SHORT REPORT

Tetracycline treatment does not eradicate *Mycoplasma genitalium*

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Sex Transm Infect 2003;79:318–319

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.^{1–3} 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.⁴

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.⁵ All positive results were confirmed by a PCR detecting the MgPa adhesin gene.⁶ 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.⁷ It is well known that tetracycline treatment might fail in NCNGU and the proposed treatment of choice in those cases is erythromycin or azithromycin.^{8,9} In vitro, *M genitalium* is less susceptible to tetracyclines but there are no published controlled treatment studies.⁴

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.

ACKNOWLEDGEMENTS

Funded by the Research Committee of Örebro County Council, Örebro Medical Centre Research Foundation. The research ethic committee of Örebro County Council approved the study 1 November 1999.

We are most grateful to the staff at the Örebro STD clinic and especially to Maritha Holmqvist, Birthe Dohn at Statens Seruminstitut provided excellent technical assistance.

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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Accepted for publication 6 February 2003

REFERENCES

- 1 Taylor-Robinson D. *Mycoplasma genitalium*—an up-date. *Int J STD AIDS* 2002;**13**:145–51.
- 2 Taylor-Robinson D, Horner PJ. The role of *Mycoplasma genitalium* in non-gonococcal urethritis. *Sex Transm Infect* 2001;**77**:229–31.
- 3 Cohen CR, Manhart LE, Bukusi EA, et al. Association between *Mycoplasma genitalium* and acute endometritis. *Lancet* 2002;**359**:765–6.
- 4 Hannan PC. Comparative susceptibilities of various AIDS-associated and human urogenital tract mycoplasmas and strains of *Mycoplasma pneumoniae* to 10 classes of antimicrobial agent in vitro. *J Med Microbiol* 1998;**47**:1115–22.
- 5 Björnelius E, Lidbrink P, Jensen JS. *Mycoplasma genitalium* in non-gonococcal urethritis—a study in Swedish male STD patients. *Int J STD AIDS* 2000;**11**:292–6.
- 6 Jensen JS, Borre MB, Dohn B. Detection of *Mycoplasma genitalium* by PCR amplification of the 16S rRNA gene. *J Clin Microbiol* 2003;**41**:261–6.
- 7 Jurstrand M, Falk L, Fredlund H, et al. Characterization of *Chlamydia trachomatis* omp 1 genotypes among sexually transmitted disease patients in Sweden. *J Clin Microbiol* 2001;**39**:3915–19.
- 8 Stamm WE, Hicks CB, Martin DH, et al. Azithromycin for empirical treatment of the nongonococcal urethritis syndrome in men. A randomized double-blind study. *JAMA* 1995;**274**:545–49.
- 9 Center for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *MMWR* 2002;**51**:33.