Reduction of asthma exacerbation rate in children by non-invasive monitoring of inflammatory markers in exhaled breath (condensate): the RASTER study

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

Summary

ID

NL-OMON36640

Source
ToetsingOnline

Brief title
Monitoring of childhood asthma by non-invasive inflammatory markers

Condition

- Bronchial disorders (excl neoplasms)

Synonym
allergic asthma, asthma, bronchial asthma

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: asthma, children, exhaled breath, exhaled breath condensate, inflammation, volatile organic compounds

Outcome measures

Primary outcome

The primary outcome measures are the number of exacerbations, the level of asthma control, and the quality of life.

I. Exacerbation:

According to an earlier study, a moderately severe exacerbation is defined as an increase in asthma symptoms (dyspnoea, chough, wheezing) and/or the use of short acting b2-agonists during not more that two days. In this case, the drop in FEV1 is not below the 80% personal maximum value. In case of a severe exacerbation, one or more of the following items occurred: 1) The FEV1 % of maximum personal value falls below 80% of the person maximal value for at least two consecutive days, and/or, 2) need for treatment with oral corticosteroids, and/or, 3) need for hospital admission.

II. Asthma control:

The level of asthma control is measured every two months by means of the Dutch validated version of the Asthma control Questionnaire of Juniper et al. This questionnaire consists of 8 items. A score of <0.9 can be considered as excellent asthma control. The questionnaire will be checked by the research

nurse.

III. Quality of life:

Every two months, quality of life is assessed in a standardised way by the Asthma Quality of Life questionnaire for children (PAQLQ) with asthma of Juniper et al..

Secondary outcome

Secondary outcome measures:

I. treatment: The dose of inhaled corticosteroid over the 1-year treatment period will be calculated and averaged as the mean daily dose.

II. treatment compliance: The difference between prescribed and remained doses of inhaled medication will be registered and will be used for calculation of treatment compliance.

III. Bronchial hyperresponsiveness: at 0 and 12 months, the PC20 histamine will be determined and course of FeNO.

IV. Costs and cost-effectiveness: ratio will be calculated as the incremental costs to prevent an exacerbation and/or improvement on the PAQLQ (40)

Study description

Background summary

Asthma is the most common chronic disease in childhood based on chronic airway inflammation. In spite of effective drugs and proper guidelines, asthma control

is worldwide far less good than expected. One of the explanations is that although asthma is an inflammatory disorder, current treatment is not guided by inflammatory markers. From previous studies of our research group it is evident that asthma exacerbations can be predicted by non-invasive inflammatory markers in exhaled breath (condensate). Adapting treatment before exacerbation are clinically manifest will reduce the exacerbation rate.

Study objective

The purpose of the present proposal is to improve care to children with asthma by including regular assessments of non-invasive inflammatory markers during the management of asthma. In this case, treatment is also guided by inflammatory markers (besides symptoms and lung function). In case an exacerbation is expected (because of signs of increased airway inflammation), therapy is already increased in order to prevent an exacerbation. When stable disease is present, tapering of medication can occur.

Study design

The study design is a double-blind randomised controlled trial (RCT) during one year. First patients enter a run-in phase consisting of three standard meetings.

Intervention

2-month diagnostic assessments of non-invasive inflammatory markers in exhaled air and exhaled breath condensate in addition to symptoms/lung function to guide treatment (active intervention group) compared to usual care (guiding of treatment by symptoms and lung function only). Intervention starts after the run-in phase.

5.1 Usual care group:
The children in the control group are treated according to the standards of the Dutch Society of General Practitioners (NHG) and the Paediatric Pulmonology section of the Dutch Society of Paediatrics (NVK) (7,8). Every two months, treatment can be changed in a stepwise manner according to the level of asthma control (see table 2). Dependent of the symptom scores and the lung function levels, treatment will be increased, not changed, or tapered off (table 2). The adaptation of treatment is performed by the independent trial coordinator.

5.2 Intervention group:
Children in the intervention group are treated in the same fashion as in the control group with one exception: treatment is also titrated on basis of exhaled biomarkers. Within two days, the results of the exhaled biomarkers will be known by the independent trial coordinator. The parents/children, physicians and trial workers will not be get information about the exhaled biomarkers. In

case of elevation of one or more of these exhaled biomarkers, treatment will be increased to the next step. When symptoms and lung function are stable but inflammation parameters still increased, tapering of maintenance treatment will not be carried out.

5.3 Exacerbations
Moderate exacerbations are treated with extra doses of reliever medication, severe exacerbations with beta-2 agonists as needed in combination with systemic corticosteroids (five-day course of oral prednisone of 2 mg/kg daily in two doses). In case of a severe exacerbation, maintenance treatment will always be intensified. When patients remain stable for two visits, treatment will be tapered of. Children are always allowed to use extra doses of a beta-2 agonist. The number of doses will be registered in the home monitor.

Table 2: Treatment algorithm in the usual care and intervention group, on basis of symptoms, lung function, or exhaled biomarkers (intervention group only)

Usual care group	Intervention group
Increase in treatment	Increase in treatment
Symptom score above range	Symptom score above range
FEV1 <90% of personal best*	FEV1 <90% of personal best
	Two or more biomarkers elevated
No change in treatment	No change in treatment
Symptom score in range	Symptom score in range
FEV1 90-95% of personal best	FEV1 90-95% of personal best
	One biomarker elevated
Tapering of treatment	Tapering of treatment
Symptom score below range, 2 times*	Symptom score below range, 1 time
FEV1 >95% of personal best, 2 times	FEV1 >95% of personal best
	No biomarker elevated

* personal best value is determined in the run-in phase
* at two subsequent assessments

Study burden and risks

The measurements of the intervention group have a completely non-invasive character, are safe and bear no health risks. On the other hand, the potential gain in quality of life and health is considerable, as the intervention will probably result in less exacerbations, a better quality of life and better asthma control. The children in the usual care group are treated according to the (inter)national guidelines on treatment of asthma.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

The specific inclusion criteria are: 1) already known with a diagnosis of asthma during at least 6 months; 2) age between 6 and 16 years; 3) reversibility to a bronchodilator (increase in FEV1 > 9% of predicted value; and/or 4) bronchial hyperresponsiveness to PC20 histamine < 8 mg/ml; and/or 5)only the use of fluticason in case of inhaled corticosteroid therapy and 6) the use of inhaled corticosteroids.

Exclusion criteria

Exclusion criteria are: 1) cardiac abnormalities; 2) mental retardation, congenital abnormalities or existence of a syndrome; 3) active smoking; 4) no technical satisfactory performance of measurements; 5) no phone line or internet assess available at home; 6) allergen immunotherapy during the study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-05-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	24-11-2010

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-04-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT01239238
CCMO	NL33101.068.10