Pharmacokinetics of nasally administered tobramycin and colistin in Cystic Fibrosis

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To investigate the clinical pharmacokinetics of tobramycin and/or colistin after nasal administration. With this pharmacokinetic parameters the safety of this treatment can be investigated.

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

Summary

ID

NL-OMON38737

Source
ToetsingOnline

Brief title
SPOEL study

Condition

- Respiratory disorders congenital
- Bacterial infectious disorders
- Respiratory tract infections

Synonym
Cystic Fibrosis, mucoviscidosis

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis

Source(s) of monetary or material Support: Haga longfonds;afdeling longziekten HagaZiekenhuis

Intervention

Keyword: Antibiotics, Cystic Fibrosis, Nasal administration, Pharmacokinetics

Outcome measures

Primary outcome

Pharmacokinetic parameters, including AUC (area under the curve), tmax (time to maximum concentration), Cmax (maximum plasma concentration), t1/2,el (terminal half-life) and F (bioavailability).

Secondary outcome

• CL (total body clearance)

• safety of the nasal irrigations with tobramycin, colistin and a combination of tobramycin and colistin, determined by systemic absorption (bioavailability)

• adverse reactions

• Visual Analogue Scale (VAS) score for (in)convenience of the nasal irrigations

Study description

Background summary

The sinonasal area of patients with Cystic Fibrosis (CF) can be a reservoir for P. aeruginosa from which cross-infection to the lungs may occur. At present adequate inhalation therapy with antibiotics for P. aeruginosa in the lungs is available. However, specific antimicrobial treatment for P. aeruginosa in the sinonasal area is not yet developed. Accurate treatment of this pathogen in the sinonasal area can prevent or postpone cross-infection to the lungs and consequently chronic lung infections. Studies of the pharmacokinetics of nasally administered tobramycin and colistin were never performed. This is the first study to investigate the clinical pharmacokinetics of these drugs. Safety

of this treatment has to be established before intervention studies on the effect of these drugs on clinical parameters are initiated. Systemic absorption can be used as surrogate parameter for safety.

Study objective

To investigate the clinical pharmacokinetics of tobramycin and/or colistin after nasal administration. With this pharmacokinetic parameters the safety of this treatment can be investigated.

Study design

Intervention study.

Intervention

Each patient irrigates the nose with tobramycin mixed with isotonic saline once, colistin dissolved in isotonic saline once and tobramycin and colistin together dissolved in isotonic saline once. In between these three administrations a minimum of 2 days is required.

Study burden and risks

Each subject visits the hospital six times. During three of those visits six venous blood samples are taken (in total 18 bloodsamples). Adverse events and serious adverse events will be closely monitored. Possible discomfort associated with nasally administered tobramycin and/or colistin could be local irritation, burning sensation in the nose, throat irritation and nose bleeds. Patients with Cystic Fibrosis could benefit from antimicrobial treatment of the sinonasal area. However, first safety of this treatment has to be established before clinical intervention studies are initiated. Due to CF-specific characteristics these pharmacokinetic models should be tested on patients with CF.

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

1. Confirmed diagnose of Cystic Fibrosis based on genotyping or a positive sweat test
2. Age >= 18 years
3. Intravenous course of tobramycin in the past, but within the age of >= 18 years, with a creatinine value measured during that same intravenous course of tobramycin

Exclusion criteria

1. Kidney dysfunction (defined as estimated Glomerular Filtration Rate of < 50 ml/min)
2. Liver dysfunction (defined as at least one of the liver enzymes >= 3 times the normal value)
3. Intravenous treatment with aminoglycosides or polymyxins <= 48 hours
4. Acute pulmonary exacerbation (defined by Fuchs criteria)
5. Allergy or intolerance for aminoglycosides or polymyxins
6. Recent surgery of ear, nose or sinuses (< 3 months before study entry)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-06-2013
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Colistin
Generic name:	colistimethate sodium
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	TOBI
Generic name:	tobramycin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	13-02-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

Approved WMO

Date:	10-04-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (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

ID: 28674
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-000117-21-NL
CCMO	NL43431.098.13
OMON	NL-OMON28674