

A CLINICAL TRIAL OF MINOCYCLINE IN UNCOMPLICATED GONOCOCCAL URETHRITIS

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In this open randomized comparative study, either 200 mg or 300 mg minocycline was administered in a single supervised oral dose to 45 adult male patients of acute gonococcal urethritis. Diagnosis was made clinically as well as on smear and culture for N. gonorrhoea. Patient was assessed again on days 3 and 7. In the 37 evaluable cases a cure rate of 63% was achieved with a 200 mg dose, and 67 with a 300 mg dose. Twenty one patients had a positive culture at the beginning of therapy, 12 of these were subjected to sensitivity by Kirby Bauer method. Three patients showed resistance to minocycline but only one of them failed the study. Both the doses were well tolerated. Single dose of minocycline can be considered as one more alternative therapy for uncomplicated gonorrhoea in males.

Key words : Minocycline, Gonorrhoea, Neisseria

Introduction

The treatment failure for the control of gonorrhoea is increasing because of a number of factors. The most important factor is treatment resistance to available antibiotics i.e. Penicillin, tetracycline, erythromycin, fucidic acid, and rifampicin.¹ Minocycline is the most effective tetracycline against *Neisseria gonorrhoea*.² This is given in a dose of 100 mg twice daily for seven days for uncomplicated acute urethritis.

The present approach for the management of STD is single dose oral supervised therapy. The efficacy of single dose therapy with minocycline has also been documented earlier,³⁻⁵ with variable sensitivity. In this present

study, the sensitivity, efficacy and safety of single oral dose of 200 mg and 300 mg minocycline was evaluated in patients of uncomplicated acute gonococcal urethritis, residing in Delhi metropolis.

Material and Methods

The trial was carried out in the STD Clinic of Dr. Ram Manohar Lohia Hospital, New Delhi. A total of 45 healthy young adult males were included in this study. The diagnosis was made on the basis of clinical signs and symptoms suggestive of gonorrhoea, gram stained smear of the discharge showing gram-negative intracellular diplococci on microscopy and positive culture for *Neisseria gonorrhoea*. The patients were randomly assigned to one of two treatment groups. Group A patients received supervised 200 mg minocycline orally as a single dose and group B patients received supervised

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300 mg minocycline orally in a single dose. The clinical signs and symptoms i.e. pus discharge per urethra, inflamed meatus, burning micturition were recorded in the proformas on day 0,3,7.

Two glass test, gram staining for intracellular diplococci, culture for *Neisseria gonorrhoea* were done at every visit. Side effects, if any, were recorded at each visit. All the patients were subjected to VDRL and ELISA test for HIV 1 and 2. The patient was considered cured when there was absence of pus discharge per urethra, clear two glass test and bacteriological negativity both on gram-stain preparation and on culture.

Results

A total of 45 male patients of uncomplicated gonococcal urethritis were included in this study. The minimum age was 16 years and maximum was 46 years. Out of 45 patients, 22 (49%) were in the sexually active group of 15 to 25 years, 18 (40%) were in the age group of 26 to 35 years and 5 (11%) were in the age group of 36 to 45 years. Of the 45 patients, 37 (82%) turned up for complete follow up. 19

patients were in the group A and 18 were in the group B. (Table I). All cases had positive gram staining for gram negative intracellular diplococci in urethral smear preparation at day 0. A total clinical and bacteriological cure was achieved in 24 (65%) patients, 12 (63%) in group A and 12 (6%) in group B.

Serological tests for HIV 1 and 2 were negative in all. The culture for *Neisseria gonorrhoea* from the pretreatment urethral specimen was positive in 21 (47%) patients. Sensitivity of the isolated strain for minocycline was tested in 12 patients and three were found resistant to minocycline in vitro. Out of these three cases, one was cured both clinically and bacteriologically (microscopic and culture), one patient after initial improvement was lost for follow-up and the third case did not improve both clinically and bacteriologically. Minocycline was well tolerated by all patients. No side effects were reported by any patient.

