

TREATMENT OF GONORRHOEA WITH AMPICILLIN ALONE AND WITH AMPICILLIN PLUS CLOXACILLIN

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SYNOPSIS

The results of 2 regimes of oral treatment of gonorrhoea are reported. Of 82 male and female patients treated with probenecid 1 g. plus ampicillin 2 g. and followed for 2 weeks, 1 relapsed (1.2%). There were no relapses among 46 male and female patients treated with probenecid 1 g. and ampicillin 1.25 g. and cloxacillin 1.25 g. It is concluded that this regime of ampicillin and cloxacillin is as satisfactory as ampicillin alone and merits further trial especially in countries with hot moist climates.

INTRODUCTION

Ampicillin, a semi-synthetic penicillin, is bactericidal and has a wide range of activity against Gram positive and Gram negative organisms. It is well absorbed when given by mouth, reaching a peak blood level of 6-7 µg/ml. 2 hours after administration of 1 g. and is still present in the blood 6 hours later (Alergant, 1963). Compared with penicillin only a small proportion becomes bound to plasma proteins so that a higher tissue concentration may be obtained at the site of infection (Kunin, 1966).

Ampicillin has been demonstrated in vitro to have a greater bactericidal effect than penicillin G. against gonococcal strains with decreased sensitivity to penicillin (Odegaard, 1962). Decreased penicillin sensitivity among gonococci has been a problem in recent years and affected 25% of gonococci isolated at Edinburgh in 1972 (Thin, 1973).

Soltz-Szots and Kikoshta (1973) recently showed that *staphylococcus aureus* may often be present in the genital tract and Sanders, Pelczar and Hoeffling (1962) suggested that penicillinase produced by certain strains of *staph. aureus* may be responsible for failure to respond to penicillin in some cases of gonorrhoea. These strains of *staph. aureus* are usually sensitive to cloxacillin (Gravenkamper, Brodie and Kirby, 1965). It was, therefore, decided to compare ampicillin (Penbritin, Beecham) alone and ampicillin plus cloxacillin (Orbenin, Beecham) in the treatment of gonor-

rhoea. Probenecid was given with the antibiotics: this preparation reduces renal tubular excretion of penicillins so raising the maximal blood level and prolonging the active level (Boger, Beatty, Pitts and Flippin, 1950). As cloxacillin is less active than ampicillin against gonorrhoea it was decided to give a larger total dose of the 2 drugs than of ampicillin alone. The object of this paper is to report the results obtained with the treatments.

MATERIAL AND METHODS

Patients

During the period of the trial all men and women who were suffering from uncomplicated gonorrhoea and were not hypersensitive to penicillin, were treated.

DIAGNOSIS

In men diagnosis of gonorrhoea was based on results of Gram stained smears and/or cultures. In women smears were taken for Gram staining but the diagnosis of gonorrhoea was based on results of cultures taken from urethra, cervix and rectum. Culture methods and penicillin sensitivity tests were the same as those described by Thin (1973) with the addition of a dry disc containing 2 mg. ampicillin (Mast Laboratories) for ampicillin sensitivity tests in the patients treated with ampicillin and probenecid. Results were reported as sensitive to ampicillin or relatively resistant to ampicillin. Relative resistance indicated that approximately 1.2 µg/ml. or more ampicillin was required. Ampicillin and cloxacillin sensitivity tests were not carried out on cultures from patient treated with these 2 drugs.

Treatment

During the first part of the study treatment comprised 1 g. probenecid and 2 g. ampicillin

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orally (Group 1). During the second part treatment was 1 g. probenecid, 1.25 g. ampicillin and 1.25 g. cloxacillin (Group 2). The drugs were taken together as a single dose under direct supervision in the clinic.

Follow-up

Patients were seen 3 days, 1 week, 2 weeks and 4 weeks after treatment. Details of examination during these visits are as described by Thin (1973).

In distinguishing relapse from re-infection, the suggestion of Evans (1966) was followed: namely, if gonococci reappear within 14 days of treatment and if the patient denies further intercourse, the infection is considered to have relapsed; the reappearance of gonococci after 14 days is considered to be due to re-infection, regardless of the patient's statements.

