Effect of Carbon Dioxide Enriched Ambient Air on Pharmacokinetics and Deposition In Bronchiectasis Patients Using Tobramycin Inhalation: A proof of concept study.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON41356

Source
ToetsingOnline

Brief title
Effect of CO2 on Deposition and Pharmacokinetics of Nebulized Tobramycin

Condition

- Bacterial infectious disorders
- Respiratory tract infections

Synonym
Bronchiëctasis, chronic lung damage

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,TEVA Pharma

Intervention

Keyword: Bronchiectasis, Carbon dioxide, Deposition, Tobramycin

Outcome measures

Primary outcome

o Feasibility of SPECT/CT scans

o Pulmonary deposition and pharmacokinetics

Secondary outcome

o Peak expiratory flow

o Respiratory parameters

o Borg score (subjective sensation of dyspnoea)

Study description

Background summary

Pseudomonas aeruginosa colonization is an independent predictor of mortality in bronchiectasis patients. Tobramycin inhalation treatment is currently only indicated for the treatment of P. aeruginosa colonization in cystic fibrosis (CF) patients. Non-CF bronchiectasis patients often experience symptom relief and improvement in lung function, however studies have failed to show significant improvement. A mainly peripheral pulmonary deposition of inhaled medication is the preferred site of choice. Enhancing deposition of inhaled antibiotics and lung recruitment may improve the response to inhaled antibiotic treatment. Inhaling a low concentration of carbon dioxide (CO_2) during antibiotic nebulization alters respiratory parameters. By changing these parameters one can try to alter the peripheral deposition of inhaled medication, which may improve treatment. Additionally, a nebulizer using a breath-actuated mode, which has a flow only during inspiration in contrast to continuous flow, could possibly also provide a better deposition. SPECT/CT is the preferred technique to obtain information on deposition of inhaled drugs.

However it is unknown if these measurements are feasible with inhalation of technetium DTPA (99mTc-DTPA) and tobramycin, due to the requirement of a relatively steady state uptake.

Study objective

1. To asses (with planar imaging) whether SPECT/CT scan are feasible in assessing pulmonary deposition of inhaled tobramycin.
2. To evaluate the effect of CO2 enriched ambient air on deposition of inhaled tobramycin in bronchiectasis patients.
3. To compare pulmonary deposition of tobramycin with the Pari LC Plus ® nebulizer and the Aero Eclipse II ® nebulizer

Study design

Prospective randomized crossover study consisting of 3 interventions:
I) Nebulization of 99mTc-DTPA and tobramycin 150 mg without carbon dioxide enriched air with an Aero Eclipse II ® nebulizer.
II) Nebulization of 99mTc-DTPA and tobramycin 150 mg with carbon dioxide enriched ambient air with an Aero Eclipse II ® nebulizer.
III) Nebulization of 99mTc-DTPA and tobramycin 300 mg without carbon dioxide enriched air with a Pari LC Plus ® nebulizer.

Phase A: SPECT/CT feasibility study with planar gamma scintigraphy (1-4 patients)
Phase B: Intervention study

After an interim analysis of the first 4 patients in phase A and B of the study we decided to discontinue the CO2 intervention (II) as of 1-1-2015 and to limit the number of blood collections.

Intervention

I) Nebulization of 99mTc-DTPA and tobramycin 150 mg without carbon dioxide enriched air with an Aero Eclipse II ® nebulizer.
II) Nebulization of 99mTc-DTPA and tobramycin 150 mg with carbon dioxide enriched ambient air with an Aero Eclipse II ® nebulizer.
III) Nebulization of 99mTc-DTPA and tobramycin 300 mg without carbon dioxide enriched air with a Pari LC Plus ® nebulizer.

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Study burden and risks

This study will consist of an inclusion visit and three study visits, all with an intervention, nuclear imaging and pharmacokinetic assessment. Tobramycin inhalation may cause minor discomfort due to bronchospasm but this does not occur in patients already on tobramycin maintenance treatment. Other side affects usually occur less frequently or only with a high intravenous dose and/or longterm treatment (see study protocol and patient information letter). The radiation burden is 1.25 mSv per 100 MBq. Enhanced deposition of inhaled antibiotics could improve treatment of P. aeruginosa in bronchiectasis patients. No direct advantages are expected in patients due to participation in this study.

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

o Bronchiectasis.
o Antibiotic inhalation therapy

Exclusion criteria

o Age <21 years.
o Chronic respiratory insufficiency defined according to the GOLD criteria (PaO2 < 60 mmHg or PaCO2 > 50 mmHg, WHO Global Initiative for Chronic Obstructive Lung Disease 2006)
o Renal insufficiency defined as renal creatinine clearance of < 30 ml/minute.
o Neuromuscular diseases.
o Impaired hearing
o Pregnant or breastfeeding.
o Bronchiectasis exacerbation during last 4 weeks.
o History of panic attacks.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-08-2013
Enrollment:	14
Type:	Actual

Medical products/devices used

Generic name:	Pari LC Plus nebulizer;AeroEclipse II nebulizer
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Tobramycin inhalation
Generic name:	(branded generic) TOBI
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	03-07-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2015
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-001541-40-NL
CCMO	NL40458.029.12
Other	NTR aangemeld, maar nog niet toegewezen