Spectinomycin in the treatment of gonorrhoea in females and males

ALAN H. FINGER

Royal Adelaide Hospital and Epidemiology Branch, Department of Health, Adelaide, Australia

During late 1971 and throughout 1972, trials of spectinomycin bihydrochloride in the treatment of gonorrhoea were carried out among randomly selected female and male patients attending the venereal diseases clinics conducted by the South Australian Department of Health in association with the Royal Adelaide Hospital.

The bacteriological work of the trials was carried out by the Institute of Medical and Veterinary Science.

Material

The 126 females and 99 males finally included in the trials comprised approximately two-thirds and one-third respectively of the total number of cases of gonorrhoea seen at the clinics during the period.

FEMALES

The mean age of the 126 female patients finally included in the trial was 20 years (range 15 to 46).

In all, 200 females were treated with spectinomycin during the trial period. Most attended the clinic as notified source contacts or secondary contacts of men proven to have gonorrhoea.

The great majority were asymptomatic and most were without definite clinical signs of infection.

After being interviewed each patient was examined and had specimens taken from both urethra and endocervix with buffered cotton-wool swabs. Smears were made and the swabs placed in Stuart's transport medium for culture on both blood agar and Amies' plates.

All cases included in the trial grew gonococci from the cervix and/or urethra confirmed by oxidase and sugar reactions.

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Each patient with a history of intercourse with a known infected male was treated immediately after examination with 4 g. spectinomycin given intramuscularly in a single dose.

Among those treated on this epidemiological basis there were 64 from whom gonococci were not isolated so they were not included in the trial. Most of these 64 had follow-up tests, all of which proved negative.

Those without a definite history of gonorrhoea contact were treated only after bacteriological proof of their infection.

Follow-up was by examination and repetition of the initial tests at 2 to 5 days, again at 7 to 10 days, and, where possible, at 14 to 21 days after treatment.

Results (Table I)

Of the 126 patients entering the trial, six were not seen again, 120 returned for the first follow-up, 92 for the second, and 34 for the third. The females regarded as having definite re-infections were those who had at least one negative post-treatment test and who subsequently had a positive test and admitted post-treatment intercourse with a male already known or subsequently proved to be infected. Those in whom there was any doubt were classed as possible treatment failures.

If only those who had at least two post-treatment tests are included, the failure rate ranged from 2.2 to 4.3 per cent.

If all those who had at least one post-treatment test are included, the rate ranged from 1.7 to 3.3 per cent.

MALES

The ages of the 99 males in the trial ranged from 13 to 38 years (mean 23).

TABLE I *Results in Females*

No. treated	Follow-up		Positive at follow-up	Re-infections	Treatment failures	Doubtful treatment failures
	Duration (days)	No. followed				
126	2-5	120	4	0	2	2*
	7-12	92	2	2	—	—
	14-21	34	1	1	—	—

*In one case the patient admitted to intercourse after treatment and in the other, although intercourse was denied, spermatozoa were noted in the cervical smear

In each case two smears were made from the urethral discharge, one of which was sent to the laboratory together with a buffered cotton-wool swab of the discharge placed in Stuart's transport medium. The other smear was examined in the clinic after methylene blue staining. Where intracellular diplococci were present, a diagnosis of gonorrhoea was presumed. The patient was then given a single intramuscular dose of 2 g. spectinomycin.

In each such case laboratory examination of a Gram-stained smear confirmed the finding of presumptive gonococci and, in all but two cases their presence was confirmed by positive culture.

Results (Table II)

Of the 99 males treated, 88 returned 1 to 4, mostly 2, days later for the first follow-up, which consisted of examination and the collection of scrapings with a heavy nichrome loop inserted 2 to 3 cm. into the urethra. These were immediately inoculated on to both Amies' and blood agar plates, placed in candle extinction jars and quickly transferred to the laboratory incubator. All proved negative.

76 patients attended mostly 7 to 10 days after treatment for further examination and urethral scrapings. All proved negative on culture.

54 attended from 2 to 5 weeks after treatment for at least one further examination at which smears and cultures were made of any obvious discharge; where there was no discharge, a two-glass urine test was made. Any urine specimen containing threads or other debris was sent for microscopy and culture.

If the three infections in which the patients denied intercourse after treatment are regarded as treatment failures, the failure rate would be three in 88 cases (3.4 per cent) or, if those with only one post treatment test are excluded, three in 76 (3.9 per cent.).

Discussion

Spectinomycin was first available as the sulphate and Willcox (1962) and Lucas, Price, Thayer, and Schroeter (1967) reported favourably on its use in two large series of cases of gonorrhoea. The dose of the sulphate required was too large for convenient administration. This problem was overcome with the development of the bihydrochloride salt.

The results of several published trials of spectinomycin hydrochloride are summarized in Table III and although all the trials are not strictly comparable they show fairly consistently that this antibiotic is an effective one-dose treatment for uncomplicated gonorrhoea. There are considerable differences in follow-up and in criteria for distinguishing between re-infections and treatment failures. Antibiotic sensitivity tests have not been reported in all trials and without them comparison between trials from different places is not strictly valid.

