Spectinomycin in gonorrhoea

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Since its introduction in 1943, penicillin has been the drug of choice in the treatment of gonorrhoea.

In recent years, however, the emergence of strains of *N. gonorrhoeae* with diminished sensitivity to penicillin makes it essential that reliable non-toxic alternatives to penicillin should be fully investigated.

In 1960, spectinomycin, a new broad-spectrum antibiotic product of *Streptomyces spectabilis*, was introduced as the sulphate salt by Messrs. Upjohn Ltd. (Mason, Dietz, and Smith, 1961) for use in genito-urinary tract infections. This preparation was found to be effective in treating gonorrhoea, the recommended dose of 2 g. for males and 3 g. for females giving cure rates of 87 to 95 and 92 per cent. respectively (Laird and Taylor, 1962; Willcox, 1963).

The sulphate salt had unacceptable side-effects including nephrotoxicity and has since been withdrawn. Spectinomycin dihydrochloride pentahydrate appears to be better tolerated and gives at least as good results as the original drug.

This paper is a report on 69 male patients treated at the Special Clinic, Cardiff Royal Infirmary, and 44 patients (35 males and 9 females) treated at the Special Clinic, Royal Gwent Hospital, Newport.

Patients and methods

Only patients with uncomplicated gonorrhoea were included in the trial. Gonococcal urethritis was diagnosed in males by Gram-stained smears examined in the clinic and most cases were confirmed by culture on Thayer-Martin medium. The patient was treated immediately with 2 g. spectinomycin intramuscularly. A second smear was examined in the laboratory. Female patients were included only if they had a positive urethral and/or cervical culture. Specimens were obtained by charging a platinum loop and inoculating the Thayer-Martin plates directly. Females received a single injection of 4 g. spectinomycin. In the case of male patients urine was examined by the two-glass method and screened for blood and protein content by Labstix (Ames and Co.) before and after treatment. Males had two tests of cure and females three. In male patients smears and cultures were taken at 48 hrs and at 7 days after treatment and in females at 48 hrs, 7 days, and 14 days after treatment. Sensitivity tests were carried out only at the Royal Gwent Hospital. Each strain of *N. gonorrhoeae* isolated was plated on to a nutrient

chocolate agar plate and incubated for 48 hrs in a candle extinction jar. Five colonies were picked off and emulsified in 1 ml. of 25 per cent. strength Ringer's solution; 0.01 ml. of this suspension (approximately 3,000 organisms) was spread over one half portion of series of nutrient chocolate agar plates containing the following concentrations of spectinomycin: 2.5, 5, 10, 20, and 40 µg. per ml. A nutrient chocolate agar plate without spectinomycin was included as an inoculum control.

The plates were incubated at 37° in a candle-jar and the results recorded after 48 hrs incubation.

A fully sensitive result was indicated by complete inhibition of growth by 20 µg. per ml. or less of the drug.

Results

During the period of the trial, 113 patients were treated. The age distributions (Table I) were 17 to 54 years for males and 17 to 41 years for females. The country of origin is shown in Table II.

TABLE I Age distribution

Age group (yrs)	No. of patients	
	Male	Female
0-14	—	—
15-19	10	2
20-24	39	4
25-29	26	2
30-34	15	—
35-39	8	—
40-44	3	1
45+	3	—
Total	104	9

TABLE II Country of origin

Ethnic group	No. of patients	
	Male	Female
Gt. Britain and Eire	98	9
Asia	2	—
Europe	1	—
Africa	1	—
Caribbean	2	—
Total	104	9

Of the 104 male patients starting the trial, three (2.9 per cent.) defaulted immediately after treatment, seven (6.7 per cent.) after 3 days (after the first test of cure), and one (1 per cent.) after the second test of cure. Of the remainder, a further eleven patients (10.5 per cent.) defaulted more than 2 weeks after treatment.

Five patients (4.8 per cent.) became re-infected at periods ranging from 3 days to 3 weeks. Three of these patients had had two negative tests of cure and two had had one negative test of cure. All five were asymptomatic before re-exposing themselves. 23 men (22.1 per cent.) developed post-gonococcal urethritis.

One male and one female patient had positive cultures for *N. gonorrhoeae* after treatment and were considered to be treatment failures (Table III). However, the female patient subsequently responded to the same dosage of spectinomycin.

TABLE III Results of treatment

Sex	No. treated	No. followed 2 weeks or more	Relapses	
			No.	Per cent. of those followed
Male	104	93	1	1.1
Female	9	9	1	1.1
Total	113	102	2	1.1

In all cases the bacteriologist's reading of the urethral smear concurred with that of the clinician making the initial diagnosis. However, in 29 cases (27.8 per cent.), the diagnosis was not confirmed by culture.

The results of the sensitivities carried out on the Royal Gwent group of patients, all of whom had positive cultures, are shown in Table IV.

TABLE IV Results of sensitivity tests

No. of strains of <i>N. gonorrhoeae</i> tested	MIC of spectinomycin ($\mu\text{g./ml.}$)				
	2.5	5	10	20	40
44	42	2	0	0	0

After an intramuscular injection of 2 g. spectinomycin, serum levels reach on average 100 $\mu\text{g./ml.}$ (minimum 35 $\mu\text{g./ml.}$) (Savage, 1972).

Both figures are many times that required for the strains isolated.

SIDE-EFFECTS

All patients were questioned specifically about possible side-effects. No patient complained of the treatment being painful or uncomfortable. One patient had transient haematuria of uncertain cause.

Discussion

Because of the small number of women in this trial no conclusions can be drawn regarding the efficacy of spectinomycin in the treatment of females. In males the failure rate of 1.1 per cent. compares favourably with most other regimens for treating

acute gonorrhoea. If one assumes that those patients who default have been cured, then the failure rate falls below 1 per cent. Such an assumption is not without justification in the present series when one considers the defaulters in more detail. Of the eleven male patients who defaulted before 2 weeks, one returned some 3 months after treatment (with an entirely unrelated complaint) saying, that as the discharge had cleared up he had not bothered to re-attend; another seven patients had one negative test of cure and one had two negative tests of cure.

The failure rate obtained in this trial is as low as that obtained by giving probenecid and 5 million units of benzyl penicillin. With this latter treatment, Gray, Phillips, and Nicol (1970) reported a failure rate as low as 0.5 per cent. in London; Thin (1973) obtained a failure rate of 1.3 per cent. in Singapore and of 1.7 per cent. in Edinburgh (Thin, 1974). On the basis of low failure rate and relative freedom from side-effects, spectinomycin can be regarded as a suitable alternative to penicillin in the treatment of acute gonorrhoea.

Summary

Of 104 male and nine female patients with uncomplicated acute gonorrhoea who were treated with spectinomycin (males 2 g., females 4 g.), two patients (one male and one female) were considered to be treatment failures. No conclusions can be drawn from the small numbers of female patients investigated. Of the 104 male patients, 93 were followed for 2 weeks or more, giving a failure rate of 1.1 per cent. The drug was well tolerated. Sensitivity tests were carried out on 44 strains of *N. gonorrhoeae*; 42 strains were sensitive to 2.5 $\mu\text{g./ml.}$ spectinomycin and all strains were sensitive to 5 $\mu\text{g./ml.}$

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