

Genomic and phenotypic characterisation of cefixime resistance in *Neisseria gonorrhoeae* in Victoria, Australia

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Background:

The emergence of resistance to extended-spectrum cephalosporins (such as ceftriaxone), the last available class of antibiotics to treat gonorrhoea, is of great concern. Despite a similar mechanism of action to ceftriaxone, cefixime has never been used to treat gonorrhoea in Australia and therefore could be used as an alternate treatment. However, little is known about the prevalence of *Neisseria gonorrhoeae* cefixime resistance in Australia.

Methods:

Here, we performed antimicrobial susceptibility testing by agar dilution and whole genome sequencing on 173 Victorian *N. gonorrhoeae* isolates collected between December 2019 and February 2020. We then determined the prevalence of cefixime resistance determinants in a collection of Victorian *N. gonorrhoeae* isolates from 2017 (n=2,048) and 2019 (n=1,084).

Results:

Our preliminary findings showed that the 173 *N. gonorrhoeae* isolates resolved into 32 individual multi-locus sequence types (MLSTs). The most prevalent MLSTs in our isolates were ST8156 (n=61), ST11864 (n=49) and ST7363 (n=39). 171/173 isolates (98.8%) were susceptible to cefixime (Minimum Inhibitory Concentration (MIC) $\leq 0.25\mu\text{g/mL}$) and 2/173 isolates (1.2%) had decreased susceptibility to cefixime (MIC $> 0.25\mu\text{g/mL}$). Notably, these two isolates were MLST7363, harboured a mosaic *penA* X allele with the Penicillin-Binding Protein 2 (PBP2) mutations: I312M, V316T, N512Y and G545S. Additionally mutations in PonA (G120K and A121D) and PBP1 (L421P) were found. In our collection of 3,132 isolates from 2017 and 2019, we found 41 isolates (1.31%) carrying the *penA* X allele (30 from 2017 and 11 from 2019), of which 32 (78.05%) were MLST7363. Additionally, these 32 isolates had near identical mutations in PonA (G120N and A121D/A121G) and PBP1 (L421P).

Conclusion:

These findings show that while decreased susceptibility to cefixime is currently rare in Victoria, it is commonly associated with one of the most prevalent, circulating MLSTs (ST7363) and thus further surveillance of this lineage and mutation profile are warranted.

Disclosure of Interest Statement: None.