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Treatment of Acute Pelvic Infections with Alphacillin (Pivampicillin Hcl)

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SUMMARY

Fifty patients with acute pelvic inflammatory disease were treated with Alphacillin (Pivampicillin Hcl). The total daily dose consisted of 1050mg, given in three divided doses. Treatment was continued for six days. Full bacteriological investigations were performed. Therapy was continued so long as the condition of the patient improved. In case of failure change to other antibiotics or surgery were considered.

The clinical response to Alphacillin was considered successful in 92% of patients. A significant observation in the trial was the low rate of residual pelvic pathology especially in patients with Acute/Chronic pelvic infection.

The drug was found to be free from complica-

tions or any serious side effects. Mild epigastric discomfort was noticed in only 3 patients.

INTRODUCTION

Pivampicillin has been marketed for clinical use during the last few years. It has been used successfully in the treatment of Gonorrhoea (Hunton et al, 1974; Shah et al, 1977), acute respiratory infections (Onadeko et al, 1976; Pines et al, 1974) and urinary tract infections (Fries et al, 1973; Roholt, 1974). There is so far one published trial on the use of alphacillin in gynaecological infections (Jordheim, 1974) in which a satisfactory therapeutic effect was reported.

Oral alphacillin (pivampicillin Hcl) is an ester of ampicillin, which is almost totally absorbed. After absorption, alphacillin is rapidly and virtually completely hydrolyzed to ampicillin by enzymes in sera, gastrointestinal mucosa, and other tissues.

Because this absorption process is so efficient, pivampicillin gives rise to peak plasma levels of ampicillin, which are about three-fold higher than those achieved after molar equivalent oral doses of ampicillin itself and they occur generally one hour after oral administration of alphacillin compared to approximately two hours after oral ampicillin.

Higher urinary concentrations of ampicillin characteristicly occur. Generally twice the amount of antibiotic can be recovered from the urine following the administration of alphacillin than with molar equivalent oral doses of ampicillin.

The direct result of these higher blood levels of ampicillin are similar high levels in all body tissues, body fluids and secretions (Jordan et al 1970). Evidence is now steadily emerging that these higher blood levels of ampicillin following pivampicillin have significant clinical advantages.

Pivampicillin has been shown to have a high spectrum of activity against gram-positive and gram-negative organisms. It is bactericidal (Gorbach 1973). It has also been shown to be well tolerated and with no serious side effects (Eni, 1971).

Grech et al (1973) reported that antibiotic therapy in patients with acute or chronic type of pelvic infection is disappointing due to a significantly high rate of residual pelvic pathology, despite favourable sensitivity of the causative pathogens to the antibiotics used. This may be due to insufficient tissue levels of the antibiotic, particularly if this is administered by the oral route.

This trial was therefore designed to evaluate the efficacy and safety of pivampicillin in the treatment of acute pelvic infections in general and in particular those patients who had previous episodes of the disease.

METHODS AND PATIENTS

Fifty patients with acute pelvic inflammatory disease were studied. These patients were admitted as emergencies in one of the Gynaecological wards at the University Teaching Hospital over a 3-month period during 1975.

A detailed history was taken on admission. This was followed by a full examination of the patient. Before antibiotic therapy was commenced, a mid-stream specimen of urine, a urethral and cervical swab were taken for microscopy, culture and sensitivity.

Bacteriological Techniques

Sterile cotton tipped swabs were used to collect bacteriological specimens from the urethra and cervix. These were placed in a sterile tube and delivered immediately to the bacteriology laboratory.

In the laboratory the swabs were treated as follows:

1. **Urethral swab.** The swab was plated in chocolate agar and incubated in carbon dioxide (candle jar). The plates were examined for growth after overnight incubation and after 48 hours.

A gram stain was also carried out on a smear from the swab and examined for pus cells and gram negative diplococci.

