

Single oral dose of 1.5 g. talampicillin in the treatment of gonorrhoea

R. R. WILLCOX

St. Mary's Hospital, London, and King Edward VII Hospital, Windsor, Berks

Summary

81 patients have been treated with single oral doses of 1.5 g. (6 tablets) of talampicillin without probenecid. The failure rate amongst those followed was only 4.2 per cent. No side-effects were reported.

These results were superior to those obtained with 2.0 g. or equivalent of ampicillin, amoxycillin, or pivampicillin with probenecid.

Talampicillin is thus the most potent ampicillin-like antibiotic so far available for the treatment of gonorrhoea and is capable of curing the disease with a smaller single dose without probenecid than is necessary for other preparations.

Introduction

Single-session treatment of gonorrhoea has considerable epidemiological and administrative advantages, and injection therapy with penicillin by this means has been generally preferred at least in the male. Employing oral medication with the newer penicillins, a cure rate comparable to that obtained by injection has been achieved only by using large single doses with the addition of probenecid. For example, in the United States Public Health Service clinics, 3.5 g. ampicillin plus 1.0 g. probenecid is recommended for those who dislike injections (PAHO, 1974).

The results of single-dose oral therapy plus probenecid vary in different parts of the United Kingdom, being less satisfactory in London (Cobbold, Rees, Parker, Woodcock, John, Latto, Redmond, and Willcox, 1973), but even there excellent results have been obtained with amoxycillin given, for example, in two split doses without probenecid (Willcox, 1974).

One of the latest penicillins to emerge is talampicillin (BRL 8988), a thiazolidine carboxylic ester of ampicillin which releases ampicillin after hydrolysis in the gut mucosa, to produce a blood concentration up to twice as high as that achieved with ampicillin trihydrate (Croydon, personal communication). Talampicillin should thus be able to cure gonorrhoea with a smaller dose than that required for ampicillin itself.

The antibiotic has been used in single oral doses without added probenecid in the treatment of 150 male patients with acute uncomplicated gonorrhoea; 69 were given 1.0 g. (four capsules) and 81 were given 1.5 g. (six capsules). The latter series is the main subject of this paper.

Material

Of the 81 patients, 37 were born in the United Kingdom, 18 were Negroes (16 from the West Indies; one from West Africa; one from Kenya), and 26 were other immigrants (6 from Eire; two each from Australia, Germany, Tunisia and Pakistan; one each from Algeria, Austria, Canada, Cyprus, Iran, Italy, Kuwait, Malta, Qatar, South Africa, Spain, and Switzerland). Their average age was 26.7 yrs (range 17 to 54); 57 were single, 22 were married, and two were separated.

43 of the patients had had no previous venereal disease but the remaining 38 patients had experienced 38 previous attacks of gonorrhoea, 26 of non-gonococcal urethritis, nine of anxiety concerning venereal disease, four each of herpes genitalis, pediculosis pubis, and syphilis, three of non-specific proctitis, two of unspecified sore, and one each of balanitis, condylomata acuminata, and tinea cruris—a total of 93 previous incidents.

Fewer Negroes had experienced previous episodes than other immigrants or men born in the United Kingdom. Amongst those who had previously attended a venereal disease clinic there was a similar average of previous episodes amongst the three groups outlined (Table I).

The disease was apparently caught from a female stranger in 36 cases, from a friend in 29 cases, and from the wife in two cases; in thirteen cases a man was involved (a friend in 7 and a stranger in 6), and in one case the source was not known. The apparent incubation period

TABLE I *History of previous venereal incident according to ethnic group*

Ethnic group	Total no. of patients	No history		Previous history		
		No. patients	Per cent.	No. of patients	No. of attacks	Average no. of attacks
Negroes	18	7	38.9	11	26	2.36
Other immigrants	26	16	61.5	10	27	2.70
UK-born	37	20	54.1	17	40	2.35
Total	81	43	53.1	38	93	2.45

was 1 to 3 days in 37 cases, 4 to 7 days in 24, 8 to 14 days in six, 15 to 21 days in three, 22 to 28 days in two, 1 to 2 months in one, and 2 to 3 months in two; it was unknown in six cases.

The duration of discharge before treatment was 1 to 3 days in 53 cases, 4 to 7 days in fourteen, 8 to 14 days in seven, 15 to 21 days in four, and more than one month in two cases; in one case it was not known. 68 patients complained of some dysuria and thirteen did not.

Case management

In all cases the disease was diagnosed by a Gram-stained smear of the urethral discharge which was confirmed by culture where possible. Six 250 mg. talampicillin capsules were then swallowed by the patient in the presence of the physician.

After treatment it was planned that the patients should return after 2 or 3 days for a post-treatment urethral smear and culture plated on to Thayer Martin medium or held in Stuart's medium. Cultures were performed in 78.9 per cent. of those who re-attended and in no case were the results of culture at variance with the smear findings.

