The role of dynamic hyperinflation in asthma

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Primary objective: To investigate the effect of supplementation of a single intramuscular dose of 80 mg triamcinolone on the level of MPT-induced dynamic hyperinflation, in adult asthma patients with demonstrated dynamic hyperinflation. (Part 1)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON43421

Source
ToetsingOnline

Brief title
Dynamic hyperinflation in asthma

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
asthma, bronchitis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Leeuwarden
Source(s) of monetary or material Support: GlaxoSmithKline,wetenschappelijke grants van Medisch Centrum Leeuwarden;Stichting Longgeneeskunde Fryslan;industrie

Intervention

Keyword: Asthma, Dynamic hyperinflation, Eosinophilic inflammation, Symptoms

Outcome measures

Primary outcome

Main study parameter:

Part 1: The change in MPT-induced dynamic hyperinflation before and 2 weeks after triamcinolone administration. We consider halving of dynamic hyperinflation as a clinical relevant result.

Part 2: The association between level of MPT-induced dynamic hyperinflation and severity and quality of specific respiratory symptoms as assessed in different respiratory questionnaires (SGRQ, CCQ, ACQ, BDI/TDI, LCADL, SOBDA).

Part 3: The association between level of MPT-induced dynamic hyperinflation and level of blood eosinophils.

Part 4: The agreement between CPET-induced dynamic hyperinflation and MPT-induced dynamic hyperinflation.

Part 5: The difference between levels of MPT-induced dynamic hyperinflation before and after bronchodilation.

Part 6: The association between the level of specific immunophenotypic parameters and level of dynamic hyperinflation.

Secondary outcome

Secondary parameters:

Part 1: The changes in questionnaire scores (ACQ, CCQ, SGRQ, BDI/TDI, LCADL, SOBDA, SNOT) and levels of FEV1 and exhaled NO before and 2 weeks after triamcinolone administration. Adverse events will be compared between the

intervention group and placebo. Baseline characteristics will be used to identify potential predictors of response.

Part 2: The association between level of MPT-induced dynamic hyperinflation and activities of daily life (BDI/TDI, LCADL, SOBDA) and nasal and ear symptoms (SNOT)

Part 3: The association between level of MPT-induced dynamic hyperinflation and health care utilisation (HCU) and baseline characteristics. The relationship between quality and quantity of different symptoms/limitations and baseline characteristics and health care utilisation.

Part 5: The association between level of pre- vs postbronchodilator MPT-induced dynamic hyperinflation and symptoms, blood eosinophils and changes in MPT-induced dynamic hyperinflation after triamcinolone.

Part 6: The association between the level of specific immunophenotypic parameters and clinical characteristics (i.a. atopy, age-at-onset asthma, smoking history), quality and quantity of symptoms, healthcare utilisation, lung function measurements (FEV1, VC, reversibility), FeNO, peripheral blood eosinophils

Study description

Background summary

Asthma is a heterogeneous condition with many clinical and inflammatory subtypes/phenotypes. Late-onset asthma is less prevalent as compared to early-onset asthma and patients with this type of asthma frequently present with atypical symptoms and fixed airflow limitation instead of reversible bronchoconstriction. Due to the lower prevalence and atypical presentation, patients with late onset asthma are at risk of being misdiagnosed as chronic

obstructive pulmonary disease (COPD), even in the absence of a significant smoking history, and treated accordingly, with only bronchodilating and no anti-inflammatory medication. Yet patients with this late-onset asthma subtype are at risk of faster decline in lung function and are prone to frequent and even life-threatening exacerbations.
There is growing evidence that ongoing eosinophilic inflammation in the small airways plays an important role. This inflammation may lead to dynamic hyperinflation, a phenomenon that might underlie the atypical COPD-like symptoms and increased risk of exacerbations. These atypical symptoms might not be detected by standard asthma control questionnaires but more so by questionnaires used in COPD.
In the present project we hypothesize that systemic eosinophilic inflammation in airway disease (asthma/COPD/asthma-COPD-overlap-syndrome (ACOS)) is associated with small airway inflammation manifesting in dynamic hyperinflation and specific symptoms, which can be reduced by systemic anti-inflammatory treatment.

