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Prevalence of Resistance to Beta-Lactam Antibiotics Among Respiratory Tract Isolates in a Hospital Situation

K. CHANDRASEKAR, S. D. RAJENDRAN*, S. A. DHANARAJ, LAKHVINDER S. BATOLAR AND B. SURESH
Department of Pharmacy Practice, JSS College of Pharmacy, Ootacamund–643 001

Antimicrobial resistance is a serious global issue. Since only empirical therapy with antibiotics is widely followed in India, it is helpful that the treating doctors have information on the prevalence of microbial resistance to the commonly prescribed antibiotics for various infections. A study of the prevalence of antimicrobial resistance among respiratory tract isolates was conducted in a secondary care Government hospital inTamil Nadu in order to gauge the existing level of antimicrobial resistance. Out of 154 isolates obtained, 138 possessed seven types of pathogenic microorganisms. This study has revealed that there exists a high level of resistance to penicillins like ampicillin, methicillin and cloxacillin and the first generation cephalosporin, cephalexin. Third generation cephalosporins, ceftriaxzone and ceftazidime, were effective against the organisms isolated.

Prevalence of antimicrobial resistance is a global issue. The level of resistance varies greatly from one part of the world to another. The problem of resistance is low in countries where the accessibility of drug is restricted and high in countries where easy accessibility of antibiotics is existing[1]. In India easy accessibility of antibiotics coupled with self medication and widespread inappropriate prescribing has led to an increasing level of resistance to various antibiotics. Antibiotics surveillance programs are rarely conducted and so the level of resistance in various parts of the country is not known. The urgent need to regularly monitor the patterns of susceptibility and resistance of various organisms to different antibiotics has been expressed.

In developed countries, antibiotics prescribed to the patients are based on the sensitivity patterns of microorganisms to various antibiotics[2]. Since the laboratory tests are expensive to the common man in India, frequently antibiotics are prescribed empirically by the medical practitioners. This leads to the development of resistance to the antibiotics commonly used. In Government hospitals, due to budget constraints, sensitivity tests on the isolates are not regularly conducted and antibiotics are empirically prescribed.

In an attempt to assist the doctors in and optimise the empirical treatment of infections, it was planned to conduct a surveillance programme on microbial resistance to antibiotics used in infectious diseases. The programme was initiated in Government Head Quarters Hospital in Ootacamund, Tamil Nadu. A preliminary survey conducted by the authors revealed that the number of patients visiting the hospital for respiratory tract infections is higher than that of other infections. Based on this, it was decided to undertake a study in patients with respiratory tract infections.

MATERIALS AND METHODS

Isolates:

During the six-month period between October 1998 and March 1999, a total of 154 isolates were collected from the patients admitted with the clinical features of lower and upper respiratory tract infections. These isolates were collected by either sputum or throat swabs following standard procedure[3,4]. Specimen collected included sputum and throat swabs. Three different media, namely,

*For correspondence

Blood Agar, Chocolate Agar and MacConkey Agar were used for culturing. The samples were initially examined microscopically to evaluate the causative agent of infection. Identification was based on colony morphology, gram staining, and by biochemical tests, which included, triple sugar iron agar test, indole production test, citrate utilization test and mannitol motility agar[5].

Antimicrobial susceptibility tests:

A standard disc diffusion (Kirby-Bauer) method was used for the susceptibility testing, because of its simplicity[6]. Mueller-Hinton agar, Blood Agar and Chocolate Agar were used in the study. The following beta-lactam antibiotic discs obtained from Hi-Media Laboratories (P) Ltd., Mumbai, were used: cephalexin (30 µg/disc), ceftazidime (30 µg/disc), ceftriaxone (30 µg/disc), ampicillin (10 µg/disc), methicillin (5 µg/disc) and cloxacillin (1 µg/disc). The final inoculum concentration was about $5x10^5$ Cfu/ml. Plates were incubated for 20 to 24 h at 35º in ambient air and inhibition zones were measured. The isolates were compared with control organisms throughout this study.

RESULTS

Of the 154 isolates obtained, 138 isolates contained seven different pathogenic microorganisms. These included 76 isolates of *Streptococcus pneumoniae*, 42 isolates of *Klebsiella pneumoniae*, 11 isolates of *Staphyloccus aureus*, 4 isolates of *Pseudomonas aureginosa*, 3 isolates of *Escherichia coli* and one isolate each of *Streptococcus pyogenes* and *Haemophilus influenzae*. The remaining 16 isolates contained non-pathogenic normal flora.

