Original Article

Efficacy of Spectinomycin versus Ceftriaxone in the Treatment of Gonorrhea

Treatment of Gonorrhea

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ABSTRACT

Objective: The aim of this study was to compare the efficacy of spectinomycin verses ceftriaxone in the treatment of gonococcal infection.

Study Design: Observational Study

Place and Duration of Study: This study was conducted at the Nowshera Medical College, Nowshera Pakistan during the period of January 2017 to December 2018.

Materials and Methods: Purposive sampling technique was used to enroll the patients. Two hundred patients were enrolled for the study. The patients were randomly divided into two groups of 100 patients each. Group A was given injection spectinomycin 2gm intramuscularly and Group B was given Injection Ceftriaxone 500mg intramuscularly in single dosage. All the patients were reexamined after 5 days and their clinical and laboratory findings were recorded and analyzed.

Results: The patients in Group A (n=100) who were given spectinomycin Showed 94% full response, 4% partial response and 2% no response, while the patients in Group B (n=100) who were given ceftriaxone showed 90% full response, 4% partial response and 6% showed no response at all. Furthermore, increasing age does not play any statistically significant role in etiology of gonorrhea infection.

Conclusion: There is no statistically significant difference between cure rates of spectinomycin and ceftriaxone. However, due to pain at injection site, less effective in pharyngeal gonorrhea, contraindication in pregnancy and breast feeding, the spectinomycin may be reserved only for ceftriaxone resistant cases.

Key Words: Neisseria Gonorrhea, Spectinomycin, Ceftriaxone

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INTRODUCTION

Gonorrhea is known to mankind since medieval time. It is a purulent inflammation of the urogenital tract caused by Neisseria gonorrhea, a gram- negative diplococcic and is highly contagious among the sexually transmitted diseases [1]. Presence of risk factors like unprotected sex, multiple sexual partners and previous history of infection with N. gonorrhea in both genders are responsible for its transmission. It can also be transmitted vertically to baby from infected mother during delivery causing ophthalmic neonatorum [2,3].

The chances of transmission of infection through single unprotected sexual contact from male to female is 80% while female to male risk of transmission is 20% [4]. if maltreated or left untreated, both men and women suffer from many obvious complications like epididymitis, encephalitis, endocarditis and arthritis, cervicitis leading to pelvic inflammatory disease (PID) which may cause ectopic pregnancy, peri hepatitis (Fitz Hugh Curtis syndrome) or infertility [3-5]. The association between gonorrhea and prostatic cancer is widely studied and no direct association has been found so far but it is proved that the risk of prostatic cancer is increased among men who report a history of gonorrhea or syphilis [6] . In the pre antibiotics era, various herbs like Cubebs (Indonesian pepper), Metals like Arsenic, Bismuth, Antimony, Gold, Silver nitrate were used for gonorrhea [7]. The advent of antibiotic in 1937, which might be tagged as sulphonamide year, revolutionized the field of chemotherapy. Sulphonamide established an effective chemotherapy against gonorrhea for some time [8]. Penicillin since its discovery in 1940 remained the mainstay of treatment for gonorrhea till 1980, when the first gonococcal isolates were identified resistant to penicillin. Then the clinical efficacy of the various drugs used in the treatment of gonorrhea have been studied and reported at different geographical locations. These studies have shown decreasing antimicrobial susceptibility among N. gonorrhea at different geographical locations of the world [9]. The emergence of antibiotics resistant strains of gonorrhea to sulpha

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drugs, penicillin, tetracycline, macrolides and quinolones is a growing challenge. In 1983 local epidemic caused by penicillin resistant strains were successfully treated by using Spectinomycin [10]. Since then spectinomycin and ceftriaxone are used more confidently in the treatment of gonorrhea with minimal resistance.

Spectinomycin is an aminocyclitol antibiotic derived from Streptomyces spectabilis, introduced in 1961 was used in patients allergic or resistant to penicillin and cephalosporin. Spectinomycin acts by inhibiting protein synthesis and elongation by binding to the bacterial 30S ribosomal subunit and interfering with peptidyl tRNA translocation. A mutation in rpsE, the gene for ribosomal protein S5, prevents the binding of spectinomycin. Spectinomycin is used for gonococcal urethritis, cervicitis and proctitis but is not effective against gonococcal pharyngitis. It is reserved for patients who cannot be treated with ceftriaxone, cefixime, azithromycin or doxycycline. Common side effects include pain at the area of injection, rash, nausea, fever and disturbed sleep pattern. It is generally safe to use during pregnancy.

