

Gentamicin in the treatment of infections due to penicillinase-producing gonococci

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SUMMARY Ninety-seven patients with infections due to penicillinase-producing *Neisseria gonorrhoeae* (PPNG) were treated with single doses of gentamicin 280 mg intramuscularly. The failure rate among those followed up was 3%. No significant side effects were recorded. Gentamicin is a valuable alternative in the treatment of infections due to PPNG strains.

Introduction

Gonorrhoea is a major public health problem and the sudden appearance of strains of gonococci that have acquired the ability to produce penicillinase, and so become totally resistant to penicillin and analogues of penicillin, has aggravated the situation. These strains were reported early in 1976,^{1 2} and in the following years have established themselves in African and Asian countries.

The newer cephalosporins have been shown to be effective in the treatment of patients infected by penicillinase-producing strains of *Neisseria gonorrhoeae* (PPNG). Good results were reported with the use of cefuroxime³ and HR 756.⁴ These drugs are, as yet, generally unavailable and are likely to be expensive when introduced into the market. The aminoglycosides have already been shown to be efficacious in its treatment in the United States⁵ and in Britain.³ Rajan *et al*⁶ obtained excellent results using kanamycin in a single dose. Strains of PPNG were reported to be susceptible in vitro to gentamicin,⁵ and hence in vivo this aminoglycoside should be a useful addition. For this reason, a trial was conducted with gentamicin sulphate in the treatment of patients with gonorrhoea due to PPNG.

Patients and methods

Patients harbouring strains of PPNG seen between March and April 1979 were included in the study. Patients who had a history of allergy to gentamicin and other aminoglycosides and those with other sexually transmissible diseases were excluded from the trial. Most of the patients were prostitutes; the

remainder consisted of patients who came for treatment and their sexual partners.

DIAGNOSIS AND TREATMENT

Infections in the prostitutes were detected during their routine fortnightly attendances, when cervical and rectal specimens were cultured on modified Thayer-Martin medium⁷ for *N gonorrhoeae*, which was identified by colonial morphology, Gram staining, and the oxidase reaction. Penicillinase production was detected by screening positive gonococcal isolates by a modification of the filter paper iodometric technique of Odugbemi *et al*.⁸ Strains giving positive results were confirmed by the rapid iodometric method.⁹

Urethral swabs were taken from all male patients for Gram staining and culture for *N gonorrhoeae*. When smears showed Gram-negative intracellular diplococci, the patient was treated provisionally as having gonorrhoea and was given our usual regimen, procaine penicillin 4.5 megaunits intramuscularly and probenecid 1 g orally. Infection by penicillinase-producing gonococci was diagnosed when on follow-up gonococci were still present and the pretreatment culture gave a growth of *N gonorrhoeae* which was shown to produce penicillinase.

In female patients and prostitutes treatment was begun only after the culture results were available.

Those patients infected with PPNG strains were treated with a dose of gentamicin 280 mg intramuscularly and seen three days later, when urethral cultures in men and endocervical and rectal cultures in women were repeated. Thereafter cultures were repeated at one week and two weeks after treatment. In addition, the serum creatinine concentrations were determined before treatment and repeated on the seventh day after treatment. A patient was considered cured when all the culture results were

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negative. Treatment failure was considered to have occurred when one or more of the post-treatment cultures yielded PPNG and reinfection had been ruled out.

SENSITIVITY TESTS

The minimum inhibitory concentration (MIC) of gentamicin was determined by the agar-plate dilution method. Two-fold concentrations of gentamicin from 0.5 µg/ml to 32 µg/ml were distributed into GC agar base (Difco) supplemented with haemoglobin and IsoVitalex. The test organisms were grown on chocolate agar and then suspended in Mueller-Hinton broth. The suspension turbidity was adjusted to correspond to 0.5 McFarland standard barium sulphate. The suspension was further diluted 1/100, and approximately 10 µl of each suspension was inoculated on to the antibiotic-containing medium by a multipoint inoculator. The plates were incubated in CO₂ tins at 35°C overnight. The MIC was determined as the lowest concentration of antibiotic that permitted the growth of no more than one colony.

Results

Ninety-seven patients with infections due to PPNG were treated with gentamicin (table I). Of these 83 were prostitutes; of the remaining 14, 11 patients were male and three female. All the prostitutes attended for follow-up culture examinations after treatment. One male patient failed to reattend.

Of the 96 patients examined bacteriologically after treatment with gentamicin, three (all prostitutes) had persistent infections. They were treated with kanamycin 2 g intramuscularly and responded well. In the remaining 93 patients their infections were cured, giving a cure rate of 97%.

There were no obvious side effects. The serum creatinine values remained within the normal range. The patients tolerated the injections very well with little discomfort. Only one patient complained of moderately severe giddiness half an hour after the injection. This was transient and lasted for about two hours.

TABLE I Results of treatment of infections due to strains of PPNG with gentamicin sulphate 280 mg intramuscularly

Results	Prostitutes	Others	Total	
			No	%
Treatment failure	3	0	3	3
Cured	80	13	93	96
Defaulted	0	1	1	1
Total	83	14	97	100

SENSITIVITY TESTS

The sensitivity of the penicillinase-producing gonococci to gentamicin was tested in 72 of the patients (table II). All strains were susceptible to 8 µg/ml or less of the antibiotic. Strains from the three treatment failures were sensitive to 8 µg/ml gentamicin.

Discussion

Soon after their emergence early in 1976, penicillinase-producing gonococci gained a foothold in Africa and in the Far East. Although these strains are susceptible to some of the aminoglycoside antibiotics, there is still a need to look for alternatives.

In this study a cure rate of 97% was obtained with gentamicin when used in a single dose of 280 mg. The PPNG strains recovered from the three patients who failed to respond to treatment were sensitive to 8 µg/ml gentamicin. This concentration is easily obtained in tissue with the dosage used. Persistence of the infection in these three patients could thus have been due to reinfection. Taking this into consideration the actual cure rate may in fact have been higher.

TABLE II Sensitivity of *N gonorrhoeae* to gentamicin

MIC (µg/ml)	No of strains
2	1
4	14
8	57

None of the patients treated showed evidence of ototoxicity or renal toxicity. Published evidence¹⁰ has suggested that these side effects should not occur when only one or two doses are given. Gentamicin in similar dosages has been used to treat uncomplicated gonococcal infection.^{11 12} None of these workers observed any serious side effects.

Gentamicin fulfils many of the criteria of a useful agent for the treatment of infections due to penicillinase-producing gonococci. It is effective, easily administered, and requires only a single dose, making it a valuable alternative for the treatment of PPNG infections. Because of the good treatment response obtained in this study, its use should be discouraged in the treatment of infections due to non-penicillinase-producing strains of *N gonorrhoeae*. Its indiscriminate widespread use may encourage the emergence of resistant strains, thus diminishing its usefulness as a valuable alternative antibiotic for the more difficult penicillinase-producing strains of *N gonorrhoeae*.

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