PHARMACOKINETICS OF INTRAVENOUS CEFOTAXIME IN CHILDREN

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The study described in this protocol is designed to determine the pharmacokinetics of cefotaxime and its metabolite, desacetyl-cefotaxime, in children on continuous intravenous infusion of cefotaxime. Using these data we will be able to delineate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Fungal infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON34521

Source
ToetsingOnline

Brief title
pharmacokineticx of intraveneus cefotaxime in children

Condition

- Fungal infectious disorders

Synonym
bacterial infectious diseases; bacterial infections

Research involving
Human

Sponsors and support

Primary sponsor: Canisius Wilhelmina Ziekenhuis
Source(s) of monetary or material Support: Canisius Wilhelmina Ziekenhuis

Intervention

Keyword: cefotaxime, children, pharmacokinetics

Outcome measures

Primary outcome

The primary parameters in this study will be:

* T1/2 (half-life during elimination phase) and Vss (volume of distribution in steady state) of cefotaxime and desacetyl-cefotaxime

* Total body clearance, AUC (area under the time-concentration curve), MRT (mean residence time)

Interpretation of pharmacokinetic parameters

* Plasma concentrations and AUC*s of cefotaxime will be compared to the MIC (minimal inhibitory concentration) of the microbe to be eliminated

* Cefotaxime/desacetyl-cefotaxime (cef/des ratio) ratio*s will be calculated to determine liver metabolism

* The T1/2 of cefotaxime and desacetyl-cefotaxime will be related to the GFR (glomerular filtration)

* All pharmacokinetic parameters will be related to the personal characteristics of the subjects

Secondary outcome

not applicable

Study description

Background summary

Cefotaxime is a bactericide third phase cephalosporin with an activity against gram-positive streptococcal species, including S. pneumoniae, and against gram-negative Haemophilus and Neisseria species. The metabolite, desacetyl-cefotaxime, acts synergistically with cefotaxime against, for instance, Bacterioides species [1, 2]. The drug has been used in paediatrics for decennia to treat neonatal infections, pulmonary and urinary tract infections, and as prophylaxis after gastro-intestinal surgery. Despite its widespread use in paediatrics, the literature on cefotaxime pharmacokinetics in children is scanty. In particular, there is a lack of information concerning continuous intravenous infusion of cefotaxime, as it is used in our hospital for over 15 years. In adults, by contrast, several studies are available indicating the advantages of continuous infusion of beta-lactam antibiotics. As the time above the minimal inhibitory concentration (MIC) is much longer during continuous infusion, the killing rate of bacteria is greater [3, 4]. Current literature, limited to intermittent dosing of cefotaxime in children, shows a prolonged half life in neonates because of diminished renal excretion [5-9]. Recent work from our group, based on continuous infusion, revealed great variability in cefotaxime concentrations in neonates [10]. This might be due to the contribution to total cefotaxime body clearance of liver metabolism and renal excretion, which both increase during the first week of life. This study focused on neonates, although differences in metabolism and excretion are expected in older children as well. For instance, some drugs are absorbed, metabolised and excreted faster or more slowly compared to adults [11]. In children, drug dosing should be very precise: low enough to prevent adverse effects, but high enough to reach serum concentrations enabling the eradication of the micro-organisms causing the infection. To accomplish this, study is needed on the pharmacokinetics of drugs in different age groups. This study is aimed to contribute to the knowledge of pharmacokinetics of cefotaxime in children of all ages. Thereby we will get information whether the current dosing regimen is accurate or needs adjustments.

Study objective

The study described in this protocol is designed to determine the pharmacokinetics of cefotaxime and its metabolite, desacetyl-cefotaxime, in children on continuous intravenous infusion of cefotaxime. Using these data we will be able to delineate further the dose regimen for continuous intravenous infusion of cefotaxime in children.

Study design

Observational study

Study burden and risks

Burden
- maximum of 3 capillary punctures
- total blood taken: 1,2 ml over 3-5 days

Risks
- pain and fear: will be reduced by a good preparation by nurses.
- haematoma
- in neonates: anemia, though not expected because of minimal blood taken and spread over 5 days

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Patients who receive intravenous treatment with cefotaxime
2. Patients < 18 years
3. Written informed consent from the patient and/or their legal guardian

Exclusion criteria

Patients with a known allergy to cefotaxime or related compounds

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2010
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	claforan
Generic name:	cefotaxime
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-09-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2010-019676-72-NL
CCMO	NL32245.091.10