CLINICAL EFFICACY OF SULBACTAM/AMPICILLIN IN THE TREATMENT OF MODERATELY SEVERE BACTERIAL INFECTIONS

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ABSTRACT

20 patients with moderately severe bacterial infections were studied to determine the clinical efficacy and safety of parenteral sulbactam/ampicillin. There were 9 female and 11 male patients. Their mean age was 51 years. 8 patients had pnemonia, 5 urinary tract infection, 4 cellulitis of the leg and 3 had pustular tonsillitis. 85% of patients had resolution of fever and symptoms within 48 hours of commencing treatment. 95% had successful treatment outcome. The organisms isolated included E. Coli, Klebsiella sp, Branhamella catarrhalis and Bacillus species. In 2 patients, the organisms isolated demonstrated in-vitro ampicillin resistance. However, they recovered fully with sulbactam/ampicillin therapy. No adverse side-effects were reported and dosage adjustment was not required in the elderly.

Key Words: Sulbactam/Ampicillin combination (Unasyn)
Bacterial infections

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INTRODUCTION

The occurence of beta-lactamase producing organisms have limited the usefulness of ampicillin as the first-line wide-spectrum antibiotic. A survey of 27 European institutions revealed highly resistant gram-negative rods (1). This problem is likely to increase world-wide in the coming years. Sulbactam sodium, a beta-lactamase inhibitor which acts by binding irreversibly to most lactamases (2, 3) has been shown to protect antibiotics such as ampicillin when used in combination (4).

This study was aimed to evaluate the clinical efficacy and safety of parenteral sulbactam/ampicillin combination (Unasyn) in the treatment of moderately severe bacterial infections.

METHOD

Patient selection

20 patients who required hospitalisation as a result of bacterial infections were studied during the period of October 1987 to July 1988. Inclusion criteria were: 1) males and non-pregnant females between ages 13 — 80 years; 2) clinical evidence of respiratory tract infections, urinary tract infections, skin or soft tissue infections; 3) diagnosis supported by a suggestive medical history, abnormal physical findings and an increased leucocyte count. Abnormal radiographic findings were necessary in patients with pneumonias.

Exclusion criteria: a) pregnant or breast-feeding females or females likely to become pregnant during the study; b) terminally ill patients whose condition precluded evaluation of a therapeutic response; c) patients receiving concomitant antibacterial therapy; d) known allergy to the beta-lactam group of antibiotics; e) severe life-threatening infections; f) significant renal impairment (serum creatinine > 2mg%).

Patients were assessed daily for any side-effects to the drug. The daily highest recorded oral temperature was noted. Fever was defined as a recorded oral temperature of > 37.5°C. Blood, sputum or urine specimens were sent for isolation of organisms when necessary. Verbal consent was obtained prior to entry into the study.

Dosage and administration

All patients were given a combination of 500mg Sulbactam and 1gm Ampicillin (Unasyn) 8 hourly for 5 to 7 days. The sterile powder was diluted in 50ml normal saline or 5% dextrose solution and infused over 30 minutes.

Definition of response

A cure was defined as the complete resolution of all presenting symptoms and signs and absence of fever, normalisation of the total white count, pyuria or abnormal radiological findings at the end of therapy. An improvement was defined as the persistence of symptoms and signs despite general improvement and well-being of the patient at the end of therapy, absence of fever and normalisation of the total white count. Both cure and improvement were considered as successful treatment outcome. A failure occurred when the patient showed no clinical response at the end of therapy or when he or she deteriorated while on treatment and required a change of antibiotics.

RESULTS

9 female and 11 male patients were studied. Their ages ranged from 20 — 78 years with a mean age of 51 years. 6 patients were aged between 66 and 78 years, with a mean age of 71.8 years. The patients' diagnoses is shown in Table 1. The duration of illness prior to admission ranged from 2 days to 2 weeks (mean: 6 days). 13 patients had concomitant medical illness (Table 2).

Normalisation of temperature and full resolution of symptoms within 24 hours were attained in 50% and 40% of patients respectively. After 48 hours of therapy, 80% patients had complete resolution of fever and symptoms.

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TABLE 1
DIAGNOSIS OF PATIENTS

Diagnosis	No of patient
Pneumonias	8
Urinary tract infections	5
Cellulitis of leg	4
Pustular tonsillitis	3

TABLE 2
CONCOMITANT DISEASES IN PATIENTS

Patient no.	Diseases
1	Left renal calculus
2	Hypertension
4	Hypertension, Diabetes mellitus
8	Diabetes mellitus, Ischaemic heart disease
9	Hypertension, Diabetes mellitus
10	Hypertension
12	Chronic obstructive airways disease
14	Right renal calculus, Left hemiparesis
16	Hypertension, Bronchial asthma
17	Diabetes mellitus
19	Pneumoconiosis, Chronic liver disease
20	Chronic obstructive airway disease

This rapid resolution of symptoms contributed greatly to the feeling of well-being in the patients. Several patients requested for early discharge due to this rapid improvement. (Fig 1) The duration of hospitalisation and clinical response is shown in Table 3.

