Oral Fosfomycin versus Ciprofloxacin for Febrile Urinary Tract Infection in Men: a pilot study

No registrations found.

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

Summary

ID

NL-OMON22870

Source
Nationaal Trial Register

Brief title
FOS-MEN

Health condition

Urinary tract infections

Sponsors and support

Primary sponsor: None
Source(s) of monetary or material Support: none

Intervention

Outcome measures

Primary outcome

Clinical cure rate (i.e., resolution of symptoms and fever) among evaluable patients through the 10- to 18-day posttherapy visit.

Secondary outcome

10-18 days post-treatment:
- bacteriologic cure rate i.e. urine culture
- all-cause mortality
- adverse events
70- to 84 days post-treatment:
- clinical cure rate
- all-cause mortality
- relapse rate of UTI

- The plasma concentration of fosfomycin (mg/L) + 1, 1.5, 3, 5, and 8 hours after the first study administration
- The plasma concentration of fosfomycin (mg/L) just before, +1, 1.5, 2, 3 hours after third study administration or later
- The urine concentration of fosfomycin (mg/L), as measured following the methods (section 5) 1-24 hours after the first study administration
- The urine concentration of fosfomycin (mg/L) 48-72 hours after the first study administration or later

Study description

Background summary

Rationale: Due to rising resistance of Enterobacteriaceae against the orally available antibiotics ciprofloxacin and trimethoprim-sulfamethoxazole, difficulties arise in the treatment
of febrile urinary tract infection (FUTI) in men. Fosfomycin possesses a high bactericidal activity to Escherichia coli with resistance rates of 1%. Fosfomycin 3000mg, dosed every 24 hours, reaches sufficient antibiotic levels in urine, prostate and bladder, has good tolerability and is considered safe. Therefore, fosfomycin is a potential alternative antibiotic option for treatment of FUTI in men.

Objective: To determine the efficacy of oral fosfomycin, in the treatment of FUTI after initial empirical treatment with intravenous antibiotics.

Study design: An open label multicenter pilot study

Study population: Consenting men (≥18 years), on appropriate intravenous therapy for FUTI caused by E. coli and fulfilling criteria for an iv-to-oral switch.

Intervention: After an empirical intravenous antibiotic treatment an iv-oral switch to oral fosfomycin 3000mg, every 24 hours, up to 14 days. Patients will be compared to historical controls who were included in a randomized trial with similar inclusion criteria and who were

treated with oral ciprofloxacin.

Eligible patients who refuse to be treated with fosfomycin, will be treated with ciprofloxacin. Those patients will be asked to participate in the trial for observational purposes only as they can serve as control patients as well.

Main study parameters/endpoints: The primary endpoint is the clinical cure rate (resolution of symptoms) 10 to 18 days post-treatment (= test of cure, TOC). Secondary endpoints are clinical cure rate during late follow-up (LFU, 70 to 84 days post-treatment), microbiological cure rate, time to resolution of symptoms, rate of UTI relapse and rate of adverse events. A pharmacokinetic substudy is part of the study and end points are blood and urine concentrations of fosfomycin after oral ingestion.

Study objective

Oral fosfomycin efficacy is as good as ciprofloxacin in men with E. coli FUTI after initial empirical treatment with intravenous antibiotics.

Study design

The primary outcome will be assesed on day 24-32. Secondary outcomes will be assesed on day 24-32 and 84-94.
Plasma pharmacokinetics data will be assesed at day 0 and day 3 till day 14.

Intervention

Oral fosfomycin 3 gram each 24 hours with duration of 14 days minus days of intravenous antibiotic,

Contacts

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Eligibility criteria

Inclusion criteria

1. Competent male 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
5. Hospital admission for presumed FUTI and empirical intravenous antibiotic treatment with beta-lactams
6. Positive urine (> 103 CFU/ml) culture and/or blood culture with E. coli susceptible to fosfomycin, ciprofloxacin and the empirical intravenous beta-lactam treatment
7. Fullfilment of criteria for safe iv to oral switch (hemodynamic stability, ability to consume oral antibiotics, no gastrointestinal problems which affect absorption)

Exclusion criteria

1. Known allergy to fosfomycin or ciprofloxacin
2. Patients with known polycystic kidney disease
3. Patients on permanent renal replacement therapy (hemodialysis or peritoneal dialysis)
4. Patients with history of kidney transplantation
5. Patients with a permanent urinary catheter
6. Patients with chronic renal failure (eGFR < 30 ml/min/1.73m3)
7. Patients with renal abcess or pyonephrosis
8. Patients with chronic bacterial prostatitis (defined as recurrent UTI with the same uropathogen and no other clarifying underlying urological disorder)
9. Patients with any diagnosed metastatic E. coli foci
10. Patients with a double-J or nephrostomy catheter
11. Concomitant systemic antibiotic treatment for another reason than FUTI
12. Residence outside the Netherlands
13. Inability to speak or read Dutch

Specific exclusion criteria for the FOS-MEN-pharm substudy is
1. Incontinency for urine, which results in the inability to properly get urine samples.

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:	Recruiting
Start date (anticipated):	01-07-2020
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	26-06-2020
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	NL8728
Other	METC Leiden-Den Haag-Delft. : 18-105

Study results