SHORT COMMUNICATIONS

A COMBINATION OF AMOXICILLIN AND CLAVULANIC ACID IN THE TREATMENT OF PYODERMA IN CHILDREN

P K Kar

The efficacy and safety of amoxicillin plus clavulanic acid was compared with that of amoxicillin, erythromycin and co-trimoxazole in an open label, randomized trial in 50 children in each group (total 200) with mild to severe pyodermas. Majority (47%) had impetigo. Fifty (25%) children had mild pyoderma, 56 (28%) had moderate and 94 (47%) children had severe pyoderma. Pure growth of *S aureus* was isolated in 130 (65%) children, *S pyogenes* in 42 (21%) and both organisms in 28 (14%) children. In mild to moderate pyoderma either of the drug tried was equally effective. In severe pyoderma, 24 of twenty five (96%) children receiving amoxicillin plus clavulanic acid, 18 of twenty (90%) children in amoxicillin group, 20 of twenty four (83.3%) children in erythromycin group ard 13 of twenty five (52%) children in co-trimoxazole group showed clinical cure on therapy. Amoxicillin combined with clavulanic acid was well tolerated in children and there was no significant side effect except mild diarrhoea in two cases (4%) which was well controlled by taking the drug with meals.

Key Words: Amoxicillin, Clavulanic acid, Pyoderma

Introduction

The prevalence of beta-lactamase producing strain has resulted in *S aureus* resistance in vitro to penicillin G and to the broad spectrum penicillins, ampicillin and amoxicillin.[1] To confront the problem of its vulnerability to beta-lactamase, amoxicillin has been combined with a beta-lactamase inhibitor such as clavulanic acid[2] which is also active against beta-lactamase producing strains of staphylococci.[3]

An attempt was made to study the efficacy of amoxicillin combined with clavulanic acid (ACA) in the management of pyoderma in children.

Materials and Methods

Two hundred children in the age group of 10 months-12 years suffering from pyoderma were selected at random. Materials from the lesions were taken for Gram stain and culture in nutrient agar and blood agar. Antibiotic susceptibility tests were carried out with the organism isolated.

A complete blood count with differential leucocyte count, serum creatinine, blood urea nitrogen, serum glutamic oxaloacetic transaminase and routine urine analysis were carried out. Children were divided in to four groups. Fifty children in each group were given 125 mg amoxicillin plus 30 mg clavulanate per 5 ml of suspension, equivalent to 20 mg amoxicillin/kg/day in three divided doses; amoxicillin 20 mg/kg/day in three divided doses; erythromycin 30 mg/kg/day in four divided doses or co-trimoxazole (8 mg trimethoprim+40 mg sulfamethoxazole/kg/day) in two divided doses in children. The duration of therapy was 10 days.

All patients were instructed to clean the lesions with soap and water and normal saline compress where indicated. Clinical response was evaluated on one of the days 3 to 5; days

From the Department of Dermatology, STD and Leprosy, 151 Base Hospital C/o 99 APO, India.

Address correspondence to : Lt Col P K Kar

7 to 10 days and 10 to 14 days after completion of therapy. Repeat cultures were obtained if appropriate at any of these visits. Patients were considered cured clinically if the lesions resolved during therapy and did not recur within 10-14 days following discontinuation of the antibiotic.

Children who had an allergy to the above drugs or hepatic, renal dysfunction by history or by laboratory evaluation, were excluded from the study.

Results

Out of two hundred children 94 (47%) were suffering from impetigo, 27 (13.5%) had ecthyma, folliculitis 24 (12%), furunculosis 8 (4%), periporitis 12 (6%) and infected scabies in 35 (17.5%) children. Fifty (25%) children had mild pyoderma (1-10 lesions), 56 (28%) had moderate (11-20 lesions) and 94 (47%) children had severe pyoderma (more than 20 lesions). Pure growth of *S aureus* was isolated in 130 (65%) children, *S pyogenes* in 42 (21%) and both organisms in 28 (14%) children. Table I shows the antimicrobial susceptibilities of the bacterial isolates.

Table I. Antibiotic sensitivity tests

Antibiotic	Staph aureus				S pyogenes			
	Sensitive		Resistance		Sensitive		Resistance	
	No	%	No	%	No	%	No	%
Penicillin	67	44.9	82	55.1	53	86.3	8	13.2
Erythromycin	143	95.9	6	4.1	57	93.4	4	6.6
Co-trimoxazole	141	94.6	8	5.4	58	95	3	5
Amoxicillin	136	91.2	13	8.8	59	96.7	2	3.3

The clinical outcomes of the four treatment groups are shown in table II. All four medications proved safe. No patient developed laboratory evidence of haematologic, hepatic or renal dysfunction. Two children in ACA group, two children in amoxicillin group and one each in erythromycin and co-trimoxazole group developed mild diarrhoea.

Discussion

Pyoderma is a very common bacterial skin infection and constitutes highest percentage of skin infection in children.[4] Pyoderma sometimes appears as the main clinical presentation in scabies.[5] Impetigo constitutes the highest percentage of pyodermas in children.[6] In the past, *S pyogenes*, was considered to be the primary pathogen causing impetigo in children.[7] With the clinical presentation of bullous impetigo, *S aureus* was considered to play a role in the pathogenesis. *S pyogenes* is still highly sensitive to penicillin, but this is no longer the case with staphylococci which have developed resistance to penicillins. This resistance is most commonly due to the secretion of beta-lactamases leading to hydrolysis of the beta-lactam ring of the antibiotic molecule.

