Background: Gonococcal infections are increasing in prevalence in many parts of the world. Increasing prevalence is compounded by increasing resistance to first line antimicrobials in therapy. The grim reality of cephalosporin resistance. Drug-resistant N. gonorrhoeae (NG) has been declared an urgent threat by the Centers for Disease Control, and prevalence of isolates with reduced susceptibility has been observed in 12 American states in recent years. Lack in 2nd and 3rd generation clinical breakpoint recommendation for NG isolates.

Antimicrobial Susceptibility of Clinical Isolates of Neisseria gonorrhoeae to Unconventional Antimicrobials with Therapeutic Potential: Results of the Canadian Antimicrobial Resistance Initiative for Neisseria gonorrhoeae (CARING) Project

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ABSTRACT

The ideal treatment for gonorrhea is a highly potent antimicrobial with a long half-life that is orally bioavailable, allows patients to engage in sexual activity while at the time of presentation. Fluoroquinolones and oral third generation cephalosporins such as cefixime were the choice of therapy because these criteria were met. However, multi-drug resistant N. gonorrhoeae is now a growing concern worldwide. (1) Emergence of cephalosporin-resistant isolates has occurred in isolated areas and reduced susceptibility to cephalosporins remains uncommon but is widespread (1). Azithromycin resistance is also reported globally and resistance to fluoroquinolones, tetracyclines and penicillins is now common and widespread (1). With isolates with reduced cephalosporin susceptibility increasing in North America (2, 3), a crisis of unmettable gonorrhea is looming (1). The purpose of this study was to investigate the in vitro activity of various currently marketed antimicrobials against a collection of N. gonorrhoeae isolates from across Canada.

RESULTS

Materials & Methods

Isolates were submitted to the National Microbiology Laboratory as part of the Public Health Agency of Canada’s National Surveillance of Antimicrobial Susceptibilities of Gonococci. Isolates are isolated in Chlamydia trachomatis and Neisseria gonorrhoeae laboratories identify resistance to at least one antibiotic or if the provincial laboratories do not perform any antimicrobial susceptibility testing. Between 900 and 1200 isolates are submitted per year. A sample of 75 isolates were selected for this study. Minimum inhibitory concentration (MIC) was determined by broth microdilution (4) on GC base supplemented with IsoVitalex™, cefixime, ceftriaxone, ciprofloxacin, spectinomycin, tetracycline, erythromycin, azithromycin, gentamicin, levofloxacin, ciprofloxacin, and nafcillin/Vancomycin, spectinomycin, tetracycline, and linezolid. Where available, CLSI breakpoints were used to interpret MICs (5).

TABLE 1: MIC₅₀, MIC₉₀ and susceptibility of isolates to conventional and unconventional antimicrobials

A high susceptibility rate was observed for cefixime, ceftriaxone and spectinomycin. Using 2007 FDA breakpoints (6) for azithromycin (MIC ≤ 1 μg/mL), 82.7% of isolates were susceptible to azithromycin. Using EUCAST breakpoints (7) (MIC ≤ 0.25 μg/mL), 57.3% of isolates were susceptible. Among marketed unconventional antimicrobials, activity was generally very good and comparable for linezolid, nearly all isolates had MICs below the susceptibility breakpoints of other organisms for which the agents are used. Gentamicin and netilmicin were approximately 2 and 4 times more potent, respectively, than spectinomycin. Among isolates with reduced susceptibility to cefixime (MIC ≥ 0.25 μg/mL), ceftriaxone and spectinomycin remained active. Among isolates with reduced susceptibility to cefixime (MIC ≥ 0.25 μg/mL), ceftriaxone and spectinomycin remained active. Among isolates with reduced susceptibility to cefixime (MIC ≥ 0.25 μg/mL), activity of the unconventional non-beta-lactam antimicrobials was comparable to the activity among those with low cefixime MIC. A strong correlation between MICs of all the beta-lactams was observed, supporting a common mechanism of reduced susceptibility to all the beta-lactams.

TABLE 2: MIC₅₀, MIC₉₀ and susceptibility of cefixime non-susceptible isolates

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REFERENCES