Modelling of saliva amikacin and flucloxacillin concentrations in neonates receiving amikacin and flucloxacillin treatment

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Primary objectiveTo establish whether saliva samples could be used as an alternative for blood samples in the therapeutic drug monitoring for amikacin and flucloxacillin. To meet this objective, a PK mod-el will be developed for amikacin and…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON55002

Source
ToetsingOnline

Brief title
Saliva amikacin and flucloxacillin concentrations in neonates

Condition

- Bacterial infectious disorders

Synonym
antibiotic treatment

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Amikacin, Flucloxacillin, Neonates, Saliva

Outcome measures

Primary outcome

The concentration-time profile of saliva and plasma amikacin and flucloxacillin

levels in neonates.

Secondary outcome

The saliva-plasma ratio amikacin and flucloxacillin, pharmacokinetic

parameters, such as clearance (CL) and volume of distribution (Vd) will be

estimated from the data during model building, identification of covariates.

Study description

Background summary

Neonates are often admitted to the neonatology ward due to suspected infection. In the Neth-erlands, amikacin and flucloxacillin are the antibiotics of choice after 72h for the treatment of late-onset sepsis. Amikacin has a small therapeutic index and therefore, therapeutic drug monitoring has to be performed. This is done by taking two blood samples (peak and trough levels), which causes a considerable burden for the neonate. TDM of flucloxacillin is not (yet) performed on a routine basis. However, TDM of flucloxacillin is considered when the therapy seems ineffective or it concerns an infection caused by S. aureus, due to higher MIC*s. A non-invasive method of therapeutic drug monitoring, for example in saliva, may be beneficial.
In the literature, little is known about the amikacin or flucloxacillin concentrations in saliva. However, general principles of drug distribution apply on to the salivary distribution of drugs. Both amikacin and flucloxacillin have physicochemical properties that are favorable for the distribution in saliva. Currently, a study is conducted in the AMC in which saliva gentamicin (also a aminoglycoside) concentrations are monitored in neonates. So far, the results from this study are promising (Mathôt, oral communication).

This study aims to determine a correlation between saliva and plasma amikacin and flucloxa-cillin concentrations in different neonatal subgroups. The relationship between amikacin and flucloxacillin concentrations in plasma and saliva will be described by a population PK model.

Study objective

Primary objective
To establish whether saliva samples could be used as an alternative for blood samples in the therapeutic drug monitoring for amikacin and flucloxacillin. To meet this objective, a PK mod-el will be developed for amikacin and flucloxacillin saliva concentrations.
Secondary objective
To describe the relation between the saliva PK model and the plasma PK model.

Study design

Observational non-interventional study to establish the potential of measuring amikacin and flucloxacillin saliva concentrations for the use of therapeutic drug monitoring.

Study burden and risks

The peak- and through serum concentrations of amikacin and flucloxacillin are determined according to clinical routine. No additional blood samples are scheduled for this study.
The saliva samples are drawn using the SalivaBio Infant's Swab. These swabs are designed specifically for the collection of saliva of young infants and can be held during sampling, eliminating the risk of asphyxiation. The time-points of saliva sampling are paired with clinical routine (i.e. before feeding), so the infants are not disturbed more frequently when participating in this study.
The population that would benefit from the results from this study is highly specific. Therefore, the subjects included in this study should be representative for this study. A model derived from adults is unlikely to predict amikacin and flucloxacillin levels in neonates, partly due to differences in permeability of the salivary glands between these two age groups. It TDM of saliva concentrations is found to be a valid alternative, it will be no longer required to draw blood from neonates for TDM of amikacin and flucloxacillin in the future.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

1. Treatment with amikacin and flucloxacillin i.v.
2. Signed informed consent from both parents or legal guardians, according to local law and regulations
3. Admission to the neonatology ward, pediatrics/pediatric surgery department, obstetrics department or maternity ward of the AMC

Exclusion criteria

1. Congenital disease of the salivary glands
2. Parent refusal
3. Inability to sample saliva
4. Inability to sample blood or monitor drug levels during treatment

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-10-2020
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	22-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2020
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
CCMO	NL72011.018.19