TROBICIN (ACTINOSPECTACIN) IN NON-GONOCOCCAL URETHRITIS*

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Trobicin (Actinospectacin) is a new antibiotic obtained from *Streptomyces spectabilis* developed by the Research Laboratories of Messrs. Upjohn. It is prepared as a white powder, 1.4–1.6 g. of which is dissolved in distilled water. It has been stated to have a wide range of antibacterial activity and has already been shown (Willcox, 1962) to be effective in cases of acute gonorrhoea in males when given by a single intramuscular injection. It appears to be well tolerated. The present paper describes the use of Trobicin in a single injection, alone or in combination with sulphadiazine, in the treatment of non-gonococcal urethritis in the male.

Material

Of the 72 patients included in this study, 27 were Negroes (23 from the West Indies and four from West Africa). The Negroes represented 43.3 per cent. (13) of those receiving Trobicin alone and 33.3 per cent. (14) of those receiving combined treatment.

Of the remainder, 28 were from the United Kingdom, four from Eire, two from Cyprus, two from Italy, and one each from Australia, Burma, Ceylon, Greece, Iraq, Pakistan, Saudi Arabia, Spain, and Sweden. The average age was 28.3 years (range 17 to 61). Eighteen were married and 54 single.

25 patients (including five Negroes) had had no previous venereal incident, but the remainder had had between them no less than 62 previous attacks of gonorrhoea, 51 of non-gonococcal urethritis, three of syphilis, three of non-specific genital sores, and two of venereophobia. The 27 Negroes accounted for sixty of the 121 previous attacks (average 2.2) and the 45 others for the remainder (average 1.4).

The discharge had been present before treatment for 1 to 3 days in 38 cases, 4 to 7 in 23, 8 to 14 in five, 15 to 21 in five, and longer than one month in one. Dysuria was complained of by all but 21 patients.

The disease had apparently been contracted from a stranger in 37 cases, from a friend in 27, and from the wife in eight.

The apparent incubation period was 1 to 3 days in 22 cases, 4 to 7 in eight, 8 to 14 in twelve, 15 to 21 in five, 22 to 28 in four, and over 28 days in eleven, and was unknown in ten.

Gonococci were excluded in the urethral smear before treatment in all cases. The routine Wassermann reaction and VDRL (or Kahn) test were both negative in 69 cases, and both were positive in three cases, including one West Indian. The gonococcal complement-fixation reaction was negative in all of 27 patients tested.

Case Management

Medication.—Thirty patients each received a single intramuscular injection of 1.4 g. Trobicin (Actinospectacin).

42 patients each received a single injection of 1.6 g. Trobicin with 10 g. sulphadiazine to be taken in four daily doses over 5 days. In the first ten cases a special diluent was used for the antibiotic, but in the remainder the white powder was dissolved in 10 ml. distilled water which was injected at first into both buttocks, and latterly into one buttock.

Follow-up.—Following treatment the patients were seen again 3 to 7 days later and were instructed to attend at 14, 21, 28, 56, and 84 days from treatment. At each visit they were examined for urethral discharge, a smear being taken if present, and the urine was inspected for haze and threads. It was planned to have at least two examinations of the prostatic fluid for pus during surveillance and to perform final serum tests for syphilis at 3 months, but not all patients attended at the times requested.

Results

Group I. Trobicin Alone.—Of the thirty patients treated (Table I, overleaf), 27 were followed and sixteen of them (59.2 per cent.) required re-treatment for non-gonococcal urethritis within 3 months. No

* Received for publication October 2, 1962.

criteria exist to distinguish relapse from re-infection and no attempt is made to do so, except that recurrences observed after 3 months are automatically regarded as re-infections and are excluded.

TABLE I
RESULTS OF TREATING THIRTY PATIENTS WITH SINGLE INJECTIONS OF 1.4 g. TROBICIN

Length of Follow-up	No. Followed	No. Satisfactory	Gc +	Re-treated for N.G.U.
0	30	—	—	—
1-7 days	27	3	—	8
8-14 days	16	2	—	4
15-21 days	10	1	—	—
22-28 days	9	—	—	—
1-2 mths	9	—	—	3
2-3 mths	6	—	—	1
Over 3 mths	5	3	—	2
Total Followed	27	9	—	18

The results in Negroes and others are analysed in Table II, which shows no increased failure rate in Negro patients. The over-all recurrence rate of 59.2 per cent. in non-gonococcal urethritis is similar to that obtained with a placebo.

TABLE II
RESULTS IN NEGROES AND OTHERS IN GROUP I

Race	No. Treated	No. Followed	Failures	
			No.	Per cent.
Negro	13	12	6	50.0
Other	17	15	10	66.7
Total Cases ..	30	27	16	59.2

Trobicin given alone in single intra-muscular doses of 1.4 g. thus appears to have no demonstrable effect in non-gonococcal urethritis.

Group II. Single Injections of Trobicin combined with Sulphonamides.—A combination of one injection of streptomycin sulphate (which by itself is followed by a failure rate of approximately 40 per cent.) with sulphonamides has been widely used in the treatment of non-gonococcal urethritis. It was felt worthwhile, therefore, to treat another series of patients with single injections of 1.6 g. Trobicin combined with 10 g. sulphadiazine given over 5 days.

Of 42 patients so treated (Table III), 34 were followed and thirteen of them (38.2 per cent.) required re-treatment within 3 months. Two recurrences observed after 3 months are excluded.