The susceptibilities of these isolates to various antimicrobial agents tested are summarised in Table I and figs. 1-3. The susceptibilities of the commonly found microorganisms to the beta-lactam group of antibiotics

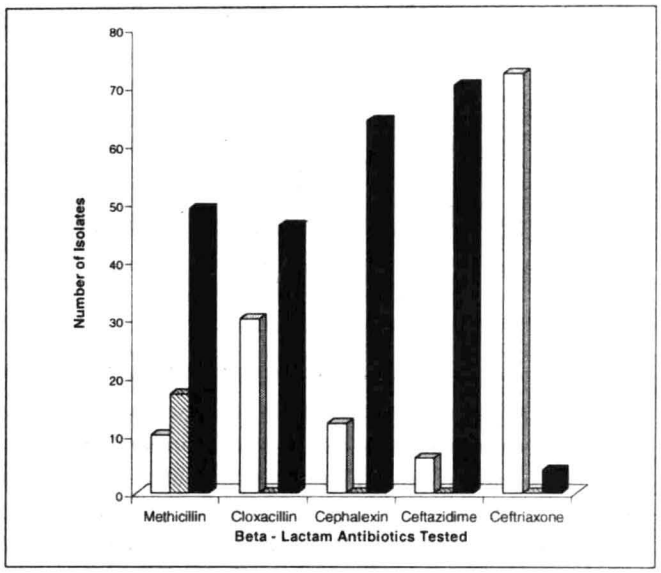

Fig. 1: Antibiogram of *S. pneumoniae* to beta-lactam antibiotics

Total number of isolates is 76. X– axis represents number of isolates and Y– axis indicates beta-lactam antibiotics tested; S stands for susceptible organisms (□), I represents organisms with intermediate susceptibility (▨) and R indicates resistant organisms (■).

TABLE 1: SENSITIVITY PATTERN OF MICROORGANISMS ISOLATED FROM THE RESPIRATORY TRACT TO THE ANTIBIOTICS TESTED

Name of the drug	*S. pneu* (76 isolates)			*K. pneu* (42 isolates)			*S. aureu* (11 isolates)			*P. aerug* (4 isolates)			*E. coli* (3 isolates)			*S. pyogenes* (1 isolate)			*H. influe* (1 isolate)		
	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R
Ampicillin	10	17	49	0	9	33	0	4	7	0	0	4	0	0	3	0	1	0	*	*	*
Methicillin	30	0	46	*	*	*	3	0	8	*	*	*	*	*	*	1	0	0	*	*	*
Cloxacillin	12	0	64	*	*	*	3	0	8	*	*	*	*	*	*	0	0	1	*	*	*
Cephalexin	6	0	70	0	6	36	5	1	5	0	0	4	0	3	0	0	0	1	0	0	1
Ceftazidime	72	0	4	42	0	0	11	0	0	2	2	0	3	0	0	1	0	0	1	0	0
Ceftriaxone	66	7	3	36	0	6	9	2	0	2	0	2	3	0	0	1	0	0	1	0	0

S represents susceptible organisms, I means organisms with intermediate susceptibility and R indicates resistant to microorganisms listed: (*S. pneu- S. pneumoniae, K. pneu- K. pneumoniae, S. aureu- S. aureus, P. aerug- P. aeruginosa, and H. influe- H. influenzae*)

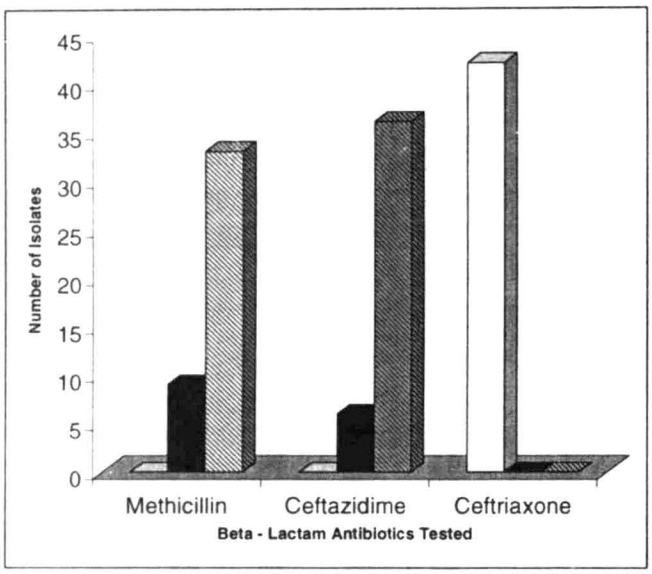

Fig. 2: Antibiogram of *K. pneumoniae* to beta-lactam antibiotics

Total number of isolates – 42. X– axis represents number of isolates and Y– axis indicates beta-lactam antibiotics tested; S stands for susceptible organisms (□), I represents organisms with intermediate susceptibility (▨) and R indicates resistant organisms (■).

