the intestinal and nasopharyngeal microbiota in patients with CAP.

These data will be associated with several clinical parameters, including, but not limited to:

• Patient demographics and medical history, at enrolment

• Date of hospital admission and discharge, transfer or death

• Date of high care unit/intensive care unit admission and discharge, transfer or death, if applicable

• Clinical outcome: hospital discharge, transfer or in-hospital death

• Mortality at day 90

Secondary outcome

Secondary it will be evaluated whether microbiome derived signals are of influence in differences found in methylation in these study groups.

Study description

Background summary

Community acquired pneumonia represents a major health care problem and mortality and morbidity associated with severe pneumonia remains considerable, despite state of the art care.
While the role of altered DNA methylation in cancer has been widely studied, knowledge of its impact on antibacterial defense is highly limited. In addition the gut microbiota contributes to host defense against bacterial pneumonia.
This study aims to explore a completely novel research area linking the extent of DNA methylation in blood leukocyte (monocytes and neutrophils) and function of gut and nasopharyngeal microbiota on the influence of innate immune responses to and host defense against community acquired pneumonia.

Study objective

Primary Objectives:
1.To obtain insight in the role of altered DNA methylation in blood leukocytes (monocytes and neutrophils) in innate immune responses and host defense in patients with CAP.
2.To determine the composition and function of the gut and nasopharyngeal microbiota in patients with CAP.

Secondary Objective:
1.To assess the influence of the gut microbiota on leukocyte DNA methylation in patients with CAP
2. To assess the influence of coagulation markers in innate immune responses and host defense in patients with CAP.
3. To assess the influence of whole blood transcriptome profiles in patients with CAP.
4. To compare the presence of gut epithelial integrity and bacterial translocation in patients with CAP and healthy volunteers.
5. To compare differences within the host response and immune systems of patients suffering from a COVID-19 CAP, regular CAP and healthy volunteers

Study design

Observational study among patients with CAP at the Emergency Department and Internal Medicine Ward of the Academic Medical Center Amsterdam.

From above mentioned patients, blood (52.5ml) will be withdrawn at presentation to analyze DNA methylation of purified monocytes and neutrophils which will be linked with DNA methyltransferase and ten eleven translocation (TET) activity,

RNA expression and a selection of innate immune function tests. In addition, 2 rectal swabs and 1 nasopharyngeal swab will be obtained to investigate the role of gut and nasopharyngeal microbiota composition and function (metagenomics). Another blood sample (12.5ml), along with 2 rectal swabs and 1 nasopharyngeal swab, will be collected at day 2/3 of hospitalisation. More patient material (47.5 ml of blood, 2 rectal swabs and 1 nasopharyngeal swab) will be obtained upon day 90 (-7/+21 days), when patients will be seen at the outpatient clinic of the AMC for follow up. Healthy volunteers will be subjected to a single blood draw of 85 ml. Moreover, 2 rectal swabs and 1 nasopharyngeal swabs will be obtained.

Study burden and risks

Participating in this observational study will not directly benefit the participant. The study will provide information about the influence of leukocyte DNA methylation and the gut microbiota on host defense mechanisms during CAP. The knowledge obtained in this study can potentially benefit CAP patients in the future by providing alternative immune modulating treatment options that modify the host response. The burden and risks for patients participating in the ELDER-BIOME study is minimal. We will take a total of 112.5ml blood, 6 rectal swabs and 3 nasopharyngeal swabs upon inclusion up to day 90. Healthy volunteers will be subjected to a 85ml blood draw, 2 rectal swabs and 1 nasopharyngeal swabs at a single time point.

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) Age >= 18 y
2) Clinical suspicion of a new episode of acute respiratory tract infection
3) The presence of a new or increased infiltrate on chest radiography or computed tomography (CT) or a positive SARS-CoV-2 PCR on nasopharyngeal swab within 14 days prior to admission
4) Presence of two or more diagnostic clinical criteria:
- Cough
- Production of purulent sputum or a change in the character of sputum
- Temperature >38°C or <36.1°C
- Auscultatory findings consistent with pneumonia, including rales, evidence of pulmonary consolidation (dullness on percussion, bronchial breath sounds, or egophony), or both
- Leukocytosis (>10×109 white cells per liter or >15% bands)
- C-reactive protein level of more than 3 times the upper limit of the normal range
- Dyspnea, tachypnea, or hypoxemia

Exclusion criteria

1) No informed consent is provided by patient
2) Patients who had recently been hospitalized (for >48 hours in the previous 2 weeks) or who resided in long-term care facilities
3) Patients with a colostomy
4) Patient is enrolled in an interventional clinical study of an anti-infective or immunomodulatory therapy

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):	03-10-2016
Enrollment:	843
Type:	Actual

Ethics review

Approved WMO Date:	06-09-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL57847.018.16