

Treatment of gonorrhoea with trimethoprim-sulphamethoxazole and probenecid plus procaine penicillin in Rwanda

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Since its introduction in 1967, many authors in industrialized countries have reported excellent results in the treatment of gonorrhoea with a combination of trimethoprim and sulphamethoxazole (Csonka and Knight, 1967; Schofield, Moffett, Masterton, and McGill, 1969; Carroll and Nicol, 1970; Ullmann, Niordson, and Zachariae, 1971; Siboulet, 1971; Rodin and Seth, 1972; van Dijk and Tan Lim, 1973). Unsatisfactory results were reported by Wright and Grimble (1970), and an intermediate result by Evans, Churcher, and Human (1972). For developing countries, with their overwhelming demand for gonorrhoea treatment, few therapeutic studies are available. Arya, Pearson, Rao, and Blowers (1970) reported an unsatisfactory cure rate with low doses of trimethoprim-sulphamethoxazole (T-SM) but a high cure rate with higher doses. Kloosman (1972) reported excellent results with three different single-dose schedules of T-SM in South Africa. Arya and Bosa (1973) evaluated the efficacy of different penicillin schedules in Uganda.

The aim of this study is to evaluate the efficacy (a) of our standard gonorrhoea treatment in Rwanda: probenecid 1 g. by mouth followed after 1 hr by 4.8 m.u. procaine penicillin intramuscularly and (b) of trimethoprim-sulphamethoxazole* in two different treatment schedules: a single dose of eight tablets, and a dosage of twenty tablets spread over 4 days.

Material and methods

The trial took place from November, 1972, until July, 1973, at the Venereal Disease Consultation of the Institut National de Santé, in Butare, Rwanda. 204 men with acute gonococcal urethritis were included in the study and were randomly allocated to one of the three treatment schedules. Known recidivists, defaulters, and persons who could not attend for follow-up were excluded. Gram-

stained urethral smears were taken in all subjects; in each case typical Gram-negative intracellular diplococci were seen. Cultures were done in 77 cases.

The treatment schedules were as follows:

A. T-SM: one dose of eight tablets taken under supervision of the medical staff.

B. T-SM: two tablets in the morning and three in the evening for 4 days, a total of 20 tablets.

C. Probenecid 1 g. by mouth followed after 1 hr by 4.8 m.u. procaine penicillin intramuscularly (half the dose into each buttock).

Three patients of Group B did not take the tablets properly while one patient did not receive the exact dose of penicillin. This explains why only 200 men were included: 68 patients in Group A, 65 patients in Group B, and 67 in Group C.

Follow-up examinations were done at 5, 10, and 15 days after the end of treatment. The patients were asked to attend in the morning having held their urine overnight, but not all complied with this request. At each visit a clinical examination was carried out and a smear taken if any urethral exudate was present.

Recurrence was diagnosed if the smear showed intracellular or extracellular Gram-negative diplococci; those with only leucocytes were diagnosed as having post-gonococcal urethritis (PGU). A two-glass urine test was performed in 43 patients who showed no urethral exudate at the 10 day follow-up examination; 14 in Group A, 12 in Group B, and 17 in Group C.

No attempt was made to obtain a follow-up of longer than 2 weeks because of the possibility of re-exposure and the high risk of re-infection.

The 28 recurrences within 2 weeks of follow-up were classified as failures or re-infections according to their history of re-exposure.

The cure rate was calculated in two different ways: (a) As the number of failures related to the total number treated. Those who did not return for follow-up can be accepted as being symptomatically cured, the Venereal Disease Consultancy of the Institute being the only facility for treatment in the area.

(b) As the number of failures related to the number followed, excluding the re-infections (Arya and Bosa, 1973).

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*Bactrim-Roche—each tablet contains 400 mg. sulphamethoxazole and 80 mg. trimethoprim

Results

The Table summarizes the results of treatment in 200 male patients with acute gonorrhoea, according to treatment schedule. Among the patients followed, and excluding re-infections, the results were:

(A) T-SM in a single dose of eight tablets cured 83.4 per cent. of patients, a not very satisfactory cure rate.

(B) T-SM two tablets in the morning and three in the evening for 4 days cured 91.9 per cent. of patients, an intermediate rate.

(C) Probenecid 1 g. followed by procaine penicillin 4.8 m.u. cured 96.6 per cent. of patients.

There were no major reactions after T-SM therapy and only one person complained of minor gastrointestinal disturbance. There were also no reactions after the penicillin therapy and, although the injection of such a large volume must cause some discomfort, the treatment was readily accepted.

The Figure, giving the cumulative number of recurrences (failures plus re-infections) during the 2 weeks follow-up period, shows more clearly the respective efficacy of the three treatment schedules.

Of the fifty persons considered cured of gonorrhoea in Group A, two continued to have an urethral discharge (PGU); but of fourteen urine specimens examined 10 days after treatment, six showed a first-glass pyuria of 20 leucocytes or more in the centrifuged deposit ($\times 400$).

Of the 45 patients considered cured of gonorrhoea in Group B, no person remained with an urethral discharge, and 10 days after the end of treatment only three out of twelve examined had a first-glass pyuria of 20 leucocytes or more.

Of the 57 patients cured in Group C, three had a non-gonococcal urethral discharge, and six out of seventeen examined 10 days after treatment had a first-glass pyuria of 20 leucocytes or more.

