The effect of tiotropium-bromide on deep inspiration-induced bronchodilation and airway responsiveness in asthma.

Published: 17-10-2006
Last updated: 20-05-2024

1) To examine the effect of 3 weeks of 18*g tiotropium bromide once daily on the degree of bronchodilation following deep inspiration at a given level of bronchoconstriction.2) To examine the effect of 3 weeks of 18*g tiotropium bromide once daily...

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

Summary

ID

NL-OMON30190

Source
ToetsingOnline

Brief title
Tiotropium-bromide and airway mechanics

Condition

- Bronchial disorders (excl neoplasms)

Synonym
allergic bronchitis, asthma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Subsidie van Boehringer Ingelheim.

Intervention

Keyword: airway responsiveness, anticholinergics, asthma, deep inspiration-induced bronchodilation

Outcome measures

Primary outcome

M/P ratio at 40% fall in V'40P

Maximal dose and response to histamine

Change of the Resistance of the respiratory system by deep inspiration (Rrs) at

8, 12 and 16 Hz

Secondary outcome

baseline FEV1, FVC and FEV1/FVC ratio

Resistance of the respiratory system at 8, 12 and 16 Hz

Reactance of the respiratory system at 8, 12 and 16 Hz

PC20 histamine

PC40 histamine

Study description

Background summary

In healthy subjects deep inspirations can protect against airway narrowing (bronchoprotection) and can also reverse induced bronchoconstriction (bronchodilation). These effects of deep inspiration are impaired or even absent in patients with asthma. In vitro work on the airway smooth muscle cell has shown that periodical stretching is in particular necessary to keep the muscle cell flexible and in a less contractile state. Stretching of the airway smooth muscle cell, or the response to stretch, might be altered in patients with asthma. Chronic blockage of muscarinic receptors of airway smooth muscle by tiotropium bromide may change the fixed state of the airway smooth muscle cell in asthma into a more flexible and less contractile state. This would allow stretches implied by breathing to be effective in reducing smooth muscle

cell contraction and enhancing deep inspiration induced bronchodilation. We therefore hypothesize that a three-week treatment with the anti-cholinergic agent tiotropium-bromide will improve the degree of bronchodilation following deep inspiration. In addition we hypothesize that the maximal response of the airways to histamine will decrease.

Study objective

1) To examine the effect of 3 weeks of 18*g tiotropium bromide once daily on the degree of bronchodilation following deep inspiration at a given level of bronchoconstriction.
2) To examine the effect of 3 weeks of 18*g tiotropium bromide once daily on the maximal response of the airways to histamine.

Study design

Lung function, Resistance of the respiratory system, airway hyperresponsiveness, maximal dose response curves and deep inspiration induced bronchodilation will be measured before, 7 days, and 21 days after treatment with tiotropium-bromide 18 mcg once daily or placebo. All measurements will be performed 180 minutes post tiotropium-bromide or placebo inhalation. The maximal dose response curve will be stopped at a fall in FEV1 of more than 50% or when reaching the last dose (32 mg/ml). During the challenge lung function will be measured using both maximal and partial flow volume curves to measure deep inspiraiton induced bronchodilation (M/P ratio). After the last dose resistance of the respiratory system will be measured before, during and after a deep inspiration.

Intervention

One group will receive 18mcg tiotropium-bromide once daily for 21 days. The other group will receive placebo.

Study burden and risks

In total 4 histamine challenges with lungfunction and resistance measurements will be performed per patient over 4 visits. One skin prick test will be performed and medical history will be asked. Each patient will attend the department for 17 hours over a period of 4 weeks.
There are no appreciable risks during this study. All tests are regularly performed at the department for diagnostic reasons. No invasive measurements are done.

Contacts

Public
Academisch Medisch Centrum

postbus 9600
2300 RC Leiden
Nederland
Scientific
Academisch Medisch Centrum

postbus 9600
2300 RC Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

18-40 yrs
history of episodic wheezing and/or dyspnoea
FEV1 > 70% of predicted
Hyperresponsive in standard histamine challenge (PC20histamine < 8 mg/ml)
Atopic
Non smoking or ex-smoking (for at least 12 months, < 5 pack years)
No usage of inhaled corticosteroids for 4 weeks prior to and during the study

Exclusion criteria

< 18 yrs or > 40 yrs

no history of episodic wheezing and/or dyspnea
FEV1 < 70% predicted
Not hyperresponsive in standard histamine challenge (PC20histamine > 8 mg/ml)
Not allergic
smoking or ex-smoking > 5 Pack Years
Usage of inhaled corticosteroids within 4 weeks prior to and during the study

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2017
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	spiriva
Generic name:	tiotropium-bromide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	17-10-2006

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2006-003385-34-NL
CCMO	NL12584.058.06