Pilot study: Fosfomycin levels in prostate tissue after oral and iv administration

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

Summary

ID

NL-OMON44736

Source
ToetsingOnline

Brief title
PROSAB-2

Condition

- Bacterial infectious disorders

Synonym
prostate infection, prostatitis

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: indien mogelijk door geld van het Haga Wetenschapsfonds;anders door de afdelingen Urologie en Ziekenhuisapotheek

Intervention

Keyword: fosfomycin, profylaxis, prostate, TURP

Outcome measures

Primary outcome

To investigate prostate tissue concentrations of fosfomycin in relation to the

MIC of 32 mg/g after a single iv or oral dose

Secondary outcome

To determine the relation between plasma and tissue concentrations of fosfomycin

To determine plasma and intraprostatic concentration over time.

Study description

Background summary

Infections of the prostate caused by multidrug-resistant gram-negative bacteria are a growing problem. In particular resistance to fluoroquinolones and cephalosporines is problematic, as these drugs are widely used as treatment for prostatitis and as profylaxis prior to prostate biopsy and transurethral resection of the prostate (TURP). The increase of resistance is prompting the re-assessment of *older* agents. Fosfomycin is such an agent, and particularly interesting as many of the multidrug-resistant bacteria remain susceptible to this antibiotic.

To prevent and to treat infections, adequate tissue concentrations of fosfomycin need to be achieved. Until now, little is known about the penetration of fosfomycin in prostate tissue.

Study objective

To measure intraprostatic concentrations and serum levels of fosfomycine after a single oral or intravenous dose prior to TURP. This is done to achieve more insight in whether fosfomycin is a suitable antibiotic to use as profylaxis or treatment of prostatitis

Study design

There will be no randomization or blinding. The first 15 subjects included in the study will receive 3 gr fosfomycin tromethamine 2 hours before TURP (group A), the second 15 subjects will receive 2 gr fosfomycin disodium directly prior to TURP (group B).
In addition, intravenous cefazolin 1 hour before surgery will be used as standard antibiotic prophylaxis (1 gram in patients <80 kg, 2 grams in patients >80 kg)
At the start of the TURP procedure a plasma sample of 4-6 ml will be drawn. Peak serum concentrations of intravenous fosfomycin occur immediately after the administration. Peak serum concentrations of oral fosfomycin occur two hours after a 3 g dose. At the end of the procedure, a second blood sample will be drawn. A third blood sample will be drawn the morning after the operation (as a standard procedure, a blood sample is drawn the morning after the operation to determine creatinine en hemoglobin levels in every patient undergoing a TURP)

Currently all tissue removed during transurethral resection of the prostate is brought to the pathology department. For this study the 2cc prostate tissue first acquired will be separated and the 2cc prostate tissue last acquired as well, and these samples will be sent to the department of pharmacy for further processing. Times of first removed tissue and of last removed tissue will be accurately recorded.

For pathological investigation, in any TUR-P, a maximum of 10 cc tissue will be included for microscopical analysis. Any material exceeding this 10 cc will be discarded. That*s why a cut-off of 15 grams of resected tissue is chosen as a exclusion criterion, so that there will be no tissue processed for this study that would otherwise be analyzed for pathological investigation.

Prostate samples will be carefully washed to remove all blood contamination and will be weighed prior to being frozen. This is necessary to make sure the measured tissue concentration is not affected by fosfomycin present in any blood left behind in the tissue.
Antibiotic concentration in plasma and prostate tissue samples will be determined by a validated liquid-chromatography-tandem mass spectrometry analysis method.

Intervention

administration of 2 grams iv fosfomycin at the start of the procedure, or 3 grams orally 2 ours prior to surgery

Study burden and risks

The burden for patients included in this study consists of 2 venipunctures during the TURP. Part of these patients will undergo this procedure under general aenthesia, en therefore will not notice it.

Patients in this study risk experiencing side effects of the administered medication. As it consist of only one gift, chances that this will happen are considered low.

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

a planned transurethral resection of the prostate in patiënts with complaints caused by benign prostatic hyperplasia (BPH)

Exclusion criteria

suspicion of or proven malignancy of the prostate
known allergy to fosfomycine
renal insufficiency (eGFR < 40 ml/min)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-05-2016
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Infectofos
Generic name:	fosfomycin disodium
Product type:	Medicine
Brand name:	Monuril
Generic name:	fosfomycin tromethamine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	20-11-2015

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
Approved WMO Date:	20-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (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	EUCTR2015-000626-11-NL
CCMO	NL52511.098.15