Reconstituting the microbiome after pneumonia.

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Primary objective: 1. To prove the concept that 90-day treatment with probiotics can restore microbiome composition and diversity in patients treated for community-acquired pneumonia. Secondary objective: 1. Investigate possible differences in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON49196

Source
ToetsingOnline

Brief title
RECAP

Condition

- Bacterial infectious disorders

Synonym
Community-acquired pneumonia, lung infection, pneumonia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Topconsortia voor Kennis en Innovatie grant.,Winclove Probiotics

Intervention

Keyword: microbiome, pneumonia, probiotics

Outcome measures

Primary outcome

1. Difference in microbiome diversity and composition between groups, analysed

by deep 16s RNA sequencing.

Secondary outcome

1. Incidence of adverse events.

2. Difference in mean cytokine response levels between groups.

3. Incidence and duration of antibiotic-associated diarrhoea, based on

Bristol-stool scale scores.

4. To link cytokine response levels to microbiome composition and clinical

endpoints.

Study description

Background summary

Community-acquired pneumonia (CAP) is the most important infection in terms of numbers of patients for which antibiotics are given in the hospital. Readmission and new infections in the year after hospital admission for pneumonia is frequent, varying from 15% up to 40% in certain subgroups. It is known that after a severe pneumonia and subsequent antibiotic treatment, the gut microbiome is severely perturbed. There is a link between the extent of this dysbiosis and the readmission rates for pneumonia and sepsis.

In recent years we deepened our understanding of the pivotal role that the microbiome plays in the local and systemic immune system. Reconstituting the severely perturbed microbiome after antibiotic treatment for pneumonia could improve the immune status of patients and thereby ultimately lower readmission and infection rates.

We hypothesize that 90-day treatment with a selected probiotics-mixture could reconstitute the microbiome diversity after antibiotic treatment for CAP. This pilot study could pave the way for a larger clinical trial powered to investigate whether probiotics can diminish readmission and new infection rates in the year after hospital admission for community-acquired pneumonia.

Study objective

Primary objective:
1. To prove the concept that 90-day treatment with probiotics can restore microbiome composition and diversity in patients treated for community-acquired pneumonia.

Secondary objective:
1. Investigate possible differences in number of adverse events between groups.
2. To obtain insight in innate immune responses during CAP and the probiotic intervention.
3. Determine incidence and duration of antibiotic-associated diarrhoea between groups.
4. To link microbiome composition to innate immune responses and clinical endpoints.

Study design

Pilot study, double blind, placebo-controlled randomized controlled trial.

Intervention

After hospitalization and in-hospital antibiotic treatment for CAP, if patients meet in/exclusion criteria (e.g. no sepsis, no ICU), one group will receive a probiotic mixture (Ecologic AAD) twice daily for 90 days, while the other group will receive a placebo twice daily for 90 days.
Patients will start with the intervention at the moment they are discharged from the hospital.

Study burden and risks

The burden for patients participating in the RECAP study is as follows:
- We will take 30ml of blood, 6 rectal swabs and 3 nasopharyngeal swabs divided over three time-points (day of inclusion, day 2-3 of admission, day 90 of the intervention). The first two sampling time-points are in-hospital, while the day 90 day sampling time-point is either at the patients home or, if possible, combined with an outpatient appointment. Patients will need to consume either a probiotics or placebo mixture twice daily for 90 days. This mixture can be drank after being dissolved in a glass of water. Patients will be asked to keep

a defecation diary during the 90-day regimen of either probiotics or placebo. Additionally, we ask patients to fill out a comprehensive questionnaire at day 90 (see appendix).

- Oral use of probiotics is deemed safe in the latest studies and systematic reviews (see introduction and chapter 6). Three previous studies have been performed with this specific probiotic mixture (Ecologic AAD), of which two randomized controlled trials. In those studies, no difference in number of adverse events was described between the groups. To lower remaining risks, the intervention will only start after the patient is discharged from the hospital. Furthermore, the exclusion criteria exclude the most seriously ill patients from this study.

- Participation in this interventional randomized-controlled trial could potentially benefit the patients in the probiotics-group. We hypothesize that probiotics can reconstitute gut microbiota diversity, thereby improving the immune status and possibly lowering readmission rates. Patients randomly assigned to the placebo-group will receive standard of care and will not benefit from participating in this study. The knowledge obtained about the effects of probiotics on the microbiome after pneumonia could potentially benefit future CAP patients.

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

Age >= 18 y
• Clinical suspicion of a new episode of acute respiratory tract infection for which treatment with antibiotics is deemed necessary.
• Presence of two or more diagnostic clinical criteria:
o Cough
o Production of purulent sputum or a change in the character of sputum
o Temperature >38°C or <36.1°C
o Auscultatory findings consistent with pneumonia, including rales, evidence of pulmonary consolidation (dullness on
o percussion, bronchial breath sounds, or egophony), or both
o Leukocytosis (>10×10^9 white cells per liter or >15% bands)
o C-reactive protein level more than 3 times the upper limit of the normal range
o Dyspnoea, tachypnea, or hypoxemia

Exclusion criteria

No informed consent is provided by patient or its legal representative
Admission to Intensive Care facilities in the current episode
Presence of enterobacteriaceae or staphylococcus aureus bacteraemia
Suspicion/diagnosis of aspiration pneumonia
More than 7 days use of probiotics or antibiotics within the last 2 months
Patients diagnosed with chronic bowel disease and/or colostomy.
Patient is enrolled in an interventional clinical study of an anti-infective or immunomodulatory therapy.
Pregnancy.
Parenteral feeding or enteral tube feeding.
Patients who are readmitted to the hospital during the 90-day intervention period will terminate the intervention. Follow-up will be continued without further sampling.
Patients who are prescribed new antibiotic treatment by the general practitioner during the 90 day intervention period will terminate the intervention. Follow-up will be continued without further sampling.
Patients who are immunocompromised due to active chemotherapy, uncontrolled HIV infection, stem-cell transplantation, haematological malignancies or high-dose

immunosuppressive drugs.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-10-2019
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	12-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-08-2019
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:	15-12-2020
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

ID: 21647
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL67870.018.18
OMON	NL-OMON21647