Clinical outcome of routine treatment of patients with Pelvic Inflammatory Disease and/or Tubo Ovarial Abcess in the presence or absence of Mycoplasma genitalium (MG)

Published: 02-07-2020
Last updated: 11-07-2024

The primary aim of the present study is to investigate whether current standard treatment for PID is clinically effective in patients in whom Mycoplasma genitalium (MG) is present. A secondary aim of the study is to asses whether this treatment is...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mycoplasmal infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON54533

Source
ToetsingOnline

Brief title
Clinical outcome of PID- and TOA-patients with and without MG

Condition

- Mycoplasmal infectious disorders
- Ovarian and fallopian tube disorders

Synonym
PID

Research involving
Human

Sponsors and support

Primary sponsor: GGD Amsterdam
Source(s) of monetary or material Support: Hologic (kits worden voor dit onderzoek verstrekt),Onderzoeksfonds OLVG en Research and Development Fund OLVG

Intervention

Keyword: Mycoplasma genitalium, PID, TOA

Outcome measures

Primary outcome

Clinical outcome of PID and/or TOA is based on fever, abdominal pain, cervical

leucorrhoea during speculum examination, painful genitalia interna, other

clinical signs and CRP.

Secondary outcome

1) The presence and persistence of MG-DNA in vaginal swabs.

2) Antibiotic resistance prevalence in MG positive cases.

Study description

Background summary

One of the most common and serious infections of nonpregnant women of reproductive age is pelvic inflammatory disease (PID). PID is caused by ascending bacteria and can be complicated by tubo-ovarian abscesses (TOA). These TOA*s can rupture and cause sepsis, resulting in life-threatening situations.

In the Netherlands, pelvic inflammatory disease (PID) is empirically treated with ofloxacin/levofloxacin and metronidazole after exclusion of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) as causative pathogens. Numerous studies implicate a role for Mycoplasma genitalium (MG) in the development of PID. A pooled estimate relative risk for PID if MG is present is 2.14 (95% CI 1.31-3.49). However, some studies indicate that there is no major role of MG in the development of PID. In addition, whether specific treatment for MG improves short-term and long-term outcome is unsure. A recent review

recommends that prospective studies evaluate whether screening programs and targeted treatment of MG improve reproductive outcomes in women are necessary to guide public health policy for this emerging pathogen. Nonetheless, recent British (BASHH) as well as international (IUSTI) guidelines recommend MG testing, molecular determination of antimicrobial resistance and specific treatment, including partner treatment (6, 7). In contrast, neither the US CDC guideline, nor the Dutch NHG, NVOG and multidisciplinary STD guidelines for PID treatment do recommend MG testing in case of PID (2, 9). Patients with non-NG, non-CT PID are routinely treated with ofloxacin (2 dd 400 mg po) or levofloxacin (2 dd 500 mg iv), in combination with metronidazole (oral 500mg 2 dd) for 14 days; or the alternative regimen consisting of a single dose ceftriaxon (500 mg im) for the treatment of a possible NG infection, followed by doxycyclin (oral 2 dd 100 mg) in combination with metronidazole (oral 500 mg 2dd) for 14 days.

Treatment of MG with the fluoroquinolones ofloxacin or levofloxacin is probably suboptimal, since both antibiotics are only moderately active against MG. Both ofloxacin and levofloxacin have higher Minimal Inhibatory Concentrations (MIC) values than the fluoroquinolone moxifloxacin. However, clinical effectivity of these antibiotics for MG has so far only been tested for male patients with urethritis, using a lower dosage and a shorter treatment duration in comparison to schedules mentioned above. The European guidelines on MG infections recommend to treat uncomplicated MG infections with azithromycin (po 500 mg on day one, then 250 mg on days 2-5) or josamycin (po 500 mg 3 dd for 10 days). Resistance against azithromycin is increasing and is in many countries higher than 30%. The European guidelines recommend to treat uncomplicated azithromycin-resistant MG infections with moxifloxacin (po 400 mg for 7-10 days). Unfortunately, resistance against the second line treatment is also already reported. Advised third-line treatment consists of doxycycline (po 100 mg 2 dd for 14 days), however this will only eradicate MG in 30% of the patients. Alternatively pristinamycin (po 1g 4 dd for 10 days) can be used, of which the cure rate of macrolide resistance MG is around 75%. Neither josamycin nor pristinamycin is registered in the Netherlands. The recommended treatment for complicated MG infections, such as PID and epididymitis, is moxifloxacin (po 400 mg dd for 14 days).

If MG is a causative organism in PID, an optimal treatment of MG in PID will improve final outcome, possibly also with regard to long-term consequences in fertility. It could also decrease the number of reinfections after treatment of PID if partners are appropriately treated. However, widespread use of MG testing will increase costs for diagnostic testing. In addition, it can be expected that as soon as MG is recognized as an important pathogen in PID, efforts will be started to test and treat also MG in asymptomatic patients (both male and female) with a risk of STD. The number of tests for MG might in that case become equal to the number of tests for CT, at least for the heterosexual population. In 2017, 105,000 CT tests were performed for the heterosexual population in STI clinics, and probably the same number of tests

at GP offices and other settings. Moreover, since resistance to azithromycin (preferred treatment outside of PID for susceptible MG strains) occurs in 30-50% of MG positive patients, additional antimicrobial susceptibility testing will be required at additional costs. In addition, in case of MG infection a test of cure is recommended, increasing diagnostic costs even more. Finally, if 10% of all tested patients will be MG-positive and 50% of them will need treatment with moxifloxacin, 11,000 patients might require a 10-14 day treatment. Moreover, extensive treatment of MG potentially induces antimicrobial resistance in other pathogens. We therefore aim to study how relevant MG testing and treatment is for clinical sequelae.

