Efficacy of peripherally targeted inhaled rhDNase for persistent obstructive asthma in childhood.

No registrations found.

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21320

Source
NTR

Brief title
IDOL

Health condition

asthma with persistent obstructive pulmonary function.

Sponsors and support

Primary sponsor: ErasmusMC Rotterdam
Source(s) of monetary or material Support: E.M. Bakker receives a 4-year grant of Roche Nederland B.V. for her PhD research.

Intervention

Outcome measures

Primary outcome

Primary endpoint will be the change in FEF75 as a result of treatment. FEF75 is the most suitable endpoint since it is sensitive to peripheral airways obstruction.

Secondary outcome

Secondary endpoints will include:

1. Lung clearance index (LCI) measurements as assessed by multiple breath washout;

2. Cumulative symptom diary scores evaluating asthma symptoms in the 2nd week of intervention (e.g. shortness of breath, cough, exercise intolerance, bronchodilator use etc.);

3. FENO;

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

Study description

Background summary

Rationale: 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. 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 hypothesize 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.
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 gas mixing, FENO values and symptom scores in children with asthma and persistent obstructive pulmonary function.
Study design: This study will be a randomized placebo-controlled cross-over clinical trial.
Study population: Children with asthma and persistent airway obstruction, aged 6-18 years.
Intervention: All patients will be treated with 2 weeks of placebo and 2 weeks of rhDNase, separated by a 4-week washout period. Children will be randomized to start with rhDNase or

placebo.

Study objective

rhDNase improves lung function in children with persistent asthma who have persistent obstructive pulmonary function;

Treatment of mucus impaction is an interesting alternative approach to treat peripheral airflow limitation in asthmatic patients. 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 asthmatic patients. Based on these findings we think that additional treatment benefit can be obtained when mucus plugging is targeted as part of asthma treatment. Especially for those asthmatic children with persistent peripheral airways obstruction, rhDNase is a well known and safe drug that could be used for this treatment. Therefore we hypothesize that rhDNase has additional effect on lung function in children with persistent asthma who have persistent obstructive pulmonary function.

Intervention

Nebulization with rhDNase or placebo once daily (each participant is treated for 2 weeks with rhDNase and for 2 weeks with placebo).

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Eligibility criteria

Inclusion criteria

1. Age 6 – 18 years;

2. Asthma diagnosed according to GINA guidelines;

3 Attending the outpatient clinic for at least one year;

4.Treatment with at least 400 mg/day inhaled Budesonide or equivalent (dose constant for at least 6 months) and bronchodilators as needed or daily;

5. Clinically stable asthma while using a constant dose of ICS for at least three months;

6. Ability to perform lung function tests (assessed by trained lung function technician);

7. Persistent peripheral airways obstruction as assessed by pulmonary function testing, defined as: dissociation between FVC and FEF75 values: FEF75 at least 20% (absolute % predicted) lower than FVC;

8. FVC within normal limits (for this study defined as FVC > 80% pred).

Exclusion criteria

1. Asthma exacerbation with hospital admission in last 3 months;

2. Intensive Care Unit (ICU) admission for asthma within the last year;

3. Current respiratory tract infection;

4. Inability to follow instructions of the investigator;

5. Inability to inhale rhDNase;

6. Concomitant medical conditions that effect inhaled treatment (e.g. cleft palate, severe malacia);

7. Neuromuscular disease;

8. Smoking.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2006
Enrollment:	60
Type:	Actual

Ethics review

Not applicable

Application type:	Not applicable

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	NL612
NTR-old	NTR671
Other	: 2412325-2
ISRCTN	ISRCTN71537084

Study results

Summary results

1. Fuchs, H.J., et al., Effect of aerosolized recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. The Pulmozyme Study Group. N Engl J Med, 1994. 331(10): p. 637-42.
2. King, M., et al., Rheology of cystic fibrosis sputum after in vitro treatment with hypertonic saline alone and in combination with recombinant human deoxyribonuclease I. Am J Respir Crit Care Med, 1997. 156(1): p. 173-7.
3. Hodson, M.E. and P.L. Shah, DNase trials in cystic fibrosis. Eur Respir J, 1995. 8(10): p. 1786-91.
4. Greally, P., Human recombinant DNase for mucus plugging in status asthmaticus. Lancet, 1995. 346(8987): p. 1423-4
5. Durward, A., V. Forte, and S.D. Shemie, Resolution of mucus plugging and atelectasis after intratracheal rhDNase therapy in a mechanically ventilated child with refractory status asthmaticus. Crit Care Med, 2000. 28(2): p. 560-2.