

CLINICAL EFFICACY OF THE VARIOUS DRUGS USED IN THE TREATMENT OF GONORRHOEA

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Background: Gonorrhoea is a purulent inflammation of mucus membrane of the genital tract and is a highly contagious sexually transmitted disease (STD) caused by the bacterium *Neisseria gonorrhoeae*. Both men and women can be infected through a variety of sexual contact behaviours including vaginal, anal or oral intercourses. This comparative study was carried out in New Gulail Polyclinic Jeddah, KSA from Jan 2003 to March 2004 to find the clinical efficacy of ciprofloxacin, ceftriaxone and spectinomycin, the three commonly used drugs, in the treatment of gonorrhoea. **Methods:** A total number of 300 patients suffering from gonorrhoea were included in this study. They were randomly divided into 3 groups of 100 patients each. Group-A patients were given Tablet Ciprofloxacin 500 mg, Group-B patients Injection Ceftriaxone 500 mg, and Group-C patients were put on Injection Spectinomycin 2 gm, all in stat dosage. On the 5th day following the treatment, all patients were re-examined and their clinical and laboratory findings were recorded and analysed. **Results:** On the 5th day following treatment the Group-A (n=100) showed 9 (9%) partial response and 11 (11%) cases showed no response to Ciprofloxacin. In the Group-B (n=100), 4 (4%) patients showed partial response and 6 (6%) patients showed no response to Ceftriaxone. In Group-C, out of 100 patients, 4 (4%) cases reported with partial response and 2 (2%) patients showed no response to Spectinomycin. The efficacy of these anti-microbial agents was the same in both the genders. **Conclusion:** Anti-microbial susceptibility of *N. gonorrhoeae* to various antibiotics is gradually decreasing. In order to ensure full cure, all gonorrhoea patients should be followed-up after a single dosage of any antibiotic. Further research should continue for newer, effective, and preferably oral medication for the treatment of gonorrhoea.

Keywords: *Neisseria gonorrhoeae*, sexually transmitted infection, STD, Sexually Transmitted Disease, Gonorrhoea

INTRODUCTION

Gonorrhoea is a purulent inflammation of mucus membrane of the genital tract and is a highly contagious sexually transmitted disease caused by the bacterium *Neisseria gonorrhoeae*.¹ Both men and women can be infected through a variety of sexual contact behaviours including vaginal, anal or oral intercourses.² The risk of infection for men who have unprotected vaginal intercourse with an infected partner is about 20% after a single exposure; whereas it is as high as 80% from men to women.³ The disease can also be transmitted to infant from infected mother during delivery causing ophthalmia neonatorum.² If maltreated or left untreated, both men and women suffer from many obvious complications like sterility, encephalitis, endocarditis and arthritis, and in women also complications like pelvic inflammatory disease (PID) which may cause ectopic pregnancy or infertility.⁴ Prostatic cancer risk is increased among men who report a history of gonorrhoea or syphilis.⁵

The clinical efficacy of the various drugs used in the treatment of gonorrhoea have been studied and reported at different geographical locations. These studies have shown decreasing antimicrobial susceptibility among *N. gonorrhoeae* at different geographical locations of the world.⁶⁻⁹

In Jeddah city, regarding the incidence of gonorrhoea there is no official statistics, but looking at the large number of such patients we are getting in our hospital the incidence of gonorrhoea looks quite high.

So, the purpose of this study is to assess the clinical efficacy of the three antimicrobial drugs like Ciprofloxacin, Ceftriaxone and Spectinomycin commonly used in the treatment of gonorrhoea.

MATERIALS AND METHODS

This study was conducted on permission of the Ethical Committee of New Gulail Polyclinic Jeddah, KSA. Informed consent was obtained from all subjects included in the study.

