AUGMENTIN (AMOXYCILLIN AND CLAVULANIC ACID) IN THE TREATMENT OF URINARY TRACT INFECTIONS AND SKIN AND SOFT TISSUE INFECTIONS

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SYNOPSIS

Twenty patients with urinary tract infections and fifteen patients with skin and soft tissue infections were treated with Augmentin, a combination of Amoxycillin with the β-lactamase inhibitor clavulanic acid.

Sixteen patients (80%) with urinary tract infections responded to treatment. Thirteen patients were bacteriologically assessable. Augmentin was effective in ten, giving a success rate of 77%. Augmentin was effective in six out of eight patients infected with Amoxycillin resistant organisms.

Thirteen patients (87%) with skin and soft tissue infections were effectively treated. Ten patients were bacteriologically assessable, eight of them (80%) responded to treatment. Four of the patients were caused by Amoxycillin resistant staphylococcus aureus either alone or in combination with Streptococcus pyogenes.

Side effects were limited to nausea (3%), rash (3%) and transient leukopenia (3%).

INTRODUCTION

In the past decade many gram-negative species have shown widespread resistance to many β-lactam antibiotics. One approach to overcome this problem has been the discovery of compounds which inhibit bacterial β-lactamases. Clavulanic acid is a naturally occuring β-lactam product of Streptococcus clavuligerus and is a potent inhibitor of bacterial β-lactamases, although it has little intrinsic antibacterial activity.

In the present study, the clinical efficacy, safety, and tolerance of clavulanate as a formulation with Amoxycillin trihydrate has been studied in the treatment of urinary tract and skin and soft tissue infections.

MATERIAL AND METHOD

Twenty patients with urinary tract infection were selected for treatment with one Augmentin tablet (Amoxycillin trihydrate 250 mg, clavulanate 125 mg) thrice daily for seven days. All of them had acute symptomatology suggesting of urinary tract infections. Two urinary cultures were taken before treatment. Urine specimens were cultured bacteriologically at the laboratory in the Singapore General Hospital. Standardised platinium loop calibrated to deliver 0.01 ml and 0.001 ml of urine were used to determine the number of bacteria in each mililiter of urine. Each urine specimen was inoculated onto blood agar and eosin methylene blue agar plates. After overnight incubation at 37°C, bacterial colonies on the blood agar plates were counted and the quantitative counts were determined. Isolates of microorganism were identified by standard procedure (1). Sensitivity to antibiotics incuding amoxycillin (25 ug) and augmentin (30 ug) were performed using the disc diffusion method of Bauer et al (2). Two further urine specimens were taken on day 3, day 8, day 14 and six weeks later.

Fifteen patients with skin and soft tissue infections were given two Augmentin tablets thrice daily for ten days. These patients were primarily skin sepsis — 11 patients, infected trauma — 3 patients, and infected eczema — 1 patient. Bacteriological cultures were done before treatment and day after completion of treatment. The wound swabs or pus were also cultured on blood agar and eosin methylene blue agar, and were then placed in cooked meat media. The cooked meat and agar plates were inoculated aerobically at 37°C. The following morning, the plates were read and organisms identified by biochemical reactions. The β-haemolytic Streptococci were grouped using the Phadebact. Streptococci Testing (Pharmacia Diagnostic AB). Sensitivity testing of the bacteria were performed using the method of Bauer et al (2). If there was no bacterial growth on primary culture, a secondary subculture was performed from the cooked meat media. Two further specimens were taken post treatment for bacteriological culture whenever possible. Safety and tolerance were monitored with routine blood counts, biochemistry and urinalysis before treatment and at the end of treatment. Daily clinical assessment of the patients was done in all in-patients. Outpatients cases were reviewed at special clinic at frequent intervals.

Response to treatment was assessed by relief of symptoms, when relevant, and by examination of specimens for bacteriological analysis.

RESULTS

a) Urinary tract infections (Table 1)

Twenty patients were treated with one tablet of Augmentin three times a day. Sixteen patients (80%) were clinically effective. Thirteen patients had positive bacteriological cultures pretreatment with one culture having two different organisms isolated. Four organisms were sensitive to Amoxycillin, ten were resistant, twelve were sensitive to Augmentin and two were resistant. Augmentin was effective bacteriologically in ten patients, giving a success rate of 77%. Augmentin was effective in six out of eight patients infected with Amoxycillin resistant organisms.

