Experimental Human Rhinovirus Infection, a randomized placebo-controlled pilot study

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Our primary objective is to set up the Human Rhinovirus (HRV)-model in our centre, using HRV serotype 16 (HRV-16). Secondary objectives:1. To determine the incubation period of HRV-16 infection.2. To determine the effects of HRV-16 infection on cold...

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

Summary

ID

NL-OMON37030

Source
ToetsingOnline

Brief title
EHRVI

Condition

- Viral infectious disorders

Synonym
common cold, Rhinovirus infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,EFRO subsidie,Immunoforce consortium bestaande uit: biotechnologische firma's, europese EFRO

gelden en academische fondsen.

Intervention

Keyword: common cold, HRV

Outcome measures

Primary outcome

The primary outcome measure is the infection rate (defined by a positive viral culture, qPCR and/or a four-fold rise in antibody titre) of healthy volunteers inoculated with a standardized dose of HRV-16.

Secondary outcome

- Incubation period of HRV-16 infection.

- Symptom scores measured by diary cards (WURSS 21 scoring method)

- Temperature

- Forced expiratory volume at a timed interval of 1 second (FEV1), and forced expiratory flow 25-75% (FEF 25-75%).

- Leukocyte counts and differentiation (NK-cells, CD4 / CD8, neutrophils), and cytokine levels in nasal washes (including but not limited to IL-8, IL-1β, CCL5)

- Leukocyte counts and circulating plasma cytokines (including but not limited to TNF-α, IL-6, IL-10, IFN-γ, IL-8, CCL5)

- The cytokine response (including but not limited to TNF-α, IL-6, IL-10,

IFN-γ), of leukocytes ex vivo stimulated with different stimuli (including but

not limited to LPS, HRV, Staphylococcus aureus).

- Composition of the gut microbiota

- The host transcriptome and metabolome

- Composition of the nasal-pharyngeal microbiota

Study description

Background summary

The importance of the common cold derives primarily from its frequency and from its enormous socioeconomic impact. Human Rhinoviruses (HRVs) are the major cause of the common cold, being responsible for 30-50% of all acute respiratory illnesses with no causal remedies for hand. A model to investigate the pathophysiology of HRV infection and to test compounds that could treat or protect one from infection or developing symptoms would therefore be very valuable. With this HRV model it is also possible to investigate crosstalk between bacteria and viruses. This is very relevant because, following a viral infection, bacterial superinfections are common in clinical practice, and underlying mechanisms and subsequent possible therapies that could prevent this remain to be discovered.

Study objective

Our primary objective is to set up the Human Rhinovirus (HRV)-model in our centre, using HRV serotype 16 (HRV-16).

Secondary objectives:
1. To determine the incubation period of HRV-16 infection.

2. To determine the effects of HRV-16 infection on cold symptoms, temperature, and spirometry.

3. To determine suitable inflammatory parameters (and their kinetics) that play a role in the HRV-16-induced local inflammatory response by measuring leukocyte counts and differentiation as well as cytokine levels in nasal washes.

4. To determine whether HRV-16 infection can induce a systemic immune response and its kinetics by measuring leukocyte counts and differentiation. and circulating plasma cytokines.

5. To determine the effect of HRV-16 seropositivity on the clinical and immunological response to re-infection with HRV-16.

6. To determine if a subject is protected against re-infection with HRV-16 within one week (tolerance formation to HRV), and if so which mechanisms play a role (local immune response parameters, systemic immune response parameters).

7. To determine whether HRV-16 infection modulates the immune response of circulating leukocytes by measuring the cytokine response, of leukocytes ex vivo stimulated with different inflammatory stimuli.

8. To determine the effects of HRV-16 (re-)infection on the nasal, oral and faecal microbiota

9. To determine the effects of HRV-16 (re)infection on the host transcriptome

10. To determine the effects of HRV-16 (re)infection on the host metabolome

Study design

A parallel, randomized placebo-controlled pilot study in healthy male and female volunteers. The subjects will be randomized to become either inoculated with HRV-16 (n=20; 10 male + 10 female) or with placebo (NaCl 0.9%, n=20, 10 male + 10 female). After one week a second inoculation with HRV-16 will be performed in both groups.

Intervention

Human rhinovirus 16 (HRV-16)

Study burden and risks

Subjects have to visit the hospital on a total of 13 occasions (about 10 minutes each visit). Upon screening, a medical interview is conducted. Subjects have to keep a symptoms diary. In total, approximately 500 ml of blood will be drawn (on 13 occasions via venapuncture). This is not associated with side effects (500 mL is also drawn at the blood bank without any side effects). Furthermore, 13 nasal washes will be performed, which can lead to slight

irritation of the nasal mucosa but is not associated with riskss. HRV infection is associated with short-term symptoms of a cold. Worldwide, thousands of subjects have been exposed to experimental rhinovirus infection, of which more than 600 to HRV-16. Serious adverse events related to rhinovirus infection have never beendocumented. Therefore, this model can be considered a safe and highly reproducible model. Moreover, 52 volunteers have already been exposed to the HRV-16 virus from the batch that we want to use in this study.

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

- Written informed consent
- Age >=18 and <=35
- Healthy

- Use of contraceptives (for female subjects only)

Exclusion criteria

- Pregnancy or lactating
- Pre-existent lung disease, including asthma
- A history of allergic rhinitis with positive allergen skin tests
- Use of any medication
- Use of alcohol > 5/day or >20/wk
- Use of any drugs
- Current smoker or more than 5 pack-year history
- Frequently have nosebleeds
- Recent nasal or otologic surgery
- Febrile illness or a common cold within four weeks before the HRV challenge
- Currently participating in another clinical trial
- Use of antibiotics, norit, laxatives (up till 6 months prior to inclusion), cholestyramine, acid burn inhibitors or immune suppressive agents (up till 3 months prior to inclusion), and pre- and probiotics (up till 1 month prior to inclusion).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-03-2013
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	13-11-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-03-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2012-004938-42-NL
CCMO	NL42503.091.12