The role of the airway smooth muscle layer in asthma

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24761

Source
NTR

Brief title
Genomics in asthma

Health condition

allergic asthma, airway smooth muscle, genomics, microarray, gene expression, Forced Oscillation Technique
allergisch astma, luchtweg glad spierweefsel, gen expressie

Sponsors and support

Primary sponsor: Academic Medical Center Amsterdam
Contactperson:
P.J. Sterk
Dept. of Pulmonology (F5-259)
Academic Medical Center
University Hospital of Amsterdam
Meibergdreef 9
NL-1105AZ, Amsterdam, The Netherlands
Tel: 31-20-566 4356
Fax: 31-20-566 9001
Email: p.j.sterk@amc.uva.nl
Source(s) of monetary or material Support: Nederlands Astma Fonds

Intervention

Outcome measures

Primary outcome

A genomic analysis of the airway smooth muscle layer of asthmatics and healthy, non-asthmatics by using laser capture microdissection (LCM) technique.

Secondary outcome

The profiles of ASM will be associated with physiologic parameters obtained by lung function tests, eNO, and FOT.

The profiles of ASM will be associated with biochemical parameters obtained by immunohistochemistry.

The presence and type of bronchial pathogens will be associated with clinical severity, and with the degree and profile of airways inflammation, airway remodelling and airway hyperresponsiveness by viral real-time multiplex PCR and bacterial PCR analysis.

Study description

Background summary

Asthma is a worldwide disease with symptoms that are characteristic and well described. However the pathophysiologic mechanisms leading to the observed functional changes are still unknown. Recently, interest has been shown in the ASM layer as an important structure contributing to the pathophysiologic feature of asthma. Several studies have shown that the phenotype of ASM is changed with asthma and it is postulated that ASM itself can contribute to the regulation and perpetuation of airways inflammation in asthma. Mast cells and progenitor cells of the ASM also tend to play an important role in asthma. Furthermore, the beneficial effects of corticosteroids on the clinical status and lung function are well described. However it is not clear whether this is solely based on its anti-inflammatory effect or that steroids also have other local actions. Therefore, the airway smooth muscle layer could be the common pathway in determining variable airways obstruction in asthma.

In this current study we will primarily investigate the role of the airway smooth muscle layer in asthmatic patients. More specifically, the phenotypic profiles of the ASM layer at the gene-level will be analysed using an unbiased genomics approach. Furthermore, we will examine the possible local effects of oral corticosteroids on the gene expression profile of ASM cells. This study is innovative as three areas of a respiratory disease will be linked and analysed: physiology, pathology and biochemistry.

Study objective

We hypothesize that the phenotypic profiles of the ASM layer at the gene-level is different between asthmatic and healthy patients, is associated with measures of variable airways obstruction and with the inflammatory infiltrate within and outside the ASM layer, and that the ASM gene profile changes after treatment with steroids.

Study design

Screening phase: Day -17 to -4;

Study phase 1: Day -3 to 0;

Study phase 2: Day 1 to 14.

Intervention

During screening, patients will undergo a physical examination, skin prick test, spirometry, and methacholine bronchoprovocation test, and when applicable a urine pregnancy test. During the two study phases, measurements of eNO and resistance of the respiratory system (by using FOT) will be performed. Additionally, bronchoscopy will be performed to obtain biopsy material.
During study phase 2, asthmatic patients will be randomized into 2 groups. One group will receive Prednisolone tablets 0.5mg/kg/day for 14 consecutive days, the other group will receive placebo.

Contacts

Public
Dept. of Pulmonology (F5-260)
Academic Medical Center
University Hospital of Amsterdam

C.Y. Yick
Meibergdreef 9

Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5669111 / 566 4359
Scientific
Dept. of Pulmonology (F5-260)
Academic Medical Center
University Hospital of Amsterdam

C.Y. Yick
Meibergdreef 9

Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5669111 / 566 4359

Eligibility criteria

Inclusion criteria

Asthmatic patients:

1. Age between 18 – 50 years

2. History of episodic chest tightness and wheezing

3. Intermittent or mild persistent asthma according to the criteria by the Global Initiative for Asthma

4. Non-smoking or stopped smoking more than 12 months ago and 5 pack years or less

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

6. Occasional usage of inhaled short-acting ß2-agonists as rescue medication is allowed, prior and during the study

7. 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

8. Baseline FEV1 ≥ 70% of predicted

9. Airway hyperresponsiveness, indicated by a positive methacholine challenge with PC20 ≤8 mg/ml

10. Positive skin prick test (SPT) to one or more of the 12 common aeroallergen extracts, defined as a wheal ≥ 3mm in diameter

11. No other clinically significant abnormality on history and clinical examination

Healthy patients:
1. Age between 18 – 50 years;

2. Non-smoking or stopped smoking more than 12 months and 5 pack years or less;

3. Baseline FEV1 ≥ 70% of predicted;

4. Negative methacholine challenge or PC20 >8 mg/ml;

5. 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;

6. Negative history of pulmonary and any other relevant diseases.

Additionally, non-asthmatic non-allergic patients must have a negative skin prick test (SPT) to one of the 12 common aeroallergen extracts, whereas non-asthmatic allergic patients must have a positive SPT.

Exclusion criteria

Both groups of patients:

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

2. Women who are pregnant or lactating or who have a positive urine pregnancy test at screening

3. Chronic use of any other medication for treatment of lung disease other than short-acting ß2-agonists

4. Participation in any clinical investigational drug treatment protocol within the preceding 30 days

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

6. Concomitant disease or condition which could interfere with the conduct of the study, or for which the treatment might interfere with the conduct of the study, or which would, in the opinion of the investigator, pose an unacceptable risk to the patient in this study

7. Unwillingness or inability to comply with the study protocol for any other reason

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2008
Enrollment:	48
Type:	Actual

Ethics review

Positive opinion

Date:	05-05-2008
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 33978
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL1260
NTR-old	NTR1306
CCMO	NL22615.018.08
ISRCTN	ISRCTN wordt niet meer aangevraagd
OMON	NL-OMON33978

Study results

Summary results
N/A