Exposure to orally administered antibiotics during the initial phase of infection in non-critically ill, febrile patients

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23093

Source
Nationaal Trial Register

Brief title
EXPO-AB

Health condition

Febrile illnesses

Sponsors and support

Primary sponsor: N.A.
Source(s) of monetary or material Support: N.A.

Intervention

Outcome measures

Primary outcome

AUC (the area under the plasma concentration versus time curve) calculated after oral

administration of ciprofloxacin and amoxicillin, which will be compared between the febrile and afebrile phase

Secondary outcome

Cmax (the maximum plasma concentration) and Tmax (time to reach the maximum plasma concentration) of ciprofloxacin and amoxicillin, which will be compared between the febrile and afebrile phase. And, the PTA (probability of target attainment) with the administered dose. Ciprofloxacin has a concentration-dependent bacterial killing activity, with prolonged persistent effects and is thus dependent on maximizing plasma concentrations and the duration of time drug concentrations exceed the MIC, expressed in AUC/MIC. The PD target of total plasma concentrations is AUC/MIC ≥125. Amoxicillin has a time-dependent bacterial killing activity and is thus dependent on the duration of time that drug concentrations exceed the MIC, expressed as percentage of a dosing interval de concentrations exceeds the MIC, %fT>MIC. The PD target of total plasma concentrations is >50%fT>MIC

Study description

Background summary

Rationale: Patients hospitalized with serious infectious diseases are in general initially treated with parental antimicrobial therapy. In case of a favourable response after 48-72h, intravenous (IV) antibiotic therapy is followed by an oral course of antibiotic therapy. This switch to oral therapy has been shown to lower the length of hospital stay, the risk of new infections and healthcare costs, without compromising the clinical outcome. The initial treatment when patients are acutely ill is started intravenously, because of the high likelihood that adequate antibiotic plasma levels are achieved. It is possible that adequate plasma concentrations are also achieved with oral antibiotics. If this is the case, we might be able to obtain the evident benefits of oral therapy earlier than the currently set time frame.

Objective: The primary objective is to determine whether the exposure to orally administered ciprofloxacin and amoxicillin is altered in hospitalized non-critically ill patients when they are acutely ill and febrile, i.e. first 24 hours of antibiotic therapy, compared to when they are afebrile, i.e. >48 hours after start of therapy. The secondary objective is to determine whether target attainment can be achieved with oral treatment regimens.

Study design: Longitudinal cohort study with repeated measurements

Study population: Hospitalized non-critically ill, febrile patients, aged 18 years or above, with an indication for IV antibiotic therapy.
Intervention (if applicable): The exposure to ciprofloxacin and amoxicillin will be investigated separately in two studies, using the same study design and procedures. Patients will receive a single oral tablet of the study antibiotic when they are febrile and again when they are afebrile, in addition to the antibiotic treatment prescribed by the treating physician. To

measure the antibiotic plasma concentrations, blood samples will be obtained at 4 time points on both study days.

Main study parameters/endpoints: Endpoints are AUC, Cmax and Tmax, calculated after oral administration of ciprofloxacin and amoxicillin, which will be compared between the febrile and afebrile phase. In addition, the amount of patients that achieve target attainment, expressed as percentage of the total number of subjects will be assessed in both phases.

Study objective

To determine whether the exposure to orally administered ciprofloxacin and amoxicillin is altered in hospitalized non-critically ill patients when they are acutely ill and febrile compared to when they are afebrile. With this knowledge the possibility of an earlier IV-to-oral switch therapy can be assessed.

Study design

two study day visits for each patient.

Intervention

Subjects will receive a single oral dose of ciprofloxacin or amoxicillin in addition to the IV antibiotic treatment prescribed for their febrile illness during their initial phase of disease when they are febrile, and again when they are afebrile. During both study visits, a maximum of 4 blood samples will be collected after ingestion of the antibiotic to measure the antibiotic plasma concentrations.

Contacts

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Eligibility criteria

Inclusion criteria

 Age ≥18 years
 Acute febrile illness, defined as an temperature ≥38.5 C and in need of IV antibiotic therapy for an infection for which amoxicillin or ciprofloxacin are registered treatments
 Admitted to the internal medicine ward (including pulmonology and gastroenterology)
 Able to take oral medication, that is no abdominal pathology or history of abdominal pathology that may alter absorption (i.e. vomiting, mucositis, diarrhoea, malabsorption syndrome, former abdominal surgery affecting absorption)
 Able and willing to give informed consent

Exclusion criteria

 Critically ill patients, admitted to the ICU, or infectious patients of the general ward who became critically ill and got transferred to the ICU during the research period.
 Comorbidity affecting absorption: hepatic impairment, i.e. active hepatitis, hepatic failure, liver cirrhosis or severe renal impairment (GFR <30),
 Neutropenic patients (neutrophil count <1000/µl) and patients treated with chemotherapy within 28 days prior to the study.
 Contraindications to use ciprofloxacin or amoxicillin
o Ciprofloxacin: allergy to fluoroquinolones, concomitant administration of tizanidine
o Amoxicillin: allergy to penicillins or proven allergy to another beta-lactam agent (e.g. cephalosporin, carbapenem or monobactam).
 Penicillin/fluoroquinolone treatment during the week prior to study enrolment
 Pregnancy
 History of alcohol and drug abuse.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	23-06-2019
Enrollment:	50
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion Date:	05-06-2019
Application type:	First submission

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
NTR-new	NL7782
Other	METC AMC : METC 2019_083

Study results