Three hundred patients coming to New Gulail Polyclinic Jeddah, KSA hospital during the period of January 2003 to March 2004 with the diagnosis of gonorrhoea were included in this study. Their history, clinical and laboratory findings were recorded into a specific proforma. The age of the subjects ranged was from 14–55 years, 229 were males and 71 were females. In male patients the clinical diagnosis was almost straight forward with cloudy urethral discharge and dysuria after a recent history of sexual exposure. Their urine examination and gram staining of urethral discharge were carried out to confirm the diagnosis. In all female patients high vaginal swabs were collected for

gram staining and/or culture for the confirmation. Because females often do not show any symptoms, the intracellular presence of gram negative diplococci in vaginal discharge was the main diagnostic criteria.¹⁰

The patients were randomly divided into 3 groups of 100 patients in each group with no regard for the gender. Group-A patients were given tablet Ciprofloxacin 500 mg orally, Group-B patients were given injection Ceftriaxone 500 mg I/V and Group-C patients were given injection Spectinomycin 2 gm I/M, all in a stat dosage.

After 5 days following the initial treatment all patients were re-examined clinically along with laboratory investigations and data were recorded for the analysis.

At follow up, urine microscopy, along with gram staining and microscopy of the prostatic fluid in males and vaginal secretion in females were carried out and recorded on a proforma.

RESULTS

All the 300 patients, 229 (76.33%) males and 71 (23.66%) females with the ages of 14–55 years, included in this study were clinically diagnosed cases of gonorrhoea.

Table-1 shows age and sex distribution of the patients, those between ages of 20–40 years were mostly the sufferers.

Table-2 shows clinical presentation of both male and female patients. The chief complaints of all male patients were typical thick yellow urethral discharge with dysuria. In females purulent and yellow vaginal discharge was the main complaint, while dysuria and lower abdominal discomfort was reported in 41 cases. Per vaginal examinations of those cases revealed that the primary site of infection was the endocervix. To confirm the diagnosis apart from urine routine examination, Gram staining of the vaginal discharge for the presence of gram negative diplococci in pus cells was carried out in all cases.

Table-3 shows clinical efficacy of antimicrobial drugs in gonorrhoea. The criteria used to differentiate between partial response and no response at all were symptoms of dysuria and/or urethral discharge in males and vaginal discharge in females, gram staining and microscopy of the prostatic fluid in males and vaginal secretion in females.

Group-A (n=100) patients were treated with Tab. Ciprofloxacin (500mg) single dose orally on the 1st day and on follow up at 5th day 80 (80%) patients reported with full cure. A total of 9 (9%) cases complained of dysuria only. In these cases gram staining of prostatic fluid in males and vaginal secretion in females revealed the presence of diplococci in pus cells (++) and urine examination showed pus cells (+++). We considered those cases as partially responsive, while the

rest of the 11 (11%) patients did not respond at all having no improvement in symptoms and laboratory investigations. Hence in a total of 20% of the patients, ciprofloxacin was clinically ineffective.

Group-B (n=100) patients received Injection Ceftriaxone 500 mg single dose I/V on the 1st day, and on follow up on 5th day 90 (90%) patients were found to be cured. Four (4%) patients complained of mild dysuria on 5th day. Gram staining, of prostatic secretion in males and vaginal secretions in females, revealed intracellular presence of gram-negative diplococci (+) and microscopic examination of urine showed pus cells (++) . These cases were considered to be partially responsive to that drug. The remaining 6 (6%) cases were absolutely non-responsive to this drug having complaints and laboratory findings same as before. Hence in a total of 10% of the cases in this group, ceftriaxone was clinically ineffective.

Group-C (n=100) patients were treated with Injection Spectinomycin (2 gm) single dose I/M on the 1st day, and on 5th day 94 (94%) patients were found to be fully cured. A total of 4 (4%) cases showed partial response to the drug with the complaints of mild dysuria only. Gram staining, of prostatic secretion in males and vaginal secretion in females of these patients revealed gram negative diplococci (+) and urine examination showed pus cells (++) . A total of 2 (2%) cases did not respond to this drug with both clinical as well as laboratory findings same as before. Hence in 6% of the cases spectinomycin was clinically ineffective. There was no difference in efficacy of the antimicrobial agents in both genders.

