The Effect of Inhaled Salmeterol on Inflammation after Bronchial Instillation of Allergen or Allergen/Lipopolysaccharide in Asthma.

No registrations found.

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

Summary

ID

NL-OMON26298

Source
Nationaal Trial Register

Brief title
N/A

Health condition

Mild asthma, allergen induced inflammation

Sponsors and support

Primary sponsor: Academic Medical Center Amsterdam, dept. Pulmonology
Source(s) of monetary or material Support: GlaxoSmithKline

Intervention

Outcome measures

Primary outcome

Neutrophil, eosinophil and mast cell responses:

1. Total leukocyte counts and differentials (BAL and blood);

2. Neutrophil activation (surface expression of CD11b as assessed by FACS);

3. Neutrophil degranulation (myeloperoxidase (MPO); by ELISA);

4. Eosinophil degranulation (eosinophil cationic protein (ECP); by ELISA);

5. Mast cell degranulation (chymase, tryptase, IP-10, c-kit ligand).

Activation of cytokine network:

1. Proinflammatory cytokines: TNF-á, IL-6, IL-5 (BAL and serum);

2. Anti-inflammatory cytokines: IL-10.

Activation of the chemokine network:

1. CXC chemokines: IL-8, GRO-á;

2. CC chemokines: MCP-1, MIP-1á, MIP-1â.

Secondary outcome

Response of alveolar macrophages:

Alveolar macrophages will be isolated using CD71 microbeads and autoMACS. RNA will be isolated from these cells and used for micro-array and multiplex ligation-dependent probe amplification (MLPA) (12). MLPA analyses will focus on activation of inflammation genes including TF (12,13,14).

Study description

Background summary

Summary: The Effect of Inhaled Salmeterol on Inflammation after Bronchial Instillation of Allergen or Allergen/Lipopolysaccharide in Asthma.

Rationale: Inhaled salmeterol was previously shown to inhibit lipopolysaccharide (LPS, endotoxin) induced lung inflammation in healthy volunteers. Moreover, there are indications

that salmeterol inhibits allergen-induced bronchial inflammation in asthma. Natural house dust and house dust mite extracts contain house dust mite allergens as well as variable concentrations of LPS. Little is known about the interaction of LPS-induced activation of the innate immune system and allergen-induced allergic reactions.

Objective: In this study we will examine whether inhaled salmeterol inhibits house dust mite allergen-induced lung inflammation in mild asthmatics that are on maintenance treatment with low dose inhaled corticosteroids. If so, salmeterol may prove useful as for maintenance treatment of asthma in addition to inhaled corticosteroids. Moreover, we will examine the effect of LPS on house dust mite allergen-induced bronchial inflammation in asthma.

Study design: This is an investigator-initiated, randomized, single centre, single blinded, controlled study.

Study population: The study population consists of 32 patients with house dust mite allergy and mild asthma on maintenance treatment with fluticasone propionate 100 ìg bid.

Intervention: 16 patients will inhale 100 ìg of salmeterol 30 minutes before bronchial instillation of house dust mite allergen (selected on low LPS content, n=8) or house dust mite allergen with additional LPS (n=8). The control group will not receive pre-treatment with salmeterol.

Main study parameters/endpoints:

Neutrophil, eosinophil and mast cell responses:

1. Total leukocyte counts and differentials (BAL and blood);

2. Neutrophil activation (surface expression of CD11b as assessed by FACS);

3. Neutrophil degranulation (myeloperoxidase (MPO); by ELISA);

4. Eosinophil degranulation (eosinophil cationic protein (ECP); by ELISA);

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Activation of cytokine network:

1. Proinflammatory cytokines: TNF-á, IL-6, IL-5 (BAL and serum);

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Activation of the chemokine network:

1. CXC chemokines: IL-8, GRO-á;

2. CC chemokines: MCP-1, MIP-1á, MIP-1â.

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 as well as based on literature is well tolerated by mild asthmatics. Each bronchoscopy will be preceded by a blood draw (2 x 40 mL). The risk of and discomfort caused by bronchial instillation of LPS is small and limited to a moderate rise in body temperature. Allergen may induce bronchus obstruction in patients who did not receive pre-treatment with salmeterol. This will be monitored by spirometry and Atrovent 40 ìg will be available as rescue medication during the study for all subjects. The results of the study may be important for the group of asthmatic patients as it will shed light on the interaction of LPS and allergen on the bronchial inflammation in asthma. Salmeterol is primarily regarded as a bronchodilatory drug, but it was shown to inhibit LPS induced bronchial inflammation in healthy subjects. Moreover, there are some indications that it also inhibits allergen-induced bronchial inflammation in asthmatics. Demonstration of inhibition of allergen and allergen/LPS-induced bronchial inflammation in asthmatics will broaden the applicability of salmeterol for maintenance treatment for all groups of allergic asthma.

Study objective

Salmeterol has an inhibitory effect on both allergen and allergen/LPS induced inflammation in asthmatics while on maintenance treatment with low dose corticosteroids.

Study design

Screening visit and after 4 weeks run-in with fluticason treatment.

Intervention

16 patients will inhale 100 ìg of salmeterol 30 minutes before bronchial instillation of house dust mite allergen (selected on low LPS content, n=8) or house dust mite allergen with additional LPS (n=8). The control group will not receive pre-treatment with salmeterol.

Contacts

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Eligibility criteria

Inclusion criteria

1. Intermittent to mild asthmatics between 18 and 45 years of age;

2. Allergy for house dust mite documented by a positive RAST;

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 while treated with fluticasone propionate 100ìg bid during 2 weeks before the study;

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 at randomization.

Exclusion criteria

1. Comorbidity;

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 oral steroids within the 4 weeks before start of run in;

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;

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

8. Inability to use only the run-in medication plus rescue medication supplied for this study. If subjects use other pulmonary medications these will be replaced by the run-in medication.

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):	15-06-2009
Enrollment:	32
Type:	Actual

Ethics review

Positive opinion

Date:	08-05-2009
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	NL697
NTR-old	NTR1807
Other	MEC Academisch Medisch Centrum : 08/241
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A