2. **Cervical swab.** This was plated on blood agar, chocolate agar and MacConkey agar respectively. The blood agar and chocolate agar plates were incubated in carbon dioxide (candle jar) and the MacConkey agar aerobically for 24 hours. If no growth was obtained they were incubated for a further 24—48 hours before being discarded as no growth.

3. **Mid stream specimen of urine.** The centrifuged deposit was examined microscopically. If more than 3 pus cells per high power field were seen in the urine was cultured quantitatively on blood agar and MacConkey agar. Pure growths of over 10,000/ml. were identified and tested for antibiotic sensitivity. Sensitivity tests were read after 18—24 hours. Sensitivity tests were performed against penicillin, streptomycin, trimethoprim, ampicillin, chloramphenicol, tetracycline and gentamycin.

Treatment

This was commenced soon after the patient was examined. Two capsules each containing 175 mg. of alphacillin (pivampicillin Hcl) were administered orally every 8 hours for a period of 6 days. The nursing staff were instructed to give the capsules after a meal or with a glass of milk.

Therapy was continued provided the condition of the patient improved. If the patient showed no improvement another antibiotic to which the micro-organisms were sensitive was considered. An alternative management was surgical intervention if there

was evidence of a spreading infection or imminent rupture of an abcess.

RESULTS

Predisposing factors

Table 1 shows that 31 patients (62%) reported that the onset of symptoms followed a menstrual period. Nine other patients (18%) related the onset of their symptoms to a recent confinement or abortion. Three patients (6%) gave a history of recent sexual contact. No related factors were identified in 7 patients (14%).

TABLE I

PREDISPOSING FACTORS

Postmenstrual	31	62%
Postpartum	5	10%
Post Abortal	4	8%
Post Intercourse	3	6%
Unrelated	7	14%
TOTAL	50	100%
Mixed infection rate:		37.7%

Twenty four patients (48%) in this series had no history of previous pelvic infection, while 26 patients (52%) claimed to have had previous episodes of the disease which necessitated treatment with antibiotics.

Diagnosis

The diagnosis was made after taking into consideration certain criteria of symptomatology, clinical signs and the course of the disease. Therefore diagnosis in each case (Table 2) attempted to portray which pelvic organs were involved in the inflammatory process and to what extent. Surgery became indicated in 4 patients. Three of these had tubo-ovarian abcesses which did not respond to conservative management, even after the antibiotic regime was changed. In two of these patients the abcesses were drained abdominally and in the other it was excised. The fourth patient had a pyosalpinx, which was also drained abdominally.

TABLE II

DIAGNOSIS

Salpingitis	23
Tubo-Ovarian Abcess	5
Pyosalpinx	2
Pelvic Peritonitis	18
Pelvic Abcess	2
	50

Bacteriological Findings

The spectrum of pathogenic organisms which were identified on culture from the urine, urethral and cervical swabs are shown in Table 3. A positive culture in one or more of the specimens was reported in 39 patients (78%). No organisms were cultured in 6 patients (12%). The reports on the remaining 5 patients were not traced. In 17 patients more than one organism was identified, giving a mixed infection rate of 37.7%.

TABLE III

BACTERIOLOGICAL FINDINGS FROM THE URINE, URETHRAL AND CERVICAL SWABS.

Positive	39	78%
Gonococcus	9	23.1%
Escherichia Coli	11	28.2%
Non-Haemolytic Streptococci	19	48.7%
Staphylococcus Aureus	14	35.9%
Proteus	3	7.7%
Klebsiella	11	28.2%
Mixed Infections	17	37.7%
Negative	6	12%
Not Available	5	

The strains of the various pathogens isolated were all sensitive to ampicillin with the exception of 3 patients. In all three patients treatment with pivampicillin was discontinued due to poor response and another antibiotic regime started. However, conservative management failed in all three patients and surgery became necessary. One of these patients had a mixed infection of Proteus and Klebsiella, which were sensitive only to gentamycin and septrin. In the second patient the culture grew staphylococcus Aureus, sensitive to Septrin. The culture from the third patient grew Eschericia Coli, which was sensitive to Gentamycine.

