Development and validation of a pharmacokinetic model of flucloxacillin for dosing in patients with impaired renal function

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Development and prospective validation of a pharmacokinetic model of flucloxacillin for dosing in patients with impaired renal function.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON41120

Source
ToetsingOnline

Brief title
PK-model Flucloxacillin

Condition

- Other condition
- Bacterial infectious disorders

Synonym
impaired renal function

Health condition

Nierfunctiestoornissen

Research involving

Human

Sponsors and support

Primary sponsor: Atrium Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Flucloxacillin, Impaired renal function, Pharmacokinetic modeling, Pharmacokinetics

Outcome measures

Primary outcome

Main study endpoint is the development of a PK-model for dosing of

flucloxacillin in patients with impaired renal function.

Secondary outcome

Secondary endpoint is the predictive value of the model for dosing of

flucloxacillin in patients with impaired renal function.

Study description

Background summary

So far, only one study described the disposition of flucloxacillin and its active metabolite 5-hydroxyflucloxacillin in patients with impaired renal function. This study was conducted by Thijssen and colleagues and included only 5 patients with creatinine clearances ranging from 10-15 ml/min. Although the study demonstrated a reduction in renal clearance, higher peak concentrations and accumulation of the active metabolite 5-hydroxyflucloxacillin, the authors concluded that dose adjustment is not necessary because of the low toxic potential of penicillins. Based on the results of this single preliminary study, dose adjustment for flucloxacillin is not recommended by the Royal Dutch Pharmacists Association (KNMP) in patients with impaired renal function (eGFR >10 ml/min). However, the SPC warns that high intravenous doses of flucloxacillin in patients with impaired renal function are associated with neurological abnormalities like convulsions. This has also been reported several times in hospitals in The Hague where continuous infusion of

flucloxacillin in patients with impaired renal function resulted in high plasma concentrations of flucloxacillin (>100 mg/l) and were associated with the occurrence of convulsions. This indicates that dose adjustment might be necessary in patients with impaired renal function. Therefore, more information is needed on dosing of flucloxacillin in case of impaired renal function. Presumed is that a pharmacokinetic model will lead to better individual dosing of flucloxacillin, especially in patients with impaired renal function.

Study objective

Development and prospective validation of a pharmacokinetic model of flucloxacillin for dosing in patients with impaired renal function.

Study design

This study includes PK-modeling. Based on retrospective data from colleagues in The Hague an initial pharmacokinetic model will be developed. This model will be validated with Monte Carlo simulation and confirmed using new data from patients included in a clinical trial. For these patients a prediction will be done what the expected plasmaconcentration will be at a defined moment, based on the patients properties like body weight, age, renal function. At this time point a plasma sample will be drawn and the measured concentration will be compared with the predicted concentration. De difference between the two levels is an indication of the precision of the model. The difference should be less than 20%.

Study burden and risks

Not applicable.

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

- adults treated with oral or intravenous flucloxacillin
- normal and impaired renal function expressed as MDRD and corrected for BSA (body surface area)

Exclusion criteria

- patients younger than 18 years of age;
- legally incapable patients;
- contra-indication or allergy to the treatment with flucloxacillin;
- pregnant patients;
- patients receiving dialysis.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2015
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	05-06-2014
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	NL48078.096.14