

## SHORT REPORT

Tetracycline treatment does not eradicate *Mycoplasma genitalium*

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**Objectives:** To study the treatment efficacy of tetracyclines and azithromycin in *Mycoplasma genitalium* positive patients attending an STD clinic.

**Methods:** All *M genitalium* positive patients (34 men and 26 women) attending an STD clinic during a 6 month period were treated with antibiotics. All patients known to be partners of *M genitalium* positive patients and those who were *M genitalium* positive, but not initially treated, were treated with azithromycin. Patients with urethritis and/or cervicitis were treated with tetracyclines before their *M genitalium* status was known.

**Results:** 10 of 14 women (71%) and 10 of 16 men (63%) treated with tetracyclines were *M genitalium* positive at follow up, whereas all patients treated with azithromycin (16 men and 20 women) were *M genitalium* negative, at the 4 week follow up visit.

**Conclusions:** These results suggest that tetracyclines are not sufficient to eradicate *M genitalium*. Randomised controlled treatment trials are urgently needed.

Consistent and increasing data indicate that *Mycoplasma genitalium* has a causative role in non-chlamydial-non-gonococcal urethritis (NCNGU) and/or cervicitis and it may also be a cause of endometritis.<sup>1–3</sup> No comparative studies have been published as to whether the standard treatment for *Chlamydia trachomatis* and non-gonococcal urethritis (NGU) with tetracyclines or macrolides is effective in *M genitalium* infection. An in vitro study by Hannan indicates that *M genitalium* is highly susceptible to azithromycin but not to doxycycline and ciprofloxacin.<sup>4</sup>

The aim of this open pilot study was to compare the antibiotic treatment efficacy of tetracyclines and azithromycin in *M genitalium* infected patients.

## SUBJECTS AND METHODS

A prevalence study of 519 men and 464 women attending the Örebro STD clinic was performed between 1 February and 31 July 2000 comparing signs and symptoms between *M genitalium* and *C trachomatis* genital infections. Two of 519 men had gonorrhoea but were negative for *C trachomatis* and *M genitalium*. In three of 464 attending women, samples for *M genitalium* were not taken. *M genitalium* was detected in 26 women and 34 men, and four of each gender, had a concurrent infection with *C trachomatis*. Patients with urethritis (>4 PMNL/high power field) and/or cervicitis (PMNL >epithelial cells in vaginal wet mount) were treated with doxycycline, 200 mg the first day and 100 mg the following 8 days, or lymecycline 300 mg twice daily for 10 days. However, some patients were treated otherwise, because of conditions such as epididymitis, prostatitis, and suspected low compliance, and therefore three of the *M genitalium* positive male patients were treated with ofloxacin, 30 days of doxycycline, or single dose

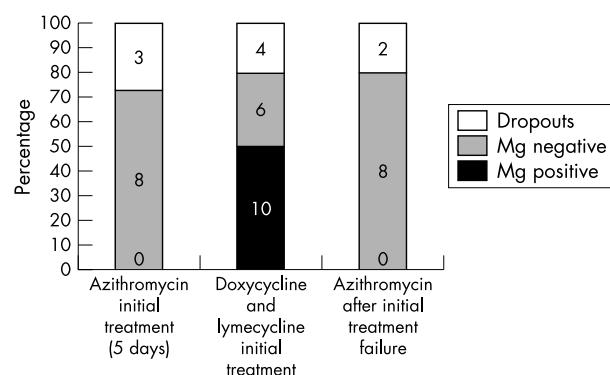
azithromycin, respectively. All patients not receiving treatment initially but having a positive *M genitalium* test were treated with azithromycin 500 mg the first day and 250 mg for the following 4 days. Steady partners to patients with an *M genitalium* infection were treated with azithromycin for 5 days. All *M genitalium* patients were asked to return 4–5 weeks after treatment commenced. After the follow up visit, those treated with tetracyclines initially but still *M genitalium* positive or with remaining symptoms of urethritis or cervicitis were treated with a 5 day course of azithromycin.

Attending men had first void urine (FVU) samples collected. *C trachomatis* was detected by the Cobas Amplicor Chlamydia trachomatis test (Roche Diagnostic Systems, Inc, Branchburg, NJ, USA). *M genitalium* was detected by polymerase chain reaction (PCR) using primers detecting the *M genitalium* 16S rRNA gene.<sup>5</sup> All positive results were confirmed by a PCR detecting the MgPa adhesin gene.<sup>6</sup> Samples for *Neisseria gonorrhoeae* (culture) were taken in 88 men.