Inhibitors of the enzymes beta-lactamases, such as clavulanic acid have been shown to be extremely active at inhibiting staphylococcal beta-lactamase.[8] Alone, it possesses very limited intrinsic antibacterial activity. It has been shown, however, in vitro and clinically to potentiate the antibacterial activity of beta-lactam antibiotics specially amoxicillin and other penicillins. Clavulanic acid is rapidly absorbed after oral administration and its pharmacokinetic profile is similar to amoxicillin with a half life of 1 hour.[9]

Fleisher and associates[10] reported the first successful use of ACA in children in the

Table II. Result of treatment and follow up

Type of cases	No. of treated	Clinically cleared		Percentage cleared
		Ist Week	2nd Week	
Group I				
Mild	13	13	-	100
Moderate	12	8	4	100
Severe	25	6	18	96
Group II				
Mild	14	12	2	100
Moderate	16	10	6	100
Severe	20	02	16	90
Group III				
Mild	11	10	01	100
Moderate	15	10	05	100
Severe	24	04	16	83.3
Group IV				
Mild	12	8	4	100
Moderate	13	6	7	100
Severe	25	1	12	52

Group I : ACA; Group II : Amoxicillin; Group III : Erythromycin; Croup IV : Co-trimoxazole

treatment of impetigo and impetigo complicated by cellulitis in 41 patients aged 6 months to 12 years. Clinical cure was obtained in eighteen of 21 patients (86%) receiving ACA. Wachs et al[11] experienced satisfactory bacteriologic and clinical response in treating 43 (90%) of 48 patients suffering from mild to moderate skin and skin-structure infections.

Reisser et al[12] have treated 43 children with skin and soft tissue infection and achieved clinical cure in 37 (97%) children who received ACA. Jaffe et al[13] have treated 21 children suffering from skin and soft tissue infections and achieved clinical cure in 18 (95%) children.

We report results of a similar clinical trial on a larger patient population with a greater variety of types of skin infections in children. In our study, *S aureus* was isolated as sole pathogen in 130 (65%) children. In other 28 (14%) cases where it was isolated, it was present in combination with *S pyogenes*. Thus it may be necessary to direct therapy against the *S aureus* as well as the *S pyogenes* while treating pyodermas.

Amoxicillin and clavulanic acid combination was well tolerated in children. Mild diarrhoea was the most common adverse event in 2 (4%) children each in amoxicillin group whether it was given alone or given in combination with clavulanic acid. Diarrhoea was controlled when the ACA was given soon after the meal. Diarrhoea has been reported with amoxicillin-clavulanate to be as low as 0.8% to as high as 15%.[14]

Since in clinical practice, it is not routine to obtain cultures of skin lesions in children presenting with uncomplicated pyoderma, a shift in the nature of the potentially causative pathogens may require a change in the empiric antimicrobial therapy. ACA combination can be used safely in moderate to severe pyodermas in chidren before the availability of antibiotic susceptibility test.[10-13]

References

1. Finland M. Changing patterns of susceptibility of common bacterial pathogens to antimicrobials. Ann Intern Med 1972; 76: 1009-36.
2. Wise PJ, Neu HC. Experience with amoxicillin: an overall summary of clinical trials in the United States. J Infect Dis 1974; 129 (suppl): 266-75.
3. Neu HC, Fu KP. Clavulanic acid, a novel inhibitor of beta-lactamases. Antimicrob Agents Chemother 1978; 14:650-5.
4. Mehta G, Prakash K, Sharma KB. Streptococcal pyoderma and acute glomerulonephritis in children. Ind J Med Res 1980, 71: 692-700.
5. Hati AK, Chaudhary DSR, Gupta R. Clinico parasitological studies on scabies. Ind J Dermatol Venereol 1974; 40: 3-6.
6. Ramani TV, Jayakar PA. Bacteriological study of 100 cases of pyodermas with special reference to staphylococci-their antibiotic sensitivity and phage pattern. Ind J Dermatol Venereol Leprol 1980; 46:282-6.
7. Peter G, Smith A L. Group A streptococcal infections of the skin and pharynx. New Engl J Med 1977; 297: 311-6.
8. Hunter PA, Coleman K, Fisher J, et al. In vitro synergetic properties of clavulanic acid with ampicillin, amoxicillin and ticarcillin. J Antimicrob Chemother 1980; 6: 455-70.
9. Diagneault EA, Hinton PA, Rebert TA, et al. Relationship between potassium clavunate and bioavailabillity of amoxicillin. J Clin Pharmacol 1982; 22:4-7.
10. Fleisher GA, Wilmett CM, Compes JM. Amoxicillin combined with clavulanic acid for the treatment of soft tissue infections in children. Antimicrob Agents Chemother 1983; 24: 679-84.
11. Wachs GN, Nelen TM, Parish LC. Comparison of cefadroxil and amoxicillin/clavulanate in mild, moderate skin and skin-structure infections. Adv Ther 1992; 9: 69-80.
12. Risser WL, Paplan SL, Mason EO, et al. Treatment of soft tissue infections in children with amoxicillin-clavulanic acid combination or cefaclor. Current Ther Res 1985; 37: 747-53.
13. Jaffe A, O'Brien CA, Reed MD, et al. Randomized comparative evaluation of augmentin and cefactor in pediatric skin and soft-tissue infections. Current Ther Res 1985; 38: 160-8.
14. Weber DJ, Tolkoff-Rubin NE. Amoxicillin and potassium clavulanate: an antibiotic combination. J Pharmacother 1984; 4: 122-36.