

The role of dynamic hyperinflation in asthma.

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Systemic eosinophilic inflammation in airway disease (asthma/COPD/asthma-COPD-overlap-syndroom (ACOS)) is associated with small airway inflammation manifesting in dynamic hyperinflation and specific symptoms, which can be reduced by systemic anti-...

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| Ethische beoordeling | Positief advies |
| Status | Werving gestart |
| Type aandoening | - |
| Onderzoekstype | Interventie onderzoek |

Samenvatting

ID

NL-OMON25886

Bron

NTR

Aandoening

Asthma, adults, dynamic hyperinflation, small airway inflammation

Ondersteuning

Primaire sponsor: Medical Centre Leeuwarden

Overige ondersteuning: Part of these studie is financed by grants of the Medical Centre Leeuwarden Academy, Stichting Longgeneeskunde Fryslan and GSK

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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 immunophenotypic 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 (≥ 18 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 (≤ 10 packyears) and have airway obstruction ($FEV_1/FVC \leq 80\%$ 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.

Doel van het onderzoek

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.

Onderzoeksopzet

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 \geq 10%), patients will be randomized to one of the two treatment arms, with stratification for level of blood eosinophils (strata $<0.4 \times 10^6/L$ or $\geq 0.4 \times 10^6/L$). 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.

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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%

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

- 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.

Onderzoeksopzet

Opzet

| | |
|------------------|-----------------------|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |
| Controle: | Placebo |

Deelname

| | |
|-------------------------|----------------------|
| Nederland | |
| Status: | Werving gestart |
| (Verwachte) startdatum: | 01-04-2016 |
| Aantal proefpersonen: | 100 |
| Type: | Verwachte startdatum |

Ethische beoordeling

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|-----------------|------------------|
| Positief advies | |
| Datum: | 27-05-2016 |
| Soort: | Eerste indiening |

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

| Register | ID |
|----------------|------------|
| NTR-new | NL5720 |
| NTR-old | NTR5873 |
| Ander register | : RTPO 969 |

Resultaten

Samenvatting resultaten

N/A