

SUSCEPTIBILITY OF *NEISSERIA GONORRHOEAE* TO GENTAMICIN, CHLORAMPHENICOL AND OTHER ANTIBIOTICS IN MANAUS, AMAZON, BRAZIL

SUSCETIBILIDADE DA NEISSERIA GONORRHOEAE A GENTAMICINA, A CLORANFENICOL E A OUTROS ANTIBIÓTICOS EM MANAUS, AMAZONAS, BRASIL

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ABSTRACT

We notify the antimicrobial tests of 83 *N. gonorrhoeae* isolates. The results showed that it is not viable to use penicillin and tetracycline to treat the disease. The resistance to quinolones has not precluded therapy yet. All gonococci were sensitive to ceftriaxone, and the low level of resistance to gentamicin and chloramphenicol may suggest their usage as a future therapeutic option.

Keywords: *Neisseria gonorrhoeae*; antimicrobial; gentamicins; chloramphenicol; resistance.

RESUMO

Reportamos os resultados de testes de suscetibilidade realizados com 83 isolados de *N. gonorrhoeae*. Os resultados demonstram que não é viável a utilização de penicilina e tetraciclina para o tratamento da doença. A frequência de resistência às quinolonas detectada neste corte ainda possibilita sua utilização na terapêutica. Todos os gonococos testados foram sensíveis à ceftriaxona. O reduzido nível de resistência à gentamicina e ao cloranfenicol demonstra que esses antibióticos podem ser utilizados como opção terapêutica futura.

Palavras-chave: *Neisseria gonorrhoeae*; antimicrobiano; gentamicinas; cloranfenicol; resistência.

NOTE

In 2008, 106,1 million new cases of gonorrhea in adults were estimated all over the world, out of which 11 million only in the American continent⁽¹⁾. In 2013, Alfredo da Matta Foundation (FUAM – Manaus, Amazonas, Brazil) reported 3,482 sexually transmitted diseases (STD) cases, out of which 14.6% were gonococcal infection. Currently gonorrhea is the second most common reported disease at FUAM, following condyloma (27.9%) and syphilis (14.2%)⁽²⁾. As in vitro susceptibility to oral cephalosporins has declined in several regions⁽³⁻⁵⁾, we evaluated the susceptibility of 83 *N. gonorrhoeae* isolates to different antibiotics, including chloramphenicol and gentamicin as possible future therapeutic options. Through May–November 2009, samples were collected consecutively from 200 patients of both sexes, aged 18 or older, who spontaneously went to the STD clinic at Alfredo da Matta Foundation with urethral or cervical discharge. *N. gonorrhoeae* was identified as described previously⁽⁶⁾. The E-test (bioMérieux AB, Solna, Sweden) method was used for antimicrobial susceptibility tests. The criteria recommended by WHO⁽⁶⁾, CSLI⁽⁷⁾, EUCAST⁽⁸⁾ and Van Dick

et al.⁽⁹⁾ were applied for the interpretation of the results of susceptibility tests. For the phenotypic characterization of gonococci resistant to penicillin and tetracycline, we used those described by Bhuiyan et al.⁽¹⁰⁾. Due to the absence of criteria for gentamicin, we used those mentioned by Brown⁽¹¹⁾, in which Minimal Inhibitory Concentration (MIC) ≤ 4 mg/L was defined as sensible, 8–16 mg/L as reduced sensitivity and ≥ 32 mg/L as resistant. Two hundred patients were included in this study (65% male and 35% female) aged from 18–48 (medium of 26 years). After samples were collected, 83 (41.5%) were positive to *N. gonorrhoeae*, out of which 65.5% were urethral and 34.5% cervical. Resistance to azithromycin was of 1.2%; to ofloxacin and ciprofloxacin, 2.4%; to chloramphenicol, 3.6%; to penicillin, 20.5% — 16.7% of which were PPNG (Penicillinase-Producing *Neisseria gonorrhoeae*) and 3.8% CMRNG (Chromosomally Mediated Resistant *Neisseria gonorrhoeae*) —; and to tetracycline, 54.2%, with 4.8% TRNG (Tetracycline-Resistant *Neisseria gonorrhoeae*). All isolates were susceptible to ceftriaxone and gentamicin (**Table 1**). Resistance reduction of 1.3% to penicillin and of 25.8% to tetracycline was observed when compared with studies carried out in the same region in 2005⁽¹²⁾. The reduction of the resistance of gonococci to both antibiotics may have been the result of some associated factors as follows: those antibiotics are not used at STD clinic in FUAM anymore; governmental measures rule the antibiotic market and the recommendations of standard guidelines⁽¹³⁾ to use different kinds of antimicrobials to treat gonorrhea. Regarding quinolones, our findings confirm the presence of resistant gonococci in the region⁽¹⁴⁾, but the frequency of resistance detected does not preclude their usage

