Effect van koolstof nanopartikels op ontsteking en stolling in de luchtwegen.

No registrations found.

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

Summary

ID

NL-OMON29149

Source
NTR

Brief title
CARBON-study

Health condition

carbon nanoparticles - air pollution - lung inflammation - coagulation
koolstof nanopartikels - luchtvervuiling - luchtwegontsteking - stolling

Sponsors and support

Primary sponsor: Academic Medical Center (AMC) Amsterdam. Department of Pulmonology
Source(s) of monetary or material Support: Sponsor

Intervention

Outcome measures

Primary outcome

1. Total leukocyte count and differentials in bronchoalveolar lavage fluid;

2. Activation of coagulation and fibrinolysis in bronchoalveolar lavage fluid.

Secondary outcome

1. Amino acid pattern in exhaled breath condensate;

2. Metabolomic fingerprint as obtained by Liquid chromatography-mass spectrometry (LC-MS);

3. Safety outcome parameters (Physical complaints of the volunteer, Blood pressure, Heart rate, Temperature, Lungfunction, Oxygen saturation, (Serious) Adverse Events.

Study description

Background summary

Rationale:

Particulate matter as part of air pollution consists of a complex mixture, consisting of different types and variably sized particles of combustion products. Inhalation of particulate matter is associated with increased morbidity and mortality due to cardiovascular and pulmonary events. Previous studies revealed multiple possible pathophysiologic mechanisms including pulmonary and systemic inflammation, oxidative stress, increased coagulation, and altered autonomic function.

Several investigators already tried to examine which properties of particulate matter are critical in causing injury. Upon inhalation, the bronchial mucosa is the first contact area of particulate matter and the host. It is still unknown which host responses predominate in the bronchial mucosa and whether they are associated with systemic responses in humans in vivo. Ultrafine (nano)particles smaller than 0.1 ìm are likely candidates for triggering local host responses because of their ability to penetrate lung cells. We hypothesize that carbon black nanoparticles cause dose-dependent local and systemic inflammation and activation of coagulation pathways in healthy humans in vivo.

Objective:

To investigate the safety, the inflammatory response and activation of coagulation pathways of escalating doses of carbon black nanoparticles after bronchial segmental instillation.

Study design:

This is an investigator-initiated, randomized controlled, single centre, single blinded, dose-

escalation study.

Study population:

The study population consists of 24 healthy male volunteers.

Intervention:

Study subjects will receive carbon black nanoparticles by bronchial instillation, and sterile saline will be instilled in the contra lateral lung. In this study we will use carbon black nanoparticles, without significant content of organic species, metals or endotoxins.

Main study parameters/endpoints:

1. Pulmonary (BALF) and systemic (Serum) inflammation according to leukocyte counts and differentials, C- reactive protein, and activation of cytokines and chemokines;

2. Local and systemic activation of coagulation pathways and fibrinolysis (BALF).

Secondary outcomes are safety parameters like adverse events, hemodynamic measurements, and lung function tests.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The burden associated with this study includes a screening visit, during which an intake interview, a physical examination, routine blood tests and lung function will be done. At the study day, all subjects will undergo two bronchoscopies, which in our own experience from previous studies, as well as based on literature is well tolerated. Each bronchoscopy will be preceded by a blood draw (2 x 40 ml) and collection of exhaled breath condensate. Although previous inhalation studies with particulate matter revealed no significant risks or discomfort, bronchial instillation of carbon black nanoparticles may induce bronchus obstruction. For this reason there will be close monitoring by spirometry and salbutamol 100 ìg will be available as rescue medication during the study for all subjects.
Relevance: This study will report for the first time a detailed analysis of the dose dependent in vivo effects of carbon black nanoparticles on inflammation and coagulation pathways in the lungs of healthy volunteers.

Study objective

We hypothesize that the response of the bronchial mucosa to nanoparticles is a critical determinant of their pathophysiological effects in humans in vivo. More specifically, we postulate that carbon nanoparticles cause dose-dependent local and systemic activation of inflammatory and coagulation pathways in the bronchial mucosa.

Study design

Screening visit and 2 weeks later studyday. 1 week later contact by phone to check for adverse reactions.

Intervention

Volunteers will receive a bronchial instillation of a carbon nanoparticle suspension.

Controls will receive a bronchial instillation with saline.

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy, male subjects between 18 and 45 years of age;

2. No clinically significant findings during physical examination and haematological and biochemical screening;

3. Baseline FEV1 > than 80% of predicted value;

4. Able to communicate well with the investigator and to comply with the requirements of the study;

5. Written informed consent;

6. No current smoking for at least 1 year and less than 5 pack years of smoking history.

Exclusion criteria

1. History of pulmonary or any other relevant disease;

2. History of enhanced bleeding tendency;

3. A history of smoking within the last 12 months, or regular consumption of greater than three units of alcohol per day;

4. Administration of any investigational drug within 30 days of study initiation;

5. Donation of blood within 60 days, or loss of greater than 400 ml of blood within 12 weeks of study initiation;

6. History of serious drug-related reactions, including hypersensitivity.

Study design

Design

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

Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2011
Enrollment:	24
Type:	Actual

Ethics review

Positive opinion

Date:	11-07-2011
Application type:	First submission

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
NTR-new	NL2835
NTR-old	NTR2976
Other	METC AMC : 2011_043
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A