Doxycycline pre-treatment to improve the efficacy of combination minocycline and metronidazole for macrolide-resistant *Mycoplasma genitalium* infections

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Background: *Mycoplasma genitalium* is an antibiotic-resistant sexually transmitted infection with limited therapeutic options. A recent study of patients attending Melbourne Sexual Health Centre found that a 14-day regimen of minocycline and metronidazole (minocycline+metronidazole) achieved microbial cure in 76.7% (n=56/73, 95%CI: 65.4–85.8%) of macrolide-resistant infections, with an efficacy of 90.3% (n=28/31, 95%CI: 74.2–98.0%) in patients who received seven days of preceding doxycycline. We evaluated the efficacy and tolerability of oral doxycycline prior to minocycline+metronidazole in a larger cohort.

Methods: Microbial cure was defined as a negative test-of-cure using transcription-mediated amplification 14–90 days after completing minocycline+metronidazole. The proportion cured and 95% confidence intervals (CIs) were calculated. Univariable and multivariable logistic regression analyses were performed to examine factors associated with cure. Data on adverse effects were collected.

Results: Overall microbial cure following minocycline+metronidazole was 80.9% (n=212/262, 95%CI: 75.6–85.5%). Microbial cure among 181 patients who received doxycycline pre-treatment was 82.3% (95%CI: 76.0–87.6%) compared with 77.8% (95%CI: 67.1–86.3%) among 81 patients who did not (*p*=0.387); individuals who had failed prior regimens were more likely to experience cure with doxycycline pre-treatment. Cervicovaginal infections were more likely to be cured by a minocycline+metronidazole regimen than urethral infections. Gastrointestinal and central nervous system adverse effects were not significantly increased with doxycycline.

Conclusion: Doxycycline pre-treatment did not significantly enhance the efficacy of minocycline+metronidazole. Cure rates are comparable to those reported for moxifloxacin in Australia, but this generic regimen cures 80% of infections with dual-

class resistance and is more accessible globally. Efficacy appears higher in cervicovaginal infections, perhaps due its influence on vaginal dysbiosis.

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