Acute and chronic inflammatory responses induced by smoking in individuals being susceptible and non-susceptible for development of COPD: from specific disease phenotyping towards novel made therapy (study 1).

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• To define mediators involved in the early induction of COPD in susceptible smokers (and so to define new drug targets)• To develop new biological and clinical markers for the early diagnosis and monitoring of COPD• To characterize the switch to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital respiratory tract disorders
Study type	Observational invasive

Summary

ID

NL-OMON31923

Source
ToetsingOnline

Brief title
Acute smoking in COPD

Condition

- Congenital respiratory tract disorders

Synonym
chronic ibstructive brochitis(COPD), emphysema

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: GlaxoSmithKline,TI Pharma (Overheid;farmaceutische industrie;kenniscentra)

Intervention

Keyword: COPD, inflammation, smoking, susceptibility

Outcome measures

Primary outcome

• Local inflammation before and after cigarette smoking assessed by exhaled breath condensate, microprobe sampling and bronchial biopsies.

• Systemic inflammation before and after cigarette smoking assessed by the expression of established and newly developed markers on innate immune cells associated with pre-activation.

• Extensive clinical characterisation including life style factors, lung function, CT scanning of the lung.

• Corticosteroid responsiveness of epithelial cells in vitro.

• Distribution of candidate genes (SNPs) for COPD between the 5 different groups and associations with the inflammatory responses on acute smoking.

Secondary outcome

n.a.

Study description

Background summary

COPD is ranked number 3 by the WHO list of important diseases worldwide and is the only disease with increasing mortality. The pathogenesis of cigarette smoke-induced COPD is obscure, therefore more insight is needed to design effective anti-inflammatory agents. We hypothesize that healthy individuals who are susceptible to smoking demonstrate a higher and aberrant inflammatory response to cigarette smoke. This susceptibility is caused by heterogeneous factors and is associated with various polymorphic genes that interact with each other and with the environment.

Study objective

• To define mediators involved in the early induction of COPD in susceptible smokers (and so to define new drug targets)
• To develop new biological and clinical markers for the early diagnosis and monitoring of COPD
• To characterize the switch to chronicity of COPD and demonstrate phase differences between local pulmonary and systemic components
• To compare between susceptible and non-susceptible individuals the corticosteroid responsiveness of bronchial epithelial cells in vitro, and to study the mechanisms of smoking-induced corticosteroid unresponsiveness.
• To study the role of candidate genes that may play a role in the development of fixed airway obstruction, and to identify clues for patient*s responsiveness to specific drugs.

Study design

This is an observational study without a therapeutical intervention.

Study burden and risks

• Totally 22 hours will be spend in the hospital during 5 visits
• Metacholine provocation may cause temporary bronchoconstriction in subjects with increased hyperresponsiveness.
• CT-scanning of the lung is associated with a radiation burden of 0,8-1,6 mSv depending on the weight of the participant.
• Two bronchoscopies with taking central biopsies after local anaesthesia with lidocaine 2%.
• Smoking 3-4 cigarettes during one hour.
• Sputuminduction with possible airway obstruction and dyspnoe.

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 18-75 years
• Age, pack years, FEV1/FVC and FEV1% predicted must fit in one of the 5 groups of table 4.1
• Able to stop smoking for 10 days and start smoking 3-4 cigarettes within 1 hour
• Physically and mentally able to undergo the total study protocol
• Written informed consent

Exclusion criteria

• Participation in another study
• Alpha-1-antitrypsin deficiency
• Selected grade 1-3 co-morbidity listed in the ACE-27

• Active pulmonary infection like tuberculosis, pneumonia, flue, tracheobronchitis
• Active extra-pulmonary infection like hepatitis A-C, cystitis, gastro-enteritis etc
• Pulmonary diseases like sarcoidosis, IPF, silicosis, hypersensitivity pneumonitis
• Life threatening diseases like carcinoma, AIDS (including HIV+), acute leukaemia etc
• Medication that may affect the results of the study: NSAID*s, immunosuppressive agents like prednisolon, metotrexate, azathioprine,Sintrom tablets

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2008
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL23440.042.08
Other	Wordt nog gedaan