

USE OF CEFOTAXIME IN GONORRHOEA

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SYNOPSIS

Cefotaxime (Claforan), a third generation cephalosporin, in single intramuscular doses of 500 mg given concomitantly with probenecid 1 gm orally, was used to treat 100 men and women with gonorrhoea caused by penicillinase-producing *Neisseria gonorrhoeae* (PPNG) and non-PPNG. The overall cure rate was 99%. Cure rates for PPNG and non-PPNG infections were 98.2% and 100% respectively. The tolerance to the drug was good. It can be concluded that this drug is effective and safe in treating both PPNG and non-PPNG infections.

INTRODUCTION

Since the first introduction of penicillin in 1941, the treatment of gonorrhoea has changed drastically over the years. This was due primarily to the acquisition of increasing levels of resistance to penicillin among the gonococcal isolates, especially those isolated from the Far East (1). The recent emergence of beta-lactamase producing, or penicillinase-producing *Neisseria gonorrhoeae* (PPNG) which has become widespread in South East Asia and Western Africa, further impairs the effective management and control of gonorrhoea with these drugs.

In Thailand, PPNG was first isolated in 1977. Since then this strain has gained a strong foothold and became endemic in this country, resulting in an ever increasing failure rate in the treatment of gonorrhoea with penicillin (2). There is thus a need to search for effective alternatives capable of a single-dose success in the treatment of such infections. This study was therefore designed to evaluate the efficacy of cefotaxime (Claforan), a new cephalosporin with high beta-lactamase stability, in the treatment of gonorrhoea caused by both PPNG and non-PPNG strains, and also to determine the antibiotic susceptibility of local strains of *Neisseria gonorrhoeae* to this antibiotic.

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MATERIAL AND METHOD

Study Population

This study was conducted in adults of either sex with clinical evidence suggestive of gonorrhoea. The infection was confirmed bacteriologically. The patients, provided they were not allergic to cephalosporins, were each given a single intramuscular injection of 500 mg of cefotaxime with concomitant probenecid, 1 gm orally.

Any adverse effects reported by the patients in relation to the treatment were recorded. The patients were then asked to return for repeated clinical and bacteriological examinations on the third, seventh and fourteenth day. They were also instructed to refrain from further sexual activities until follow-up had indicated clearance of the infection. Only those treated patients with confirmed positive culture results, and had been followed-up for at least one week, were included in the final analysis.

Bacteriological Investigations.

Urethral discharge or endocervical swab specimens were subjected to microscopic examination after Gram staining in the clinic. For cultures, the specimens were inoculated directly onto modified Thayer-Martin medium and incubated at 35°C for 24-48 hours in CO₂ canisters. Identification of *Neisseria gonorrhoeae* was by colonial morphology, oxidase test, Gram staining and sugar utilization. All cultures giving positive results were tested routinely for the presence of penicillinase by the disc diffusion technique using a penicillin disc (10 IU) and confirmed by rapid iodometric method.

RESULTS

One hundred patients with bacteriologically confirmed gonorrhoea and satisfying the study criteria were included in the report (Table 1). Of these infections, 56 were due to PPNG and 44 to non-PPNG.

Table 1: Demographic Data

No. of patients	100
Male	90
Female	10
Age (years)	
Mean \pm S.D.	24.3 \pm 6.1
Range	16 — 51
Weight (Kg)	
Mean \pm S.D.	54.4 \pm 6.1
Range	40 — 66

Past History

Among the 97 patients surveyed, 56 gave previous history of sexually transmitted diseases of which 39 (70%) were due to gonococcal infection.

Present History

The incubation period varied from 1 — 31 days with a mean \pm S.D. of 8.4 \pm 6.2 days. It was reported to be less than 1 week in 58%, 1 to 2 weeks in 27% and more than 2 weeks in 15% of the patients included in the study.

The mean duration of symptoms before seeking treatment varied from 1 to 20 days with a mean \pm S.D. of 4.3 \pm 3.6 days. Treatment was sought within 2 days by 37%, bet-

ween 3 to 4 days by 32%, between 5 to 6 days by 10% and after more than 6 days by 21% of the patients treated.

Treatment Response

Of the 100 patients followed up, 99 were cured and 1 failed to respond to treatment (Table 2). 55 (98.2%) of the 56 patients with PPNG infections, including 3 who had failed to previous antibiotic therapy (2 to penicillin; 1 to kanamycin) were cured. Similarly all the 44 patients with non-PPNG infections were also cured.

