Diagnostic utility of *Mycoplasma genitalium* antimicrobial resistance markers – state of play for individualized treatment

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Background:
Mycoplasma genitalium is a sexually-transmitted infection which is becoming increasingly difficult to treat. A lack of effective antimicrobials, coupled with the rising rates of resistance to mainstay treatments including macrolides and fluoroquinolones complicates patient management. Given this, there is an important need for commercial diagnostic tests for precision treatment of *M. genitalium* infections.

Methods:
We investigated the prevalence of *M. genitalium* antimicrobial resistance markers for macrolides (23S rRNA) and fluoroquinolones (*parC* and *gyrA* genes). These were correlated with patient outcomes, focusing primarily on fluoroquinolones, since there are limited commercial tests to detect fluoroquinolone resistance in *M. genitalium*.

Results:
Macrolide resistance remains strongly linked to five 23S rRNA mutations (87%; 95% CI 76-94%); and the prevalence of specific mutations in Europe has recently changed. Regarding fluoroquinolone resistance, the ParC-S83I mutation remains the most common and is strongly associated with moxifloxacin treatment failure (62.5%; 95% CI 45.8-77.3). Importantly, ParC wildtype is strongly predictive of treatment success with fluoroquinolones (98.3%; 95% CI 93.9-99.8), and hence this diagnostic marker is also useful in ‘ruling in’ treatment with fluoroquinolones. Other ParC mutations have been identified, however the majority of these mutations are not strongly linked to treatment failure, and so their role in individualized treatment remains controversial. Recently, data has emerged on the important role for dual ParC and GyrA mutations in moxifloxacin treatment failure. Notably, the ParC-S83I mutation commonly co-occurs with the GyrA-M95I mutation; and the presence of these dual mutations substantially increases the risk of treatment failure with fluoroquinolones, when compared to the ParC-S83I mutation alone (80.6% vs 43.2%, $p = 0.0027$).

Conclusion:

Diagnostic assays have considerable value for enhanced individualized treatment for *M. genitalium*. Commercial assays focused on detection of markers like those above, are crucial for maintaining high levels of cure for *M. genitalium* infections.

Disclosure of Interest Statement:
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