An exploratory pharmacokinetic and pharmacodynamic study of beta-lactam and fluoroquinolone in ICU patients

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

Summary

ID

NL-OMON43959

Source
ToetsingOnline

Brief title
EXPAT

Condition

- Bacterial infectious disorders

Synonym
Sepsis;bacterial infection

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Antibiotics, ICU, Pharmacokinetics, Pharmaodynamics

Outcome measures

Primary outcome

Achievement of the PK/PD targets: time that free (unbound) fraction of beta-lactam concentration remains above the MIC during a dosing interval (100%*T>MIC and 100%*T>4xMIC) and for the fluoroquinolone the Area Under the concentration-time Curve for the free (unbound) fraction of above the MIC (fAUC/MIC) ratio, maximum serum concentration (fCmax) and the fCmax/MIC ratio.

Secondary outcome

Comparison of observed PK/PD indices of the individual antibiotics with the length of ICU stay and sickness severity scores in ICU patients.

Study description

Background summary

Emerging evidence supports the importance of optimized antibiotics exposure in intensive care unit (ICU) patients, while evidence based antibiotic dosing in ICU patients in clinical practice is limited. Changes in pharmacokinetic (PK) parameters of antibiotics in subpopulations of critically ill patient have been defined in previous studies. However, there are no data from studies assessing whether the issues identified in a controlled research environment correspond to clinical practice. Assessment is essential in order to determine whether actions, such as the use of therapeutic drug monitoring (TDM), are required to change our existing antibiotic prescribing practices in ICU patients. The potential benefits of a TDM-based approach include a better outcome because of more appropriate antibiotic concentrations, but also less resistance development and avoidance of toxicity. It is most commonly used when the PK and therefore the optimal dose of a drug for an individual patient are difficult to predict. In clinical practice, this approach has been routinely used for many years for vancomycin and aminoglycosides. However, expansion of this practice to beta-lactam and fluoroquinolone antibiotics, which are frequently used to

treat infections in critically ill patients, has not been widely tested as a routine intervention. This is very unfortunate, because the contemporary antibiotic dosing is debatable in severely ill patients as most dosing references have been derived from studies that do not consider the occurrence of pathophysiological changes in critical illness.

Study objective

The aim of this study is to describe the utility of beta-lactam and fluoroquinolone TDM programs in tertiary ICUs. Therefore, the main objective is to document whether empirical antibiotic dosing regimens of these antibiotics achieve defined therapeutic target concentrations, 2 days after start of the therapy in ICU patients.

Study design

The design is a multicenter, prospective, observational pharmacokinetic and pharmacodynamic study.

Study burden and risks

Blood sampling can hurt and give a bruise. Altogether we take off 25 ml extra blood. This volume presents no problems in adults.

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

All the patients admitted to the ICU or internal medicine ward and given standard of care intravenous therapy of either one or both of the target antibiotic classes are included. Antibiotic initiation based on clinical suspicion of infection and/or cultured pathogens susceptible to the target drugs, initial dosage prescription, and duration of therapy are at the discretion of the attending physician. ;In order to be eligible to participate in this study, a subject must also meet all of the following criteria:
* Written informed consent has been obtained from the patient or their legally authorized representative.
* Receiving intravenous antibiotic therapy of the target drugs.
* Suitable intravenous/intra-arterial access to facilitate sample collection.
* Treatment should be aimed for at least at 3 days.
* Bacterial isolates sample are obtainable before start of the target drugs.

Exclusion criteria

* Consent not obtained.
* <18 years of age.
* Antibiotic cessation within 72h after start of the therapie.
* Medium care and burn wound patients admitted to the ICU.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-01-2016
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	20-10-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL53551.078.15