Effect of Carbon Nanoparticles on Inflammation and Coagulation after Bronchial Segmental Instillation. A dose escalation study

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We will investigate the local and systemic effects of carbon nanoparticles on inflammation and coagulation in humans by bronchial segmental challenge

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON36310

Source
ToetsingOnline

Brief title
Effect of Carbon Nanoparticles on Inflammation and Coagulation

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Respiratory tract infections

Synonym
pulmonary inflammation and activation of coagulation

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: financiële bijdrage van de farmaceutische industrie,GlaxoSmithKline

Intervention

Keyword: Carbon, Coagulation, Inflammation, Nanoparticles

Outcome measures

Primary outcome

Neutrophil, eosinophil and mast cell responses in blood and bronchoalveolar

lavage fluid (BALF):

* Total leukocyte counts and differentials

* Neutrophil response (LTB4, myeloperoxidase (MPO))

* Eosinophil response (eosinophil cationic protein (ECP))

* Mast cell response (chymase, tryptase)

Activation of cytokine- and chemokine network :

* Proinflammatory cytokines: TNF-*, IL-5, IL-6, IL-17, VEGF, c-kit ligand,

* Anti-inflammatory cytokines : IL-10

* CXC chemokines: IL-8, GRO-*, IP-10

* CC chemokines: MCP-1, MIP-1*, MIP-1*

General: C-reactive protein measurement

Secondary outcome

Activation of coagulation and fibrinolysis (BALF and/or blood):

* Coagulation: TAT complexes, F1+2 prothrombin fragment, soluble tissue factor,

D-dimers

* Fibrinolysis: PA activity, tPA, PAI-1, PAP complexes

* Anticoagulant proteins: protein C, activated protein C, antithrombin, soluble

thrombomodulin

Amino acid pattern in exhaled breath condensate

Metabolomic fingerprint as obtained by Liquid chromatography-mass spectrometry

(LC-MS)

Lung functions will be assessed before and after the provocations.

Study description

Background summary

Multiple epidemiologic studies have shown a strong association between exposure to particulate matter (PM) as part of air pollution and increased morbidity and mortality due to cardiovascular and pulmonary events. Particulate matter is derived by incomplete combustion of motor fuel and consists of a complex mixture of different types and variably sized particles. Nanoparticles have a diameter of less than 0.1 *m. Because of their higher deposition efficiency in the pulmonary region and their ability to penetrate lung cells, they are likely candidates for causing the pulmonary injury associated with particulate matter. The specific effects of inhalation of carbon nanoparticles are largely unknown.

Study objective

We will investigate the local and systemic effects of carbon nanoparticles on inflammation and coagulation in humans by bronchial segmental challenge

Study design

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

Intervention

Subjects will receive saline in one lungsegment and in the other lung they will be challenged with also saline (placebo, n=8), saline with 10 *g carbon nanoparticles (n=4), saline with 50 *g carbon nanoparticles (n=4) or saline with 100 *g carbon nanoparticles(n=8).

Study burden and risks

The burden associated with this study includes a screening visit, during which an intake interview, a physical examination, routine blood tests (40ml) 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 *g will be available as rescue medication during the study for all subjects.

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

* Healthy male subjects between 18 and 45 years of age
* No clinically significant findings during physical examination and haematological and biochemical screening.
* Baseline FEV1 > than 80% of predicted value.
* No current smoking for at least 1 year and less than 5 pack years of smoking history

Exclusion criteria

* History of any relevant disease
* A history of smoking within the last 12 months, or regular consumption of greater than three units of alcohol per day
* Administration of any investigational drug within 30 days of study initiation
* Donation of blood within 60 days, or loss of greater than 400 ml of blood within 12 weeks of study initiation
* 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

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-01-2012
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	22-12-2011
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	NL35297.018.11