IN VITRO COMPARATIVE ACTIVITY OF EIGHT ANTIPSEUDOMONAL AGENTS

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ABSTRACT

Five hundred and thirty strains of *Pseudomonas aeruginosa* isolated from indoor patients were tested against three chemical groups comprising eight antibiotics. High degree of resistant strains ranging from 38.0% to 61.8% were seen against carbenicillin, piperacillin and gentamicin. However amikacin, ciprofloxacin, ceftazidime, netilmicin and norfloxacin showed comparatively better activity with resistant strains ranging from 7.8% to 22.8%. A notably higher rate of resistance was seen in urinary isolates.

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KEY WORDS : *Pseudomonas*; Beta-lactams; Aminoglycosides; Quinolones.

Introduction

P*seudomonas aeruginosa*, a widely distributed organism, is a major human pathogen. The organism is invasive, toxigenic and produces infections in patients with abnormal host defences. It is currently recognised as one of the leading causes of severe hospital associated infections [1]. In the recent years, an increased frequency of resistant strains to several antibiotics has been experienced [2]. In view of this a study was conducted where hospital associated strains of *Pseudomonas aeruginosa* were tested in vitro against three broad groups of beta-lactams, aminoglycosides and quinolones and their comparative activity was evaluated.

Material and Methods

Five hundred and thirty isolates of *Pseudomonas aeruginosa* were recovered from clinical samples of patients admitted in Army Hospital Delhi Cantt during 1991-92. Of these 272 isolates were from urine, 177 from pus and skin swabs, 45 from blood and 36 from sputum and others. The samples were received from various critical care units including renal transplant centre, burn centre and

neonatal units. Different enriched and selective media were used and *Pseudomonas aeruginosa* strains were confirmed by Gram stain, growth on oxidative fermentative media, pigment production and oxidase reaction. The isolates from significant bacteriuria samples were grouped as urinary isolates. The other group was from pus and other body fluids samples. All the isolates were tested against eight antibiotics : carbenicillin, piperacillin, ceftazidime, gentamicin, netilmicin, amikacin, ciprofloxacin and norfloxacin taken from three chemical groups of beta-lactams, aminoglycosides and quinolones. Mueller-Hinton medium was used for antibiotic sensitivity testing carried out by Stokes' comparative method [3].

The antibiotic disc concentration of each drug procured from HiMedia Laboratories and M/s Fulford (India) Ltd was as follows : carbenicillin and piperacillin 100 µg each; ceftazidime and netilmicin 30 µg each; and gentamicin, amikacin, ciprofloxacin and norfloxacin 10 µg each.

Results

The chemical group and antibiotic wise resistant pattern of the organism is shown in

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the Table 1. A notable higher rate of resistant organisms was seen in urinary isolates as compared to isolates from pus and other body fluids. Very high rates of resistant strains, i.e. 38.0% to 61.8% were seen against carbenicillin, gentamicin and piperacillin. The other antibiotics like amikacin, ciprofloxacin, ceftazidime, netilmicin and norfloxacin showed better activity with resistant organisms ranging from 7.8% to 22.8%.

Discussion

Pseudomonas aeruginosa is an important hospital associated pathogen causing a high degree of morbidity and mortality [1,2]. The organism is increasingly becoming resistant to many antibiotics [2]. The most common group of drugs being used against the pathogen are beta-lactams, aminoglycosides and quinolones. The common beta-lactams in use are carbenicillin, piperacillin and cephalosporins. The major mechanism of resistance to beta-lactams found in *Pseudomonas aeruginosa* is expression of beta-lactamase [4], which is usually chromosomal and/or plasmid mediated. The well tried aminoglycosides have been in use against pseudomonal species for several years. The antibiotics of the group in use are gentamicin, amikacin, netilmicin, sisomicin, kanamycin and streptomycin. The resistance mechanism of this group to pseudomonas is mainly due to

penetration barrier and enzymatic modification of the drugs [4].

The quinolones consist of potent antibacterials like nalidixic acid, norfloxacin, ciprofloxacin, ofloxacin and many others. All these drugs are highly active against Gram negative and positive organisms and are well tried against *Pseudomonas aeruginosa*. Two major mechanisms of resistance of *Pseudomonas* to quinolones are altered target (DNA gyrase) and reduced antibiotic uptake [5,6].

In our study, *in vitro* activity of eight antipseudomonal agents has been evaluated. The overall percentage of resistant strains from urinary isolates was more as compared to the strains from pus and other body fluids (Table 1). This was also experienced in a recent similar study [7]. In the broad group beta-lactams, ceftazidime showed least resistant strains ranging from 12.4% to 21.7% ($p < 0.001$) as compared to 38.0% to 61.9% in carbenicillin and 43.6% to 44.9% in piperacillin (Table 1). In the aminoglycoside group, amikacin showed the least number of resistant strains ranging from 7.8% to 11.0% ($p < 0.001$ & < 0.05) as against 14.7% to 19.9% in netilmicin and 57.4% to 59.6% in gentamicin. Ciprofloxacin showed better results in quinolones with isolates resistant percentage of 10.1 to 18.8 as compared to 14.7% to 22.8% in norfloxacin. However, this fell short of statistical significance.

TABLE 1
Resistance profile of *Pseudomonas aeruginosa* in hospital infections.

Chemical group	Antibiotic	Pus & other (n= 258)		Urine (n=272)	
		Resistant strains	%	Resistant strains	%
Beta-lactams	Carbenicillin	98	38.0 ^a	168	61.8 ^d
	Piperacillin	112	43.6 ^b	122	44.9 ^e
	Ceftazidime	32	12.4 ^c	59	21.7 ^f
Aminoglycosides	Gentamicin	148	57.4 ^g	162	59.6 ^j
	Netilmicin	38	14.7 ^h	54	19.9 ^k
	Amikacin	20	7.8 ⁱ	30	11.0 ^l
Quinolones	Ciprofloxacin	26	10.1	51	18.8
	Norfloxacin	38	14.7	62	22.8

p values : a vs c, b vs c, g vs i, d vs f, e vs f, j vs l, and k vs l = < 0.001 , h vs i = < 0.05 , ciprofloxacin vs norfloxacin = not significant

Previous studies in India and abroad have shown variable percentages of resistant organisms to different anti-pseudomonal agents [7-9]. In a recently conducted study in India, Sugandhi and Shivananda [9] have experienced that most of the pseudomonal strains were resistant to commonly used drugs like carbenicillin (55%) and gentamicin (84%) but the strains showed very little resistance to ciprofloxacin, 4% and 0% to netilmicin. Fujita *et al* [10] in 1991 reported 21% strains resistant to piperacillin, 22% to ceftazidime, 26% to amikacin and 33% to ofloxacin. The results in our study are fairly comparable with the studies mentioned, though the percentage of resistant strains to various drugs is some times different. This may be due to extensive use of these drugs in the community and also production of various enzymes inactivating the drugs or reduction of uptake of the antibiotic by the pathogen [5,6].

The analysis of data indicates broad guidelines in that, drugs showing maximum efficacy (amikacin and ciprofloxacin) be reserved for life threatening infections. Netilmicin and ceftazidime may be used as standard antipseudomonal agents. The use of carbenicillin, piperacillin and gentamicin should be restricted for sometime allowing time for the antimicrobial susceptibility profile to change before reintroducing these drugs. At that time the earlier drugs may be withdrawn.

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