The role of the intestinal microbiome in enteric and systemic vaccine immune responses

Published: 24-06-2015
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Primary Objective: to investigate the role of the gut microbiota in RVV immune response
Secondary Objectives: To investigate the role of the gut microbiota in tetanus and pneumococcal vaccine immune responses

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44814

Source
ToetsingOnline

Brief title
Rota-biome

Condition

- Other condition
- Gastrointestinal infections
- Viral infectious disorders

Synonym
immunity, rotavirus vaccine

Health condition

vaccin immunogeniciteit

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: immunogenicity, microbiome, rotavirus, vaccine

Outcome measures

Primary outcome

Main study parameters/endpoints: The main study endpoint is the 28-day post vaccination anti-RV IgA serum response.

Secondary outcome

Secondary study parameters are the height, slope and time to positivity of the post-vaccination anti-RV IgA, anti-pneumococcal antibodies and anti-tetanus toxoid antibodies, and fecal rotavirus antigen shedding days 1-7 post rotavirus vaccination. Differences in the composition and diversity of the intestinal microbiota before and after antibiotic use and between groups. Isolation and stimulation of peripheral blood mononuclear cells (PBMC) pre and post vaccination with vaccines. Correlation between self-reported diet (4 day log) and microbiome composition.

Study description

Background summary

Rationale: Rotavirus (RV) is the leading cause of diarrhea-related death in children under five years of age, particularly in Africa and Asia. Rotavirus vaccines (RVV) have the potential to dramatically reduce rotavirus morbidity

and mortality, however rotavirus vaccine efficacy is lowest in the poorest countries with the highest child mortality rate.
We hypothesize that differences in gut microbiome colonization, composition and diversity might be contributing to the diminished RVV efficacy observed in developing countries. We propose evaluating the effects of intestinal microbiota differences obtained through antibiotics on RVV immune responses.
To obtain a better mechanistic understanding of the relationship between the intestinal microbiota and vaccine immune responses, this study also proposes evaluating the effect of antibiotic microbiota manipulation on two well-studied and classic systemic vaccines: the tetanus vaccine and the pneumococcal vaccine (Pneumo23).

Study objective

Primary Objective: to investigate the role of the gut microbiota in RVV immune response

Secondary Objectives: To investigate the role of the gut microbiota in tetanus and pneumococcal vaccine immune responses

Study design

Study design: Randomized, controlled intervention study in adult human volunteers

Intervention

Intervention:
Arm 1 (control): no antibiotic depletion then RotarixTM, Tetanus and Pneumococcus vaccination;
Arm 2: broad-spectrum antibiotic depletion (ciprofloxacin, vancomyin, metronidazole) then RotarixTM, Tetanus, and Pneumococcus vaccination;
Arm 3: Gram-positive depletion (oral vancomycin) then RotarixTM, Tetanus, and Pneumococcus vaccination

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The burden of this study includes vaccination (one oral two intramuscular), oral antibiotics, and 5 visits after the screening visit to the hospital, spread out over 5 1/2 weeks. Intramuscular vaccinations can give local irritation, pain, muscle soreness and aching.

Vaccination can give transient malaise and infrequently, fever.

Oral antibiotic use could lead to gastrointestinal symptoms and (rarely) allergic reactions.

The results of this study might lead to interventions that could improve the immunogenicity of rotavirus vaccine in developing countries, potentially preventing hundreds of thousands of deaths due to rotavirus disease over the next 15 years. It could also elucidate important immune mechanisms involved in oral and systemic vaccination.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9 Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9 Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

* Healthy, as determined by a responsible physician, based on a medical evaluation including medical history, physical examination and laboratory tests carried out within 28 days prior to starting antibiotics (day -9). A subject with a clinical abnormality or laboratory parameter outside the reference range may be included if the investigator agrees that the finding is unlikely to introduce additional risk factors and will not interfere with the study procedures
* Male between 18 and 35 years of age, inclusive at the time of signing the informed consent
* Capable of giving written informed consent and able to comply with the requirements and restrictions listed in the informed consent form
* Normal defecation pattern (defined as *3x/ day and *3x/week)

Exclusion criteria

* Baseline anti-rotavirus immunglobluin A level greater than 20 IU/mL or equivalent geometric mean titer.
* Subject has had a major illness in the past 3 months or any significant chronic medical illness that the investigator would deem unfavorable for enrollment, including inflammatory diseases.
* Subject with any history of immunodeficiency
Subject with a history of thrombocytopenia or bleeding disorder
* Subjects with a history of any type of malignancy
* Subject has a past or current gastrointestinal disease which may influence the gut microbiota
* Current or chronic history of liver disease, or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones)
* History of alcoholism and/or drinking more than an average of 5 units of alcohol per day
* The subject has received an investigational product within three months of day 0 of the current study
* Use of prescription or non-prescription drugs and herbal and dietary supplements within 6 months unless in the opinion of the investigator the medication will not interfere with the study procedures or compromise subject safety
* Recent (< 12 months) use of antibiotics (any kind, except for dermal antibiotics)
* Known allergy to antibiotics (any kind)
* Allergy to any vaccine components (any kind, including allergy to egg white, thiomersal and phenol) or past adverse reaction of any kind to a tetanus or pneumococcal vaccination
* Subject has difficulty in donating blood or accessibility of a vein in left or right arm
* Subject has donated more than 350 mL of blood in last 3 months
* Difficulty swallowing pills
* Body mass index >28 kg/m2
* Any other issue that, in the opinion of the investigator, could be harmful to the subject or compromise interpretation of the data

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2015
Enrollment:	63
Type:	Actual

Ethics review

Approved WMO Date:	24-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2017
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	NL52510.018.15