Gene Expression and Genome Wide Association Study on remission of asthma

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Main objective: To investigate differential gene-expression in nasal epithelium of asthmatics in complete remission, in clinical remission, not in remission and healthy controls.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational invasive

Summary

ID

NL-OMON40066

Source
ToetsingOnline

Brief title
Gene Expression and GWAS on remission of asthma

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma, hyperresponsivenes

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Möller foundation

Intervention

Keyword: asthma, Gene-expression, GWAS, remission

Outcome measures

Primary outcome

The main outcome parameter is the expression level of mRNA. These expression levels will be compared between patients in complete asthma remission, clinical asthma remission, no asthma remission and healthy controls.

Secondary outcome

1. The genetic variation at DNA-level will be used to perform a GWAs study on the presence of asthma remission.

2. Association of IL1RL1 gene variation, with IL1RL1 T lymphocyte expression with and without IL-33 stimulation.

3. Investigate the differences in DNA-methylation between asthmatics and patients in clinical or complete remission

4. Cultivate nasal epithelial cells for hypothesis-testing in functional studies based on results of the genetic expression and association analyses.

5. To compare the small airway parameters Scond and Sacin between patients in complete remission of asthma, clinical remission of asthma and patients with current asthma.

Study description

Background summary

Recently, we have shown that some asthmatics show complete asthma remission in adulthood. Investigating the mechanisms leading to this spontaneous remission

of asthma may provide new avenues for better understanding of asthma remission and may eventually lead to new intervention strategies. In 2008 we have started a genome wide association study (GWAS) on asthma. Additionally one can search for expression of genes in tissue, like epithelial cells. Some of the asthma patients (59) participating in the GWAS were in clinical or complete remission. In 1987, a group of asthmatics visited the UMCG for a follow-up study of R.J. Roorda, the Roorda cohort. The patients all had childhood asthma with hyperresponsiveness as a child. We now are interested in investigating who is in remission of asthma and to search for genetic background of this remission by gene expression profiling in epithelial cells. The NORM study will be used as a control population and all participants have been fully screened.

Study objective

Main objective: To investigate differential gene-expression in nasal epithelium of asthmatics in complete remission, in clinical remission, not in remission and healthy controls.

Study design

We study two cohorts with new clinical and functional characterization:
1) The Roorda cohort: A follow-up study of the Roorda cohort (age > 18 years). Patients are asked to visit the UMCG to perform spirometry with reversibility, metacholine challenge test, NO measurements, skin prick test, blood parameters of a.o. allergy and DNA isolation and a nose brush. In subjects who still have currently active asthma, peripheral blood mononuclear cells will be isolated and stored for T lymphocyte purification. IL1RL1 receptor expression on T cells will be assessed using flowcytometry. Moreover, using its ligand IL33, we will stimulate the IL1RL1 receptor and investigate the strength of IL1RL1 receptor signal transduction using activation of intracellular signaling intermediates including ERK, p38 MAP kinase and NF*B as an outcome. We will relate both outcomes to IL1RL1 genotypes.
2) DAG cohort: Patients in clinical or total remission in the DAG cohort will be asked to perform NO measurements, a nose brush and determination of a.o. allergy in blood.

Study burden and risks

The burden to the individual participants will be performing a reversibility test, metacholine challenge test, NO measurements and blood samples and nose brushes that will be taken. This implies that the person may experience some breathlessness that will fade away immediately after giving a bronchodilator after the metacholine challenge, and they will experience some discomfort when blood samples and nose brushes are taken. It is expected that the burden of these measurements lasts for a short period of time (i.e. 15 minutes).

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

Roorda cohort and the DAG cohort (asthma)
1. Age 18 years or older
2. Previous diagnosis of asthma
3. Bronchial hyperresponsiveness in childhood (Roorda Cohort)
4. In clinical or complete remission of asthma (DAG cohort)
NORM study (healthy)
1. Age 18 years or older
2. FEV1 pre bronchodilator > 80% predicted
3. No bronchial hyperresponsiveness; PC20 metacholinebromide >32 mg/ml
4. Never diagnosed with asthma

Exclusion criteria

For all cohorts
1. Presence of serious concomitant diseases (Cancer, Cardiovascular disorders)
2. Pregnancy
Additional exclusion criterium for metacholine challenge testing:
3. FEV1 below 1.2 L

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2012
Enrollment:	277
Type:	Actual

Ethics review

Approved WMO Date:	16-11-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-05-2013
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL40817.042.12
Other	wordt geregistreerd bij clinical trials, nummer volgt