Rhinovirus type 16-induced exacerbation in asthma.

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We hypothesize that the ASM phenotype of asthmatic patients: 1. Changes during an experimental, rhinovirus type 16 (RV16)-induced exacerbation; 2. Is associated with enhanced airway inflammation and hyperresponsiveness during an experimental, RV16...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26994

Bron
NTR

Verkorte titel
Gene expression analysis in asthma

Aandoening

allergic asthma/allergisch astma, Airway Smooth Muscle (ASM)/ luchtweg glad spierweefsel, gene expression analysis/genexpressie analyse, RNA whole transcriptome sequencing

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC)
Dept. of Respiratory Medicine
1105AZ Amsterdam
The Netherlands
Overige ondersteuning: The Netherlands Asthma Foundation

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To investigate the consequences of an experimental, RV16-induced exacerbation on the gene expression profile of airway smooth muscle (ASM) using RNA whole transcriptome sequencing.

Toelichting onderzoek

Achtergrond van het onderzoek

Asthma is characterized by episodic symptoms and variable airways obstruction accompanied with airway inflammation and airway remodelling. It appears that extracellular matrix (ECM) components within the airway smooth muscle (ASM) are altered in asthma and that ASM mass inversely correlates with lung function (FEV1). In addition, it has been observed that mast cell infiltration in ASM represents a typical aspect of inflammation in asthma, which is associated with airway hyperresponsiveness and impaired bronchodilation following a deep breath. Additionally, evidence has shown that dendritic cell (DC)-derived cytokines change the synthetic properties of ASM, suggesting that the distinct DC-phenotype in asthma might influence ASM phenotype.

Both inflammation and hyperresponsiveness are enhanced during an exacerbation. It has been observed that viral infection of the airways is a major factor causing these exacerbations. There is good evidence that this occurs by mechanisms related to epithelial and inflammatory cell pathways. Furthermore, the phenotype of the ASM layer is shown to be altered by viral infection, suggesting that smooth muscle and its direct environment are key determinants of the changes in airway function as observed during clinical episodes of both well- and poorly-controlled asthma. However, the precise mechanisms underlying this process are still poorly understood, resulting in the impediment of the development of adequate prophylaxis and treatment of exacerbations.

Doel van het onderzoek

We hypothesize that the ASM phenotype of asthmatic patients:

1. Changes during an experimental, rhinovirus type 16 (RV16)-induced exacerbation;

2. Is associated with enhanced airway inflammation and hyperresponsiveness during an experimental, RV16-induced exacerbation.

Furthermore, we hypothesize that gene expression of the epithelial cells from the airway wall:

1. Changes in asthmatic patients during an experimental, RV16-induced exacerbation;

2. Changes differently between asthmatic and control-group subjects during an experimental, RV16-induced exacerbation.

Onderzoeksopzet

Day -9: Screeningsvisit;

Day -1: Bronchoscopy pre-RV16 exposure;

Day 0: RV16 exposure;

Day 6: Bronchoscopy post-RV16 exposure;

Day 42: Follow-up visit.

Onderzoeksproduct en/of interventie

Spirometry, bronchoprovocation with methacholine, allergy skin prick test, measurement of respiratory impedance using Forced Oscillation Technique, eNO measurement, bronchoscopy with brushes and biopsies, venapunction, once-only exposure to low-dose rhinovirus type 16 (10 TCID50).

All participants will be exposed to a low dose (10 TCID50) RV16, the common cold virus. This will take place once-only during visit 3 of the study. The RV16 inoculum will be diluted in sterile NaCl and a total volume of 0.75mL will be sprayed through one nostril using an atomizer.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Asthmatic patients will be selected using the following inclusion criteria:

1. Age between 18 – 50 years;

2. History of episodic chest tightness and wheezing;

3. Controlled asthma according to the criteria by the Global Initiative for Asthma;

4. Non-smoking or stopped smoking > 12 months ago and ≤ 5 pack years;

5. Clinically stable, no exacerbations within the last 6 weeks prior to the study;

6. Steroid-naïve or those patients who are currently not on corticosteroids and have not taken any corticosteroids by any dosing-routes within 8 weeks prior to the study. Occasional usage of inhaled short-acting Beta2-agonists as rescue medication is allowed, prior and during the study;

7. Baseline FEV1 > 70% of predicted;

8. Airway hyperresponsiveness, indicated by a positive acetyl-ß-methylcholine bromide

(MeBr) challenge with PC20 < 9.8 mg/ml;

9. Positive skin prick test to one or more of the 12 common aeroallergen extracts, defined as a wheal with an average diameter of > 3mm.

Control-group, non-asthmatic subjects are recruited using the following inclusion criteria:

1. Age between 18 – 50 years;

2. Non-smoking or stopped smoking > 12 months and ≤ 5 pack years;

3. Baseline FEV1 > 70% of predicted;

4. Acetyl-ß-methylcholine bromide challenge with PC20 > 9.8 mg/ml;

5. Negative skin prick test to one or more of the 12 common aeroallergen extracts;

6. Steroid-naïve or those participants who are currently not on corticosteroids and have not taken any corticosteroids by any dosing-routes within 8 weeks prior to the study;

7. Negative history of pulmonary or any other relevant diseases.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Exclusion criteria for both patient-groups are as follows:

1. Presence of antibodies directed against RV16 in serum, measured at visit 1;

2. History of clinical significant hypotensive episodes or symptoms of fainting, dizziness, or light-headedness;

3. Women who are pregnant, lactating or who have a positive urine pregnancy test at visit 1;

4. Chronic use of any other medication for treatment of lung disease other than short-acting Beta2-agonists;

5. Ongoing use of tobacco products of any kind or previous usage with ≥ 6 total pack years.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-12-2011
Aantal proefpersonen:	24
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	22-06-2010
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2264
NTR-old	NTR2390
Ander register	: AF 3.2.09.065
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A