

## SUSCEPTIBILITY OF NEISSERIA GONORRHOEAE TO PENICILLIN AND CO-TRIMOXAZOLE IN VITRO AND THEIR COMPARATIVE EFFICACY IN GONORRHOEA

R. K. PANDHI \* R. A. BHUJWALA †  
S. C. SHUKLA \* SHRINIWAS AND L. K. BHUTANI †

### Summary

19.6% and 3.0% isolates of *N. gonorrhoeae* were found respectively to be resistant to penicillin and co-trimoxazole during the period of this study.

Penicillin (procaine penicillin, 1.5 mega units + crystalline penicillin, 1.5 mega units) given intra-muscularly as a single injection was found to be slightly more effective compared to co-trimoxazole (Septran) 4 tablets twice daily X 2 days. Co-trimoxazole is a good alternative drug to penicillin and can be used in patients who are either allergic to penicillin or where penicillin has failed to cure the gonococcal infection. Co-trimoxazole was quite effective in the treatment of gonococcal subacute prostatitis.

Penicillin continues to be the drug of choice in the treatment of gonorrhoea, the world over. The emergence of relatively resistant strains in various parts of India<sup>1,4</sup> and various other countries<sup>5</sup> and penicillinase producing *Neisseria gonorrhoeae* in other parts of the world<sup>6</sup> poses a serious problem in the treatment and control of gonorrhoea. Hence, there is a need for regular monitoring and reviewing the resistance of gonorrhoeae to penicillin at periodic intervals in a particular

area and to assess the therapeutic efficacy of the penicillin dosage employed, and/or to consider the use of alternative chemotherapeutic agents for the treatment of gonorrhoea.

The present study was undertaken to find out the *in vitro* sensitivity of *N. gonorrhoeae* to penicillin and co-trimoxazole (Septran) and to compare the efficacy of these two drugs in the treatment of gonorrhoea, in patients attending the Sexually Transmitted Diseases Clinic, Department of Dermato-Venereology, All India Institute of Medical Sciences, New Delhi.

### Subjects and Method

The clinical diagnosis of gonorrhoea was in every case confirmed by smear examination, culture on chocolate agar and Thayer Martin medium<sup>7</sup> with the addition of polymyxin B (25 units/ml) and nystatin (12.5 units/ml) as modification, oxidase production and sugar fermentation tests.

\* Department of Dermato-Venereology

† Department of Microbiology

All India Institute of Medical Sciences,  
New Delhi-110029

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The *in vitro* sensitivity of isolated strains of *N. gonorrhoeae* to penicillin was determined by estimating the minimum inhibitory concentration (MIC) of penicillin by plate dilution method. A strain was considered to be sensitive if the MIC was < 0.12 iu/ml.

Disc diffusion technique<sup>8</sup> was used for testing the sensitivity to co-trimoxazole, employing 25 mcg of co-trimoxazole per disc on Wellco test sensitivity agar supplemented with 10% lysed blood. Strains with a zone of inhibition measuring more than 22 mm were regarded as sensitive, those having a zone less than 14 mm as resistant, and those having a zone 14-22 mm as partially sensitive as per the recommendations of Burroughs Wellcome Laboratories, England.

The patients were assigned at random to one of the following treatment schedules :-

1. Penicillin: Inj. procaine penicillin-1.5 megaunits + crystalline penicillin 1.5 megaunits given intramuscularly after a test dose.
2. Co-trimoxazole (Septran-each tablet containing 400 mg of sulphamethoxazole + 80 mg of trimethoprim), 4 tablets twice daily for 2 days.

Patients were examined on day 2nd, 4th, 7th and 14th or after upto 3-4 weeks. Urethral or cervical discharge or scrapings, were collected in duplicate, one for smear and the other for culture examination on each visit. Blood VDRL was done before starting the treatment and then after 3-4 weeks interval for exclusion of syphilis.

**Results**

97 out of 107 patients completed the follow up for a minimum of 2

weeks. 57/97 received co-trimoxazole and 40/97 penicillin therapy. Majority of patients, 75/97 (77.3%) were in the age group of 21-30 years. Only 3 females with culturally proved gonococcal cervicitis were seen during the period of study. 69/97 (71.1%) patients were unmarried. About 3/4th of the patients (73/93) reported within 1-10 days of beginning of symptoms. Most of the patients 92/97 (94.8%) had anterior urethritis and 2 (2.1%) had subacute prostatitis and 3 females were suffering from cervicitis.

86/107 (80.4%) strains were found to be sensitive to penicillin and 21/107 (19.6%) strains were relatively resistant to penicillin. In 5 out of these 21 strains, the MIC was found to be less than 1.00 unit and more than 0.5 unit of penicillin and 3 strains were even resistant to 2.0 units of penicillin (Table 1). 97 out of 100 (97%) strains of *N. gonorrhoeae* were found to be sensitive to co-trimoxazole *in vitro*.