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Table 1 – Antimicrobial susceptibility test of 83 clinical isolates of *N. gonorrhoeae*.

Antibiotics	Susceptibility test – Etest								
	Susceptible			Reduced sensitivity			Resistant		
	n	%	mic-µg/mL	n	%	mic-µg/mL	n	%	mic-µg/mL
Azithromycin•	79	95.2	0.16–0.250	3	3.6	0.5	1	1.2	1
Ceftriaxone♦	83	100	0.002–0.032	ND	ND	–	ND	ND	ND
Ciprofloxacin♦	81	97.6	0.002–0.008	0	0.0	–	2	2.4	6–8
Chloramphenicol•	67	80.7	0.047–0.5	13	15.7	0.7–1.5	3	3.6	2–4
Gentamicin*	83	100	0.016–4	0	0.0	–	0	0.0	–
Ofloxacin♦	81	97.6	0.002–0.125	0	0.0	–	2	2.4	6–8
Tetracycline♦	23	27.7	0.047–0.250	15	18.1	0.380–1	45	54.2	1.5–16
Penicillin♦	23	27.7	0.012–0.064	43	51.8	0.094–1	17	20.5	2–32

• WHO (2013)⁶, EUCAST (2014)⁸ and Van Dick et al. (2000)⁹; * Brown et al. (2010)¹¹; ♦WHO (2013)⁶; CLSI (2013)⁷; ND: not determined. The breakpoints have not been determined yet.

in therapy. There was no resistance to ceftriaxone in this study, but it is noteworthy that gonococcus with reduced sensitivity to this antibiotic⁽¹⁵⁾ (MIC of 0.064 µg/mL) had been reported in the region before⁽¹⁴⁾. Concerning azithromycin, the frequency of 1.2% of resistance enables the use of this antibiotic as a therapeutic option at the currently recommended dose⁽⁵⁾ if necessary. Thiamphenicol, a chloramphenicol derivate, has been successfully used in Brazil⁽¹⁶⁾ to treat gonorrhea, and its resistance below 5%⁽¹⁷⁾ makes it an alternative therapeutic option. The absence of resistance to gentamicin is encouraging, but an isolate showed MIC of 6 µg/mL, which needed monitoring. Studies with gentamicin were conducted in some countries^(18–20) and their good perspectives encourage its use for gonorrhea treatment⁽²¹⁾. Comparing our results with the other countries in South America⁽²²⁾, we notice that decrease of resistance to penicillin and tetracycline has also been detected. However, 11% of resistance to ciprofloxacin has been reported in 8 countries, as well as to azithromycin, gentamicin and chloramphenicol. As in our findings, no gonococcal with ceftriaxone resistance in those countries has been reported either. In Brazil, a single ciprofloxacin oral dose of 500 mg or 250 mg of intramuscular ceftriaxone is currently recommended as first-line treatment for gonorrhea⁽¹³⁾. In spite of the increasing ineffectiveness of antibiotics used in the treatment of gonorrhea in other countries⁽²³⁾, this study demonstrated that quinolones and ceftriaxone are still effective in the therapy of gonorrhea at FUAM. Chloramphenicol and gentamicin might be used as possible future therapeutic option⁽²⁴⁾ or in cases in which ciprofloxacin is not recommended as: pregnant women, patients under 18 years old and cephalosporin-allergic patients.

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