Do microRNAs control inflammatory mediator production by airway epithelial cells from patients with asthma and COPD?

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Ethical review	Approved WMO
Status	Pending
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Observational invasive

Summary

ID

NL-OMON31684

Source
ToetsingOnline

Brief title
miR in asthma and COPD

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
asthma, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Nederlands Astma Fonds

Intervention

Keyword: airway epithelium, astma, COPD, inflammation

Outcome measures

Primary outcome

With this project we will analyze around five proteins in a semi-quantitative manner and determine the microRNA profiles in airway epithelial cells from patients with asthma or COPD or that of healthy individuals. In both analyses we will use endogenous standards allowing us to compare the analyses between the study groups. These analyses will be linked to clinical details.

Secondary outcome

There are no secondary study parameters

Study description

Background summary

The airways of patients with asthma or chronic obstructive pulmonary disease (COPD) are inflamed. Inflammation and inflammation-induced tissue remodelling contribute to the clinic, and thus intervention is aimed at reducing inflammation. Inflammation is directed by inflammatory mediators that are produced amongst others by the airway epithelium. Earlier, studies have indicated that airway epithelial cells from patients have an increased basal expression and after stimulation an exaggerated production of inflammatory mediators. It is assumed that the airway epithelium contributes to the chronic airway inflammation in asthma and COPD.
The production of inflammatory mediators is strictly regulated. Previous studies have shown that the post-transcriptional regulation of inflammatory mediator expression is easily disturbed, which results in an exaggerated prodcution of inflammatory mediators. Post-transcriptional regulation, in particular mRNA degradation, is probably regulated by a family of RNA-binding proteins and microRNAs. These microRNAs are recently recognized small RNAs that

do not encode for a protein but rather interact with mRNAs.

Study objective

Besides more basic research into which RNA-binding proteins and microRNAs regulate the expression of inflammatory mediators in airway epithelial cells, we will also assess these proteins and microRNAs in airway epithelial cells from patients with asthma and COPD as opposed to that of controls. We hypothesize that differences in the expression of these proteins and/or of these microRNAs provide an explanation for the exaggerated production of inflammatory mediators by airway epithelial cells from patients. We expect to reveal potential targets for intervention as well as why corticosteroids downregulate the production of inflammatory mediators in asthma but not in COPD.

Study design

Patients with mild asthma or mild COPD and healthy matched controls will be subjected to three sequential brushes to remove epithelial cells from the mucosal surface. These cells will be used in two approaches. On the one hand, part of the epithelial cells will be processed immediately to collect protein and RNA. On the other hand epithelial cells will be cultured for several weeks afterwhich protein and RNA will be isolated. By directly processing the epithelial cells we make a snapshot of RNA and protein expression in situ, whereas the analyses on the cultured cells will reveal whether any differences in protein and RNA expression are an intrinsic characteristic of the epithelial cells or are caused by the local milieu (in situ). For this study we expect that the analyses of material from 15 individuals per group suffices. In our application, however, we mention 20 individuals per group, anticipating some difficulties in culturing the cells from patients and healthy individuals.

Study burden and risks

After anamnesis and a physical examination, individuals will be subjected to a lung function test and 10 mls of blood will be sampled, which are considered to be a mild burden. Bronchoscopy is an invasive technique that, despite the use of the anaesthetic lidocain, inflicts an unpleasant feeling and thus a considerable burden to the individual. A bronchoscopy may give rise to a dry cough and some distress at the nose, where the bronchsope is inserted. During brushing a superficial bleeding may develop which normally stops rapidly. The bronchoscopy will take about 5 minutes to complete.

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

Asthma: non-smoking, allergic, intermittent to mild persistent asthma (history of episodic wheeze and shortness of breath). FEV1 predicted > 70% and PC20 histamine between 0.25 to 8 mg/ml.
COPD: middle-age onset of symptoms, cigarette consumption of at least 15 pack-years and a post-bronchodilator FEV1/VC ratio smaller than 0.7. Reversibility in FEV1 assessed after the apropriate abstaining of bronchodilators, and measured follwing high dose of beta2-agonist inhalation was below 11% of predicted.
Healthy individuals: no lung pathology

Exclusion criteria

Exacerbation requiring oral steroids or antibiotics for 3 months before the study and no lower respiratory tract infection for 4 weeks before the study. Inhaled corticosteroids, antibiotics, theophylline, sodium cromoglycate, or antileukotrienes were not allowed 4 weeks before and during the study. Specific exclusion criteria: for COPD patients: allergy; for asthma patients: smoking

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2008
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

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	NL20648.018.07