TABLE 1

Showing the pattern of *in vitro* sensitivity of *N. gonorrhoeae* to penicillin

MIC (iu/ml)	Number of strains		Total
	Sensitive	Resistant	
0.03	46 (42.1%)		46
0.06	26 (24.3%)		26
0.12	14 (13.1%)	21 (19.6%)*	35
Total	86 (79.5%)	21 (19.6%)	107

* Sensitive to 0.24 units (MIC < 0.24 units and > 0.12 units)	13
Sensitive to 0.5 units (MIC < 0.5 units and > 0.24 units)	1
Sensitive to 1.0 unit (MIC < 1.0 units and > 0.5 units)	2
No further sensitivity done	2
Resistant to 2.0 units	3
No further sensitivity done	
Total	21

The failure rate with penicillin and co-trimoxazole therapy was found to

TABLE 2

Showing the results of the treatment

Type of treatment	Total number of cases	Number of cases cured	Percentage of cure	Percentage of failure
Co-trimoxazole *	57	47	82.5	17.5
Penicillin †	40	35	85.5	12.5

\* Dose of co-trimoxazole 4 tab. twice a day for 2 days

† Dose of penicillin - Inj procaine penicillin 1.5 mega units + crys alline penicillin 1.5 mega units I. M. single injection.

be 12.5 and 17.5% respectively (Table 2). 5/10 cases of co-trimoxazole failure were lost to follow up one each out of five remaining co-trimoxazole failure cases responded to penicillin and erythromycin and 3 others got cured by tetracycline therapy (Table 3).

3/5 penicillin failure cases were cured by co-trimoxazole therapy, the fourth patient did not respond to co-trimoxazole but was cured by tetracycline (2 g/day x 2) and the fifth was lost to follow up (Table 4).

In all the 10/57 co-trimoxazole failure cases, the organisms were found to be sensitive to the drug *in vitro*. The three cases, where the organisms were resistant to co-trimoxazole *in vitro*, had anyway been given penicillin in the randomized

therapy schedule. 6/40 patients were cured by penicillin therapy, though the MIC was found to be more than 0.12 units of penicillin and in 3/40 cases, the penicillin therapy was a failure, even though the MIC was less than 0.12 units of penicillin.

### Comments

Results of *in vitro* sensitivity from different parts of the world as well as from different centres in India have shown an alarmingly high incidence of strains of *N. gonorrhoeae* relatively resistant to penicillin<sup>1,3,5</sup>. In the present study, 19.6% of strains of *N. gonorrhoeae* were found to be having MIC of penicillin > 0.12 iu/ml. We have recently reported on the prevalence of relatively resistant strains (> 50.0%) with MIC > 0.12 iu/ml from

TABLE 3

Showing follow up of co-trimoxazole failure cases

Total number of co-trimoxazole failure cases	10/57
* Number of cases lost to follow-up	5/10
Number of cases cured by penicillin	1/10
† Number of cases cured by tetracycline	3/10
‡ Number of cases cured by erythromycin	1/10

\* 1/5 patient was allergic to penicillin and he did not respond to tetracycline (2g/day X 2 days). After that he was lost to follow-up.

† These 3 cases were allergic to penicillin, hence treated with tetracycline (2g/day X 2 days).

‡ This patient did not respond to 4 g of tetracycline or 1.2 g of doxycycline, was cured by 15 g of erythromycin and was allergic to penicillin.

TABLE 4

Showing follow up of penicillin failure cases

Total number of penicillin failure cases	5/40
Number of cases lost to follow up	1/5
Number of cases cured by co-trimoxazole	3/5
Number of cases cured by tetracycline	1/5

the isolates made during the year 1973-79<sup>4</sup>. Earlier, 90% and 56% of isolates in Madras and Bombay were reported to be having MIC of penicillin  $> 0.12$  iu<sup>1,2</sup>. Hence there is a need for monitoring the sensitivity pattern of *N. gonorrhoeae* at periodic intervals from different parts of country. 97% strains of *N. gonorrhoeae* were found to be sensitive to co-trimoxazole in the present study. Sowmini et al<sup>9</sup> from Madras reported 88.8% of strains to be sensitive to co-trimoxazole.

The results of the present study showed that penicillin therapy in the dosage of 1.5 mega units of procaine penicillin + 1.5mega units of crystalline penicillin, given as a single injection, is better than co-trimoxazole therapy (4 tablets of co-trimoxazole twice daily x 2 days), showing a failure rate of 12.5% as against 17.5% with co-trimoxazole. The latter was reported to be a highly effective drug in the treatment of gonorrhoeae in other countries and by several workers<sup>10,12</sup>. From India, Reddy et al<sup>13</sup> reported a failure rate of 8.7% with co-trimoxazole (Septran); but the number of cases included in that study was only 23, rather small for drawing any conclusion. Sowmini et al<sup>9</sup> reported a failure rate of 12.0% with co-trimoxazole when given as 4 tablets twice daily for 5 days. In the present study, though co-trimoxazole therapy resulted in a failure rate of 17.5% in acute gonorrhoea, 3/5 penicillin failure cases did respond to co-trimoxazole therapy. In addition, co-trimoxazole given for 4 days to 2/2 cases of subacute gonoco-

cal prostatitis, seen during the course of this study, completely cured the patients. Both these observations are quite encouraging.

The earlier results of treatment with penicillin in dosage of procaine penicillin 1.2 mega units and 2.4 mega units from this very clinic gave a failure rate of 28.9% and 17.5% respectively<sup>14</sup>. The dosage of penicillin employed in the present study gave slightly better results compared to 2.4 mega units used earlier.

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## FALSE

Fluorescent patterns of immunoglobulin and complement staining at the dermo-epidermal junction in rosacea have been described by several authors<sup>1,2</sup> but denied by few<sup>3</sup>. It has been shown that all conditions with telangiectasia can cause positivity of the BZ; but this may be false positivity and could be due to oedema and the infiltrate which by compressing the dermal components of the papilla producing a band-like effect<sup>4</sup>. Even though many workers have demonstrated the BZ positivity, the etiological significance of this is far from clear.

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