High-altitude treatment versus treatment at sea level in patients with severe, refractory asthma: a pragmatic randomized controlled trial

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON47209

Source
ToetsingOnline

Brief title
High altitude treatment in severe refractory asthma

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Asthma, Bronchial disease

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Astmacentrum Davos, onderdeel van MC Groep

Source(s) of monetary or material Support: MC groep

Intervention

Keyword: asthma, high altitude, pulmonary rehabilitation, randomized controlled trial

Outcome measures

Primary outcome

Asthma-specific quality of life assessed with the Asthma Quality of life

questionnaire

Secondary outcome

1) Asthma control (self- administered questionnaire Asthma Control

Questionnaire)

2) Medication use: daily oral and inhaled glucocorticoid dose

3) Walking endurance (incremental shuttle walk test)

4) Markers of systemic and airway inflammation (eosinophils in peripheral

blood; exhaled nitric oxide fraction (FeNO)

5) Pulmonary Function Testing including reversibility.

6) Rhino-sinusitis health status (20-question Sino-Nasal Outcome Test)

7) Problems in health status (Nijmegen Clinical Screening Instrument)

8) Asthma-related healthcare resource utilization

9) Number of work or school / college days missed due to asthma.

10) Global perceived effect of pulmonary rehabilitation.

11) Care-related Quality of life

Study description

Background summary

Patients with sever asthma suffer from insufficient asthma control despite optimal medical treatmentand and frequent exacerbations.Severe asthma has a large impact on the patient's quality of life. In the recent guideline *Diagnostiek en behandeling van ernstig astma, 2013* pulmonary rehabilitation at high altitude is considered a treatment option for these patients. High altitude treatment combines asthma treatment with exposure to a trigger poor environment. Part of the high altitude treatment effect is attributed to changes in environmental triggers (low humidity air, lower general air pollution, absence of house dust mite allergen exposure and lower microbial exposure). The Dutch asthma centre in Davos (CH) at an altitude of 1650 metres is a tertiary asthma centre offering rehabilitation treatment to patients with severe asthma. Despite a long history of high altitude treatment in severe asthma, its relative short and long-term effectiveness compared to sea level treatment is unknown due to a lack of high-quality controlled studies. The Dutch Health Insurance Board (Zorginstituut Nederland) has commissioned a comparative study to investigate the short and long-term effectiveness of high-altitude pulmonary rehabilitation compared with rehabilitation at sea level in patients with severe, refractory asthma.

Study objective

The primary objectives are twofold:
1) to compare the effect of 12 weeks of multidisciplinary pulmonary rehabilitation in a high-altitude centre with comparable rehabilitation in a sea level centre on asthma-specific quality of life (assessed with the Asthma Quality of Life Questionnaire, AQLQ) in patients with severe, refractory asthma;
2) to compare the AQLQ values over a one-year period in subjects who received 12 weeks of multidisciplinary pulmonary rehabilitation in a high-altitude centre versus rehabilitation in a sea level centre, adjusting for differences in exposure to environmental triggers, both outdoor and indoor. Environmental exposure will also be monitored in both the high-altitude centre and sea level centre.
Secondary objectives are:
1) to compare the effect of 12 weeks of multidisciplinary pulmonary rehabilitation in a high-altitude centre with the same in sea level centre(s) on asthma control questionnaire (ACQ) and other secondary outcomes (care-related quality of life, cardiopulmonary fitness, medication use, pulmo-nary function and inflammation) in patients with severe, refractory asthma
2) to compare the asthma control questionnaire (ACQ) scores over a one-year period in subjects who received 12 weeks of multidisciplinary pulmonary rehabilitation in high-altitude or in sea level centre
3) to investigate the impact of environmental exposure to allergens, microbial content, PM10 and NOx in the subject*s home on short and long term treatment

effectiveness

Study design

a parallel, pragmatic, clinical trial with random allocation to high-altitude or sea level multidisciplinary pulmonary rehabilitation

Intervention

12 weeks of intensive pulmonary multidisciplinary rehabilitation either in the high altitude centre in Davos or in a lung centre in The Netherlands. In both centres, the rehabilitation programme is personalized by using a modular approach with standardized treatment modules according to the DBC *Complex longfalen (longrevalidatie)*.

Study burden and risks

The burden associated with participation consists of the assessments at baseline, every 3 weeks of the intervention period and the follow up assessments (3, 6, 9 and 12 months after the end of rehabilitation). Risks of assessments are minimal as all the assessments are standard assessments within usual care. Both treatment options for intensive pulmonary multidisciplinary rehabilitation, at high altitude and at sea level, are recognized as part of standard care.

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

Adult subjects with asthma, requiring treatment with guideline suggested medications for GINA steps 4 * 5 asthma (receiving inhaled CS (*500 *g fluticasone or equivalent) and LABA as maintenance therapy) for the previous year or systemic CS *6 months / year, that remain **uncontrolled** despite this therapy, for which multidisciplinary pulmonary rehabilitation in a tertiary lung centre is indicated. Uncontrolled asthma is defined by the presence of at least one of the following criteria:
1) poor symptom control: ACQ consistently *1.5, ACT <20 (or **not well controlled** by NAEPP / GINA guidelines)
2) frequent severe exacerbations: two or more bursts of systemic CS (>3 days each) in the previous year
3) serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
4) airflow limitation: after appropriate bronchodilator withhold postbronchodilator FEV1 <80% of predicted (in the face of a reduced FEV1 / FVC, defined as FEV1 / FVC z-score <1.64).;Additional inclusion criteria
1) age *18 and <75 years
2) inhaler technique is optimized
3) adherence to asthma medication is optimized
4) environmental control measures to limit exposure to allergens are taken
5) optimal treatment of comorbidity
6) no medication which can aggravate asthma
7) patient is a non-smoker or stopped smoking at least 6 months before study entry
8) patient has been treated by a pulmonologist in the past 6 months

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study if he / she:
1) participated in a clinical trial in the preceding three months
2) has known alcohol abuse or a severe unstable psychiatric condition requiring treatment
3) has unstable cardiovascular status

4) is pregnant or planning to become pregnant;
5) suffers from other lung disease that impact on asthma symptoms
6) is using long-term oxygen therapy at sea level (exclusion criterium for treatment at high-altitude at the Dutch Asthma Centre Davos)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-09-2015
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	15-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23233
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL53835.018.15
OMON	NL-OMON23233

Study results

Date completed:	01-04-2019
Results posted:	25-04-2019
Actual enrolment:	173

First publication
12-04-2019