Microbiome and lower respiratory tract infections in children

Published: 12-02-2013
Last updated: 26-04-2024

Primary objective: To compare the NP microbiome composition and the presence of viruses in children hospitalized for a LRTI to the NP microbiome composition and the presence of viruses in healthy age- and gender-matched controls. Secondary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON44725

Source
ToetsingOnline

Brief title
Microbiome and LRTI

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
bronchitis or pneumonia, Lower respiratory tract infections

Research involving
Human

Sponsors and support

Primary sponsor: Spaarne Ziekenhuis
Source(s) of monetary or material Support: de kosten voor het onderzoek komen ten laste van de verrichter en niet ten laste van de ziektenkostenverzekering

Intervention

Keyword: LRTI, Microbiome

Outcome measures

Primary outcome

NP microbiome composition and viral presence in the nasopharynx of children

hospitalized for a LRTI and in healthy age-and gender-matched controls.

Secondary outcome

1.NP microbiome composition and viruses of LRTI cases after recovery.

2.Clinical data from the medical record, routine chest X-ray results and

routine laboratory blood parameters of children hospitalized for LRTI.

3.Microbiota in saliva (oral cavity) and faeces (intestines).

Study description

Background summary

Lower respiratory tract infections (LRTI) are a major cause of morbidity in young children in high- income countries and the major cause of mortality in developing countries. The etiology of LRTI is often polymicrobial involving well-known viral or bacterial pathogens and also combinations of both.

LRTI pathogens all originate from the nasopharynx . Most of the time these bacteria are regular residents of the nasopharynx of asymptomatic individuals and live there together with other presumed harmless commensals, without causing disease. Together they are a complex bacterial community, called the nasopharyngeal (NP) bacterial microbiome. Next to bacteria, viral presence is also found in the nasopharynx during respiratory tract infection and in asymptomatic individuals.

Studies of the microbiome have only recently become feasible with the development of molecular methods, since 40-80% of microbiome bacteria cannot be detected by conventional culture techniques. Novel molecular techniques as 454 pyrosequencing
enable us to measure in detail the composition of complex microbial communities

in various states of health and disease.

The reason for progression from nasopharyngeal bacterial or viral carriage towards invasive or symptomatic respiratory infectious disease is unknown. The composition of the NP microbiome may be highly relevant for health or susceptibility to disease. For instance, acquisition of a viral common cold may alter bacterial outgrowth of common colonizers of the nasopharynx like S. pneumoniae. Subsequently these bacteria may spread and cause pneumonia. This development towards infectious disease by commensals like S. pneumoniae may however not only depend on viral acquisition, but also on the total NP microbiome of which S. Pneumoniae is part. A well- balanced composition may play a role in the containment of potential pathogens by preventing outgrowth. LRTI may occur as the balance is disturbed and host defense is insufficient.

The intestinal microbiome is important for its presumed correlation to several diseases. Also respiratory immunity seems to be affected by the intestinal microbiome. In addition the digestive system is believed to function as the largest reservoir for exchanging antibiotic resistance genes between commensals and bacteria passing through the gastro-intestinal tract. Antibiotic consumption may also have influence on the equilibrium of the microbiome on the other various body sides, like the nasopharynx, which will render a child more susceptible for a new infection.

In this study we will focus on the microbiome composition of the nasopharynx, the oral cavity and intestines during health and LRTI. This may lead to new insights in the pathogenesis of LRTI and create possibilities for future preventive strategies.

Study objective

Primary objective:
To compare the NP microbiome composition and the presence of viruses in children hospitalized for a LRTI to the NP microbiome composition and the presence of viruses in healthy age- and gender-matched controls.

Secondary objectives:
1.To study the differences in composition of the NP microbiome in children hospitalized for a LRTI during disease and after recovery.
2.To study the correlation between clinical, radiological and laboratory findings and the bacterial and viral presence as well as their density in the nasopharynx during LRTI.
3.To study the relation between the NP- and oral- and intestinal microbiome during health and LRTI.

Exploratory Objectives:
To explore the influence of host and environmental factors such as age and use of antibiotics on the composition of the NP-, lower respiratory tract-, oral-

and intestinal microbiome.
To explore the relation between the NP microbiome in to the bacteria and viruses present in the lungs of children with severe LRTI

Study design

Case control study. The NP-, oral- and intestinal microbiome of children hospitalized for a LRTI will be compared with the NP-, oral- and intestinal microbiome of healthy age- and gender-matched children within the same period of time.

Study burden and risks

Participation in this study holds no more risks than negligible risk and no benefits. We believe that the risk of this study is no more than negligible for the participants since all sampling methods are non-invasive and generally accepted as fully save. Sampling moments will take place during hospitalization and on regular visits to the outpatient department or "consultatiebureau" to minimize burden and time spent for the study participants. There is no personal benefit for the child or the parents.
We will follow the code of conduct relating to expressions of objection by minors participating in medical research, as stated by the CCMO.
The sampling moments including signing of the informed consent will take about 30 minutes of participant*s time.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

All groups:
Children * 4 weeks and * 5 years and;Non-severe LRTI group:
Hospitalized for a LRTI at a general pediatric ward. ;Severe LRTI group:
Hospitalized at the intensive care ward for a severe LRTI;Control group must fulfil all the following criteria:
1. Children matched with LRTI case for age (in years). In addition children < 1 year will be matched for months in two categories: 4 weeks - 6 months or 6 months - 1 year.
2. Matched with hospital admission date of LRTI case + maximal two weeks.
3. Matched for gender.
4. No fever and/or respiratory tract infection (except rhinitis) in the previous four weeks.
5. No antibiotics in the previous 3 months.

Exclusion criteria

- Severe concomitant disease (severe congenital heart disease, bronchopulmonary dysplasia, prematurity <32 weeks, cystic fibrosis, sickle cell disease, congenital or acquired immunodeficiency disorders, cardiovascular disease, neuromuscular disorders, oncology patients or major congenital anomalies) and/or
- Nosocomial infection and/or
- Language barrier

Study design

Design

Study type:	Observational non 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):	10-09-2013
Enrollment:	975
Type:	Actual

Ethics review

Approved WMO Date:	12-02-2013
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	27-02-2013
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	03-05-2013
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	26-09-2013
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	17-12-2013

Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	07-01-2014
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	13-11-2014
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	09-11-2015
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	18-07-2017
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)

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	NL42019.094.12