Table-1: Age and sex distribution of patients

Age (yrs)	Total		Males		Females		M:F
	No.	%	No.	%	No.	%	
<20	122	40.6	94	77.0	28	22.9	3.3:1
20–40	148	49.4	115	77.7	33	22.2	3.4:1
>40	30	10.0	20	66.6	10	33.3	2:1
Total	300	100	229	–	71	–	–

Table-2: Clinical presentation of the patients

Symptoms	Number	Males	%	Females	%
Urethral discharge	229	229	100	–	–
Vaginal discharge	71	–	–	71	100
Dysuria	270	229	85	41	57.7

Table-3: Clinical efficacy of antimicrobials in the treatment of gonorrhoea

Group	Drugs	Single Dose	Fully sensitive	Partially sensitive	Insensitive
A (n=100)	Ciprofloxacin	500 mg	80	9	11
B (n=100)	Ceftriaxone	500 mg	90	4	6
C (n=100)	Spectinomycin	2 gm	94	4	2

DISCUSSION

Gonorrhoea is highly contagious STD and is commonly referred to as ‘the clap’.¹ Due to effective public awareness campaigns in developed countries the incidence of gonorrhoea has declined significantly¹⁰, but in Jeddah the incidence is steadily rising where 80%

patients of gonorrhoea are foreigners, who either cannot afford, or are not allowed to bring their families and hence are involved in extramarital sex; and due to lack of public awareness campaigns on STD in the Kingdom.

If treated early, gonorrhoea can be cured. But unfortunately most of the women with gonorrhoea do not experience symptoms which could alert them to seek medical advice.³

This study indicated that most of the gonorrhoea victims are of 20–40 yrs of age and the number of male patients was significantly higher than females. All male patients had the complaints of urethral discharge with dysuria whereas the females reported with vaginal discharge and dysuria and it is in agreement with studies done in other countries.^{3,12–14}

Antimicrobial resistance (AMR) of *N. gonorrhoeae* is a major problem and is another cause of increase in the number of gonorrhoea cases in some parts of the world.¹³ For this reason its treatment is becoming difficult and expensive.¹⁶ The antimicrobial resistance of *N. gonorrhoeae* occurs as plasmid mediated resistance to Penicillin and Tetracycline,^{11,15,17} and chromosomally mediated resistance to Penicillin, Tetracycline, Spectinomycin and recently to Fluoroquinolones.^{17,19} The resistance to Fluoroquinolones is prevalent worldwide^{18,22} and in some countries it is no longer considered as the appropriate first line treatment for gonorrhoea.²⁴ In our study ciprofloxacin was ineffective in 20% of the cases either partially (9%) or completely (11%). The resistance to Ceftriaxone is reported in many studies,^{17,20,22} and it was ineffective in 10% of our cases. Spectinomycin was found clinically ineffective in 6% of the cases compared to other studies.^{20,21,25}

CONCLUSION

Antimicrobial susceptibility of *N. gonorrhoeae* to various drugs is decreasing. All gonorrhoea cases should be followed up after a single dose of any antibiotic. Further search to discover new effective, cheap, and preferably oral medications is required. Public awareness campaign can play an important role to decrease the incidence of gonorrhoea and its resistance to antibiotics.

REFERENCES

1. Britigan BE, Cohen MS, Sparling PF. Gonococcal infection; a model of molecular pathogenesis. *N Engl J Med* 1985;312:683–94.
2. Woods CR. Gonococcal infections in neonates and young children. *Semin Pediatr Infect Dis* 2005;16:258–70.
3. Barlow D, Phillips I. Gonorrhoea in women—diagnostic, clinical and therapeutic aspects. *Lancet*, 1978;I(8067):761–4.
4. Johnson RA. Diagnosis and treatment of common sexually transmitted diseases in women. *Clin Cornerstone* 2000;3(1):1–11.
5. Hayes RB, Pottern LM, Strickler H, Rabkin C, Pope V, Swanson

