De rol van corticosteroiden op de coagulatie en inflammatie bij astma.

No registrations found.

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

Summary

ID

NL-OMON27682

Source
NTR

Brief title
ROCOCO

Health condition

Asthma
Corticosteroids
Coagulation
Inflammation

Sponsors and support

Primary sponsor: Dept. Respiratory Medicine, Academic Medical Center University of Amsterdam the Netherlands
Netherlands Asthma Foundation
Source(s) of monetary or material Support: Dept. Respiratory Medicine, Academic Medical Center University of Amsterdam the Netherlands
Netherlands Asthma Foundation

Intervention

Outcome measures

Primary outcome

Primary endpoint will be the change in TATc and PAPc in blood.

Secondary outcome

Secondary endpoints will be changes in markers of hemostasis and inflammation in blood, induced sputum and exhaled breath.

Study description

Background summary

Asthma is a chronic inflammatory disease of the airways characterised by variable airways obstruction and although asthma can be well controlled in most patients by treatment with inhaled corticosteroids, there is a small subset of patients requiring oral corticosteroids for asthma control. High levels of glucocorticoids, either endogenous or exogenous, have been shown to induce hypercoagulability and an increased risk of venous thromboembolism.

In asthma corticosteroids, either inhaled or oral, have been shown to influence hemostasis. In patients with moderate asthma inhaled corticosteroids decrease the activation of coagulation, while in severe asthmatic patients a further activation of coagulation may occur. Oral corticosteroids further activate coagulation during an acute exacerbation.

In addition, asthma itself has also been associated with a prothrombotic state, and preliminary data from our group have shown an increased risk of pulmonary embolism in patients with severe asthma that was associated with chronic oral corticosteroid use and frequent asthma exacerbations.

Therefore, an activated coagulation system might enhance the inflammatory process in the airways of asthmatics and contribute to therapy resistance in those with severe disease.

Study objective

We hypothesize that:

1. Patients with mild-moderate and severe asthma have an increased procoagulant activity as compared to healthy controls;

2. Oral corticosteroids activate coagulation in healthy controls and increase the procoagulant activity in mild-moderate and severe asthmatic patients;

3. Increase of hypercoagulation is correlated with asthma severity and use of high dose corticosteroids.

Study design

At baseline, day 1 and day 11.

Intervention

Patients will be randomized to receive either prednisolon (once daily 0,5mg/kg) or identical placebo for 10 days.

Contacts

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Eligibility criteria

Inclusion criteria

All subjects:

1. Age between 18 – 75 years;

2. Non-smoking or stopped smoking more than 12 months ago and 10 pack years or less;

3. Able to give written and dated informed consent prior to any study-specific procedures.

Healthy controls:

1. Baseline FEV1 80% of predicted;

2. Methacholine PC20> 8 mg/ml 29;

3. No usage of steroids by any dosing route;

4. Negative allergy testing by skin prick test or specific IgE;

5. Negative history of pulmonary and any other relevant diseases.

Patients with asthma:

1. All patients have previous evidence of variable airways obstruction within the last 5 years, as documented by at least one of the following:

A. Reversibility in forced expiratory volume in one second (FEV1) of ≥12% predicted after 4 puffs of a 100 µg salbutamol dose-aerosol, administered via a spacer;

B. A mean diurnal variation in peak expiratory flow (PEF) ≥15% (highest PEF - lowest PEF) per mean PEF on ≥4 days per week for a minimum of 2 weeks;

C. An increase in FEV1 of ≥400 mL after a course of prednisolone 0.5 mg•kg−1•day−1 for 14 days;

D. A provocative concentration causing a 20% fall in FEV1 with histamine or methacholine <8 mg/mL.29.

2. Clinically stable, for patients with mild asthma this means no exacerbations within the last 8 weeks prior to the study;

3. No other clinically significant abnormality on history and clinical examination;

4. The use of short and long-acting 2-agonists, leukotriene receptor antagonist, short or long acting anticholinergic agonists are allowed provided that the dose of these drugs remains stable during the study.

Mild/Moderate asthmatic patients:

1. Baseline FEV1 70% of predicted 30;

2. Low- to medium-dose use of inhaled corticosteroids (ICS) (fluticason ≤ 500 µg/day or equivalent drug).

Severe asthmatic patients:

1. Severe asthma according to the recently published consensus criteria of the Innovative Medicine Initiative (IMI)31;

2. High- and ultrahigh dose of ICS (Fluticasone ≥1000 µg/day or equivalent drug);

3. On stable doses of inhaled corticosteroids during the previous 4 weeks and during the study.

Exclusion criteria

Exclusion criteria for all patient-groups are as follows:

1. Women who are pregnant or lactating or who have a positive urine pregnancy test at screening;

2. Participation in any clinical investigational drug treatment protocol within the preceding 30 days;

3. Use of heparin, LMWH, or vitamin K antagonists;

4. Use of omalizumab during the last 6 months before randomization;

5. Use of prednisolone during the last 8 weeks before randomization;

6. Ongoing use of tobacco products of any kind or previous usage with a total pack year ≥ 10 years;

7. General contraindications for the use of corticosteroid use, including a known diagnosis of peptic ulcers, osteoporosis, psychoses, infections, diabetes and hypertension, or symptoms and signs compatible with one of the above diagnoses;

8. Concomitant disease or condition which could interfere with the conduct of the study, or for which the treatment might interfere with the conduct of the study, or which would, in the opinion of the investigator, pose an unacceptable risk to the patient in this study;

9. Unwillingness or inability to comply with the study protocol for any other reason.

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):	01-11-2011
Enrollment:	90
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	12-10-2011
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	NL2953
NTR-old	NTR3101
Other	AF / EudraCT number : 3.2.11.021 / 2010-023931-40;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A