Peripheral targeting of inhaled rhDNase for chronic obstructive asthma in childhood.

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Primary Objective: To investigate the effect of treatment with nebulized rhDNase on pulmonary function in children with asthma and persistent obstructive pulmonary function.Secondary Objectives: To investigate the effect of treatment with nebulized...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON34039

Source
ToetsingOnline

Brief title
IDOL (Inhaled DNase in Asthmatic children with Obstructive Lung function)

Condition

- Respiratory disorders NEC

Synonym
asthma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Roche Nederland B.V.,unrestricted grant Roche Nederland B.V.

Intervention

Keyword: administration, asthma, inhalation, obstruction, respiratory function tests

Outcome measures

Primary outcome

The primary study parameter is the percent change in FEF75.

Secondary outcome

Secondary endpoints will include:

§ Lung clearance index (LCI) measurements as assessed by multiple breath

washout;

§ Cumulative symptom diary scores evaluating asthma symptoms in the 2nd week of

intervention (e.g. shortness of breath, cough, exercise intolerance,

bronchodilator use etc.);

§ FENO;

§ Other values obtained in the flow volume curve: FEV1, FVC, PEF.

Study description

Background summary

One of the aims of the pharmacological management of asthma is to normalize pulmonary function. In fact, in many children with asthma treated with ICS and inhaled b2-agonists, pulmonary function tests return to (nearly) normal values[4]. However, airflow limitation (airways obstruction) persists in a proportion of these patients. The pathogenesis of this persistent obstruction is unclear. Airway wall inflammation and edema, increased bronchomotor tone, increased sputum volume, increased sputum viscoelasticity and decreased mucociliary clearance all play an important role in the pathogenesis of airways obstruction in childhood asthma. Since absolute airway resistance is higher in childhood than in adulthood, it is likely that mucus retention contributes substantially to airways obstruction in childhood asthma.
In severe asthma dramatic improvement has been described in a few patients

after inhalation of the mucolytic rhDNase. In addition in pathology studies extensive mucus plugging has been described in asthma patients. Based on these findings we think that additional treatment benefit can be obtained when mucus plugging is targeted as part of asthma treatment in children with asthma and persistent airways obstruction.
Therefore we would like to investigate the additional effect of rhDNase treatment in children with asthma and persistent obstructive pulmonary function.

Study objective

Primary Objective: To investigate the effect of treatment with nebulized rhDNase on pulmonary function in children with asthma and persistent obstructive pulmonary function.
Secondary Objectives: To investigate the effect of treatment with nebulized rhDNase on lung clearance index (LCI), FENO values and symptom scores in children with asthma and persistent obstructive pulmonary function.

Study design

This study will be a randomized placebo-controlled clinical trial.

Intervention

All patients will be treated with 3 weeks of placebo or 3 weeks of rhDNase, followed by a 4-week follow-up period. After the 4 weeks of follow-up, one study visit to the hospital is scheduled and lung function tests are performed. Children will be randomized to receive rhDNase or placebo.

Study burden and risks

The target population of this study are children rather than adults, because this early and persistent airflow limitation is a typical feature of childhood asthma. Furthermore, asthma characteristics, mechanisms and severity are age-specific. Firstly, the presentation of asthma differs between children and adults. In childhood, asthma is less affected by other pulmonary disorders, or by loss of elastic recoil of the lung. The clinical picture is more often characterized by reversible airways obstruction, unlike in adults. Small improvements in airways obstruction are easier to recognize and, above all, clinically relevant.
Secondly, baseline airway resistance depends on geometric factors and on airway mechanics, being much higher in children than in adults. If viscous mucus is clinically relevant in worsening airway obstruction, it is most likely to occur in children because of their much smaller airway size, facilitating mucus impaction in the smallest airways.

Children participating in this study will be treated at home and will come to the hospital for 4 study visits. At each visit, pulmonary function tests will be performed (non-invasive). During the two 3-week periods of treatment, patients will be asked to fill in a symptom diary.
The risks associated with participation are small. RhDNase is a registered drug since 1994 for the treatment of mucous impaction in CF. In addition DNase has been extensively used for the treatment of patients with atelectasis due to a variety of pulmonary diseases like PCD, asthma, RSV brochiolitis or due to mechanical ventilation. Administration of rhDNase to children for chronic or acute respiratory symptoms is proven to be safe in multiple studies.
Serious and life threatening side effects have not been described. Side effects, most frequently reported in CF-studies, were mild and included pharyngitis, rhinitis and hoarseness, which resolved spontaneously.

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

Age 6 - 18 years;
Asthma diagnosed according to GINA guidelines;
Treatment with at least 400 microg/day inhaled Budesonide or equivalent (dose constant for at least 6 months) and bronchodilators as needed or daily;
Clinically stable asthma while using a constant dose of inhaled corticosteroids (ICS);
Persistent peripheral airways obstruction as assessed by pulmonary function testing, defined as:
o Dissociation between FVC and FEF75 values: FEF75 at least 20% (absolute % predicted) lower than FVC. ;FVC within normal limits (for this study defined as FVC > 80% pred).

Exclusion criteria

Asthma exacerbation with hospital admission in last 3 months;
Intensive Care Unit (ICU) admission for asthma in last year;
Current respiratory tract infection;
Inability to follow instructions of the investigator;
Inability to inhale rhDNase;
Concomitant medical conditions that effect inhaled treatment (e.g. cleft palate, severe airway malacia);
Neuromuscular disease;
Smoking.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-03-2007
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pulmozyme
Generic name:	recombinant human DNase (rhDNase)
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-07-2006
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-09-2006
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-06-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2006-002337-20-NL
CCMO	NL12582.078.06