CEFTAZIDIME IN FEBRILE SLE PATIENTS

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SYNOPSIS

Ceftazidime, a β-lactase cephalosporin was administered to 12 febrile SLE patients with infection. 7 of 12 patients had Pseudomonas bacteremia, 3 Staph aureus and 2 each of E Coli and Salmonella Gp B. The clinical response rate to Ceftazidime was 92%. No adverse effects to Ceftazidime were encountered.

Ceftazidime appears an effective and safe anti-microbial in the initial therapy of febrile, infected lupus patients.

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INTRODUCTION

Fever is a common problem in patients with SLE. Apart from disease flares, infections are of paramount concern in febrile, immunocompromised lupus patients. Infections can be serious and life-threatening. The selection of appropriate antimicrobial combinations in the initial therapy of a patient suspected of infection is crucial. Ceftazidime, a β-lactamase stable cephalosporin has broad anti-bacterial activity against many gram-positive and most gram-negative bacillary pathogens. In addition it has increased activity against Pseudomonas aeruginosa.

In this study, we evaluated the efficacy of Ceftazidime in the treatment of lupus patients with moderate or severe bacterial infection with clinical assessment of the response, and the safety and tolerance of Ceftazidime.

MATERIALS AND METHODS

12 patients with SLE and fever and who had suspected or proven infections entered the study. Patients who received antibotics in the preceding 48 hours were excluded. Ceftazidime was used as a single antimicrobial agent except where a known or mixed infection was present, combination antibotics were used.

Drug Administration

Ceftazidime was administered by intravenous infusion. A dose of 3-6gm per day was used depending on the size of the patient and the type of infection.

Laboratory Tests

Test for haemoglobin, white cell count, platelet count and prothrombin time, serum chemistry determinations which included values for creatinine, transaminases, alkaline phosphatase and urinalysis were performed before, during and after therapy to evaluate development of any toxic reactions. Clinical cure refers to elimination of signs and symptoms of infection. Patients who failed to respond to monotherapy after 72 hours were considered as treatment failures.

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RESULTS

12 female SLE patients received Ceftazidime for a total of 7 days. The mean age of the patients was 33.7 years. Blood cultures yielded positive bacteriological growth in 11 patients. Pseudomonas aeruginosa was the commonest organism isolated, being present in 7 of 12 cultures. 3 patients had Staphylococcal aureus bactermia, 2 Salmonellosis, 1 had urinary tract infection and another septic arthritis. 4 patients were neutropenic (total white < 4000). 1 patient had a rapidly fatal infection. 11 patients were on corticosteroids, the dose of which ranged from 2.5mg on alternate day to 60mg daily. Two were on the immunosuppressive agent Azathioprine (Imuran) — Table 1 and 2. The antibiotic profile of the organisms cultured is shown in Table 2A.

Table 1

PATIENT CHARACTERISTICS	
No. of SLE patients	12
Female : Male	12 : 0
Mean age (years)	33.7 (range 16 — 58)
Race (Chinese/ Indian/Malay)	8/2/2
Duration of treatment (days)	7

DISCUSSION

Patients with SLE have an increased risk of infection.[1] This increased susceptibility to infections is seen particularly in those on high dose corticosteroids and in those with renal failure.[2] Other predisposing factors are granulocyte and phagocyte dysfunction, impaired bacterial activity and hyposplenism.[3,5] The micro-organisms commonly reported to be associated with infections in SLE are summarised in Table 3. The predominance of Gram-negative bacilli, namely Klebsiella sp, E Coli and Pseudomonas aeruginosa has important implications in the selection of empirical microbial therapy in lupus patients with infections. In addition, Staphylococcal infections should be kept in mind. Fungal infection is less common but candida may produce systemic infection and present a major diagnostic and therapeutic challenge.