Even with these reservations, however, the results of the current trial have confirmed the efficacy of spectinomycin.

Gonorrhoea treatment trials are beset with inherent difficulties, not the least of which is the

TABLE II *Results in Males*

No. treated	Follow-up		Positive at follow-up	Re-infection	Possible treatment failures
	Duration (days)	No. followed			
99	1-4	88	0	—	—
	7-10	76	0	—	—
	14-35	54	8	5	3

TABLE III *Results obtained in other areas*

Authors	Date	Country	Males		Female	
			No. treated	Cure rate (per cent.) ^a	No. treated	Cure rate (per cent.) ^a
Cornelius and Domesick	1970	U.S.A.	108	100	28	100
Duncan, Holder, Roberts, and Knox	1972	U.S.A.				
		(1) ¹	82	90	77	96
		(2) ¹¹	70	93	89	95
Gallai, Sylvestre, and Brault	1972	Canada	200	100	—	—
Hafermann, Cooper and Murphy	1973	S.E. Asia	289	95	—	—
Holder, Roberts, Duncan, and Knox	1972	U.S.A.	15 ^b	87	—	—
Labowitz, Porter, and Holloway	1970	U.S.A.	30	94	25	84
Platts	1970	N. Zealand	38	97	20	95
Reyn, Schmidt, Trier, and Bentzon	1973	Denmark	61	98	52	100
Smithurst	1972	Queensland	197	95	34	91
Tuza and Hatos	1973	New South Wales	124	97	—	—

^aExpressed to nearest whole number

(1)¹ Using 2 g.

(2)¹¹ Using 4 g.

^bHomosexual males

interpretation of each post-treatment infection as being due either to treatment failure or to re-infection.

In this series there were post-treatment infections in five males and five females in which differentiation was easy, whereas there were infections in three males and two females in which there remained serious and unresolvable doubts as to their origin.

Had routine antibiotic sensitivity tests been made on all gonococcal isolates in this trial, apart from aiding comparability of results as mentioned above, there may have been some objective evidence of re-infection had any case shown marked sensitivity differences between pre- and post-treatment isolates.

In numerous reported gonorrhoea treatment trials, especially in males, it has been assumed that infections noted later than 2 weeks (in some cases, even 1 week) after treatment were re-infections. Such an assumption, however convenient, appears to be too simple. In this trial the three possible treatment failures in males were all found only in the third test carried out from 2 to 5 weeks after treatment.

Spectinomycin usually takes effect very rapidly. In eleven men who returned almost exactly 24 hours after treatment, either very little or no discharge was evident and many of those treated remarked on the apparent overnight disappearance of the discharge. However, similar very rapid clearances are common with adequate penicillin or ampicillin and probenecid treatment.

No side-effects were reported, but about 5 per cent. of both males and females volunteered that they had suffered pain at the injection site for 1 or 2 days.

The doses of spectinomycin used were those the manufacturers recommend. In view of the now common use of the same dose of penicillin or ampicillin for both males and females with gonorrhoea, the need for the larger dose of spectinomycin in females is doubtful and could well be further investigated. In one published trial (Duncan, Holder, Roberts, and Knox, 1972) equivalent results were recorded in a group of females receiving 2 g. and another receiving 4 g. doses.

The results of reported treatment trials using large single doses of penicillin or ampicillin with probenecid show the same order of efficacy as do this and other spectinomycin trials.

Conclusion

Spectinomycin is probably the best alternative treatment available in penicillin sensitive patients and in penicillin insensitive infections. It would appear prudent to hold spectinomycin in reserve while penicillin and ampicillin are still effective, practical, and very much less expensive to use for routine treatment of gonorrhoea. At this stage of its

use it is impossible to know whether or when gonococci may accommodate themselves to the new antibiotic.

Summary

126 female patients with proven gonococcal infection were treated with 4 g. spectinomycin bihydrochloride given intramuscularly in a single dose. In 120 cases followed up there were four possible treatment failures, giving a cure rate of 96.7 per cent.

99 male patients with acute gonococcal urethritis were treated with a single dose of 2 g. spectinomycin bihydrochloride. Of 88 cases followed up, there were three possible treatment failures, giving a cure rate of 96.6 per cent.

Spectinomycin is an important addition to gonorrhoea therapy but should be reserved for penicillin sensitive patients and penicillin insensitive infections.

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La spectinomycine dans le traitement de la gonococcie féminine et masculine

SOMMAIRE

126 femmes atteintes d'une infection gonococcique certaine furent traitées par 4 g de bichlorhydrate de spectinomycine en injection intramusculaire unique. Pour 120 cas suivis, il y eut quatre échecs possibles, soit un taux de guérison de 96,7 pour cent.

99 hommes atteints d'urétrite gonococcique aiguë furent traités par une dose unique de 2 g de bichlorhydrate de spectinomycine. Pour 88 cas suivis, il y eut trois échecs possibles, soit un taux de guérison de 96,6 pour cent.

La spectinomycine est un important appoint au traitement de la gonococcie mais doit être réservée aux malades sensibilisés à la pénicilline et aux infections non sensibles à la pénicilline.