Infuence of the day-night rhythm on renal clearance of tobramycin in cystic fibrosis patients.

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The circadian rhythm influences the renal clearance of tobramycin in cystic fibrosis patients.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25851

Bron
Nationaal Trial Register

Verkorte titel
CIRCA

Aandoening

cystic fibrosis
cystische fibrose
kidney damage
nierschade

Ondersteuning

Primaire sponsor: Haga Medical Center, The Hague
Overige ondersteuning: not funded by external sources

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To compare the renal clearance of tobramycin in CF patients receiving a daily intravenous dose in the morning against patients receiving a daily intravenous dose of tobramycin in the evening.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

Aminoglycosides are a cornerstone for the treatment of cystic fibrosis patients, who have a chronic pulmonary infection with Pseudomonas aeruginosa1. This class of antibiotics is very effective against infections with Pseudomonas aeruginosa, which is the most important pathogen in cystic fibrosis. Repeated or extended dosing of aminoglycosides may cause damage to the proximal tubuli, resulting in renal impairment. Renal impairment affects up to 40 % of adult CF patients, measured after estimation using an appropriate formula. The true number is probably even greater. Life expectancy of CF patients is extending as a result of better treatment. This makes toxicity caused by intravenous aminoglycosides now more relevant than for instance 30 years ago. The TOPIC study has shown that once-daily dosing of aminoglycosides is at least as effective and may be less toxic compared to multiple daily dosing. A recent post-hoc analysis of the TOPIC study data revealed that this difference was probably caused by the fact that 53 out of the 71 patients received their active dose between 16:00 and 20:00 h. This may be the result of a circadian rhythm in drug clearance. It is our hypothesis the circadian rhythm (and mobility) influences the renal elimination rate of tobramycin in CF patients.

Objective:

Main objective: To compare the renal elimination rate constant in CF patients receiving a daily intravenous dose of tobramycin in the morning against patients receiving a daily intravenous dose of tobramycin in the evening.

Secondary objective: To compare biochemical signs of nephrotoxicity in patients who receive their dose of tobramycin in the morning against patients who receive their dose of tobramycin in the evening.

Study design:

Open randomized trial.

Study population:

Adult cystic fibrosis patients, admitted to hospital for treatment of pulmonary exacerbation.

Intervention:

Subjects will be randomized to receive their daily dose of tobramycin in the morning or in the evening.

Main study parameters/endpoints:

The primary end point will be a significant or non-significant difference in the elimination rate constant (Kel) between CF patients receiving a daily intravenous dose of tobramycin in the morning and CF patients receiving a daily intravenous dose of tobramycin in the evening.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The only extra burden associated with participation is three 24-hour urine collections. There are no extra risks associated with participation other than the risks associated with standard treatment.

Doel van het onderzoek

The circadian rhythm influences the renal clearance of tobramycin in cystic fibrosis patients.

Onderzoeksopzet

Renal clearance of tobramycin and biochemical paramaters of kidney function will be evaluated on day 1, 7 and day 14 of tobramycin therapy.

Onderzoeksproduct en/of interventie

Subjects will be randomized to receive their daily dose of tobramycin in the morning or in the evening.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age: ≥ 18 years;

2. A diagnosis of cystic fibrosis (ie, sweat chloride ≥ 60 mmol/L or a genotype associated with cystic fibrosis);

3. Chronic infection with Pseudomonas aeruginosa with the most recently isolated organism showing sensitivity to tobramycin;

4. Pulmonary exacerbation as defined by Fuchs and colleagues.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Use of nephrotoxic drugs (NSAID´s, furosemide, vancomycin);

2. Allergy for aminoglycosides;

3. Granulocytopenia (<1,0 x 109/L);

4. Pregnancy;

5. Calculated GFR < 40 ml/min;

6. Pre-existing hearing impairment (≥ 20 dB hearing level at any two frequencies between 2kHz and 8 kHz on the standard audiogram).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-06-2008
Aantal proefpersonen:	22
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	27-02-2012

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3165
NTR-old	NTR3309
Ander register	: 08-107

Resultaten

Samenvatting resultaten
N/A