Prevention of recurrent urinary tract infections by multi-drug resistant bacteria, by intravesical administration of gentamicin.

Published: 07-01-2014
Last updated: 15-05-2024

Objective: The main objective is to demonstrate superiority of the intravesical overnight instillation of gentamicin versus oral antibiotic prophylaxis in reducing the number of recurrences of UTI and extending the time-interval to a next UTI, in...

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

Summary

ID

NL-OMON38402

Source
ToetsingOnline

Brief title
SPRING

Condition

- Bacterial infectious disorders
- Urinary tract signs and symptoms

Synonym
Recurrent urinary tract infection

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw subsidie Goed Gebruik Geneesmiddelen;projectnr 80-83600-98-10218

Intervention

Keyword: intravesical gentamicin, multidrug resistant microorganisms, prophylaxis, urinary tract infection

Outcome measures

Primary outcome

Main study parameters/endpoints: The primary end point is defined as the number

of UTI per patient after initiation of the study during the first 6 months

(prophylactic treatment) and during 12 months (total follow up).

Secondary outcome

Secondary endpoints include the time to first, second and third UTI after start

of intravesical gentamicin or oral antimicrobial prophylaxis, the

microbiological cure rate in males with chronic bacterial prostatitis, the need

for oral and/or intravenous antibiotic-courses for UTI in hospital/day-care

setting during the year of the study, patients* satisfaction with the treatment

and the development of antimicrobial resistance of uropathogens and commensal

flora.

Study description

Background summary

Rationale: Management of patients with recurrent urinary tract infections (UTI) is challenging, even more so in the era of rising antimicrobial resistance. Multidrug-resistance is currently leading to an increased need for intravenous

treatment of UTIs with reserve antibiotics and subsequent hospitalizations. Prophylaxis with low dose oral antibiotics, as recommended by current guidelines, is often limited by multidrug-resistance of uropathogens, and if possible may even further extent the development of resistance. In such patients with recurrent UTI due to multi-drug resistant uropathogens, intravesical gentamicin installation is a potential valuable treatment option for either suppression or prevention of UTI. Locally administered aminoglycosides bypass systemic toxicity and development of antimicrobial resistance is unlikely because of high urinary levels and lack of antibiotic pressure on commensal gut flora.

Study objective

Objective: The main objective is to demonstrate superiority of the intravesical overnight instillation of gentamicin versus oral antibiotic prophylaxis in reducing the number of recurrences of UTI and extending the time-interval to a next UTI, in adults with recurrent UTIs. Secondary objectives include assessment of the acceptability and the safety of intravesical installation of gentamicin and the influence on development of antibiotic resistance of uropathogens.

Study design

Study design: Randomized, controlled, open-label, intervention study.

Intervention

Intervention: The intervention group receives intravesical installations of gentamicin during a period of 24 weeks (once daily for 2 weeks, every other day for 10 weeks, twice weekly for 12 weeks). The control group receives low dose oral antibiotic prophylaxis based on prior susceptibility pattern of isolated uropathogens and patient characteristics, reflecting current standard care.

Study burden and risks

Nature and extent of the burden and risks associated with participation and benefit:
In this therapeutical trial treatment with intravesical gentamicin will be compared to current standard of care. Subjects participating in the study will receive a baseline evaluation including standard diagnostic procedures in patients with recurrent UTI. Follow up consists of 7 outpatient clinic visits, 7 blood samples, 6 urine cultures, and 2 cultures of perineal/vaginal flora. Symptoms, treatment details, side effects and quality of life will be evaluated by standardized questionnaires obtained on each follow up visit.
By direct instillation of gentamicin in the bladder, high concentrations can be reached without concerns on systemic side effects. Systemic uptake of

gentamicin will be monitored during treatment; in case of detectable gentamicin serum levels, intravesical treatment might be discontinued as judged by the principal investigators.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

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 or above.
2. A history of recurrent cystitis, defined as:
a. females: at least 2 episodes of UTI in the last 6 months or 3 in the last 12 months
b. males: at least 2 episodes of UTI in the last 12 months (including recurrent cystitis likely due to chronic bacterial prostatitis).
3. At least one episode of these infections is documented by urine culture with the isolation of *10^3 CFU/mL of an identified MDR pathogen. Multidrug resistance is defined as acquired

non-susceptibility to at least one agent in three or more antimicrobial classes.
4. All other episodes at least by one urinary symptom* and positive urinary nitrate test or leukocyturia (as depicted by positive leukocyte esterase test or microscopy).
5. No clinical symptoms of UTI at enrolment.

Exclusion criteria

1. Urinary culture in prior 6 months tested positive for high-level gentamicin resistant enterobacteriaceae or enterococci (MIC >128 mg/L).
2. Abnormalities of the upper urinary tract, including presence of urinary stones.
3. Patients with a permanent urinary catheter.
4. Complete urinary incontinence.
5. Patients with stage 5 chronic kidney disease (GFR <15 ml/min).
6. Patients with known hypersensitivity to gentamicin.
7. Pregnancy or lactation.
8. Inability to provide informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-03-2014
Enrollment:	170
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	gentamicin
Generic name:	gentamicin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-01-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-01-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-02-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-08-2015
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

ID: 23211
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-002995-42-NL
CCMO	NL46991.058.13
OMON	NL-OMON23211