Respiratory infections in asthma: the role of host defense against infections, allergic inflammation and vitamin D

Published: 07-08-2008
Last updated: 07-05-2024

We hypothesize that local AMPs expression in the airways of patients with asthma is decreased as a result of allergic inflammation. Furthermore, we hypothesize that local AMP expression can partly be restored by vitamin D substitution therapy. We...

Ethical review	Approved WMO
Status	Pending
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON31956

Source
ToetsingOnline

Brief title
asthma and vitamin D

Condition

- Allergic conditions
- Bacterial infectious disorders
- Bronchial disorders (excl neoplasms)

Synonym
asthma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: astra zenica nl

Intervention

Keyword: allergic inflammation, asthma, host defense, vitamin D

Outcome measures

Primary outcome

- antimicrobial peptides in nasal secretions and sputum

- 1,25 (OH) vitamin D in serum

- mediators of allergic inflammation in nasal secretions and sputum

Secondary outcome

- sputum cell differentials

- bacterial and viral load

- 25 (OH) vitamin D in serum

- exhaled NO-measurements

- PTH levels

Study description

Background summary

Morbidity in asthma is strongly determined by disease exacerbations and associated respiratory infections. Recurrent respiratory infections are one of the most important risk factors for frequent exacerbations in difficult-to-treat asthma. Antimicrobial peptides (AMPs) are important effector molecules in innate immunity that act as endogenous antibiotics in host defense against respiratory infections. Little is known about the expression and activity of AMPs in asthma. Recent studies show that both allergic inflammation and vitamin D are important regulators of production of AMPs. Both human and mouse studies show that the Th2 cytokines that are a characteristic of allergic inflammation in asthma, suppress expression of AMPs. Other studies show that active vitamin D, 1,25 (OH) vitamin D, is an important regulator of AMPs expression, as demonstrated both in vitro in cell culture and in vivo after

topical application onto the skin.

Study objective

We hypothesize that local AMPs expression in the airways of patients with asthma is decreased as a result of allergic inflammation. Furthermore, we hypothesize that local AMP expression can partly be restored by vitamin D substitution therapy. We aim to test our hypothesis by investigating AMPs in sputum and nasal secretions from patients with mild to moderate asthma and non-atopic controls. In addition, we will study the effects of oral vitamin D administration in asthma and controls on local expression of AMPs in the airways. The results from the present study will provide insight into host defense against respiratory infections in asthma, and will show the feasibility of using vitamin D treatment to increase this local immunity.

Study design

The levels and activity of antimicrobial polypeptides (AMPs) in airway secretions in patients with mild-to-moderate asthma will be compared to non-atopic controls.

Intervention

The subjects will receive 2 microgram 1,25 (OH) vitamin D (calcitriol) or placebo once daily during seven days (unless discontinued based on assessment on day 4). The wash out time between the intervention in the cross over design will be two weeks.

Study burden and risks

Standardized test as a skin prick test, methacholine challenge, sputum induction, exhaled NO and spirometry are applied worldwide for the examination of patients with asthma and are proven to be save.
Nasal secretions will be collected using a narrow-tipped vacuum device to mildly stimulate nasal secretion. This procedure is safe and non-invasive.
Venous blood for the laboratory assessment will be collected at all visits using standard procedure. The intervention with 2 microgram 1,25 (OH) vitamin D (calcitriol) or placebo during seven days is monitored by measuring creatinine and calcium in venous blood before and at day 4 of the intervention. An independent physician will check the serum levels and stop treatment if calcium levels exceed 2.65 mmol/l (albumin-adjusted). In this group of patients no hypercalcaemia is expected.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
2333 ZA Leiden
Nederland
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
2333 ZA Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Age 18-45 yrs
-BMI< 27
-History of episodic symptoms of wheezing, breathlessness, cough or chest tightness (>12 months)
-FEV1>70 % of predicted
-Hyperresponsive in standard methacholine challenge (PC20methacholine< 9,6 mg/ml)
-Atopic, as reflected by one or more wheal (> 3 mm) response to skin prick test (SPT) with 10 common airborne allergen extracts (HAL)

Exclusion criteria

-Age <18 yrs or > 45 yrs
-BMI> 27
-Smoking or ex-smoking (for less than 12 months > 5 pack years)
-Usage of inhaled or nasal corticosteroids within last 4 weeks or oral corticosteroids within 3 months prior to and during the study
-Usage of vitamin D supplements
-Pragnancy

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2008
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL21913.058.08