Intestinal microbiota composition after antibiotic treatment in early life

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON46989

Source
ToetsingOnline

Brief title
The INCA study

Condition

- Gastrointestinal conditions NEC
- Allergic conditions
- Respiratory tract infections

Synonym
composition of intestinal microbiota, development of allergy

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van Economische Zaken;via Food & Nutrition Delta (FND)

Intervention

Keyword: antibiotics, immunology, infants, neonatal intestinal microbiota

Outcome measures

Primary outcome

The primary endpoint of the study is the incidence of eczema in antibiotic treated children versus healthy controls. Besides that, the incidence of food allergy, URTI, LRTI and GITI will be monitored. This will illustrate whether early antibiotic treatment may influence the developing immune system. Objective evaluation will be done by measuring vaccination response, length and weight (weight/growth curves) and recall doctor*s diagnoses from the GP (primary care visits for URTI, LRTI, GITI, food allergy, atopic dermatitis). Even so, usage of medication will be determined by checking pharmacist*s medication records and by asking the parents to report antibiotic treatment of their child on the monthly checklists.

Secondary outcome

The secundary outcomes of the study are potential differences in the development of intestinal microbiota (i.e. microbiota composition) in infants exposed to antibiotic therapy in early life (first 2 weeks) versus infants that did not receive antibiotic treatment during that period.

The samples are subjected to microbiota composition profiling by means of a PCR-based interspace profiling technique (IS-pro, IS-Disgnostics, Amsterdam). Composition of faecal samples will be analyzed by targeting bacterial groups that are present (e.g. Bifidobacteria, Enterobacteriaceae, Streptococci,

Lactobacilli, Bacteroides, Proteobacteria) and by pyrosequencing technique at

the University of Wageningen (head Prof. J. Knol). .

Study description

Background summary

Evidence is growing that an aberrant microbiota composition can have clinical effects. It is yet unknown to what extend the neonatal use of antibiotics can have a detrimental effect on the gastrointestinal microbiota, for how long this gastrointestinal imbalance will remain, to what extend the microbiota will normalize and what the effects are on the developing immune system. Several studies showed distinct associations between aberrant colonization patterns and reduced microbial diversity and an increased risk of developing atopic Th2 type diseases on one hand, such as allergy, wheezing and asthma, and auto-inflammatory Th1 diseases on the other hand, like inflammatory bowel disease (IBD), diabetes and obesity
Answering these questions can be important, since there is evidence that manipulation of the infant microbiota by using pre-or probiotics can restore ecological balance of the microbiota. Future studies should demonstrate if development of allergic diseases might be influenced by (restoring) the ecological intestinal microbiota balance. Also, targeted intervention may have beneficial effects on gastrointestinal imbalance due to early antibiotic exposure.

Study objective

In this prospective observational cohort study we aim to study the potential clinical consequences of antibiotic use in early life, by focussing on the incidence of eczema, as well as food allergy, upper respiratory tract infections (URTI), lower respiratory tract infections (LRTI) and gastrointestinal infections (GITI) in the first year of life. Also, vaccination response will be measured at 1 year of age. Differentiation will be made between a group of neonates who received antibiotics in the first days of their life, and control infants who were not exposed to antibiotics in the neonatal period.
Besides that, the perturbations in the gastrointestinal microbiota due to antibiotic use in early life will be studied, since it is hypothesized that altered microbiota may be an important underlying mechnism for impediments in the developing immune system.

Study design

At baseline, parents have to fill out an (online) questionnaire containing questions on key events family history, family composition, co morbidity and medication. They have to complete daily checklists, on which they tick off the presence of 8 symptoms.
A total of 8 faecal samples need to be collected at specific time points during the first year of life. Also, at the age of 2 years, a fecal sample needs to be collected. All parents will be offered collection vials for easy collection of the fecal samples.
Participation will end around the 1st birthday of the infant after a scheduled outpatient consultation. At that time instruction will be given for the fecal sample collection around the 2nd birthday of their child.
When the child has reached the age of 4-5 years old, parents will be approached for an online questionnaire concerning allergic disorders, gastro-intestinal disorders and general health and growth. In addition, permission will be asked to approach the general practitioner for doctor diagnosed conditions as mentioned above. Moreover, parents will be asked to collect one more fecal sample.

Participants will be recruited at the maternity ward or neonatal ward of the St. Antonius Hospital, Meander Medisch Centrum Amersfoort as well as the Tergooi Hospitals Blaricum/Hilversum and Gelre Hospitals Apeldoorn. In total 150 couples of whom their baby is suspected to suffer from a perinatal infection are recruited (antibiotic treated group). Newborns with a low probability of neonatal infection (no treatment but 24-48 hours of observation) and healthy newborns, born in the hospital, will be included to form the control group (in total 300 couples recruited).
During the study period, parents are free in their choice of breastfeeding and/or feeding formula as well as their feeding regime; no specific formula feeds and/or regime will be provided by the research group.

Study burden and risks

See page 12 of the protocol.

Potential side-effects: The study involves collection of faecal samples, one blood sampling and information gathering by requesting parents to fill out checklists. No negative side-effects of the study content are expected.

Unwanted effects and other risks: Unwanted effects and other risks are not to be foreseen.

Inconveniences and risks related to study related procedures: During this study there are no procedures which would pose any risk to the participants. Blood sampling (on the back of the hand) may be inconvenient shortly, but doesn*t cause increased risk for the participant (compared to blood sampling in adults). A local anesthetic will be used to relieve the inconvenience.

Strains for the parents: The main strain for the parents is ticking off of the weekly checklist (max 10 minutes every week). Former studies showed that parents quickly do this 'out of habit' and don't encounter this as a strain. Collecting the faecal samples takes ~5 minutes per sample.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Term born babies (i.e. > 36 weeks gestational age)
(Short) stay on maternal ward OR admission to neonatal ward because of antibiotic treatment
Signed informed consent by the parents

Exclusion criteria

Prematurity (i.e. gestational age < 36 weeks)
Congenital illness or malformations
Maternal probiotic use (well considered) < last 6 weeks of pregnancy
Severe perinatal infections for which neonatal intensive care transfer is needed
Insufficient knowledge of the Ducht language (by the parents)

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):	11-01-2012
Enrollment:	450
Type:	Actual

Ethics review

Approved WMO Date:	11-10-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-11-2011

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-03-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	24-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
ClinicalTrials.gov	NCT02536560
CCMO	NL37233.100.11