Ceftriaxone a third-generation broad spectrum cephalosporin introduced in United States in 1984 and approved for respiratory, genitourinary, gastrointestinal, meningococcal, gonococcal and soft tissues infections, respectively. Adverse effects reported are hypersensitivity, pancytopenia, glossitis and pseudo-cholelithiasis[11]. There is a tentative evidence that ceftriaxone is relatively safe during pregnancy and breastfeeding rather than spectinomycin.

MATERIALS AND METHODS

This study was conducted in Nowshera Medical College, Nowshera after permission from institutional ethical committee. Informed consent was taken from all subjects included in the study before administration of the drugs.

Two hundred patients coming to medical and gynae departments during the period of January 2017 to December 2018 with the diagnosis of gonorrhea were included in this study. Their history, clinical and laboratory findings were recorded on a specific proforma. The age of the subjects was ranged between 14–55 years of which 152 were males and 48 were females. In male patients, the clinical diagnosis was almost straightforward with cloudy urethral discharge and dysuria after a recent history of sexual exposure [12]. Urine examination and gram staining of urethral discharge were carried out to confirm the diagnosis. High vaginal swabs of all female patients were collected for gram staining and culture confirmation. Because females often do not show any symptoms, the intracellular presence of gram-negative diplococcic in vaginal discharge was the main diagnostic criteria. The patients were randomly divided into 2 groups of 100 patients without any regard for the gender. Group-A patients were given single dose spectinomycin 2 grams intramuscularly, Group-B patients were given single dose Ceftriaxone 500 mg intramuscularly. It was thought that I/M injection has depot effect in gonococcal infection but it is reported by Workowski in 2010 that ceftriaxone I/M and I/V has the same plasma concentration after 24 hours. After 5 days following the initial treatment all the patients were re-examined clinically along with laboratory investigations and data was 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 200 patients in the study including 52 males (76.33%) and 48 females (23.66%) with age range between 14–55 years, were clinically diagnosed cases of gonorrhea. Table-1 shows age and gender distribution of the patients and also impact of age on the occurrence of gonorrhea

To confirm the diagnosis, apart from urine routine examination, gram staining of the vaginal discharge for the presence of gram-negative diplococcic in pus cells was carried out in all female patients. Table-III shows clinical response of antimicrobial drugs in gonorrhea. 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 who were given inj. spectinomycin on the first day, were followed up on 5th day. 94 patients (94%) reported with full cure. A total of 4 (4%) cases complained of dysuria only.

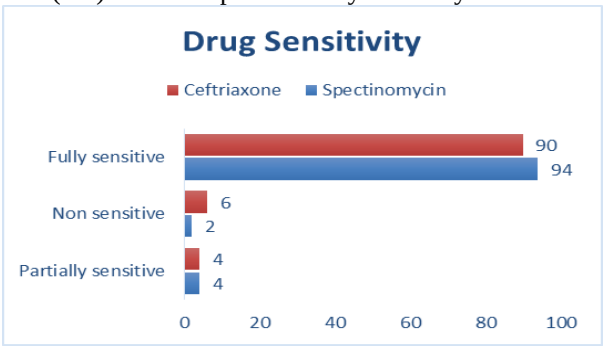

Figure No.1: Drug sensitivity response of ceftriaxone and spectinomycin

Table No. 1: Age and sex distribution of Patients

Age in years	Total	Male	Female	P-value	OR(95%CI)
< 20	81	62	19	Reference	Reference
20-40	99	77	22	0.98	0.93(0.46-1.87
> 40	20	13	7	0.44	1.75(0.615.03)

In these cases, gram staining of prostatic fluid in males and vaginal secretion in females revealed the presence of diplococcic in pus cells (++) and urine examination showed pus cells (+++). We considered those cases as partially responsive, while the rest of the 2 patients (2%) did not respond at all having no improvement in symptoms and laboratory investigations. Hence in a total of 6% of the patients, spectinomycin was clinically ineffective. Group-B (n=100) patients received Injection Ceftriaxone 500 mg single dose I/M on the 1st day, and were followed up on 5th day. 90 patients (90%) were found to be cured. Four patients (4%) 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 diplococcic (+) and microscopic examination of urine showed pus cells (++). These cases were considered to be partially responsive to ceftriaxone.