TABLE *Results of treatment*

Group	Dosage	Number treated	Number followed	Results				Cure rate per cent.	
				Cures	Re-infections	Failures	(1)	(2)	
A	T-SM, single dose of 8 tablets	68	64	50	4	10 ^a	85.3	83.4	
B	T-SM, 5 tablets a day for 4 days (20 tablets)	65	54	45	5	4 ^b	93.8	91.9	
C	Probenecid 1 g. plus 4.8 m.u. procaine penicillin	67	62	57	3	2 ^c	97.0	96.6	

(1) Percentage of number treated

(2) Percentage of number followed excluding re-infections

^a Intracellular Gram-negative diplococci in 8, extracellular in 2

^b Intracellular Gram-negative diplococci in 2, extracellular in 2

^c Intracellular Gram-negative diplococci in 1, extracellular in 1

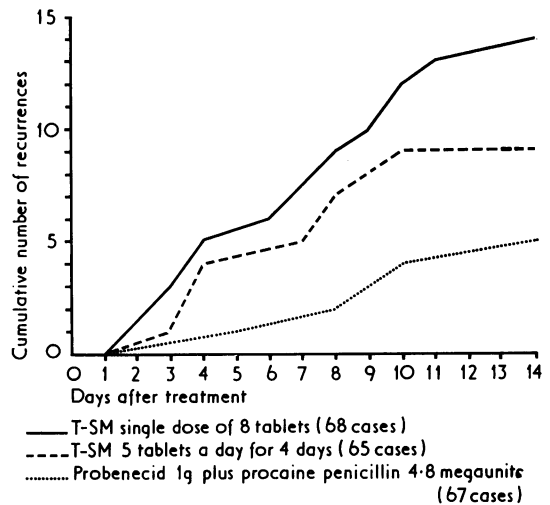


FIGURE *Cumulative number of recurrences of gonorrhoea in patients receiving three different treatment schedules*

Two persons developed a primary syphilitic infection, one 6 days after a single dose of eight tablets of T-SM, and one 15 days after twenty tablets of T-SM.

Discussion

Probenecid 1 g. followed after 1 hr by 4.8 m.u. procaine penicillin is a highly effective treatment for gonorrhoea. Rodin and Seth (1972) in London, and Arya and Bosa (1973) in Uganda, found as good results giving probenecid simultaneously with the injections and using respectively 1.2 m.u. and 3.0 m.u. procaine penicillin. Because of greater ease of administration and lower cost, 1 g. probenecid given simultaneously with 3.0 m.u. procaine penicillin could be recommended as standard treatment for gonorrhoea in Rwanda, instead of the schedule we used.

In the search for an alternative single-dose therapy, we tested T-SM in a single dose of eight tablets. The cure rate obtained of 83.4 per cent. is not very satisfactory, and lies between the 65 per cent. obtained by Arya and others (1970) with two doses of four tablets at an interval of 12 hrs, and the 98 per cent. cure obtained by Ullman and others (1971) with two doses of five tablets at an interval of 8 hours. Kloosman (1972), however, claimed a 100 per cent. cure rate with single doses of eight, ten, or 12 tablets of T-SM.

The 91.9 per cent. cure rate with the T-SM schedule of two tablets in the morning and three in the evening for 4 days is acceptable, and only slightly lower than that obtained, using a comparable total dose by Csonka and Knight (1967), Schofield and others (1969), Carroll and Nicol (1970), Arya and others (1970), Siboulet (1971), Rodin and Seth (1972), van Dijk and Tan-Lim (1973), and Svindland (1973).

Only Wright and Grimble (1970) obtained an unacceptable cure rate of 62 per cent., while the cure rate of 82 per cent. in the study of Evans and others (1972) is intermediate.

As Rodin and Seth (1972) recommended, when using a total dosage of twenty tablets it may be better to give the daily dose of four or five T-SM tablets once daily than to divide them in a twice or four times daily schedule.

Twenty tablets of T-SM is a useful second-line schedule of treatment; it is comparable with tetracycline, but has the advantage of fewer doses than the 6-day treatment with 1.5 g. tetracycline daily.

The lack of effect of T-SM on an incubating syphilitic infection (Svindland, 1973) was confirmed by the two cases of primary syphilis seen during the follow-up period.

An important consideration is that, in countries with a high incidence of infectious syphilis, the treatment used for gonorrhoea should either cure this also (as is the case with the high-dose procaine penicillin schedule) or should not influence it at all.

Summary

Probenecid 1 g. followed after 1 hr by 4.8 m.u. procaine penicillin, which is the recommended treatment for gonorrhoea in Rwanda, cured 96.6 per cent. of cases of acute gonorrhoea in men.

A single dose of eight tablets of trimethoprim-sulphamethoxazole gave a less satisfactory cure rate of 83.4 per cent., while twenty tablets of trimethoprim-sulphamethoxazole, two in the morning and three in the evening for 4 days, cured 91.9 per cent. of patients.

Lack of effect of trimethoprim-sulphamethoxazole on incubating syphilis was confirmed by the development of primary syphilis in two patients during the 2-week follow-up period.

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Traitement de la gonococcie par le triméthoprime-sulfaméthoxazole et par le probénécide plus la pénicilline-procaïne au Ruanda

SOMMAIRE

Le traitement recommandé pour la gonococcie au Ruanda: 1 g. de probénécide suivi une heure après par 4,8 millions d'unité de pénicilline-procaïne, guérit 96,6 pour cent des cas de gonococcie masculine aiguë.

Une dose unique de 8 comprimés de triméthoprime-sulfaméthoxazole donna un taux de guérison moins satisfaisant de 83,4 pour cent alors que 20 comprimés de triméthoprime-sulfaméthoxazole, deux le matin et trois le soir pendant 4 jours, a guéri 91,9 pour cent des malades.

L'absence d'effet du triméthoprime-sulfaméthoxazole sur la syphilis en incubation a été confirmé par la constatation d'une syphilis primaire chez deux malades pendant la période de surveillance de deux semaines.