Effect of intravenous recombinant human APC on coagulation and inflammation in house dust mite and lipopolysaccharide induced allergic asthma.

No registrations found.

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

Summary

ID

NL-OMON22425

Source
Nationaal Trial Register

Brief title
Achilles-study

Health condition

Allergic asthma, house dust mite allergy, lung inflammation, coagulation

Sponsors and support

Primary sponsor: Center for Experimental and Molecular Medicine, Academical Medical Center - University of Amsterdam
Source(s) of monetary or material Support: Dutch Asthma Foundation

Intervention

Outcome measures

Primary outcome

Influx, differentiation and possible phenotype differences of inflammatory cells.

Secondary outcome

Eight hours after instillation of HDM and LPS (t = 8 hours) a second bronchoscopy will be performed and the challenged segments will be lavaged. In BAL fluid and blood, obtained directly before bronchoscopies, leukocyte responses, the response of alveolar macrophages, activation of the cytokine and chemokine network, complement and activation of coagulation and fibrinolysis will be determined.

Study description

Background summary

Allergic lung inflammation is associated with reduced bronchoalveolar levels of endogenous activated protein C (APC). The biological effects of APC are pleiotropic, and can be roughly divided in anticoagulant and cytoprotective effects. Recombinant human Activated Protein C (rhAPC) has been shown to decrease inflammation and is known for its capability to decrease mortality of patients with severe sepsis. Recent evidence derived from animal studies, in part from our laboratory, indicates that APC is also beneficial in allergic inflammatory conditions. In this study, we will examine whether intravenous administration of rhAPC is capable to inhibit local inflammation, within a lung subsegment, induced by combined administration of house dust mite (HDM) and lipopolysaccharide (LPS) in asthma patients. LPS is a relevant in this context because it is abundant in the natural human environment (and a natural contaminant of HDM) and known to enhance HDM induced allergic inflammation in asthma patients. The primary objective of this study is to determine the effect of intravenously administered rhAPC on HDM-LPS induced allergic lung inflammation.

Study objective

Intravenously administered rhAPC has protective effects on HDM-LPS induced allergic lung inflammation.

Study design

28 asthma patients will start on intravenous treatment with rhAPC or placebo 4 hours before (t = -4 hours) bronchial instillation of HDM/LPS in a lung subsegment and bronchial instillation of saline in a contralateral lung subsegment (t = 0 hours). Intravenous treatment with rhAPC or placebo will be continued until 1 hour before initiation of the second bronchoscopy.

Intervention

Intravenous rhAPC treatment and bronchoscopy allergen challenge and lavage. At 05:00

asthma patients will start on intravenous rhAPC treatment or placebo treatment. At 09:00 patients are challenged with housedustmite+LPS in one lungsegment and Saline in a lung segment of the contralateral lung. At 16.00 intravenous treatment is halted and at 17:00 a second bronchoscopy is done to lavage the segments.

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Eligibility criteria

Inclusion criteria

1. Intermittent to mild asthmatics between 18 and 45 years of age according to the Global Initiative for Asthma (GINA) criteria;

2. Allergy for HDM documented by a positive RAST and a positive skin prick test;

3. No clinically significant findings during physical examination and hematological and biochemical screening;

4. At spirometry FEV1 more than 70% of predicted value;

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

6. Stable asthma without the use of asthma medication 2 weeks prior to the study day;

7. Written informed consent;

8. No current smoking for at least 1 year and less than 10 pack years of smoking history;

9. Both male and female subjects are eligible for the study. Female subjects of child bearing potential will use adequate anti-conceptive precautions and will be tested for pregnancy.

Exclusion criteria

1. Relevant comorbidity, pregnancy and/or recent surgical procedures;

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

3. Exacerbation and/or the use of asthma medication within 2 weeks before start;

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 enhanced bleeding tendency or abnormal clotting test results;

7. History of heparin-induced thrombocytopenia;

8. History of serious drug-related reactions, including hypersensitivity;

9. Inability to maintain stable without the use of asthma medication 2 weeks before start.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2011
Enrollment:	28
Type:	Actual

Ethics review

Positive opinion

Date:	14-06-2011
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 35983
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL2802
NTR-old	NTR2943
CCMO	NL36336.018.11
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON35983

Study results

Summary results
N/A