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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ancillary infectious topics
Study type	Interventional

Summary

ID

NL-OMON49236

Source
ToetsingOnline

Brief title
EXPO-AB

Condition

- Ancillary infectious topics

Synonym
febrile illness, infectious disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

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

Intervention

Keyword: Antibiotics, Exposure, Febrile, Oral

Outcome measures

Primary outcome

The primary endpoint is the AUC, calculated after oral administration of ciprofloxacin and amoxicillin, which will be compared between the febrile and afebrile phase.

Secondary outcome

The secondary endpoints are the Cmax and Tmax, calculated after oral administration of ciprofloxacin and amoxicillin, which will be compared between the febrile and afebrile phase. In addition, the percentage of patients that achieve target attainment will be assessed in both phases.

Study description

Background summary

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 is intravenously because of the high likelihood that adequate antibiotic plasma levels are achieved when patients are acutely ill. 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.

Study objective

The primary objective is to determine whether the exposure to oral ciprofloxacin and amoxicillin is altered in hospitalized non-critically ill, febrile patients in need of IV antibiotics when they are acutely ill and febrile, compared to when they are afebrile. The secondary objective is to determine whether target attainment can be achieved with current oral treatment dosage regimens.

Study design

Longitudinal cohort study with repeated measurements

Intervention

The exposure to ciprofloxacin and amoxicillin will be investigated separately in two studies, using the same study design and procedure. 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.

Study burden and risks

Ciprofloxacin or amoxicillin will only be administered to those patients diagnosed with a febrile illness for which the antibiotica are a registered treatment and on top of IV antibiotics that are given to these patients. The study will thus not influence the treatment of the febrile illness. Prolongation of the hospitalization or extra study visits won*t be necessary. Patients are exposed to extra venous blood sample collection (low-risk intervention), with a total of 8 samples. To enhance patients comfort we will try to collect the venous blood through an IV catheter. If this is not possible, this will be done via direct venapuncture. Data obtained from our study will have impact on current treatment strategies, which will be beneficial for future patients, science and society.

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

Age *18 years
Acute febrile illness, defined as a temperature *38.3 and in need of IV antibiotic therapy for an infection for which amoxicillin or ciprofloxacin are registered treatments
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

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-08-2019
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	amoxicillin
Generic name:	amoxicillin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	ciprofloxacin
Generic name:	ciprofloxacin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2019
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
EudraCT	EUCTR2019-001240-21-NL
CCMO	NL69024.018.19