THE MANAGEMENT OF PURULENT PENILE ULCERS IN SINGAPORE

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SYNOPSIS

The therapeutic response to purulent painful penile ulcers was studied using ceftriaxone (Rocephin) 250mg I.M. single dose, ceftriaxone 250mg I.M. daily three doses, trimethoprim-sulfamethoxazole (Bactrim) 2 tablets (160/800mg) twice daily for 7 days and trimethoprim-sulfametrole (Lidaprim) 8 tablets (640/3200mg) single oral dose.

In both H. ducreyi positive and H. ducreyi negative chancroidal ulcers ceftriaxone as a single or three injections gave a cure rate of 95% in two weeks. Trimethorprim-sulphaemthoxazole gave a cure rate of 88% and trimethoprim-sulfametrole only gave a cure rate of 45% at the end of 14 day follow-up.

Ceftriaxone as a single 250mg intramuscular dose is highly effective in the treatment of chancroidal ulcers in Singapore.

INTRODUCTION

Genital ulcer disease is a common clinical problem in primary health care clinics in the tropics. The management of genital ulcer disease is thwarted by its polymicrobial aetiology and their overlapping clinical features. However, the control of genital ulcer disease is important in the spread of sexually transmitted diseases (STD) and fundamental in the control of syphilis.

In clinical practice the laboratory is of little help in making an immediate therapeutic decision. There is no simple and reliable diagnostic test like the Gram's stain smear in genital discharge disease. The results of cultures often arrive too late to be of use for a therapeutic decision. Sophisticated tests like viral cultures and even dark field microscopy may not be available to primary health care physician. In a considerable proportion of ulcers no primary pathogen could be implicated. (1, 2, 3)

In the prevention of further transmission of STD, prompt and effective therapy is necessary. The choice of antimicrobial therapy can only be made on the basis of the epidemiological and aetiologic features of local genital ulcer disease.

At Middle Road Hospital, one aspect of genital ulcer disease that creates a therapeutic dilemma is purulent painful genital ulcers. We embarked on an aetiological assessment of purulent penile ulcers in 100 patients attending the clinic. We than proceeded to a open prospective, randomised comparative study using the following regimes:

I. ceftriaxone (Rocephin) 250mg intramuscular injections daily for 3 days.
II. ceftriaxone 250mg intramuscular single injection.
III. trimethoprim-sulfamethoxazole (Bactrim) 2 tablets (160/800mg) twice daily for 7 days.
IV trimethoprim-sulfametrole (Lidaprim) 8 tablets (640/320mg) single oral dose.

All three preparations, ceftriazone, (4) trimethoprim-sulfamethoxazole (5) and trimethoprim-sulfametrole (6) have all been known to be effective in the treatment of chancroid. It was also the aim of this study to evaluate single dose regimes as they are convenient and cost-effective in controlling STD.

PATIENTS AND METHODS

Eighty patients between the ages of 18 and 60 years with suppurative painful penile ulcers, clinically consistent with chancroidal ulcers were studied. All patients with known or suspected hypersensitivity to penicillins, cephalosporins, sulfonamides or trimethoprim were excluded. The exclusion criteria also included patients with concomitant or recent (less than a week) administration of other antibiotics and patients with syphilis. Concomitant gonorrhoea is not a contraindication for inclusion.

After the initial history and physical examination swabs for culture of Haemophilus ducreyi, N. gonorrhoeae, Chlamydia species, aerobic bacteria and herpes simplex virus were taken. A dark ground examination was done on the serous fluid from the ulcer, serological test for syphilis (VDRL) were done on the first visit and four weeks later. The serology for herpes simplex antibodies were taken on the first day and two weeks later. The details of laboratory techniques in this study has been described. (7)

All patients were asked to return on days 3, 7 and 14 and 28. Cultures for H. ducreyi were repeated if the ulcers were still present.

A *cure* was defined by eradication of H. ducreyi within three days with complete epithelialisation by 7 or 14 days.

A *improvement* is defined by eradication of H. ducreyi within 3 days with significant objective decrease in size and no purulence but where complete epithelialisation has not been achieved.

A *failure* is no eradication of H. ducreyi within 3 days or no objective, significant improvement of ulcers by day 7 or worsening of ulcers by day 3.

RESULTS

Out of the 100 patients recruited, 80 patients were available for assessment of therapeutic response. The rest defaulted treatment or excluded for other reasons. The aetiological agents isolated are listed in Table I.

TABLE I
AETIOLOGICAL AGENTS ISOLATED IN MEN WITH PURULENT PENILE ULCERS

Predominant Organisms Isolated	No.	(%)
Haemophilus ducreyi	13	(16)
Herpes simplex virus Type II	8	(10)
Neisseria gonorrhoeae	3	(4)
H. ducreyi + N. gonorrhoeae	3	(4)
Aerobic organisms only	21	(26)
No pathogens	32	(40)
TOTAL	90	(100)

The aerobic organisms isolated included staphylococci, streptococci, enterococci, coliforms and diptheroids. These are organisms sometimes isolated from the skin around the perineum. Although there were 21 ulcers with isolation of an aerobic organism, 2 of the herpes simplex ulcers and 7 of the H. ducreyi ulcers had in addition an aerobic organism isolated. In fact if the aerobes are considered secondary invaders as they most likely are then no primary pathogen was isolated in 66% of the patients.

A large number of these ulcers with no pathogens isolated would be either chancroid or infected herpes. Technical reasons and the fastidious nature of the agents could account for their lack of isolation.