Subsequently it was intended that they should be seen approximately 1 and 3 weeks later and at 2 and 3 months after treatment. At each visit the urethra was examined

for urethral discharge, a smear being taken if a discharge was present, and the urine was examined for haze and threads. It was also planned that the prostatic fluid should be examined at least once during surveillance, and that a final serum test for syphilis should be made after 3 months.

Follow-up and results

Default rates from follow up were substantial but sufficient time elapsed before writing this report for all the patients to have attended had they co-operated fully. The follow-up and results obtained are shown in Table II.

Thus, of 81 treated, 71 were followed and the status at the last visit was satisfactory in 47. Thirteen patients were re-treated for non-gonococcal infection and, judging from a history of further sexual exposure, eight were re-treated for re-infection with gonorrhoea and three (4.2 per cent. of those followed) were regarded as treatment failures. All of the suspected failures occurred within the first week and all suspected re-infections after 2 weeks of observation. Thus, if all recurrences within 1 to 2 weeks were assumed to be failures regardless of history, the failure

TABLE II *Follow-up and results*

Duration of follow-up	No. followed	Result			
		Satisfactory	Non-gonococcal infection	Re-infection	Failure
0	81	—	—	—	—
1-7 days	71	23	4	—	3
8-14 days	41	6	2	—	—
15-21 days	33	4	—	2	—
22-28 days	27	3	3	2	—
1-2 mths	19	6	3	1	—
2-3 mths	9	5	1	2	—
More than 3 mths	1	—	—	1	—
Total	71	47	13	8	3

TABLE III *Results according to ethnic groups*

Ethnic group	No. treated	No. followed	Result				
			Non-gonococcal infection	Reinfection		Failure	
				No.	Per cent.	No.	Per cent.
Negroes	18	15	1	3	20.0	1	6.7
Other immigrants	26	24	5	3	12.5	1	4.2
Total immigrants	44	39	6	6	15.4	2	5.1
UK-born	37	32	7	2	6.3	1	3.1
Total	81	71	13	8	11.3	3	4.2

TABLE IV *Results compared with those of 1.0 g. dose*

Dose (g.)	No. treated	No. followed	GC+recurrences within 2 wks		Failure based on history	
			No.	Per cent.	No.	Per cent.
1.0	69	61	6	9.8	8	13.1
1.5	81	71	3	4.2	3	4.2
Total	150	132	9	6.8	11	8.3

TABLE V *Comparison with other ampicillin-like compounds*

Drug	Single dose (g.)	No. treated	No. followed	GC+recurrences within 2 wks		Failure based on history	
				No.	Per cent.	No.	Per cent.
Talampicillin ^a	1.5 alone	81	71	3	4.2	3	4.2
Amoxycillin ^b	2.0+1.0 g. probenecid	78	70	6	8.6	7	10.0
Ampicillin ^c	2.0+1.0 g. probenecid	114	94	6	6.4	10	10.6
Pivampicillin ^d	2.8 ^e +1.0 g. probenecid	101	91	7	7.7	9	9.9

^aPresent series^bWillcox (1972)^cWillcox, Woodcock, Latto, John, Redmond, Parker, Rees, and Cobbold (1973)^dUnpublished data^eEquimolecular to 2 g. ampicillin

rate would still be the same. One of the three treatment failures had had non-gonococcal infection before. Three of the thirteen patients who developed non-gonococcal infection after treatment for gonorrhoea had had urethritis before.

Results according to ethnic groups (Table III)

An apparently lower failure rate was noted amongst United Kingdom-born patients, but the number of failures was too small for this to be statistically significant. However, the re-infection rate was twice as high amongst immigrant groups than in the home population.

Comparison with the results of a 1 g. dose

The results achieved with 1.5 g. were substantially better than those obtained earlier with a single dose of 1.0 g. (Table IV).

Side-effects

No side-effects were reported in any of the 150 patients treated in the two series.

Comparison with ampicillin, pivampicillin, and amoxycillin

The results obtained with 1.5 g. talampicillin alone are compared in Table V with those of other series involving single oral doses of amoxycillin, ampicillin, or pivampicillin—in each case with an added 1.0 g. probenecid.

The results obtained with talampicillin alone thus proved superior to those obtained with single doses of the other antibiotics listed *plus* probenecid.

Thanks are expressed to Beecham Pharmaceuticals Ltd for kindly providing the talampicillin (Talpen) used in this study.

References

- COBBOLD, R. J. C., REES, G. D., PARKER, R. B., WOODCOCK, K., JOHN, J., LATTO, D., REDMOND, A., and WILLCOX, R. R. (1973) *Brit. J. vener. Dis.*, **49**, 268
- Pan-American Health Association (1974) 'Report of International Traveling Seminar to the U.S.A.', Washington
- WILLCOX, R. R. (1972) *Brit. J. vener. Dis.*, **48**, 504
- (1974) *Ibid.*, **50**, 120
- , WOODCOCK, K. R., LATTO, D., JOHN, J., REDMOND, A., PARKER, R. B., REES, G. D., and COBBOLD, R. J. C. (1973) *Ibid.*, **49**, 263