SINGLE-DOSE ORAL TREAMTENT WITH CEFACLOR FOR MEN WITH UNCOMPLICATED GONOCCAL URETHRITIS

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SUMMARY

Sixty patients with uncomplicated gonococcal urethritis were treated with a single dose oral regime comprising 3 g of cefaclor and 1 g of probenecid. Forty-eight patients (80%) returned for follow-up and the overall cure rate among them was 91.6%. Among the isolates, 25 (41.7%) showed penicillinase producing Neisseria gonorrhoeae *(PPNG) strains. The cure rate for patients infected with PPNG was 85% while the cure rate for non-PPNG was 96.4%. Further work is required to establish the optimum dosage for this particular regimen.*

INTRODUCTION

The control of gonorrhoeae has been relatively difficult because of many reasons. We have no effective vaccine, we cannot use quarantine measures, nor do we have acceptable methods of chemo-prophylaxis. We have only one approach: early effective treatment of infected patients and sexual contacts of patients. To do so, we must have adequate diagnostic facilities, effective antibiotics and proper health education of patients.

The introduction of sulphonamides in 1937 and the use of penicillin since the Second World War have not stopped the worldwide increase in the incidence of gonorrhoea. Two microbiological factors play a significant part: the gradual decreasing sensitivity of the gonococcus to penicillin due to chromosomal resistance, and the emergence of Beta-lacatamase or penicillinase-producing *Neisseria gonorrhoeae* (PPNG), first reported in 1976 in England and the United States of America.[1,2] In July 1977, the Ministry of Health Malaysia, first reported the appearance of PPNG. Since then, the incidence of PPNG cases has gradually increased, and a recent study in Malaysia by the author showed that 35% of the gonococcal isolates were PPNG.[3] This shift in bacterial flora has far reaching therapeutic implications.

There have been two approaches to the Beta-lactamase problems. One has been the development of antibiotics stable to Beta-lactamase, e.g., the aminoglycosides, spectinomycin and the cephalosporins. The other has been the development of Beta-lactamase inhibitors, e.g., clavulanic acid, isolated from *Streptomyces clavuligerus.* Augmentin is a combination of amoxycillin and clavulanic acid and has been shown to be very effective in the treatment of gonococcal urethritis.[4]

Cefaclor is an acid-stable, semi-synthetic cephalosporin that is absorbed when given orally. It differs from cephalexin in that it has a chlorine atom instead of a methyl group in the carbon-3 position of the cephalexin molecule. This study is undertaken to assess the efficacy of cefaclor at a dose of 3 g given orally with 1 g probenecid in the

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treatment of uncomplicated gonorrhoea in an area where strains of penicillinase-producing *Neisseria gonorrhoeae* are prevalent.

MATERIALS AND METHODS

This is a single, blind prospective clinical trial of 60 consecutive male patients with uncomplicated gonococcal urethritis attending a private clinic in Penang.

At the initial visit, intraurethral specimens of urethral discharge were collected using platinum bacteriological loops and smears examined microscopically. A separate specimen was taken for immediate culture on Thayer. Martin medium containing vancomycin, colistin, and the anti-fungal agent, nystatin. The culture plates were incubated in a candle jar at 36°C for one day. If no growth was obtained after 24 hours, the plates were reincubated for another 24 hours. An oxidase test and gram stain were performed on colonies suspected of being gonococci.

Confirmation of *Neisseria gonorrhoeae* was performed by the Phadebact co-agglutination test technique. The agar plate diffusion method was used to determine the antibiotic sensitive pattern of all isolates. Penicillin susceptibility was tested using discs containing 10 units of penicillin G. Where the inhibition of growth was less than 20 mm in diameter, a Beta-lactamase test was done, using the iodometric methods.[5]

At the initial visit, all patients with positive results from direct microscopy were each given 3 g of cefaclor and 1 g of probenecid orally to take with a glass of water. They reported 48–72 hours after taking the medicines for physical examination and cultures of urethral specimens. Where no discharge was present, intra-urethral scrappings were performed. The criteria for failure of treatment was positive smear or culture in patients without further sexual contacts after treatment. All patients had been advised to abstain from sexual activity for two weeks after therapy.