Discussion

Since *N. gonorrhoea* shows a variable response to treatment from year to year and at times may develop relative or absolute resistance to formerly effective antibiotics, there is a constant need to evaluate the efficacy of different antibiotics as well as different schedules of the same antibiotics.⁶ Minocycline (an alkylated amino-tetracycline) is a potent, stable, less toxic drug and has a broad spectrum of activity. The drug was introduced by Lederle Laboratories in 1967.⁴ Efficacy of a single dose therapy of gonorrhoea with minocycline has been tested before. Thatcher et al,³ obtained a cure rate of 92.2% with a single dose of 200 mg and 95.5% with 300 mg as well as 400 mg.

Table I - Results of minocycline therapy in 2 groups

	Minocycline 200mg (Group A)	Minocycline 300mg (Group B)
Bacteriological cure	13	12
Clinical cure	12	12
Failure	6	6
Defaulters	5	3
Total	24	21

Jog et al,⁵ obtained a cure rate of 92% with a single dose of 300 mg minocycline. Masterton et al,⁵ used 300 and 400 mg of minocycline to achieve a success rate of 97% and 95% respectively. Baytch⁷ noted only 62% results with 300 mg single dose. Duncan et al tried 300 and 400 mg single dose and their results varied from 25% to 75%.⁸ In the present series, a single dose of 200 mg and 300 mg minocycline achieved a cure rate of 63% and 67% respectively, thus confirming earlier results.

Out of 21 cases where *N.gonorrhoea* could be cultured only 12 cases were subjected to a sensitivity test using the Kerby Bauer method. Of these 21 cases, 3 showed resistance. However, of these three cases one patient showed cure, another showed significant improvement before being lost for follow up and only one failed, indicating that there was no correlation between in vivo and in vitro findings. Jog et al,⁵ have made similar observations in their study.

Although it is an accepted fact that resistance to an antibiotic increases over the years due to indiscriminate use and cross resistance, the same may not be the case with minocycline.

Concomitant, undiagnosed non-gonococcal urethritis may account for a few of the 35% failure in our study. One case that showed bacteriological but not clinical cure was later on treated with azithromycin for NGU. Two of the eight defaulters who were followed up until day 3 showed bacteriological cure but only slight improvement in clinical signs and symptoms. Re-exposure and loss of many patients to follow-up could be other confounding variables.

It is worth noting that even a single dose of 300 mg of minocycline was well tolerated by the patients.

In conclusion, we tend to agree with Brogden et al,¹⁰ that minocycline can only be considered a possible alternative to oral and semi-synthetic penicillin with probenecid in case of uncomplicated gonorrhoea in persons allergic to the penicillins and when the organism is sensitive to minocycline.

References

1. Sparling PF. Antibiotic resistance in *Neisseria gonorrhoeae*. *Med Clin NA* 1972; 56:1133-1152.
2. Martin JE Jr., Lester A, Kellogg DS, et al. In vitro susceptibility of *Neisseria gonorrhoeae* to non-antimicrobial agent. *Appl Microbiol* 1969;21:18-25.
3. Thatcher RW, Pazin G, Domesick G. Gonorrhoeal urethritis in males, treated with a single oral dose of minocycline. *Public Health Report* 1970;85:160-162.
4. Cunha BA, Comer JB, Jonas M. The tetracyclines. *Med Clin N Amer* 1982; 66: 293 - 302.
5. Masterton G, Schofield CB. Minocycline hydrochloride as a single dose oral treatment of uncomplicated gonorrhoea in men. *Br J Vener Dis* 1976; 52: 43 - 45.
6. Pariser H, Marino AF. Treatment of gonorrhoea with minocycline. *South Med J* 1975; 68: 1210.
7. Baytch H. Minocycline in single dose therapy in the treatment of gonococcal urethritis in male patients. *Med J Austr* 1974; 1: 831 - 832.
8. Duncan WC, Glicksman JM, Knox JM, et al. Treatment of gonorrhoea with a single oral dose of minocycline. *Br J Vener Dis* 1971; 47: 364 - 367.
9. Singh OP, Prakash O, Kandhari KC. A comparative study of enriched culture media in the diagnosis of gonorrhoea. *Indian J Dermatol Venereol* 1972; 38: 280 - 236.
10. Brogden RN, Speight TM, Avery GS. Minocycline: A review of its antibacterial and pharmacokinetic properties and therapeutic use. *Drugs* 1975; 9: 251- 291.