- GM, *et al.* Sexual behaviour, STDS & risks of prostatic cancer. *Br J Cancer* 2000;82:718–25.
6. Knapp JS, Wongba C, Limpakarnjanarat K, Young NL, Parekh MC, Neal SW, *et al.* Antimicrobial susceptibilities of strains of *N. Gonorrhoeae* in Bangkok, Thailand 1994–1995. *Sex Transm Dis* 1997;24(3):142–8.
7. Johnson SR, Morse SA. Antibiotic resistance in *N. Gonorrhoeae*: Genetics and mechanisms of resistance. *Sex Transm Dis* 1988;15(4):217–24.
8. Zheng HP, Cao WL, Wu XZ, Yang LG. Antimicrobial susceptibilities of strains of *N. Gonorrhoeae* strains isolated in Guangzhou, China. 1996–2001. *Sex Transm Infect* 2003;79(5):399–402.
9. Rahman M, Sultan Z, Monira S, Alam A, Nessa K, Islam S, Antimicrobial susceptibility of *N. Gonorrhoeae* isolated in Bangladesh (1997 to 1999), rapid shift to fluoroquinolone resistance. *J Clin Microbiol* 2002;40(6):2037–40.
10. Jephcott AE. Microbiological diagnosis of gonorrhoea. *Genitourin Med* 1997;73:245–52.
11. Su X, Hutapea N, Tapsall JW, Lind I. Plasmid-mediated resistance of *Neisseria gonorrhoeae* strains isolated from female sex workers in North Sumatra, Indonesia, 1996. *Sex Transm Dis* 2003;30(2):178–82.
12. National institute of Allergy and Infectious Diseases; National institutes of Health, Department of Health and Human Services (2001-07-20). ‘Workshop Summary; Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention’ Hyatt Dulles Airport, Herndon, Virginia, pp 14.
13. Annual report of the Australian Gonococcal Surveillance Program. 1998. *Commun Dis Intell* 1999;23(7):193–7.
14. Herida M, Srdnaoni P, Goulet V. Gonorrhoea Surveillance System in France: 1986–2000. *Sex Transm Dis* 2004;31(4):209–14.
15. Bhuiya BU, Rahman M, Miah MRA, Nahar S, Islam N, Ahmed M, *et al.* Antimicrobial Susceptibilities and Plasmid Contents of *Neisseria gonorrhoeae* Isolates from Commercial Sex Workers in Dhaka, Bangladesh: Emergence of High-Level Resistance to Ciprofloxacin. *J Clin Microbiol* 1999;37(4):1130–6.
16. Centers for Disease Control & Prevention. ‘Gonorrhoea among men who have sex with men: 1993–96. *JAMA* 1997;278: 1228–9.
17. Ison CA, Martin IM. Gonorrhoea in London: Usefulness of First Line Therapies. *Sex Transm Inf* 2002;78:106–9.
18. Heffernan H, Brokenshire M, Woodhouse R, MacCarthy A, Blackmore T. Antimicrobial susceptibility among *N. gonorrhoeae* in New Zealand in 2002. *NZ Med J* 2004;117(1191):U817.
19. Ng LK, Martin I, Lau A. Trends of chromosomally mediated antimicrobial resistance in *N. gonorrhoeae* in Canada. *Sex Transm Dis* 2003;30(12):896–900.
20. Collier AC, Judson FN, Murphy VL, Leach LA, Root CJ, Handsfield HH. Comparative study on Ceftriaxone and Spectinomycin in the treatment of uncomplicated gonorrhoea in women. *Am J Med* 1984;77 (4c):68–72.
21. Eason CS, Forster GE, Walker GD, Ison CA, Harris JR, Munday PE. Spectinomycin as initial treatment for gonorrhoea. *BMJ* 1984;289 (6451):1032–4.
22. Ye S, Su X, Wang Q, Yin Y, Dai X, Sun H. Surveillance of antibiotic resistance of *N. gonorrhoeae* isolates in China, 1993–98. *Sex Transm Dis* 2002;29:242–5.
23. Echolas PM, Hyed A, Okeefe BJ, Schacht P. Single dose Ciprofloxacin for the treatment of uncomplicated gonorrhoea. *Sex Transm Dis* 1994;21(6):345–52.
24. Nissinen A, Jarvinen H, Jahkola M, Limatainen O. Antimicrobial resistance in *N. gonorrhoeae* in Finland, 1976–5. *Sex Transm Dis* 1997;24:576–81.
25. Stapinski A, Gede K. Treatment of gonorrhoea with Spectinomycin. *Pregl Dermatol* 1983;70(2):115–20.

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