Relevance of Biomarkers and Clinical Predictors of Outcome in Unselected Population with Febrile Urinary Tract Infection at Primary Care and Emergency Department in a Prospective, Randomized Cohort Trial Comparing Short (7 days) Antibiotic Treatment with Conventional Treatment (14 days)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON39150

Source
ToetsingOnline

Brief title
FUTIRST (Febrile Urinary Tract Infection Randomized Short Treatment)

Condition

- Bacterial infectious disorders
- Urinary tract signs and symptoms

Synonym
febrile urinary tract infection or pyelonephritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: acute pyelonephritis, biomarkers, febrile urinary tract infection, randomized controlled trial

Outcome measures

Primary outcome

The clinical cure rate through the 10- to 18-day posttherapy visit. Clinical

cure is defined as the resolution of fever and signs and symptoms of UTI.

Secondary outcome

This includes microbiological cure rate 10- to 18-day posttherapy, 30- and 90-

day overall mortality rate, clinical cure rate 70- to 84- day posttherapy, time

to resolution of symptoms, relapse rate of UTI, adverse events or

complications, rate of pelvic floor dysfunction, occurrence of CDAD. The course

and predictive value of clinical parameters and biomarkers in blood and urine.

Study description

Background summary

Patients with febrile urinary tract infection (fUTI) usually present with a mild illness in primary care but may rapidly develop a life-threatening condition, progressing into septic shock and multiple organ failure. The overall mortality of patients with fUTI admitted to hospital amounts to about

7-8%. Given this spectrum of clinical presentation, disease severity and outcome, this clinically well-recognizable disease represents an elegant model to develop clinical scoring systems of disease severity, and characterize new biomarkers of disease that will allow not only a timely diagnosis of urinary tract infection and the etiologic microbial agent (and/or antibiotic resistance), but also allow early identification of those patients who will progress into more severe stages of the host inflammatory response, e.g., sepsis and septic shock with multiple organ failure. To date, a set of clinical criteria to guide management of fUTI have not been established. Thus, the general practitioner or emergency department specialist will decide to hospitalize a patient or not guided by his personal perception of the patient*s illness.
In the last decades hospitalization rates of patients with acute pyelonephritis (AP) or fUTI has decreased from almost 100% to 10-30%. The outpatient management of patients with fUTI has become popular as well as oral antimicrobial treatment regiments and shortening of treatment duration. However, as such approaches are only discovered in otherwise young health non-pregnant women, the best management of fUTI in the elderly, men and patients with co-morbidity remains elusive. Again, based on personal perception of the attending physician antibiotic treatment, duration varies approximately between 7-14 days. Facing the aging of the general population, it is urgent to better define the optimal treatment for AP or fUTI in an unselected population and to identify those at risk for treatment failure or poor outcome to guide and optimize individual patient management and to prevent on the one hand unnecessary long treatment duration and hospital admission and on the other hand unsafe short duration or unsafe outpatient management.
In this study the efficacy and safety of a 7-day antimicrobial regimen compared to a 14-day antimicrobial regimen will be evaluated in an unselected population presenting with fUTI at primary care or emergency department and a clinical and/or biomarker based scoring system of disease severity will be derived to predict those at risk for treatment failure or poor outcome.

Study objective

To assess clinical parameters and biomarkers in blood and urine in predicting bacteremia, need for hospital admission, clinical and bacteriologic cure and mortality in patients with fUTI.
To determine whether a 7-day duration of antibiotic treatment of fUTI is non inferior to 14-day standard duration of treatment in unselected population presenting at primary care or emergency department.
To asses the prevalence of pelvic floor dysfunction after recovery of fUTI , the occurrence of Clostridium difficile associated diarrhea (CDAD) and the occurrence of fluoroquinolones resistant streptococci in the throat as side effects of fUTI treatment

Study design

A multi-center double blind randomized placebo controlled non-inferiority trial combined with prospective observational cohort study (for those who meet entry criteria but cannot be randomized or receive study drugs). Five hundred patients will be enrolled of which four hundred patients will be randomized to either receive standard (14 days) or short (7 days) of antibiotic treatment. Day 8 through 14 of treatment will be blinded; either oral placebo (b.i.d.) or oral ciprofloxacin (500 mg b.i.d).

Intervention

Either placebo or ciprofloxacin during the 8th through 14th day of antimicrobial treatment.

Study burden and risks

The burden of study procedures is limited.
The risk of shorter antimicrobial treatment is minimal as this is already the standard four young women without co-morbidity presenting with febrile urinary tract infection (fUTI). It is reasonable to expect this also upholds the elderly, men and people with underlying co-morbidity. Furthermore the risk of longer (too long?) antimicriobial treatment should not be underestimated. Safety is quaranteed as those subjects with a medical indication to treat fUTI for longer than 7 days or other antimicrobials then the study drug, will NOT receive the study drug but will be treated according to best clinical practice as judged by the attending physician.

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

1. Competent patient aged 18 years or above
2. One or more symptom(s) suggestive of urinary tract infection (dysuria, frequency or urgency*; perineal or suprapubic pain; costo-vertebral tenderness or flank pain)
3. Fever (ear or rectal temp of 38.2 oC or higher, or axillary temp of 38 oC or higher), or history of feeling feverish with shivering or rigors in the past 24 hours
4. Positive urine nitrate test and/or leucocyturia as depicted by positive leukocyte esterase test or microscopy

Exclusion criteria

1. Known allergy to fluoroquinolones
2. Female patients who are pregnant or lactating
3. Patients with known polycystic kidney disease
4. Patients on permanent renal replacement therapy (hemodialysis or peritoneal dialysis)
5. Patients with history of kidney transplantation
6. Residence outside country of enrolment
7. Inability to speak or read Dutch

Study design

Design

Study phase:	4
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-12-2008
Enrollment:	500
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	11-04-2008
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-01-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-01-2012
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-04-2012

Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-02-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-05-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2008-001081-80-NL
CCMO	NL22172.058.08