Response to Alphacillin Therapy

The criteria used for satisfactory clinical response to treatment were the lowering of temperature and pulse rate, decrease in the area of tenderness until it eventually disappeared and the resolution of abdominal and pelvic masses. A notable feature in the trial was the effect on the temperature and pulse rate which returned to normal within 3 days of the commencement of therapy in the majority of patients. In three patients pivampicillin therapy was discontinued and another antibiotic regime instituted because of the deterioration of the patients' condition. The patients failed to improve even after this change of therapy and therefore surgical intervention beceme necessary. Another patient in whom the cervical and

urethral swab showed a mixed infection of gonococci, Esch.coli and non-beta-haemolytic streptococci failed to improve even though the strains of the various pathogens were all sensitive to ampicillin. The patient had a laparotomy and drainage of a pyosalpinx. Pivampicillin was however continued post-operatively until the patient became afebrile.

The clinical response (Table 4A) to alphacillin in the trial was therefore considered successful in 46 patients (92%). There were 3 failures (6%). The patient in whom conservative management failed was recorded as partially successful, since no change of antibiotic was necessary to control the infection.

A pelvic examination was performed on all the patients before discharge from hospital for evidence of residual pelvic signs, such as tenderness or thickening in the adnexael regions. Table 4B shows that no residual pelvic signs were observed in those patients with no previous history of the disease (Acute P.I.D.). In the group of patients who had previous episodes of pelvic infection (Acute/Chronic P.I.D) residual pelvic pathology was recorded in 5 patients (22.7%). The four patients who were operated upon were excluded from this assessment.

TABLE IV (A & B)

THERAPEUTIC RESULTS

A. CLINICAL RESPONSE		
Success	46	92%
Partial Success	1	2%
Failure	3	6%
	50	
B. RESIDUAL PELVIC SIGNS		
Acute P.I.D.	24	Nil
Acute / Chronic P.I.	22	5

Tolerance

Mild epigastric discomfort was reported in 3 patients (Table 5). This occurred during the first two days of treatment and disappeared completely later on. Discontinuation of therapy was never necessary because of this side effect. There were no cases of vomitting and cutaneous side effects of an allergic nature were not observed.

DISCUSSION

There is evidence from this trial that Alphacillin (Pivampicillin Hcl) is effective in the treatment of acute pelvic infection due to susceptible organisms even in the presence of mixed pathogens. Its clinical response was considered successful in 92% of patients.

TABLE V

SIDE EFFECTS

Gastrointestinal Disturbances	3	6%
Vomiting	Nil	
Diarrhoea	Nil	
Allergic Skin Reaction	Nil	

Pivampicillin has the advantage of oral administration and because of its efficient absorption, it need only be given every 8 hours, unlike other oral broad spectrum antibiotics.

Clinical studies have demonstrated that pivampicillin is better absorbed from the intestinal tract than ampicillin and this is reflected in considerably higher peak ampicillin concentrations in serum and higher rate of urinary recovery of ampicillin (Daehne et al, 1971). Also the absorption of pivampicillin is not significantly influenced by administration of food (Roholt et al, 1974). This high concentration of ampicillin in the serum and tissues may have contributed to the very high success rate in this series. Another significant observation in this trial is the low rate of residual pelvic pathology in patients with acute/chronic pelvio infection. It would seem, therefore, that a comparative trial with ampicillin and pivampicillin will yield useful information.

The only side effect in this series was mild epigastric discomfort which was observed in 6% of the patients. This has been the experience of other workers (Roholt 1971; Jordheim, 1974) and Shah et al (1977) after treating acute gonorrhoea with a single dose of 1.4 gms pivampicillin irrespective of whether the patients had taken any meal prior to commencement of therapy. However, since pivampicillin, unlike ampicillin can be taken with meals and milk without depressing absorption, gastro-intestinal side effects can be minimised considerably.

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