RESULTS

In Group 1, 146 patients were treated: 82 were followed for 2 weeks after treatment and relapse occurred in 1 (1.2%) case (Table I). No patient became re-infected and post gonococcal non-specific urethritis (post-gonococcal urethritis occurred in 24 of the men followed for 1 month. Sensitivity results of the strain of gonococcus isolated from the patient in whom treatment failed were penicillin MIC 0.4 u/ml. and relatively resistant to ampicillin.

In Group 2, 50 patients were treated, 46 were followed for 2 weeks after treatment and there were no cases with relapse or re-infection (Table I). Post gonococcal urethritis occurred in 8 of the men.

Some details of follow-up are shown in Tables II and III.

TABLE I
RESULTS OF TREATMENT

	Number Treated	Number Followed *	Treatment Failures	
			Number	Per Cent
Group 1	146	82	1	1.2
Group 2	50	46	0	

*For 2 weeks

All cases in which relapse or re-infection occurred had positive results to cultures taken before and after treatment.

TABLE II
DETAILS OF FOLLOW-UP OF AMPICILLIN TREATED CASES (GROUP 1)

	No. of patients treated	Follow-up			
		3 days	1 week	2 weeks	1 month
Males	95	67	69	56	34
Females	51	34	36	26	15
Total	146	101	105	82	49

TABLE III
DETAILS OF FOLLOW-UP OF AMPICILLIN PLUS CLOXACILLIN TREATED CASES (GROUP 2)

	No. of patients treated	Follow-up			
		3 days	1 week	2 weeks	1 month
Males	25	25	25	23	6
Females	25	24	25	23	11
Total	50	49	50	46	17

Three men in Group 1, and 2 in Group 2 had positive smear results and negative culture results. Results of ampicillin and penicillin sensitivity tests among 143 cases with positive culture results in Group 1 are shown in Table IV. Six of 48 cases in Group 2 with positive culture results showed diminished sensitivity to penicillin.

TABLE IV
RESULTS OF SENSITIVITY TESTS IN GROUP 1 AMONG 143 CASES WITH POSITIVE CULTURE RESULTS

	Penicillin	
	Sensitive	Decreased Sensitivity
Ampicillin Sensitive	119	14
Ampicillin Decreased Sensitivity	2	8

Side effects were not a problem with either regime of treatment. There were none at all among patients with ampicillin. Among those

treated with ampicillin and cloxacillin 2 patients complained of a few loose stools and 1 patient complained of nausea, dizziness and 2 loose stools some hours after treatment.

During the study of Group 2 patients efforts were made to isolate organisms, such as *staph. aureus*, using Stuart's transport medium but no satisfactory results were obtained.

DISCUSSION

There was 1 (1.2%) treatment failure in Group 1 treated with probenecid and ampicillin and none in Group 2, treated with probenecid and ampicillin plus cloxacillin. Seven per cent of strains of gonococcus isolated in Group 1 showed decreased sensitivity to ampicillin and 12.5% in Group 2 showed decreased sensitivity to penicillin. Thin (1973) observed a failure rate of 1.7% among 344 patients treated with 5 m.u. benzyl penicillin plus 1 g. probenecid; 25% of the gonococci from these patients showed diminished sensitivity to penicillin. Criteria for treatment failure were the same as those reported here. Eriksson (1970 a,b) reported 3% failures among 580 patients treated with 1 g. probenecid and 2 g. ampicillin using similar criteria to ours; approximately 15% of the gonococci showed decreased sensitivity to penicillin. Bro-jorgensen and Jensen (1971) found 2% failures among 1,194 patients treated with the same regime but their criteria were a little different.

Our results with ampicillin support the view of the Lancet (1972) that ampicillin 2 g. and probenecid 1 g. is a most satisfactory treatment for gonorrhoea. Ampicillin plus cloxacillin as used here appear equally effective and merit further trial, especially in areas with hot moist climates when *staph. aureus* is more likely to occur as a secondary invader.

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