Sulphaphenazole, streptomycin and sulphaphenazole combination, trimethoprim, and erythromycin in the treatment of chancroid

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Abstract

One hundred and thirty six patients with chancroid were treated with four different treatment regimens; (A) Sulphaphenazole 1 g 12 hourly by mouth $\times$ 10 days (B) Inj streptomycin 1 g intramuscularly daily with sulphaphenazole 1 g 12 hourly orally $\times$ 10 days; (C) trimethoprim 200 mg 12 hourly by mouth $\times$ 7-10 days, and (D) erythromycin 500 mg 6 hourly orally $\times$ 7-10 days. Cure rates of 9% with sulphaphenazole alone, 48% with streptomycin and sulphaphenazole combination, 93% with trimethoprim and 100% with erythromycin were obtained. Sulphaphenazole alone or in combination with streptomycin were thus inferior in the treatment of chancroid. There is need for modification of treatment regimens recommended for chancroid in the textbooks of dermatology and venereology. Trimethoprim can be recommended as first line of treatment for chancroid in developing countries like India where resistance to trimethoprim is uncommon and erythromycin is suggested as a second line of therapy because by that time syphilis can be easily ruled out.

Chancroid is the most common cause of genital ulcers in India and accounts for 12-39% of all sexually transmitted diseases at different centres.¹⁻³ Chancroid is mostly confined to developing countries, but epidemics have been reported from Orange County, California, United States of America⁴ and Holland.⁵ Increasing resistance of *Haemophilus ducreyi* to antimicrobials⁶ and the variable response to available treatment regimens necessitates the re-evaluation of older and prevalent regimens in addition to research for newer drugs.

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Patients and methods

All patients attending STD clinic between the years 1985 to 1987 with the diagnosis of chancroid based on clinical picture and negative dark ground illumination, Tzanck smear and tissue smear were considered for inclusion in the study. Patients who had received antimicrobial therapy in the last 5 days before reporting were excluded. VDRL and HIV antibody detection was carried out in all patients. Between January 1985 and December 1986, the initial 33 patients received sulphaphenazole 1 g 12 hourly by mouth (Regimen A). Patients were reviewed after 5 days. If they showed improvement, treatment was continued for another 5 days or till the ulcer healed. If no improvement was evident injection of streptomycin 1 g intramuscularly daily was added and both were continued for 10 days (Regimen B). After the initial 3 months regimen A was discontinued because of unacceptably higher failure rates and patients were treated with regimen B.

During 1987, patients were randomly allocated to trimethoprim 200 mg 12 hourly by mouth for 7-10 days (Regimen C) and erythromycin stearate 500 mg 6 hourly orally for 7-10 days (Regimen D). Clinical details of ulcer and inguinal adenopathy (bubo) were recorded. Patients were followed weekly until the ulcers healed, when they were considered cured.

Results

One hundred and thirty six patients completed treatment and were available for follow up. All but two were men with a mean age of 27.8 years. They had had genital ulceration for 1-39 days with an average of 23 days. The majority (70%) were unmarried and had acquired the infection from prostitutes. Thirty three patients were treated with sulphaphenazole alone, 75 with streptomycin and sulphaphenazole combination, 28 with trimethoprim and 30 with erythromycin. Thirty patients who did not respond to sulphaphenazole alone were treated with a combination of streptomycin and sulphaphenazole. Demographic details of patients treated with different regimens are shown in table 1. VDRL and HIV antibody tests were negative in all patients.

Table 1 Demographic data of patients treated with different treatment regimens

S No		Treatment regimens			
		A SPZ ALONE	B SPZ + STM	C TMP	D ERY
1	Number treated	33	75	28	30
2	Mean age (years)	26.7	25.9	26.3	25.1
3	Mean duration of ulcer (days)	23	29	20	20
4	Mean number of ulcers	2.9	2.4	2.7	3.1
5	No (%) with adenitis (bubo)	18 (55)	45 (60)	9 (45)	15 (50)

SPZ—Sulphaphenazole; STM—Streptomycin; TMP—Trimethoprim; ERY—Erythromycin.

Table 2 Results of therapy with different treatment regimens

Treatment regimen	No of patients	
	Treated	No (%) cured
A Sulphaphenazole 1 g bd × 10 days	33	3 (9)
B Sulphaphenazole 1 g bd and Inj streptomycin 1 g intramuscular, daily × 10 days	75	36 (48)
C Trimethoprim 200 mg bd × 7–10 days	28	26 (93)
D Erythromycin stearate 500 mg × 7–10 days	30	30 (100)

A cure rate of 9% was obtained with sulphaphenazole alone, 48% with streptomycin and sulphaphenazole combination, 93% with trimethoprim and 100% with erythromycin (table 2). No significant difference in the resolution of bubo was observed with various treatment schedules. Vestibular side effects were not observed with the dose of streptomycin used. Trimethoprim treatment was completely devoid of untoward effects. One patient receiving erythromycin, however, complained of epigastric pain and nausea after one week of therapy.

Discussion

Haemophilus ducreyi shows wide geographic variations in its antimicrobial susceptibility.⁷ It is a fastidious organism and it is not easy to culture it with the existing laboratory facilities available in developing countries like India.^{8,9} Hence it is the clinical trials with chemotherapeutic agents and not the sensitivity testing which gives information about the usefulness of the drugs.

Sulphonamides were once the mainstay of treatment of chancroid, but resistance, both plasmid and non-plasmid mediated, is now prevalent.¹⁰ However, several textbooks of dermatology^{11,12} and venereology^{13,14} still continue to recommend them as the first line of treatment. We found sulphonamides alone to be singularly ineffective in the treatment of chancroid. Ramakrishnan *et al*¹⁵ also reported similar results from India.

Streptomycin alone is also recommended in the management of chancroid.^{13,14} However, there are many reports of *H ducreyi* being resistant to streptomycin and in fact other aminoglycosides.^{16,17} Resistance to streptomycin can be stepwise or plasmid mediated, due to presence of aminoglycoside phosphotransferases, as encountered with other gram

negative bacteria.¹⁸ We found streptomycin in combination with sulphaphenazole curative in less than half the cases and this treatment can no longer be recommended.

In Kenya, sulphamethoxazole 800 mg and trimethoprim 160 mg twice a day by mouth was found effective in 100% cases¹⁹ and subsequently single dose treatment has been found to be equally effective in both sexes.^{20,21} Since sulphonamides alone in our experience were totally ineffective, we used trimethoprim alone and found it effective in 93% patients. Plummer *et al*²⁰ reported 92% success with trimethoprim 200 mg twice a day for 5 days. Trimethoprim does not mask syphilis and hence can be used as first line of treatment in chancroid in countries where syphilis is endemic. However, a single dose of trimethoprim does not give acceptable cure rates and resistance may develop rapidly.²²

Erythromycin, recommended as the first line of therapy in chancroid by the Center for Disease Control, Atlanta²³ and WHO,²⁴ has been found effective throughout the world, though a few resistant strains from Singapore have been reported.⁷ Erythromycin gave 100% success in our experience and can be recommended as the second line of treatment in developing countries because by that time syphilis can be easily ruled out.

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