TABLE III
RESULTS OF TREATING 42 PATIENTS WITH SINGLE INJECTIONS OF 1.6 g. TROBICIN PLUS 10g. SULPHADIAZINE

Length of Follow-up	No. Followed	No. Satisfactory	Gc +	Re-currence of N.G.U.
0	42	—	—	—
1-7 days	34	3	—	2
8-14 days	29	5	1	2
15-21 days	21	1	—	3
22-28 days	17	1	—	1
1-2 mths	15	3	—	3
2-3 mths	9	3	—	2
Over 3 mths	4	1	1	2
Total Followed	34	17	2	15

The results in Negroes and others are analysed in Table IV, which shows a somewhat higher apparent failure rate in the Negroes, who, as indicated above, are more likely to be re-infected than other groups.

TABLE IV
RESULTS IN NEGROES AND OTHERS IN GROUP II

Race	No. Treated	No. Followed	Failures	
			No.	Per cent.
Negro	14	13	6	46.2
Other	28	21	7	33.3
Total Cases ..	42	34	13	38.2

The overall results in the two groups (38.2 per cent. failures) are compared with those previously obtained by the author with sulphonamides alone in Table V.

TABLE V
RESULTS WITH SULPHONAMIDES ALONE IN 215 CASES OF NON-GONOCOCCAL URETHRITIS

Sulphonamide	No. Treated	No. Followed	Failures	
			No.	Per cent.
Sulphadiazine* (short-acting) 26-28 g. . . .	55	53	21	39.6
Dosulphin (middle-acting) 12 g.	100	88	33	37.5
Sulfamoxole (long-acting) 8 g.	60	54	20	36.4
Total Cases	215	195	74	37.9

* Including a few cases with Sulphatriad.

The results obtained with Trobicin combined with sulphonamides are thus no better than those obtained with sulphonamides alone, and are less good than those obtained with single injections of 1 g.

streptomycin sulphate with sulphonamides (Table VI).

TABLE VI
RESULTS WITH STREPTOMYCIN PLUS SULPHONAMIDES
IN 100 CASES OF NON-GONOCOCCAL URETHRITIS

Schedule	No. Treated	No. Followed	Failures	
			No.	Per cent.
Streptomycin plus Dosulfin	50	43	12	27.9
Streptomycin plus Sulfamoxole	50	34	11	31.8
Totals	100	77	23	29.8

Tolerance

No systemic side-effects were noted in this series and no complaints of local pain were made by the patients. The preparation appeared to be as well tolerated as injectable penicillin and streptomycin preparations.

Summary and Conclusions

- (1) 72 male patients with uncomplicated non-gonococcal urethritis were treated with single intramuscular injections of Trobicin (Actinospectacin). In thirty cases, 1.4 g. was given alone, and in 42 cases 1.6 g. was combined with 10 g. sulphadiazine given over 5 days.
- (2) Of the thirty patients given 1.4 g. Trobicin alone, 27 were followed and there were sixteen recurrences (59.2 per cent.) of non-gonococcal urethritis within 3 months. The recurrence rate was no higher in the Negro patients than in the rest.
- (3) Of the 42 patients given 1.6 g. Trobicin combined with sulphadiazine there were thirteen recurrences (38.2 per cent.) within 3 months. The recurrence rate was somewhat higher in the Negro patients.
- (4) Previous investigations had shown a failure rate of 37.9 per cent. of those followed out of a series of 215 patients with non-gonococcal urethritis treated with sulphonamides, and of 29.8 per cent. in those fol-

lowed out of a series of 100 patients given single injections of 1 g. streptomycin sulphate plus sulphonamides.

- (5) The results so far obtained with Trobicin alone and in combination with sulphonamides would not appear to indicate that this drug has any particular activity against non-gonococcal urethritis.

Thanks are expressed to the Upjohn Company of Kalamazoo, Michigan, U.S.A. and to Dr. J. C. Jacobm of the Upjohn Company of England for kindly providing the Trobicin used in this study.

REFERENCE

- Willcox, R. R. (1962). Paper presented to the International Dermatological Congress, Washington, D.C. (In press). See also (1962) *Brit. J. vener. Dis.*, **38**, 150.

Urétrite non-gonococcique traité par la Trobicine (actinospectacine)

RÉSUMÉ

- (1) On donna une seule injection intramusculaire de Trobicine à 72 hommes atteints d'urétrite non-gonococcique simple (N.G.U.). Dans 30 cas 1,4 g. fut administré seul, et dans 42 cas 10 g. de sulphadiazine furent administrés pendant 5 jours en plus de 1,6 g. de Trobicine.
- (2) Sur 30 malades qui reçurent seulement 1,4 g. de Trobicine, 27 furent suivis et il y eut 16 rechutes (59,2%) de N.G.U. en 3 mois. La proportion de rechutes fut la même parmi les nègres que parmi le reste.
- (3) Sur les 42 malades qui reçurent 1,6 g. de Trobicine avec 10 g. de sulphadiazine, il y eut 13 rechutes (38,2%) en 3 mois. La proportion de rechutes fut un peu plus grande parmi les nègres.
- (4) Des enquêtes précédentes révélèrent 37,9% de rechutes parmi les cas suivis d'une série de 215 malades atteints de N.G.U. traités par la sulphonamide, et 29,8% de rechutes parmi les cas suivis de cent malades traités par une seule injection de 1 g. de streptomycine avec la sulphonamide.
- (5) Les résultats obtenus jusqu'à présent n'indiquent pas que la Trobicine, seule ou avec la sulphonamide, a aucune activité spécifique contre l'urétrite non-gonococcique.