The symptoms subsided within 24 hours in all the patients successfully treated with a mean \pm S.D. of 9.0 \pm 4.7 hours. The symptoms resolved within 6 hours in 18%, between 6-12 hours in 60%, between 13-18 hours in 15% and between 18-24 hours in 7% of the patients cured.

Sources of Infection

Prostitutes were the most common source of infection (92%) in males while all the 10 females in this study contracted the infection from their husbands.

Side-effects

No serious side-effects were reported. Some patients reported local pain after the injection but most often this did not last for more than 10 minutes and was in no way incapacitating to the patients.

Antibiotic Susceptibility

56 PPNG and 44 non-PPNG strains were examined for their susceptibility to cefotaxime. The PPNG were more susceptible than the non-PPNG; all the strains of PPNG were susceptible from 0.002 ug/ml to 0.064 ug/ml, in comparison to 0.004 to 0.128 ug/ml for the non-PPNG (Table 3). The respective geometric means were 0.0105 and 0.016 ug/ml for the PPNG and non-PPNG. The distribution of their MICs were statistically significant ($\chi^2 = 16.86$; $p < 0.01^*$).

DISCUSSION

Epidemiologically, gonococcal infection has been a major health problem in Thailand since 1964. The relatively common practice of self-treatment among patients and the free mobility and anonymity of the prostitutes who form the main reservoir of infection, have made control measures including surveillance, contact tracing and follow-up generally difficult.

The free availability of antibiotics in Thailand has led to an alarming increase in levels of drug resistance among the gonococci. Additionally, the recent emergence of beta-lactamase-producing, or penicillinase-producing *Neisseria gonorrhoeae* (PPNG) and the rapid spread of these organisms further impairs the control of gonorrhoea. Thus, effective therapy of clinical cases with the appropriate antibiotic is mandatory to curb the spread of these infections caused by the resistant gonococci.

At present, spectinomycin is one of the preferred single-dose alternatives for penicillin-resistance gonorrhoea. However, being a suspension rather than a true solution, it suffers the disadvantage difficulty of administration. The recent derivatives of the cephalosporins have high beta-lactamase stability (3) and are of good potentials in treating such infections. In-vitro studies have shown cefotaxime to be highly effective against both PPNG and non-PPNG strains (4). Its level of activity is many times greater than that of the other cephalosporins such as cefuroxime and cephamecins (5, 6) which are advocated for use in the treatment of penicillin-resistant

Table 2: Treatment Response

Organism	Cured		Not cured		% Success
	Male	Female	Male	Female	
PPNG	52	3	1	0	99
Non-PPNG	37	7	0	0	

Table 3: Susceptibility of *N. gonorrhoea* to Cefotaxime

Strains	Total	Minimum inhibitory concentration (ug/ml)						
		0.128	0.064	0.032	0.016	0.008	0.004	0.002
PPNG	56	0	8	9	10	11	6	12
Non-PPNG	44	2	6	9	11	5	11	0

$$\chi^2 = 16.86 \quad (p < 0.01)^{**}$$

gonorrhoea. It has also been successfully used in clinical trials to treat both PPNG and non-PPNG infections (7, 8, 9).

The results of this study has demonstrated the efficacy of cefotaxime in the treatment of gonorrhoea. The overall cure rate was 99 while that of PPNG and non-PPNG was 98.2% and 100% respectively. It is important to note that 3 patients with PPNG infections which had failed to previous therapy (2 to penicillin and 1 to kanamycin) just prior to this study, were cured.

An alarming proportion (15%) of patients in this study had an abnormally long incubation period of more than 2 weeks. 3 (21%) of these patients were reported to have an incubation period of 30 days! Similarly, 21% of the patients sought treatment more than 6 days after the first appearance of symptoms. This would pose a serious problem to the effective control of gonorrhoea as gonococcal infection is usually spread by 'carriers' who have no symptoms or those who have ignored symptoms.

The distribution of MICs of the non-PPNG were significantly different from those of the PPNG, with the non-PPNG less susceptible to cefotaxime than the PPNG. This has also been reported in Singapore (10) where the authors attributed this to possible free and uncontrolled use of other antibiotics.

The overall tolerance to cefotaxime was good, and no serious side-effects were observed. The administration of the drug was easy as the injection of cefotaxime was a true solution.

It can be concluded from the results of this study that cefotaxime, in single intramuscular dose of 500 mg given concomitantly with probenecid, 1 gm orally, is effective and safe in the treatment of gonorrhoea caused by both PPNG and non-PPNG.

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