The remaining 6 cases (6%) 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, there was no response. However, there was no statistically significant difference when we compared the use of spectinomycin versus ceftriaxone in the treatment of gonorrhea

Table No. 2: Clinical efficacy of antimicrobials in the treatment of gonorrhea

Groups	Drugs	Single dose	Fully sensitive	Partially sensitive	Non sensitive	p-value
A(n=100)	Spectinomycin	2 gm. (I/M)	94 (94%)	04 (4%)	02 (2%)	**NS***
B(n=100)	Ceftriaxone	500mg (I/M)	90 (90%)	04 (4%)	06 (6%)	
NS: Non significant						

DISCUSSION

Gonorrhea is highly contagious Sexually Transmitted Disease and due to its causation and specific clinical features, it was usually referred to as "the clap" and "the drip" before the advent of antibiotics [1]. Due to effective public awareness campaigns in the developed countries the incidence of gonorrhea has declined significantly but rising in some developing countries due to lack of public awareness campaigns. According to World health organization report the number of gonorrhea cases were 106 million in 2008 reduced to78 million in 2016 [13].

Most of the gonorrhea victims in this study are of 20–40 years of age and the number of male patients significantly higher than females producing signs symptoms of urethral discharge with dysuria by males and vaginal discharge with dysuria by females is consistent with studies done in other countries [14-16].

If treated early, gonorrhea can be cured. But unfortunately most of the women with gonorrhea do not experience symptoms which could alert them to seek medical advice.[3] No follow up visits after single dose of antibiotics, improper choice of antibiotics and emergence of resistant cases of gonococci are other causes of increasing cases of gonorrhea in some parts of the world[17]. The antimicrobial resistance of N. gonorrhea occurs as plasmid mediated resistance to Penicillin and Tetracycline [18-19] and chromosomally mediated resistance to Penicillin, Fluor quinolones, Tetracycline and Spectinomycin [19-20]. In a study conducted by Bala M in 2005 reported occasional spectinomycin resistant isolates from U.S, India and China. Our study showed spectinomycin susceptibility in 94% cases and non-responsiveness was noted in 6% cases. Spectinomycin in 6% of the cases is either partially (4%) or completely (2%) resistant. It was reported by Hands field that Neisseria gonorrhea had been eradicated in 99% cases by administering 125mg of ceftriaxone to155 patients. By using 500mg ceftriaxone, our study showed 90% eradication of the gonococci and showed resistance in 10% cases. A study conducted by Collier in 1984 showed that spectinomycin eradicated 96% anorectic and 50% pharyngeal gonorrhea, while ceftriaxone eradicated 98% anorectic and 90% pharyngeal. Judson in 1985 reported that both spectinomycin and ceftriaxone cured anorectic gonorrhea 100% and pharyngeal gonorrhea 43% and 94% respectively. Keeping in view all these studies, if ceftriaxone is used in high doses and is combined with other antibiotics it will be highly effective than spectinomycin [21 22 23].

CONCLUSION

Although spectinomycin is more effective than ceftriaxone in the treatment of uncomplicated gonorrhea but because of scarce availability, pain at the injection site and less effect on pharyngeal gonorrhea it should be reserved only for ceftriaxone resistant gonorrhea or patients hypersensitive to other antibiotics. Furthermore, ceftriaxone is relatively safe during pregnancy and breast feeding as compared to spectinomycin. Based on previous studies, being broad spectrum, effective against all anatomical sites and easily available, ceftriaxone should be used the drug of first choice for gonorrhea.

Author's Contribution:

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Drafting:	Shandana Altaf
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Revisiting Critically:	Tayaba Basharat Shandana Altaf
Final Approval of version:	Tayaba Basharat

Conflict of Interest: The study has no conflict of interest to declare by any author.

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