The role of dynamic hyperinflation in asthma.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25886

Source
Nationaal Trial Register

Health condition

Asthma, adults, dynamic hyperinflation, small airway inflammation

Sponsors and support

Primary sponsor: Medical Centre Leeuwarden
Source(s) of monetary or material Support: Part of these studie is financed by grants of the Medical Centre Leeuwarden Academy, Stichting Longgeneeskunde Fryslan and GSK

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

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 severity and quality of specific respiratory symptoms as assessed in different respiratory questionnaires (SGRQ, CCQ, ACQ).

The association between level of MPT-induced dynamic hyperinflation and dyspnea during 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 level of blood eosinophils, healthcare utilisation and baseline characteristics.
The relationship between quality and quantity of different symptoms/limitations and baseline characteristics and healthcare utilisation.

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.
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 level of dynamic hyperinflation.

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

Rationale:
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.

Hypothesis: 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.

Objectives:

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

Secondary objectives:

Part 2: To investigate the relationship between 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 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.

Study population:
In this study patients (¡Ý18 yr) who are referred to a secondary clinic for asthma or COPD will be included. Patients will have been treated according to the Global Initiative for Asthma (GINA) steps 4-5 for at least 6 months, are non-smoking (¡Ü10 packyears) and have airway obstruction (FEV1/FVC ¡Ü80% of predicted). Exclusion criteria are: contraindication for triamcinolone and pregnancy. Patients will be recruited from the pulmonary outpatient clinic of the Medical Centre Leeuwarden.

Intervention:
One group receives a single dose of triamcinolone acetonide injection (80mg) intramuscular. The other group receives placebo.

Main study parameters/endpoints:

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.

Study objective

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 design

The study consists of a baseline visit, and a follow-up period of 2 weeks (between visit 2 and 3).

Baseline (visit 1): Patients characteristics, several questionnaires, blood, lung function tests. If the MPT-induced change in dynamic hyperinflation exceeds -10%, patients will be invited for visit 2.

Visit 2: MPT, CPET.

If dynamic hyperinflation is demonstrated during CPET (IC ¡Ý-10%), patients will be randomized to one of the two treatment arms, with stratification for level of blood eosinophils (strata <0.4 106/L or ¡Ý0.4 106/L). One single i.m. injection of 2 ml/80 triamcinolone acetonide or matched placebo (2 ml NaCl 0.9%) will be given.

Two weeks thereafter (visit 3): Measurements performed at visit 1 will be repeated.

Intervention

One single i.m. injection of 2ml/80mg triamcinolone acetonide or matched placebo (2 ml NaCl 0.9%) in adult asthma patients with demostrated dynamic hyperinflation.

Contacts

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Eligibility criteria

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% of predicted

- 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, psychiatric diseases, idiopathic thrombocytopenic purpura, ulcus ventriculi, ulcus duodeni, infectious disease, infection after administration of live or live, attenuated vaccines.

- Hypersensitivity to any components of triamcinolon acetonide.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2016
Enrollment:	100
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-05-2016
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	NL5720
NTR-old	NTR5873
Other	: RTPO 969

Study results

Summary results
N/A