An exploratory pharmacokinetics and pharmacodynamics study of beta-lactam antibiotics in pediatric intensive care patients: is there a need for more precision? (EXPAT-Kids)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON54427

Source
ToetsingOnline

Brief title
EXPAT-Kids

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
critically ill patients, infections

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Erasmus MC Grant

Intervention

Keyword: Antibiotics, Pharmacokinetics, Pharmaodynamics, PICU

Outcome measures

Primary outcome

The PK/PD endpoints are the unbound concentration above the MIC at 100% (PICU target) of the dosing interval (*T*>*MICECOFF and *T*>*4 x MICECOFF). The percentage *T*>*MIC is determined by calculating the intercept of the MIC values with the concentration-time curve.

The following PK/PD indices are calculated:

• %*T>MICECOFF for each individual patient

• % of patients that achieved the target of 100% *T>MICECOFF and 100% *T>4×MICECOFF

• Target attainment for the study antibiotics and dosing regimens to reach the target of 100% *T*>*MIC and 100% *T*>*4×MIC for a range of MICs (0.03125 to 128* mg/L)

Secondary outcome

Secondary endpoints are estimated multivariate binomial and binary logistic regression models, to examining the association of target attainment with patient characteristics and clinical outcomes. We defined ICU length of stay (LOS) from the start of therapy (enrollment) as a secondary endpoint. Factors

likely to contribute to these two outcomes were analyzed for association based on clinical relevancy and previously described relationships (11). These included patient characteristics (age, gender, body mass index (BMI)), organ dysfunction score (PELOD), serum albumin, serum urea, sepsis, estimated glomerular filtration rate (eGFR >= 90 mL/min/1.73 m2), and presence of extracorporeal circuits (CRRT (continuous renal replacement therapy), ECMO (extracorporeal membrane oxygenation)).

Study description

Background summary

Morbidity and mortality in critically ill patients with infection is a global health problem. Emerging evidence supports the importance of optimized antibiotic exposure in pediatric intensive care unit (PICU) patients, while evidence based antibiotic dosing in PICU 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 of pharmacodynamic target attainment is warranted to identify whether clinical outcomes for patients admitted to the PICU can be improved. We propose an exploratory pharmacokinetic and pharmacodynamic (PK/PD) study to analyse whether current antibiotic dosing regimens of frequently used beta lactam antibiotics achieve defined therapeutic target concentrations in PICU patients.

Study objective

The aim of this study is to describe the PK/PD characteristics of frequently used beta-lactam antibiotics in PICU patients. The main objective is to identify whether current antibiotic dosing regimens of the selected beta-lactams achieve defined therapeutic target concentrations, within the first 36 hours after start of therapy in PICU patients.

Study design

The design is a multicenter, prospective, observational pharmacokinetic and

pharmacodynamic study.

Study burden and risks

With the exception of obtaining blood samples, there is no burden or risk associated with participating in this study. Risks are low and burden is minimal.

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)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

All patients admitted to the pediatric intensive care unit wards and given standard of care intravenous therapy of target antibiotic are screened for participating trial.

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 the followinng criteria:

• Written informed consent has been obtained from the patient or their legally authorized representative.
• Recruitment within 36 hours after start of antibiotic therapy
• Intravenous antibiotic therapy of the target antibiotic should be aimed for at least 2 days.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

• Premature infants
• History of anaphylaxis for the study antibiotics
• Consent not obtained
• Study antibiotic cessation before blood collection
• Prophylactic use of the study antibiotics

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-05-2021
Enrollment:	145
Type:	Anticipated

Ethics review

Approved WMO Date:	27-05-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-04-2024
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	NL76194.078.21