Infection is the major cause of death in our SLE patients.[6] It is our practice to initiate antimicrobial chemothe-

Table 2

Patient	Organism	Source	TW	Outcome	Other Antibiotics	Prednis-olone (mg)	Immunosu-ppressive (mg)
1	Salmonella Group B	Blood	1500	Cured	Nil	10	
2	E Coli	Urine	15700	Cured	Nil	2.5 eod	
3	P aeurginosa E Coli	Blood	7500	Died	Clindamycin	Nil	
4	P aeurginosa Staph aureus	Blood	700	Cured	Amikacin Cloxacillin	40	Imuran 50
5	P aeurginosa	Blood	6900	Cured		30	Imuran 50
6	P aeurginosa	Blood	2500	Cured	Nil	60	
7	Salmonella Group B	Blood	5200	Cured	Nil	30	
8	P aeurginosa	Blood	3400	Cured	Nil	7.5	
9	Staph aureus	Blood	17100	Cured	Clindamycin	30	
10	Staph aureus	Blood	5400	Cured	Clindamycin	30	
11	P aeurginosa	Blood	5900	Cured	Nil	45	
12	P aeurginosa	Blood	3300	Cured	Nil	20	

TW total white
Patients 3, 4, 9, 10 had combination antibotics
The other patients received ceftazidime only

Table 2A
SENSITIVITY TEST

Patient	Organism	Antibiotic					
		Amikacin	Ampicillin	Gentamycin	Cloxacillin	Ceftrioxone	Ceftazidime
1	Salmonella Group B	ND	+	+	ND	+	+
2	E Coli		+				
3	P aeurginosa	+		+			+
	E Coli		−	+		+	
4	P aeurginosa	+		+			
	Staph aureus		+	+	+		
5	P aeurginosa	±	−	−		−	−
6	P aeurginosa		±	+		+	+
7	Salmonella Group B		+	+		+	
8	P aeurginosa		−	+		+	
9	Staph aureus		−	+	+		+
10	Staph aureus		+	+	+		+
11	P aeurginosa		−	+		+	−
12	P aeurginosa	−	−	−		−	−

ND Not done

Table 3
INFECTION IN SLE PATIENTS — PATHOGENIC MICRO-ORGANISMS

Bacteria	Viruses	Fungi	Protozoa/Helminths
Escherichia coli Klebsiella pneumoniae Enterobacter spp. Proteus spp. Pseudomonas aeruginosa Serratia marcescens Staphylococcus aureus Staphylococcus epidermidis enterococci diphtheroids	Herpes simplex Varicella-Zoster Cytomegalovirus	Candida spp. Aspergillus fumigatus Cryptococcus neoformans	Pneumocystis carinii Strongyloides stercoralis Toxoplasma gondii

rapy early in patients with fever of 38°C or more and in whom infection is suspected. In this study, Pseudomonas aeruginosa was the commonest organism in 7 isolates, all of which were associated with bacteraemia. There were 3 cases of Staph aureus infection isolated from blood cultures and 2 cases each of E Coli and Salmonella Group B. All but one patient responded to therapy with Ceftazidime. The clinical response rate was 92%. No adverse events occurred. There was no evidence of rash, diarrhoea, haemolysis or hypo thrombinaemia in the patients. No patient had recurrence of fever or infection within 4 weeks of discontinuation of Ceftazidime.

Neutropenia (neutrophil count < 4000) was present in 5 patients. Patients with neutropenia are subject to second or multiple infection which may necessitate use of combination antimicrobial therapy.[7] A high index of suspicion of concurrent SLE and Salmonellosis has been previously emphasized.[8] Recognition of Salmonella infection may be delayed since SLE and Salmonellosis share similar clinical and laboratory denominators. These include fever, rash, pleurisy, abdominal pain, synovitis, glomerulonephritis, leucopenia, and circulating immune complexes.[9]

In summary, this study shows that inital single agent drug regimen of Ceftazidime in a febrile SLE patient with infection is a reasonable option based on its broad spectrum of activity which includes Pseudomonas aeruginosa. Mono-therapy would presumably cause lower toxicity and may be the only antibotic necessary in the majority of patients. Certain patients will require modification of antibotic therapy especially those with severe neutropenia. The limited activity of third generation cephalosporins against gram positive organisms especially Staphylococci and Group D streptococci is noteworthy although Ingram showed that Ceftazidime covers possibly Staphylococci.[10]

Empirical microbacterial drug therapy in febrile, and infected lupus patients should contain an anti-pseudomonas agent. Ceftazidime is a good choice. However, the cost of the drug is a limiting factor. Nevertheless, this must be balanced against its efficacy and side effects. Infection in SLE must be considered as potentially fatal and be treated aggressively. The right choice of antibiotic and the speed of its administration can prevent overwhelming and fatal sepsis.

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