Figure 1 — Time taken for resolution of fever and presenting systems

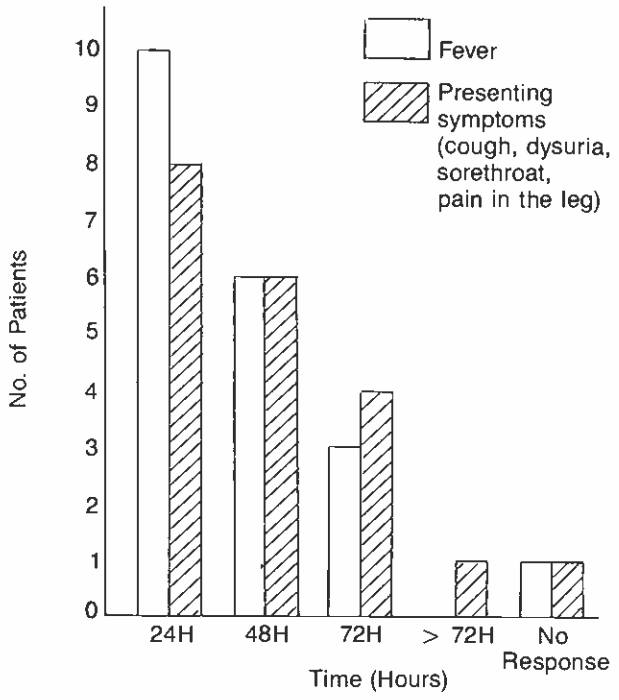

TABLE 3
RELATIONSHIP BETWEEN DURATION OF HOSPITAL STAY AND CLINICAL RESPONSE

Hospital stay (days)	Cure	Improvement	Failure
< 7	15	1	Nil
7	2	Nil	Nil
> 7	Nil	1	1

Organisms were isolated from the blood, urine or sputum specimens in 7 patients (Table 4). 5 patients had gram-negative infections. This included Escherichia coli, Klebsiella sp. Branhamella catarrhalis. The isolates which showed in-vitro resistance to ampicillin are listed in Table 5.

TABLE 4
ORGANISMS ISOLATED AND OUTCOME OF TREATMENT

Patient no	Organsim	Source	Outcome
1	E. Coli	Urine	Cure
5	E. Coli	Urine	Cure
6	E. Coli	Urine	Cure
14	Klebsiella sp.	Sputum	Cure
15	Branhamella Catarrhalis	Sputum	Cure
18	Klebsiella sp.	Blood	Cure
19	Bacillus sp.	Blood	Failure

TABLE 5
ORGANISMS WHICH SHOW RESISTANCE TO AMPICILLIN IN IN-VITRO TESTING

Patient No.	Organism	In-Vitro Ampicillin Resistance
1	E. Coli	No
5	Ps. aeruginosa	N.A.
6	Ps. species	N.A.
14	Klebsiella	Yes
15	Branhamella catarrhalis	Yes
18	Klebsiella	No
19	Bacillus sp.	N.A.

N.A. — Not available

No patient reported adverse-effects such as diarrhoea, nausea, vomiting and rash. No haematological abnormalities were noted. Liver function tests were not performed routinely in all patients. However, none showed symptoms and signs of hepatitis during their hospital stay. Patient no. 19 had a history of chronic liver disease. He did not suffer a deterioration of liver function at the completion of therapy.

17 patients had complete cure, 2 improved and 1 failed therapy.

DISCUSSION

Bacterial resistance to antibiotics presently in common use is an increasing problem. This has led to the search for agents that are effective against the majority of clinically important bacterial infections seen in hospitals. The combination of sulbactam with a penicillin that has a wide spectrum of anti-bacterial activity may be considered use-

Our study showed that Unasyn is efficacious in treating infections caused by E. Coli, Klebsiella sp. and B. catarrhalis. The cure rate was 85% and improvement rate 10%. The overall successful outcome was of the order of 95%. This high level of efficacy was accompanied by a low incidence of adverse reactions. Our study showed that sulbactam/ampicillin was safe and well tolerated. In the elderly, elimination of sulbactam/ampicillin was reported to be approximately half the rate of healthy, young adult volunteers. However, no significant drug accumulation was observed (8). No dosage adjustment was required in our group of 6 elderly patients who had successful treatment outcome.

ful in the therapy of these bacterial infections. Sulbactam/ampicillin combination has been shown to be effective in the treatment of pneumonias (5), pelvic infections (6) and urinary tract infections (7) and in infections caused by beta-lactamase producing organisms.

In conclusion, Sulbactam/Ampicillin has been shown to be well tolerated, safe and clinically effective in the treatment of moderately severe bacterial infections.

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