Doxycycline Postexposure Prophylaxis Impact on *Neisseria gonorrhoeae* Antimicrobial Susceptibility

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BACKGROUND

-Doxycycline post-exposure prophylaxis (DoxyPEP) is an effective strategy to reduce bacterial sexually transmitted infections (bSTIs) among men who have sex with men (MSM).[1-2]
-Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (Ng) threatens the effectiveness of ceftriaxone, the current first-line therapy.
-DoxyPEP could select Ng tetracycline-resistant strains.[3-4]
-Resistance determinants can cluster on successful lineages, raising concern for linked resistance, including cephalosporins.[4]

-The aim of this study is to assess DoxyPEP impact on gonorrhea antimicrobial susceptibility in a real-life setting.

METHODS

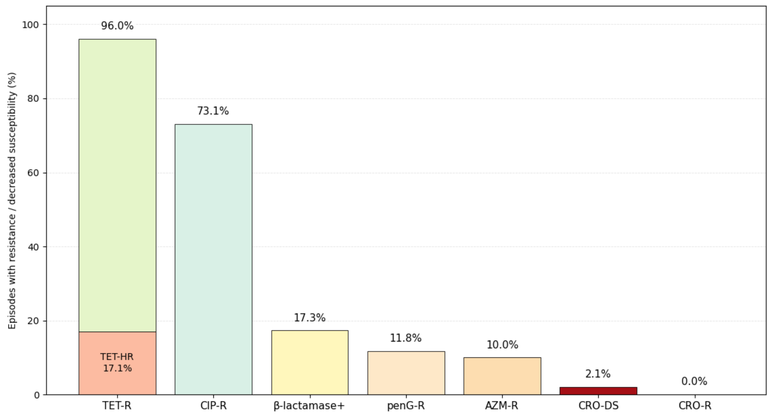
Design: Retrospective cohort study.
Setting: Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan (Italy); Jan 1st, 2022 to Jun 30th, 2025.
Population: Individuals receiving HIV care or PrEP care with at least one episode of culture-confirmed gonorrhea infection.
Exposure definition: Ng episodes after DoxyPEP initiation.
Microbiology:
-Culture from rectal, urethral and pharyngeal sites.
-MICs by gradient-test strips for ceftriaxone (CRO), ciprofloxacin (CIP), tetracycline (TET), azithromycin (AZM), benzylpenicillin (penG); β-lactamase tested.
-Interpretation: EUCAST v15.0.
-TET high-level resistance (TET-HR): MIC >8 mg/L based on ECOFF.
-CRO decreased susceptibility (CRO-DS): MIC >0.032 mg/L based on ECOFF.
Statistics:
-Generalized Estimating Equations (GEE) logistic regression to assess association between DoxyPEP use and Ng resistance rates.
-GEE models on log(MIC) to compare adjusted geometric mean MICs by DoxyPEP use.
-Models were adjusted for age, HIV status, PrEP use and number of prior bacterial STIs (as proxy of other antibiotic exposure).

RESULTS

Study population

318 individuals contributed 376 culture-positive gonorrhea episodes.
Median age was 34.8 years (IQR 30.0–39.8); 99.2% were male at birth.
At Ng diagnosis: 57.7% episodes during PrEP (217/376) and 20.2% among people living with HIV (76/376).
Prior ≥1 bacterial STI detected in 67.6% of Ng episodes (254/376).
DoxyPEP exposed Ng episodes: 20.5% (77/376).

Antimicrobial resistance in Ng isolates



Resistance

-Higher odds of TET-HR after DoxyPEP:
Univariable: OR 1.85 (95%CI 1.01–3.40), p=0.047
Adjusted GEE: aOR 1.87 (95%CI 1.01–3.47), p=0.045
-Higher odds of CRO-DS after DoxyPEP:
Univariable: OR 6.81 (95%CI 1.60–28.93), p=0.009
Adjusted GEE: aOR 8.35 (95%CI 1.67–41.71), p=0.010
-No significant association between DoxyPEP exposure and:
TET-R, CIP-R, AZM-R, penG-R, or β-lactamase positivity.

Minimum inhibitory concentrations

Geometric mean MICs were similar between DoxyPEP-exposed and unexposed episodes for all antibiotics.

Association between DoxyPEP use and resistance (aOR)

Antibiotic	Resistance Type	OR (95% CI)	p-value
Benzylpenicillin	Resistance	1.78 (0.82–3.84)	0.144
Ciprofloxacin	Resistance	0.97 (0.51–1.86)	0.930
Azithromycin	Resistance	0.73 (0.24–2.27)	0.587
Tetracycline	High-level resistance	1.87 (1.01–3.47)	**0.045**
Ceftriaxone	Reduced susceptibility	8.35 (1.67–41.71)	**0.010**
Beta-lactamase	Positive	1.80 (0.93–3.49)	0.083

Association between DoxyPEP use and MICs (aOR)

Antibiotic	Geometric Mean MIC (No DoxyPEP)	Geometric Mean MIC (DoxyPEP)	p-value
Benzylpenicillin	0.29 (0.24–0.36)	0.35 (0.23–0.53)	0.427
Ciprofloxacin	0.53 (0.33–0.86)	0.40 (0.19–0.87)	0.507
Azithromycin	0.29 (0.24–0.36)	0.29 (0.21–0.40)	0.916
Tetracycline	2.07 (1.72–2.48)	2.58 (1.86–3.57)	0.222
Ceftriaxone	0.003 (0.003–0.003)	0.003 (0.003–0.004)	0.333

Both OR and Geometric mean were adjusted for age, PrEP use, HIV status and number of prior bSTIs.

CONCLUSIONS

In this cohort TET resistance was near-universal regardless of DoxyPEP, with a significant association between DoxyPEP use and TET-HR.
Although no ceftriaxone-resistant isolates were detected and CRO-DS was rare, DoxyPEP exposure was associated with CRO-DS; however, ceftriaxone MIC distributions did not differ.
These findings highlight the need for enhanced resistance surveillance.

REFERENCES

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CONTACT INFORMATION

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