USE OF AMOXICILLIN AND CLAVULANIC ACID (AUGMENTIN) IN THE TREATMENT OF SKIN AND SOFT TISSUE INFECTIONS IN CHILDREN

Lt Col PK KAR*

(Department of Dermatology and STD, 151 Base Hospital, C/O 99 APO)

ABSTRACT

The efficacy and safety of amoxicillin plus clavulanic acid, a combination of antibiotics potentially effective against beta-lactamase producing bacteria, was compared with that of amoxicillin, erythromycin and co-trimoxazole in an open label, randomized trial in 200 children with mild to severe skin and soft tissue infections. The majority (47%) had impetigo. Fifty (25%) children had mild pyodermas, 56 (28%) had moderate and 94 (47%) children had severe pyodermas. A pure growth of *Staphylococcus aureus* was isolated from 130 (65%) children. *S. pyogenes* was isolated from 42 (21%), children and both organisms in 28 (14%) children. In mild to moderate pyoderma 84 per cent of children receiving the combination were cured clinically at the end of the 1st week, whereas 73.3 per cent children in amoxicillin group, 76.9 per cent children in erythromycin group and only 56 per cent children in co-trimoxazole group showed clinical cure at the end of the 1st week. In severe pyoderma 96 per cent children receiving amoxicillin plus clavulanic acid, 90 per cent children in amoxicillin group, 83 per cent children in erythromycin group and 52 per cent children in co-trimoxazole group showed clinical cure. Amoxicillin combined with clavulanic acid was well tolerated by children.

MJAFI 1997; 53 : 87-90

KEYWORDS : Amoxicillin; Clavulanic acid; Drug therapy, combination; Pyoderma.

Introduction

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

In this study an attempt has been made to study the efficacy of amoxicillin and clavulanic acid combination (ACA) in the management of skin and soft tissue infection in children.

Material and Methods

Two hundred children in the age range of 10 months - 12 years suffering from skin and soft tissue infections were selected at random. Children with 1-10 lesions were categorized as having mild pyoderma, those with 11-20 lesions as moderate

and those with more than 20 lesions as severe pyoderma. Material from the lesions were taken for Gram stain and culture in nutrient agar and blood agar. Antibiotic susceptibility tests were carried out on 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 4 groups of 50 each. Children in Group I were given a suspension containing 125 mg amoxicillin and 30 mg clavulanate per 5 mL, in a dose equivalent to amoxicillin 20 mg/kg/day in 3 divided doses. Groups II, III and IV received amoxicillin 20 mg/kg/day in 3 divided doses, erythromycin 30 mg/kg/day in 4 divided doses, and co-trimoxazole (trimethoprim 8 mg/kg/day + sulphamethoxazole 40 mg/kg/day) in 2 divided doses, respectively. The duration of therapy was 10 days. All patients (or their parents) were instructed to clean the lesions with soap and water.

*Classified Specialist (Dermatology & Venerology), 151 Base Hospital, C/O 99 APO

Clinical response was evaluated on one of the days of day 3 to 5, day 7 to 10, and day 10 to 14 day, after completion of therapy. Repeat cultures were obtained if necessary on any of these visits. Patients were considered clinically cured if the lesions resolved during therapy and did not recur within 14 days after discontinuation of the antibiotic.

Results

Out of the 200 children, 94 (47%) were suffering from impetigo, 27 (13.5%) had ecthyma, 24 (12%) had folliculitis, 8 (4%) had furunculosis, 12

(6%) had periporitis and 35 (17.5%) had infected scabies. Fifty (25%) of all these children were found to have mild infection, 56 (28%) had moderate and 94 (47%) children had severe infections. Pure growth of *Staph. aureus* was isolated from 130 (65%) children, *S. pyogenes* from 42 (21%) and both organisms from 28 (14%) children. Table 1 shows the antimicrobial susceptibilities of the bacteria isolated.

The clinical outcome in the 4 treatment groups is shown in Table 2. In mild to moderate pyoderma, 21 out of 25 (84%) children in Group I were cured clinically, whereas 22 out of 30

TABLE 1
Antibiotic sensitivity of isolates from 200 patients

Antibiotic	Staph. aureus				S. pyogenes			
	Sensitive No.		Resistant No.		Sensitive No.		Resistant No.	
Penicillin	67	(42.4)	91	(57.5)	62	(88.5)	8	(11.4)
Erythromycin	143	(90.5)	15	(9.4)	66	(94.2)	4	(5.7)
Co-trimoxazole	141	(89.2)	17	(10.7)	67	(95.7)	3	(4.2)
Amoxycillin	136	(86.0)	22	(13.9)	68	(97.1)	2	(2.8)

(Figures in the parenthesis denote percentage)