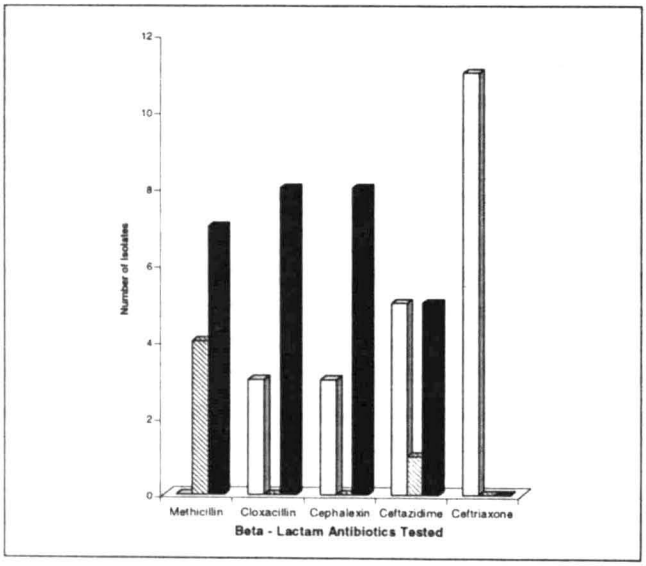

Fig. 3: Antibiogram of *S. aureus* to beta-lactam antibiotics

Total number of isolates – 11. X– axis represents number of isolates and Y– axis indicates beta-lactam antibiotics tested; S stands for susceptible organisms (□), I represents organisms with intermediate susceptibility (▨) and R indicates resistant organisms (■).

were generally poor. Out of 76 isolates of *S. pneumoniae*, only 10 (13.16%) isolates were susceptible to ampicillin, 30 (39.47%) were susceptible to methicillin, and 12 (15.79%) were susceptible to cloxacillin. Isolates of *K. pneumoniae* and *S. aureus* also showed poor susceptibilities towards these antibiotics. The susceptibility of *K. pneumoniae* to ampicillin was 0% and the susceptibility of *S. aureus* was 0% to ampicillin and 27.3% to methicillin and cloxacillin.

When these isolates were tested against cephalosporins, it was found that the sensitivity to the first generation antibiotic, cephalexin was similar to that of the penicillin group of antibiotics. Out of 76 isolates of *S. pneumoniae*, 6 (7.9%) were susceptible to cephalexin. However, the susceptibility to the third generation cephalosporins was good. Seventy two (94.7%) isolates were susceptible to ceftazidime and 66 (86.8%) isolates were susceptible to ceftriaxone. The same trend towards these antibiotics also continued for other isolates. Cephalexin was ineffective, whereas ceftazidime (100%) and ceftriaxone (85.7%) were active against *K. pneumoniae*. The observed susceptibilities of *P. aeruginosa* and *E. coli* against ceftriaxone and ceftazidime in the study are comparable to the previous reports. Some isolates showed intermediate resistance towards these antibiotics.

DISCUSSION

Beta-lactam group of antibiotics continue to be one of the most widely prescribed antibiotics the world over, including our country. Such widespread use has been shown to contribute to the development of resistance towards these antibiotics. The widespread, uncontrolled use of these drugs in community practice in our country has given rise to a high level of resistance towards these drugs as observed by us in this study. Drugs like methicillin and cloxacillin are regarded as effective against penicillinase enzyme producing microorganisms. The extent of methicillin and cloxacillin resistance observed in this study is alarming. This high level of resistance may be due to the uncontrolled and frequent use of beta-lactam antibiotics and non-compliance of patients with respect to antibiotic dosage and duration.

Staphylococcal resistance to methicillin (MRSA) is not due to the destruction of the antibiotic by beta-lactamase enzyme, but it is due to a marked decrease in the affinity of penicillin binding proteins (PBPs 1, 2

and 3)[7]. In addition, in the presence of methicillin, MRSA strains synthesize a novel penicillin binding protein, PBP 2_a. In MRSA strains both PBP 2_a and PBP 3 show very low affinity for methicillin. PBP 2_a has poor affinity for beta-lactam antibiotics and is functional even when other PBPs are blocked.

The occurrence of MRSA strains appears to be related to the use of all penicillins and not specifically to the use of penicillinase-resistant penicillins. MRSA strains are capable of producing serious diseases, and so there is an urgent need in our country for effective control of the spread of these strains. Guidelines to this effect have been published in many countries. Multi-pronged approaches including combination of screening patients and staff, mupirocin for treatment of carriers and the use of isolation wards have been successful. Methicillin resistance gene is quite unstable and *S. aureus* strains can lose this resistance if limitations on the administration of antibiotics are observed. Borderline resistant cases have also been reported. Of some interest is the finding that classical MRSA strains which possess PBP 2_a are more sensitive to beta-lactamase labile penicillins such as penicillin G, ampicillin and amoxycillin, provided that the beta-lactamase can be neutralised, which can be done by inhibitors of the enzyme such as clavulanic acid or sulbactam. However, *in vivo* studies in animal models have produced conflicting results and it appears that such combinations (e.g. amoxycilin/clavulanic acid) may not be useful for treatment of MRSA infections in humans.[8]

There is an urgent need to improve awareness on the use of antibiotics in the community. Lack of awareness on the rational use of antibiotics was evident from the results of the study. Absence of any national antibiotic policy could have aggravated the problem. Since antibiotic surveillance programmes are seldom conducted, the prevailing pattern of antibiotic resistance in various regions of the country is not known. Little information is available on microbial resistance in our geographical area. Although this report is from a single hospital, being the biggest hospital in the region it treats a majority of the indwelling population. And so these results may indicate the antimicrobial resistance status of this region.

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