Collection of nasal lavage fluid from experimentally infected healthy human volunteers for the generation of a GMP batch of HRV16

Published: 08-11-2011
Last updated: 03-05-2024

Experimental infections of humans with rhinoviruses, in particular rhinovirus 16 (HRV16) have proven to be a highly relevant and safe approach to study exacerbations in patients with asthma and COPD. The worldwide availability of stocks of HRV16 for...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Observational invasive

Summary

ID

NL-OMON34307

Source
ToetsingOnline

Brief title
HRV16 GMP

Condition

- Respiratory tract infections

Synonym
acute worsening of symptoms, exacerbation

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: asthma, COPD, exacerbation, rhinovirus

Outcome measures

Primary outcome

Viral load (PCR) and TCID 50 (dilution of viral suspension that causes

cytopathic effects in 50% of the cultured HELA cells). By both specific

techniques as well as deep sequencing we will search for contaminating viruses

and bacteria in the nasal lavages.

Secondary outcome

not applicable

Study description

Background summary

Asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory disorders of the airways. Patients with asthma or COPD frequently suffer from exacerbations, which are manifested by episodes of acute worsening of symptoms, such as shortness of breath, cough, wheezing and chest tightness in conjunction with airways obstruction. The frequent exacerbations contribute to faster deterioration of lung function compared to that in healthy individuals and thus attenuate the health status and quality of life of these patients. The mechanisms that underlie these exacerbations are poorly understood, which hampers the development of adequate prophylaxis and/or treatment of these exacerbations. Exacerbations are triggered in particular by viral respiratory infections. Of all human respiratory viruses, rhinovirus species are most frequently causing exacerbations in asthma and COPD patients.

Relevance:
These preparations are crucial to establish a new batch of HRV16, prepared according to GMP standards. This batch will enable researchers worldwide to study exacerbations of asthma and COPD, and extent that to other respiratory

diseases.

Study objective

Experimental infections of humans with rhinoviruses, in particular rhinovirus 16 (HRV16) have proven to be a highly relevant and safe approach to study exacerbations in patients with asthma and COPD. The worldwide availability of stocks of HRV16 for experimental infections is decreasing and thus there is a need for a new batch. Various groups have joined forces in a European Union project, U-BIOPRED, amongst others to prepare a state of the art HRV16 stock. The major aim of this study is to collect samples of healthy individuals after infection HRV16 that can serve as a stock to generate a GMP batch of HRV16, which will be made available to multiple research groups currently using this experimental exacerbation model.

Study design

Passage of rhinovirus in cell lines or animal models bears the risk of reducing the potency of rhinovirus to infect humans. Therefore, in vivo passage of rhinovirus in humans is required to obtain viable virus that is also infectious for humans. Six, extensively screened healthy humans will be exposed to 10 TCID50 HRV16 (low dose). Daily, i.e. up to day 8, throat swabs and nasal lavage samples will be obtained, each of which will be processed and stored separately. The swabs serve to screen for other respiratory viruses and bacteria. In nasal lavage samples we will determine HRV16 viability and load (TCID50), number of viral particles (quantitative PCR) as well as execute an extensive screening for other micro-organisms. In three nasal samples that contain high and viable HRV16 loads, and that are free of any contaminating micro-organisms, we will confirm HRV16 identity by sequencing the viral genome. By using deep sequencing we will in parallel re-assess any other RNA- and DNA-containing contaminants. When confirmed, these samples are considered fit to be used in the preparation of the GMP batch of HRV16 by Charles River, a project that will be conducted by the U-BIOPRED consortium.

Study burden and risks

Exposed individuals will develop a mild cold. The nasal washings and the throat swabs are a minor burden to the participants. This experimetnal infection protocol has been used in several hundres of individuals without any unexpected effects and thus is considered a safe procedure..

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 between 18 * 60 years
* No cold for at least 6 weeks prior to the study. A cold is present if 2 of the following 3 criteria are present:
1. a cumulative symptom score of least 14 over a 6-day period.
2. the subjective impression of a cold.
3. rhinorrhoea (<=nasal drainage/runny nose) on at least 3 days.
* No BCG vaccination
* Normal chest X-ray
* No history of lung disease; Forced Expiratory Volume (FEV)1 > 80% predicted
* No history of seasonal or perennial rhinitis or sinusitis
* Non-smoking or stopped smoking more than 12 months ago and * 5 pack years (PY)
* No other clinically significant abnormality on medical history and clinical examination
* No participation in any clinical investigational drug treatment protocol within the preceding 30 days
* Being available 9 to 12 months post infection for safety measurements
* Having a GP

Exclusion criteria

* A titer of > 4 in serum for antibodies directed against HRV16
* Participants who share the same house(hold)
* Pregnant or intending to become pregnant during the study period (till visit 9) and lactating women
* Any of the following infectious micro-organisms, diseases:
- Antibodies and PCR (on plasma) for Human T-lymphotropic virus Type I (HTLV-1) and type II (HTLV-2)
- Antibodies and PCR (on plasma) for Human Immunodeficiency Virus (HIV)
- Antibodies and PCR (on plasma) for Hepatitis A, B and C virus (HAV, HBV, HCV)
- tuberculosis (tuberculin test)
* The presence of any of the following respiratory viruses and bacteria in nasal lavage and/or throat swabs, by PCR:
- influenza A&B, Enterovirus sp., Adenovirus sp., Rhinovirus sp., human metapneumovirus, RSV, parainfluenza 1-4, human parechovirus, Bocavirus, Coronavirus sp.
- Chlamydia pneumoniae, Mycoplasma pneumonia and Legionella sp.
* Seasonal allergies at the time of the study
* Any maintenance drug usage
* Any NSAID usage 2 weeks prior to up till 7 days after inoculation
* Any other medical condition at the discretion of the study physician

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-11-2011
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	08-11-2011
Application type:	First submission
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	NL34834.018.10