TABLE 2
Results of treatment and follow-up in 4 groups of children with skin infection

Patient group	No. of children	Clinically cleared after				Percentage cleared Total
		1st week	(%)	2nd week	(%)	
Group I						
Mild	13	13	(100.0)	—		100.0
Moderate	12	8	(66.6)	4	(33.3)	100.0
Severe	25	6	(24.0)	18	(72.0)	96.0
Group II						
Mild	14	12	(85.7)	2	(14.2)	100.0
Moderate	16	10	(62.5)	6	(37.5)	100.0
Severe	20	2	(10.0)	16	(80.0)	96.0
Group III						
Mild	11	10	(90.9)	1	(9.1)	100.0
Moderate	15	10	(66.6)	5	(33.3)	100.0
Severe	24	4	(16.6)	16	(66.6)	83.3
Group IV						
Mild	12	8	(66.6)	4	(33.3)	100.0
Moderate	13	6	(46.1)	7	(53.8)	100.0
Severe	25	1	(4.0)	12	(48.0)	52.0

Group I : Amoxycillin + clavulanic acid

Group II : Amoxicillin

Group III : Erythromycin

Group IV : Co-trimoxazole

(73.3%) in Group II, 20 out of 26 (76.9%) in Group III and 14 out of 25 (56%) children in Group IV showed clinical cure at the end of the 1st week. In severe pyoderma the response was delayed but, by the end of the 2nd week, 24 of 25 (96%) children in Group I, 18 of 20 (90%) children in Group II, 20 of 24 (83.3%) children in Group III and 13 of 25 (52%) children in Group IV were clinically cured.

All 4 medications proved safe. No patient developed laboratory evidence of haematologic, hepatic or renal dysfunction. Two children in Group I, 2 in Group II and 1 each in Groups III and IV developed mild diarrhoea which was controlled by taking the drug with meals. All infections resolved without untoward incident while continuing the medication.

Discussion

Pyoderma is a very common bacterial skin and soft tissue infection and constitutes highest percentage of skin infection in children. Pyoderma sometimes appears as the main clinical presentation in scabies [4,5]. Impetigo is the commonest form of pyoderma in children. In the past *S. pyogenes* was considered to be the pathogen primarily causing impetigo in children. *Staph. aureus* was considered to play a role in the pathogenesis of bullous impetigo. *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.

The recent discovery of inhibitors of beta-lactamase, such as clavulanic acid, which possess very limited intrinsic antibacterial activity, has enabled potentiation of the antibacterial activity of beta-lactam antibiotics specially amoxicillin and other penicillins [8]. 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 treatment of impetigo and impetigo complicated by cellulitis in 41 patients aged 6 months to 12 years. Clinical cure was obtained in 18 of 21 patients (86%) re-

ceiving ACA. Wachs et al [11] had 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] treated 43 children with skin and soft tissue infections and achieved clinical cure in 37 (97%) children who received ACA. Jaffe et al [13] treated 21 children suffering from skin and soft tissue infections and achieved clinical cure in 18 (95%) children.

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

ACA was well tolerated in children. Mild diarrhoea was the most common adverse event and was controlled when ACA was given soon after a meal. Incidence of diarrhoea has been reported with ACA to be as low as 0.8 per cent and even as high as 15 per cent [14].

Since in clinical practice it is not usual to perform cultures of skin lesions in children presenting with uncomplicated pyoderma, a change in the nature of the causative pathogens may require a change in the empiric antimicrobial therapy prescribed. ACA combination is stable against beta-lactamase producing strains of *Staph. aureus*. Hence it can be used safely in moderate to severe pyodermas in children even before the results of an antibiotic susceptibility test are available [12,13].

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 B. Streptococcal pyoderma and acute glomerulonephritis in children. *Ind J Med Res* 1980; 71: 693-700.

5. Hati AK, Choudhary DSR, Gupta R. Clinico-parasitological studies on scabies. *Indian Journal of Dermatology and Venereology* 1974; 440: 3-6.
6. Ramani TV, Jaykar PA. Bacteriological study of 100 cases of pyoderms with special reference to staphylococci - their antibiotic sensitivity and phage pattern. *Indian Journal Dermatology, Venereology and Leprology* 1980; 46: 282-6.
7. Peter G, Smity AL. 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, Robert TA, et al. Relationship between potassium clavulanate and bioavailability 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. *Advances in Therapy* 1992; 9: 69-80.
12. Rissor 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 MB, et al. Randomized comparative evaluation of Augmentin and Cefaclor in paediatric skin and soft-tissue infections. *Current Ther Res* 1985; 338: 160-8.
14. Weber DJ, Tolkoff-Rubin NE. Amoxicillin and potassium clavulanate: an antibiotic combination. *J Pharmacother* 1984; 4: 122-36.