

Potential for selection of *Neisseria gonorrhoeae* ceftriaxone resistance using Doxy-PEP – the need for enhanced antimicrobial resistance surveillance.

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Background:

Increasing evidence shows doxycycline post-exposure prophylaxis (Doxy-PEP) is effective for preventing sexually transmitted infections particularly among patients using HIV PrEP. However, in using Doxy-PEP, the benefits must outweigh the potential risks. Of primary concern is the use of Doxy-PEP for gonococcal infection and the potential for co-selection of antimicrobial resistance. Once established, resistance to multiple antimicrobials is strongly associated with clonal spread and is maintained in multiple genotypes. Given the recent and concerning surge of ceftriaxone resistance strains harboring the penA-60 allele associated with ceftriaxone resistance, we sought to better understand the potential selection of gonococcal ceftriaxone resistance through doxycycline treatment.

Methods:

Published data for ceftriaxone resistant, penA-60-harboring strains/isolates to date were identified to determine the prevalence of tetracycline resistance amongst these strains. Secondly, we retrospectively conducted tetracycline minimum inhibitory concentration (MIC) testing on all *N. gonorrhoeae* isolates from NSW between 2015-2022 with decreased susceptibility or resistance to ceftriaxone (MIC \geq 0.125 mg/L)

Results:

Published data showed more than 70 strains from 14 countries harboring penA-60 allele. Tetracycline susceptibility data was available for 70% (50/71) of these strains, and of these reported strains only 16% (8/50) were susceptible to tetracyclines. Resistance to tetracyclines was high, with 70% (35/50) reported resistant. MIC testing of *N. gonorrhoeae* isolates from NSW between 2015-2022 with decreased susceptibility or resistance to ceftriaxone showed 97% (64/66) were resistant to tetracyclines. Overall, the prevalence of ceftriaxone and tetracycline co-resistance is concerning.

Conclusion:

These data indicate that *N. gonorrhoeae* exhibiting decreased susceptibility and resistance to ceftriaxone are typically resistant to tetracyclines. Hence, with ceftriaxone resistant strains already on the rise globally, there is a theoretical risk of co-selection of ceftriaxone-resistant strains in populations using Doxy-PEP.

Additional consideration must be given to enhanced antimicrobial resistance surveillance within populations using Doxy-PEP.

Disclosure of Interest Statement:

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