The overall response of the ulcers for the various drug regimes are as in Table II. Ceftriaxone three injections and single injection gave a cure rate of 95%. In the 3 injections of cerftriaxone one patient was not cured but showed improvement. This patient was complicated by phimosis and gonorrhoea (PPNG). In the single injection, the patient who failed to cure was H. ducreyi positive on the first visit, improved and cleared of H. ducreyi on day 3 and day 7. For no known reason there was a clinical relapse of ulcer without a bacteriological relapse. This patient was cured by trimethoprim-sulfamethoxazole combination for seven days. No herpes simplex was isolated from this patient.

In the trimethoprim-sulfamethoxazole combination group, the one patient who failed was from a gonococcal ulcer (PPNG) which was cured in 7 days by a single 250mg ceftriaxone injection. The other patient who only improved after 2 weeks had herpes simplex virus (type 2) isolated.

The trimethoprim-sulfametrole single dose therapy of 8 tablets only achieved a 45% cure by the end of 14 days. Of the 11 failures, four were cured by ceftriaxone 250mg single injection, three by ceftriaxone three injections, two by trimethoprim-sulfamethoxazole and two did not return after the second drug was administered. Aetiological agents involved in the failures included H.

TABLE II
PURULENT PENILE ULCERS RESPONSE TO THERAPY

Therapy	Cured by 7 days		Cured by 14 days		Improved by 14 days		Failed		Total
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.
Ceftriaxone 250mg × 3	10	(50)	9	(45)	1	(5)	—		20
Ceftriaxone 250mg × 1	12	(52)	10	(43)	—		1	(5)	23
Trimethoprim-Sulfamethoxazole 2 tabs b.d. × 7	10	(59)	5	(29)	1	(6)	1	(6)	17
Trimethoprim-Sulfametrole 8 tabls single oral dose	6	(30)	3	(14)	—		11	(55)	20
Total No.	38	(48)	27	(34)	2	(3)	13	(15)	80

TABLE III
PENILE ULCER THERAPY AND RESPONSE ACCORDING TO AETIOLOGY

Therapy	Chancroid	Chancroid + Gonorrhoea	Gonorrhoea	Herpes Simplex	Aerobic	No Pathogens
Ceftriaxone 250mg daily × 3	3 All cured	All cured	1 Improved	—	4 All cured	10 All cured
Ceftriaxone 250mg × 1	5 1 failed	—	—	1 Cured	8 All cured	8 All cured
Trimethoprim-sulfamethoxazole 2 tabls b.d. × 7	2 All cured	—	1 Failed	4 1 Improved	5 All cured	5 All cured
Trimethoprim-sulfametrole 8 tabs sinlge oral dose	3 2 failed 2 failed	—	1 Failed Failed	3 All cured All cured	4 2 cured 2 failed 2 failed	9 3cured 6 failed 6 failed

ducreyi, (2) N. gonorrhoeae, (1) aerobes (2) and no organisms isolated. (6)

The clinical response of the ulcers according to the therapy instituted and aetiology is as shown in Table III. Ceftriaxone as a group cured 10 out of 11 chancroid, all the gonorrhoea (4) and cured all aerobic ulcers and ulcers with no pathogen isolated. Trimethoprim-sulfamethoxazole was useful for chancroid and other ulcers except gonococcal ulcer.

No adverse effects to the therpay was noted except for one patient who developed headaches with trimethoprim-sulfamethoxazole but was able to complete the treatment.

DISCUSSION

From the study, we conclude that ceftriaxone (Rocephin) as a single 250mg injection and 250mg three daily injections achieved 95% cure rates for purulent penile ulcers at the end of 14 days. Trimethoprim-sulfamethoxazole two tablets twice daily for seven days was equally effective with a cure rate of 88% at the end of two weeks. However, a single dose of 8 tablets of trimethoprim-sulfametrole is not useful for purulent penile ulcers although it was highly effective for chancroid in Nairobi (6). The advantage of ceftriaxone over trimethoprim-sulfamethoxazole is that it is effective against H. ducreyi as well as *N. gonorrhoeae* (PPNG and non PPNG). Ceftriaxone can be administered as a single supervised dose with no consideration of non-compliance or absorption. Other than cost, the advantage of trimethoprim-sulfamethoxazole is that it is not treponemacidal and thus does not mask concomitant syphilis. Ceftriaxone is definitely treponemacidal both in vitro and in viro. Ceftriaxone 250mg is too low to be curative for syphilis and it is not certain to what extent this will alter the manifestation of syphilis. The maxim to raise at this point is that all penile ulcer disease patients should have a VDRL (if possible a dark field examination) at the first visit and at follow-up at 6 to 12 weeks later. We estimate that 1 to 3% of all purulent penile ulcers would have *Treponema pallidium* implicated in its aetiology. (7) In this study patients with syphilis were excluded.

Our overall experience with purulent painful penile ulcers and specifically from this study confirms that antibiotics need not be continued until complete epithelialisation of the penile ulcer. As long as the ulcer shows significant healing with clearance of pain and purulence, the ulcers heal with simple measures like saline washes. Penile ulcers often heal quickly but sometimes the inguinal bubo may persist and even get worse. In this situation, simple aspiration of the fluctuant bubo with a wide bore needle would be adequate to settle it. However, it is always prudent to extend the antibiotics for a few more days.

In managing sexually acquired penile ulcers one

must appreciate its polymicrobial aetiology. Knowing the epidemiology, clinical features and with selective use of the laboratory, the physician will be able to work out a rational diagnosis and treatment.

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