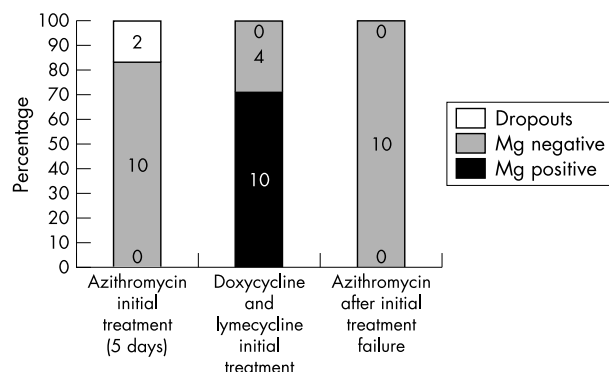
Women were tested for *M genitalium* in FVU and from endocervical specimens as described above. *C trachomatis* was detected in FVU and endocervix by PCR and culture, respectively. Endocervical and urethral samples were cultured for *N gonorrhoeae* in 65 women. Sampling for *N gonorrhoeae* culture was only performed on patients at risk, because of the low prevalence in Sweden.

## RESULTS

Three of 34 *M genitalium* positive men were not treated with the standard treatment and were excluded in the treatment comparison. Those with a concurrent *C trachomatis* infection were treated with tetracyclines (n=3) or ofloxacin (n=1). At follow up all were *C trachomatis* negative, but those receiving tetracyclines were still *M genitalium* positive. Out of 20 men treated with either doxycycline (n=14) or lymecycline (n=6), 16 reattended and 10/16 (63%) were still *M genitalium* positive after a median of 43 days (mean 39, range 27–90 days). After a second treatment with azithromycin eight of 10 reattended



**Figure 1** Outcome of antibiotic treatment in 31 *M genitalium* (Mg) infected men. The figures in bars indicate number of patients.



**Figure 2** Outcome of antibiotic treatment in 26 *M genitalium* (Mg) infected women. The figures in bars indicate number of patients.

after a median of 38 days (mean 42, range 31–79) and were all *M genitalium* negative. All eight of 11 initially treated with azithromycin who reattended were *M genitalium* negative at the follow up visit after a median of 43 days (mean 67, range 23 to 170 days) (fig 1). Among the *M genitalium* positive men initially treated with azithromycin, a subgroup of six had symptomatic urethritis. These patients could be compared to 15 *M genitalium* positive patients with symptomatic urethritis who received tetracyclines. None of those receiving the 5 day course of azithromycin were positive at follow up whereas 10 of the 15 (67%) in the tetracycline group were still *M genitalium* positive at follow up (Fisher's exact test =0.0124). None had a concurrent *C trachomatis* or *N gonorrhoeae* infection.

Fourteen *M genitalium* positive women were treated with tetracyclines (eight with doxycycline and six with lymecycline). Four of the women treated with lymecycline had a concomitant *C trachomatis* infection. Ten of the 14 (71%) women were still *M genitalium* positive, at the follow up visit after a median of 35.5 days (mean 42, range 24–90 days). These women were then treated with a 5 day course of azithromycin and all 10 reattended after a median of 31 days (mean 44, range 22–98 days) and were at that time *M genitalium* negative. Of 12 women initially treated with azithromycin (all *C trachomatis* negative) 10 reattended after a median of 32 days (mean 40, range 23–89 days) and were all *M genitalium* negative (fig 2). *N gonorrhoeae* was not isolated from any patient.

## DISCUSSION

Tetracyclines are widely used worldwide as a treatment for NGU. This treatment is excellent for chlamydial infections and most failures are the result of lack of compliance of treatment or re-infection.<sup>7</sup> It is well known that tetracycline treatment might fail in NCNGU and the proposed treatment of choice in those cases is erythromycin or azithromycin.<sup>8,9</sup> In vitro, *M genitalium* is less susceptible to tetracyclines but there are no published controlled treatment studies.<sup>4</sup>

The treatment groups from the present study of *M genitalium* infected patients were not equal in symptoms and signs and therefore not directly comparable, but in a subgroup

of *M genitalium* infected men with symptomatic urethritis there was a statistically significant difference indicating that azithromycin could be more efficient than tetracyclines.

The widely used treatment for urethritis and cervicitis with tetracyclines does not appear to be sufficient to eradicate *M genitalium* and this should be considered in treatment guidelines. A randomised controlled treatment trial is urgently needed to evaluate the efficacy of azithromycin at different dosages.

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Conflict of interest statement: None declared.

## CONTRIBUTORS

LF initiated the study, examined and sampled most of the patients, he also collected all data and wrote the first draft of the manuscript; HF was responsible for the *N gonorrhoeae* and *C trachomatis* tests, he contributed to the design of the study and analysis of the data; JSJ was responsible for the *M genitalium* tests, he provided major contributions to the design of the study and analysis of the data.

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