Table 1
Urinary tract infection — Bacteriological assessment
(1 Augmentin t.d.s.)

Serial No.	Organism isolated	Sensitivity to Amoxycillin		Sensitivity to Augmentin		Cured / Failed
		Sensitive	resistant	Sensitive	resistant	
1	proteus morganii		—		—	cured
2	Group β streptococcus		—	+		failed
3	E. Coli		—	+		cured
4	E. Coli		—	+		cured
5	E. Coli	+		+		cured
6	Staph. epidermis	+		+		cured
7	E. Coli		—	+		cured
8	Staph. aureus		—	+		cured
9	E. Coli	+		+		cured
10	E. Coli		—	+		failed
11a	E. Coli	+		+		cured
11b	Kleb sp		—	+		failed
12	E. Coli		—	+		cured
13	Acinetobacter Calcoacetines		—		—	cured
Total	14	4	10	12	2	

b) Skin and soft tissue infections (Table 2)

Fifteen patients were treated with two Augmentin tablets three times a day. Thirteen patients (87%) were clinically effective. Bacteria was isolated in ten patients, and four of these patients had mixed infection of Staphylococcus aureus and Streptococcus pyogenes. Three isolates were sensitive to Amoxycillin and six were resistant; seven were sensitive to Augmentin and two were resistant. Augmentin was effective bacteriologically in eight patients, giving a success rate of 80%. Augmentin was effective in all four patients infected with Amoxycillin resistant organisms.

Table 2
Skin & Soft tissue infection — Bacteriological assessment
(2 Augmentin t.d.s.)

Serial	Organism	Sensitivity to Amoxycillin		Sensitivity to Augmentin		Cured / Failed
No.	isolated	Sensitivie	resistant	Sensitive	resistant	
1	Staph. aureus*		—	+		cured
2	Enterobacter sp.		—		—	cured
3	Group D Streptococcus		(not done)			cured
4	Staph. aureus*	+		+		failed
5	Group G β Strep	+		+		cured
6	Staph. aureus*		—	+		cured
7	E. Coli		—		—	failed
8	Staph. aureus	+		+		cured
9	Staph aureus		—	+		cured
10	Staph. aureus*		—	+		cured
Total	10	3	6	7	2	

*All four patients have mixed infections of Staph. aureus and Streptococcus pyogenes.

c) Safety and tolerance

Three separate side effect occurred in thirty five patients. One patient (3%) had nausea and this was treated symptomatically. One patient (3%) had rash which cleared with topical application. One patient (3%) had transient leukopenia (total white counts was 2800/cmm) at the end of treatment which reverted to normal spontaneously. Augmentin was not withdrawn in any patients.

There was no significant changes in clinical chemistry (liver functions test, urea, creatinine) and urinalysis pretreatment and after completion of treatment.

DISCUSSION

The results of the clinical study demonstrate that clavulanic acid and amoxycillin trihydrate adminstered together were effective in both the urinary tract infection and skin and soft tissue infections. It also eradicates a high proportion of infections caused by amoxycillin resistant organisms.

The overall success rate for urinary tract infections was 77%. This is consistent with results from other workers (3, 4, 5).

80% of skin and soft tissue infections responded to the treatment. The majority of the infections were due to Amoxycillin resistant Staphylococcus aureus and/or Streptococcus pyogenes. Clinically, it is sometimes difficult to determine whether both Staphylococcus aureus and Streptococcus pyogenes are causing a skin infection. Augmentin could go some way in solving this problem. The result of this study further confirms previous work by Millard (6).

Ball et al(3) demonstrated that the dose of clavulanic acid appeared to be critical in patient tolerance. A doubling of calvulanic acid to 500 mg given every 8 hour was associated with a 40% prevalence of nausea in his series. This was not shown to be the case in our study of fifteen patients with skin and soft tissue infections, who were given two Augmentin tablets (Amoxycillin 500 mg and clavulanate 250 mg) every eight hours.

In summary, the data obtained in this clinical study indicate, despite the small number of patients, that Augmentin was safe and highly efficacious for the treatment of urinary tract infections and skin and soft tissue infections.

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This study carries the Clinical Trial Certificate No. 8/81 of The Ministry of Health, Singapore.

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