Short-term treatment of gonorrhoea with intramuscular and oral forms of trimethoprim-sulphamethoxazole

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SUMMARY Fifty-nine male patients and 41 female patients with uncomplicated gonorrhoea were treated with an intramuscular dose of 1600 mg sulphamethoxazole plus 320 mg trimethoprim followed by an oral dose of 2400 mg sulphamethoxazole plus 480 mg trimethoprim 12 hours later. Forty-nine out of 52 male patients and 37 out of 38 female patients who were re-examined were cured. One of the men probably had a reinfection.

Introduction

Csonka and Knight (1967) reported favourable results with a combination of trimethoprim and sulphamethoxazole in the treatment of gonorrhoea. Later several studies confirmed these results. Recently an intramuscular form of trimethoprim-sulphamethoxazole has been developed which gives high blood concentrations of short duration. To obtain a high blood level for at least 24 hours we prescribed one intramuscular dose of trimethoprim-sulphamethoxazole and one oral dose 12 hours later to evaluate its effect on uncomplicated gonorrhoea in patients of both sexes.

Material and methods

The series included 59 male and 41 female patients with uncomplicated gonorrhoea. Specimens for direct microscopy and culture were taken from the urethra in men and from the urethra, cervix, and rectal mucosa in women before treatment and at the follow-up visit seven to 14 days later. The specimens for culture were transported in Stuart's medium to the laboratory and cultured on two Thayer-Martin media, one of which also contained trimethoprim. Although treatment was given on the basis of positive microscopical evidence, only cases confirmed by culture (including fermentation reac-

tions) were included in the assessment. Sensitivity tests to penicillin G and trimethoprim-sulphamethoxazole were carried out by the plate dilution method described by Reyn *et al.* (1958).

The treatment was given as an immediate intramuscular injection of two ampoules of Bactrim (Ro 6-2580/59, F. Hoffmann-La Roche and Co. AG, Basle, Switzerland) in equal doses into both gluteal regions, each ampoule containing 800 mg sulphamethoxazole and 160 mg trimethoprim.

Twelve hours later the patient was asked to take three tablets of Bactrim Quiksolv (Ro 6-2580/55, F. Hoffmann-La Roche and Co. AG, Basle, Switzerland) dissolved in a glass of water, each tablet containing 800 mg sulphamethoxazole and 160 mg trimethoprim.

Results

The MIC values for both penicillin G and trimethoprim-sulphamethoxazole were estimated in 93 cases (Table 1). In nine cases the gonococci showed a slightly decreased sensitivity to trimethoprim-sulphamethoxazole (MICs=1.25 and 25 µg/ml) and in 23 cases the MIC of penicillin G was ≥ 0.2 IU/ml. There seemed to be no cross-resistance between penicillin G and trimethoprim-sulphamethoxazole.

Ninety out of all 100 patients returned for re-examination, which showed that 49 (94.2%) of the 52 men and 37 (97.4%) of the 38 women had negative culture results (Table 2). One of the male patients probably had a reinfection because he

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Table 1 Sensitivity-testing of 93 gonococcal strains to penicillin G and trimethoprim-sulphamethoxazole

MICs of penicillin G (IU/ml)	MICs of trimethoprim-sulphamethoxazole (µg/ml)			Total
	0.31 and 5.3	0.62 and 12.5	1.25 and 25.0 (Slightly resistant)	
<0.1	35	24	2	61
0.1	5	3	1	9
0.2	7	2	2	11
0.5	4	4	3	11
1.0	0	0	0	0
2.0	0	0	1	1
Total	51	33	9	93

Table 2 Treatment results with trimethoprim-sulphamethoxazole given in a single intramuscular dose (1600 mg + 320 mg) and a single oral dose (2400 mg and 480 mg) 12 hours later

Patients	MICs of trimethoprim-sulphamethoxazole (µg/ml)			Total
	≤0.62 and 12.5	1.25 and 25.0	Not known	
Treated (59 men, 41 women)	84	9	7	100
Re-examined	77	8	5	90
Cured	76	5	5	86
Treatment failures	0	3	0	3
Reinfections	1	0	0	1

admitted sexual contact following treatment and harboured gonococci which were highly sensitive to trimethoprim-sulphamethoxazole. All the remaining three patients with positive culture results on re-examination had gonococci which were slightly resistant to trimethoprim-sulphamethoxazole, and they denied sexual contact following treatment. Thus, it seems probable that these patients (one woman and two men) were true treatment failures. Thus, of the 90 patients who were re-examined 3.3% were treatment failures. Three (33.3%) of the nine patients with a slightly decreased sensitivity to trimethoprim-sulphamethoxazole (MICs = 1.25 and 25 µg/ml) were treatment failures.

The only side effect observed during the study was pain at the injection site in one patient; this disappeared after two days.

Discussion

The sensitivity-testing of the gonococci in the present study showed that fewer than 10% of the tested strains had a slightly decreased sensitivity to trimethoprim-sulphamethoxazole. The decreased sensitivity did not seem to cross-react with the decreased sensitivity to penicillin, which was about

25% in the present series. It seems, therefore, that trimethoprim-sulphamethoxazole is a good substitute in cases in which penicillin is ineffective.

It seems evident that the plate dilution technique for trimethoprim-sulphamethoxazole gives adequate information on the clinically valuable sensitivities of gonococci for trimethoprim-sulphamethoxazole, at least with the present treatment schedule. All treatment failures (three patients) were infected by strains with MIC values of 1.25 and 25 µg/ml for trimethoprim-sulphamethoxazole, but no cases of treatment failure occurred in the group of patients with more sensitive gonococci.

The side effects were minimal; no allergic rashes were seen and only one patient had severe pain at the injection site.

Thus, the one-day treatment schedule we used for cases of uncomplicated gonorrhoea seemed to be effective and safe in patients of both sexes.

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