An additional question is the effectiveness of treatment in patients in whom no MG has been detected. In some of them CT or NG is demonstrated, but in a large proportion of patients the causative agent is unclear. The collected data makes it possible to compare the clinical effectiveness of therapy between groups with different causative agents.

Study objective

The primary aim of the present study is to investigate whether current standard treatment for PID is clinically effective in patients in whom Mycoplasma genitalium (MG) is present. A secondary aim of the study is to asses whether this treatment is microbiologically effective.
Research questions involved in this study are the following:
1. What is the prevalence of MG in patients with PID and/or TOA?
2. What is the effectivity of PID treatment according to NHG/NVOG guidelines on persistence of MG?
3. Does persistence of MG in PID correlate with worse clinical outcome in PID on day 14 and 28?
4. What is the relation of treatment effectiveness and antibiotic resistance in MG?

Addititional question added May2024:
5. What is the clinical efficacy of PID-treatment according to NHG/NVOG guidelines, in relation to the causative agent of PID?

Study design

This prospective cohort study will take approximately 1 year. The study will include patients diagnosed with PID and/or TOA at the hospitals OLVG (both locations East and West), Meander Medical Centre (MC) and Flevo Hospital, and at the STI clinic in Amsterdam.

All patients diagnosed with PID and/or TOA will be asked to participate in this study. Patients at the hospitalswill be routinely treated with ofloxacin po (or levofloxacin iv) and metronidazol po treatment according to present NHG/NVOG

guidelines. Patients at the STI clinic will be treated with doxycyclin (1 dd 200 mg) and metronidazol, according to local guidelines. Ceftriaxone (one single dose 500 mg im) is added to the antibiotic regimen in the hospitals when patients are hospitalized and antibiotics are intravenously administrated; and will be added in case of NG infection at the STI clinic. Treatment will be evaluated clinically. Vaginal swabs, routinely obtained for testing of CT and NG, will also be tested for MG. Patients will be asked to keep a diary in which they report fever, pain and other clinical symptoms. Results of MG testing will not be communicated with the clinician and the patient until the end of follow-up at day 28.

At day 14 patients are asked to take a swab for a self-sampling test and send it to the research laboratory to test for microbes including CT, NG and MG. At day 28 the patient is asked for a control visit to evaluate clinical treatment efficacy and microbiological MG treatment efficacy.

All specimens that are positive for MG will be additionally tested for resistance to azithromycin and fluoroquinolones. Specimens and clinical data collected during the study will also be anonymously stored in a Biobank and a clinical database, respectively, for possible later studies regarding causative organisms in PID, such as bacterial vaginosis related pathogens and Trichomonas vaginalis.

If MG persists at day 28, it will be decided by the clinician whether additional antibiotic treatment, including partner treatment, is deemed necessary. Patients are asked for extra control visits (day 42 and 56) to evaluate the alternative MG clinical and microbiological treatment efficacy.

At day 1, 3, 5, 7, 14 and 28 (and in case of persistent MG with start of another antibiotic treatment at day 29, 31, 33, 35, 42 and 56) patients will be asked to report pain, fever and other clinical symptoms in a diary. In addition, MG will be tested for at the start of inclusion, at day 14 and 28 (and in case of persistent MG at day 42 and 56) after the diagnosis PID. C-reactive protein (CRP) will also be determined at inclusion and at day 28.

In case the patient detoriates under standard clinical care, the clinician can decide to change the treatment regimen. If deemed necessary in these cases, the clinician can ask for the result of the MG test. Before switching treatment, a new vaginal swab will be taken for routine diagnostics as well as for MG testing. Clinicians should report this change in regimen clearly. In all other cases, the initial MG test result will be disclosed at day 28 after the clinical evaluation of the patient.

Study burden and risks

Burden associated with participation:
- collection of an additional vaginal self-swab at day 14

- completion of diary
- test of cure visit at day 28 (if patient does not participate, this could be done by telephone)
- additional vaginal swab and blood specimen collection at day 28.

Risks associated with participation:
- not applicable

Benefits associated with participation:
- test of cure visit at physician's office
- if persistent presence of MG and persisting complaints: possibility of guided treatment

Contacts

Public
GGD Amsterdam

Nieuwe Achtergracht 100
Amsterdam 1018WT
NL
Scientific
GGD Amsterdam

Nieuwe Achtergracht 100
Amsterdam 1018WT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients with PID or TOA

Exclusion criteria

Pregnancy
Hypersensitivity to antibiotics given as standard treatment
Not being able to understand information provided in Dutch or English

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	02-07-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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
CCMO	NL72299.018.19