RESULTS

The results of treatment are shown in Table I. 12 patients (20%) defaulted from follow-up and were therefore excluded, leaving 48 patients for assessment. The percentage of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) is shown in Table II. Out of the 48 cases treated with cefaclor, there were four failures, giving an overall cure rate of 91.6%. Of the 20 PPNG infections, 17 (85%) were successfully treated, compared with 27 (96.4%) of 28 non-PPNG infections.

The age distribution of the patients is shown in Table III. The age group between 20–29 has the most number of patients and this is probably because people are sexually more active at this age group.

The clinical presentation of the patients is shown in Table IV. 57 (95%) out of 60 patients presented with a urethral discharge, and this was the commonest complaint. 49 (80%) patients complained of dysuria, while 14 (23%) only complained of increased frequency of micturition.

TABLE I
TREATMENT RESPONSE WITH CEFACLOR

Total number of cases	PPNG			Non-PPNG		
	Defaulted	Failure	Success	Defaulted	Failure	Success
60	5	3	17	7	1	27

TABLE II
PERCENTAGE OF PENICILLINASE-PRODUCING *NEISSERIA GONORRHOEAE* (PPNG)

Number of isolates	Number tested		
	PPNG	Non–PPNG	Total
60	25 (41.7%)	35 (58.3%)	60 (100%)

TABLE III
DISTRIBUTION OF PATIENTS BY AGE

Age group (yrs)	Number	Percentage
19 and below	6	10.0
20 – 29	32	53.3
30 – 39	16	26.7
40 – 49	6	10.0
50 – 59	0	0
Total	60	100

Minimal side-effects were encountered by the 48 patients who came for follow-up. Two patients complained of headache, while one complained of nausea after taking the cefaclor and the probenecid.

DISCUSSION

No event in the control of gonorrhoea in Malaysia has a more significant effect than the discovery of PPNG strains of gonorrhoea in 1977. Since then, the proportion of PPNG strains have increased, and this study showed 41.7% of all the gonococcal isolates to be Beta-lactamase secretors. Clearly, an antibiotic that is effective against both PPNG and non-PPNG should be used. This is especially so when patients cannot come back for tests of cure.

The aminoglycosides, spectinomycin and the cephalosporins are increasingly being used in the treatment of gonorrhoea. In a recent study with kanamycin, the author found an overall failure rate of 12.2%.[3] Although spectinomycin is a drug that produces acceptable cure rates in the treatment of PPNG and is recommended in the treatment of such strains, attempts to find alternative agents are necessary. Furthermore, spectinomycin has to be given intramuscularly, and some patients prefer oral medications. Many new cephalosporins, including cefuroxime, cefotaxime and cefoxitin are highly effective in the treatment of gonococcal infections: all three are given intramuscularly. Cefaclor has the advantage of being given orally.

Similar works on cefaclor can be found in the literature. Panikabutra *et al.*, found a failure rate of 4.3% among men treated with cefaclor and 1 g of probenecid, and a failure rate of 10.4% among those treated with 3 g cefaclor alone.[6] Tupasi *et al.*, reported a cure rate of 93% after a single oral dose of 3 g cefaclor in the treatment of uncomplicated gonococcal infections in women: 27 of them were infected with PPNG strains.[7]

TABLE IV
CLINICAL PRESENTATION

Clinical presentation	Number of patients	Percentage
Urethral discharge	57	95
Dysuria	49	80
Frequency of micturition	14	23

It has been shown in this trial that a combination of cefaclor and probenecid used in a single oral regime may be effective in the treatment of uncomplicated gonococcal urethritis in a region where the incidence of PPNG is high. However, further work is necessary in order to establish the optimum dosage from this regime.

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