Does pre-treatment with doxycycline improve the efficacy of combination minocycline and metronidazole for macrolide resistant *Mycoplasma genitalium* infections?

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Background:
Curing *Mycoplasma genitalium* is challenging due to rising antimicrobial resistance and limited therapeutic options. There is an urgent need for more therapeutic options. A recent series of patients attending Melbourne Sexual Health Centre (MSHC) found 14 days of minocycline and metronidazole (minocycline+metronidazole) achieved microbial cure in 76.7% (95% CI, 65.4-85.8%) of macrolide-resistant infections, indicating it may be more effective than 14 days of minocycline (67.5%; 95% CI, 58.4-75.6%). Doxycycline has been shown to reduce *M. genitalium* load and is used for STI syndromes and in resistance-guided therapy. We hypothesised that the addition of seven days of oral doxycycline prior to minocycline+metronidazole may further enhance cure and provide an effective and affordable therapeutic option.

Methods:
We evaluated microbial cure and tolerability of seven days of oral doxycycline 100mg twice daily followed by oral minocycline 100 mg BD and metronidazole 400mg BD for 14 days for macrolide-resistant *M. genitalium* infections at MSHC. Microbial cure was defined as a negative test-of-cure (TOC) using transcription mediated amplification 14–90 days after completing the regimen. Data on side effects and adherence were collected at TOC visits.

Results:
Between September 2021 and November 2024, 69 patients were treated with doxycycline followed by minocycline+metronidazole; 61/69 (88.4%, 95% CI, 78.4-94.9%) achieved microbial cure. Cure was significantly higher than that achieved with minocycline monotherapy (88.4% *vs* 67.5%, p=0.002). Preliminary data suggests it may be more effective than minocycline+metronidazole without doxycycline (88.4 *vs* 76.7%, p=0.080). Central nervous system and gastrointestinal side effects were commonly reported for all regimens.

Conclusion:
The efficacy of the minocycline+metronidazole regimen appears to be enhanced by pre-treatment with seven days of oral doxycycline with cure rates of 88%. This regimen may offer an effective and affordable option for patients with contraindications to quinolones or limited options. Clinicians should be aware of side effects.

Disclosure of Interest Statement

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