Study objective

Primary objective:
To investigate the effect of supplementation of a single intramuscular dose of 80 mg triamcinolone on the level of MPT-induced dynamic hyperinflation, in adult asthma patients with demonstrated dynamic hyperinflation. (Part 1)

Secondary objectives:
Part 2: To investigate the relationship between metronome-paced tachypnea (MPT) induced dynamic hyperinflation and respiratory symptoms and limitations in daily activities as assessed in different questionnaires.
Part 3: To investigate the relationship between MPT induced dynamic hyperinflation and eosinophilic inflammation in peripheral blood.
Part 4: To evaluate the agreement between level of dynamic hyperinflation induced by metronome-paced tachypnea (MPT) versus cardiopulmonary exercise testing (CPET).
Part 5: To evaluate the difference between levels of MPT-induced dynamic hyperinflation pre vs post bronchodilation in relationship to symptoms, blood eosinophils and triamcinolone-induced changes in dynamic hyperinflation.
Part 6: To investigate whether specific immunophenotipic characteristics are associated with (small) airway inflammation and dynamic hyperinflation.

Study design

Prospective randomised, double-blind, placebo-controlled intervention study.

Intervention

One group receives a single dose of triamcinolone acetonide injection (80mg)

intramuscular. The other group receives a placebo.

Study burden and risks

The burden associated with this study includes 3 hospital visits, during which several measurements will be done. At visit 1 several questionnaires will be completed and blood test and lung function tests (spirometry, exhaled NO, metronome-paced tachypneu (MPT)) will be performed. Eligible patients will continue to visit 2, at which a cycle exercise test will be performed and study medication will be given intramuscular. At the final visit all assessments performed at visit 1 will be repeated.
The risk and discomfort of these procedures are small. Intramuscular triamcinolone has proven to be safe and is registered for and regularly used in asthma. Possible adverse effects (1-10%) listed for regular use of i.m. triamcinolone include headache, infection and cataract. Data on side effects of a single injection are not available. As possible local adverse effects are listed: injection side reaction, pain following intramuscular injection, sterile abces, (sub)cutaneous atrophy, hyper- or hypopigmentation and Charcot like arthropathy.
The results of this study may be important for asthmatic patients, as it may help to understand the relationship between systemic eosinophilic inflammation, dynamic hyperinflation and symptoms. If indeed small airway inflammation and subsequent dynamic hyperinflation underlies the atypical pattern of symptoms and increased risk of exacerbations, it is important to identify these patients in time and to treat them adequately.
We think the potential gained insights outweigh the risks and discomfort of this study.

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

Adults with symptoms compatible with asthma or COPD
Non-smoking, *10 packyears
BMI *30
ICS (*500 mcg fluticasone equivalent) or daily oral corticosteroids combined with LABA or other controller for at least 6 months.
Stable disease, no exacerbations in last 4 weeks
FEV1/FVC *80% predicted pre-bronchodilation
MPT induced dynamic hyperinflation: * IC *-10%
CPET induced dynamic hyperinflation: * IC *-10%

Exclusion criteria

Concurrent respiratory diseases
Clinically significant cardiovascular disease
Pregnant or breastfeeding women
History of hypertension, diabetes mellitus, menorrhagia, immunodeficiency, psychiatric diseases, idiopathic thrombocytopenic purpura, ulcus ventriculi, ulcus duodeni, infectious disease and infection after administration of live or live, attenuated vaccines.
Hypersensitivity to any components of triamcinolon acetonide,

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-05-2016
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kenacort A-40
Generic name:	Triamcinolone acetonide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-05-2016
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	26-05-2016
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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
EudraCT	EUCTR2016-000357-NL
CCMO	NL55853.099.16