Short Commentary

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Susceptibility of *Neisseria gonorrhoeae* to Quinolones and Azithromycin: Its Implication in the Treatment of Pharyngeal Infection

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Short Commentary

Neisseria gonorrhoeae infections are the second most common bacterial sexually transmitted infections (STI) in our area [1-3]. Resistance to this microorganism is currently considered a global threat by the World Health Organization (WHO). Current Spanish guidelines recommend a dual therapy with extended-spectrum cephalosporines (such as cefotaxime, ceftriaxone, cefuroxime or cefixime) and azithromycin (AZT) [4]. Dual therapy has shown synergy *in-vitro* and *in-vivo* and is effective against *Chlamydia trachomatis*. In pharyngeal infections cephalosporins have shown to be less effective than quinolones; thus, UK guideline recommend ciprofloxacin (CIP) in pharyngeal infection if the isolate is known to be quinolone susceptible. On the other hand, European and German guidelines recommend quinolones as an alternative treatment in pharyngeal infections if the isolated strain is susceptible to these compounds and there are indications against using ceftriaxone [5].

Between January 2015 and December 2017, a total of 111 clinical strains of *N. gonorrhoeae* were isolated at the Microbiology Laboratory of the University Hospital of Álava (Vitoria-Gasteiz, Spain). CIP and AZT susceptibility data for all these strains was recorded and is currently being analyzed in order to determine the CIP-and AZT resistance rates among *N. gonorrhoeae*. Patients age and sex was also analyzed. Information regarding patients sexually orientation was not available. For this analysis, one isolate per patient was considered. The majority of *gonococci* (90.1%) were collected from men. The age range was 14 years to 68 years, with a median age of 32.1 years. All strains were susceptible to cefotaxime and only 7 (6.31%) were cefuroxime non-susceptible (**Figure 1**).

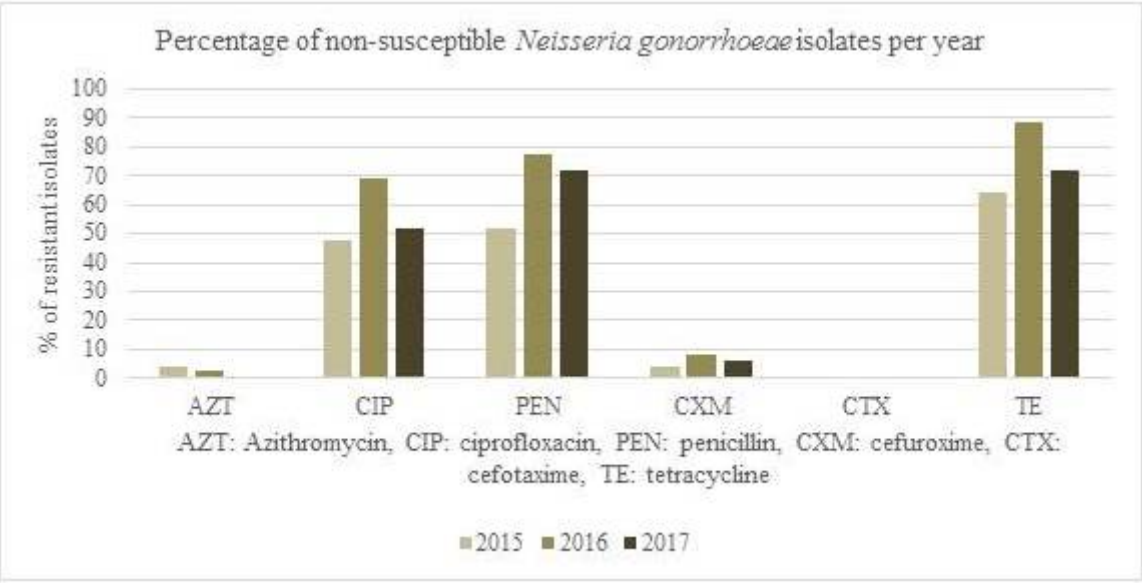

Figure 1 Percentage of resistant *Neisseria gonorrhoeae* isolates per year at the Microbiology Laboratory of the University Hospital of Álava (Vitoria-Gasteiz, Spain), January 2015-December 2017 (n=111 isolates).

As far as CIP is concerned, following Clinical 41 and Laboratory Standards Institute (CLSI) interpretative criteria, which defines the CIP susceptibility breakpoint at <0.06 mg/L, 63 (56.8%) of the strains evaluated were CIP-non-susceptible; 61 (55.0%) were CIP-resistant and 2 (1.80%) CIP-intermediate. CIP-resistant strains were isolated from patients with a mean age of 33.0 years old and were 93.4% men.

In our analysis and similar to what Ota et al., [6] have stated before, CIP-non 47 susceptible strains were more resistant to penicillin (non-susceptible rate of 85.7%) and to tetracycline (non-susceptible rate of 92.1%). Interestingly, Serra-Pladevall et al., [7] have recently found that CIP resistance rates were higher in heterosexual patients than in men who have sex with men.

Regarding AZT, current CLSI recommendations do not provide a susceptibility breakpoint but an epidemiological cutoff value defined at >2 mg/L for non-wild-*N. gonorrhoeae*. Thus, AZT susceptibility is interpreted following European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, which defines the resistant breakpoint at >0.5 mg/L. Taking this breakpoint into account, only two strains displayed minimum inhibitory concentrations (MICs) above the susceptibility breakpoint defined at 0.25 mg/L; the two of them harboured a MIC of 0.5 mg/L and would be classified as non-susceptible.

This report aims to highlight the increase of quinolone-resistant *N. gonorrhoeae* strains in the last 3 years. Our date provides further evidence that quinolones should no longer be recommended as first line therapy although in pharyngeal infections cephalosporins have shown to be less effective. In fact, if the isolated strain is known to be susceptible to quinolones, some guides recommend ciprofloxacin is these infections [2].

Only two of the analyzed strains harboured 64 non-susceptible-AZT MICs but the finding is worrisome since AZT is part of the currently used empiric regimen.

Although molecular methods are increasingly replacing conventional culture procedures, the latter are crucial in order to determine susceptibility patterns.

We would like to emphasize the importance of surveillance programs to control the emergence of these resistant strains, particularly the AZT-resistant ones, in order to update treatment recommendations and to avoid therapeutic failures.

Harmonized criteria for susceptibility testing and interpretation are needed to provide accurate advice to clinicians as well as to obtain reliable epidemiological information at local, regional or national levels.

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