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Original Research Article

The antibacterial efficacy of different antipseudomonal agents against *Pseudomonas aeruginosa*

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A B S T R A C T

K e y w o r d s

P.aeruginosa, Lower Respiratory Tract Infection, Carbapenem, Floroquinolones Cephalosporins

Pseudomonas aeruginosa is a leading cause of nosocomial infections. The risk of emergence of antibiotic resistance may vary with different antibiotic treatments. To compare the risks of emergence of resistance associated with three antipseudomonal agents, carbapenems (meropenem and imipenem), floroquinolones (Ciprofloxacin and levofloxacin) and cephalosporins (cefepime and ceftazidime) were studied. In this cross-sectional study, we investigated a total of 64 *P. aeruginosa* isolates obtained from Lower Respiratory Tract Infection (LRTI) patients. The carbapenems (89%) were found to be more effective in vitro than cephalosporins (46.9%) and fluoroquinolones (34.5%). Our study shows a carbapenems may be of value for treatment of LRTI.

Introduction

Severe cases of acute exacerbations of chronic bronchitis (AECB) and community-acquired pneumonia (CAP) are included in Lower respiratory tract infections (LRTIs) also involve hospital acquired pneumonia (HAP); the latter consists of ventilator-associated pneumonia (VAP) and healthcare-associated pneumonia (HCAP) (Grossman *et al.,* 2005). *P. aeruginosa* is one of the most common gram-negative bacterial causes of health care-acquired infections (Gaynes and Edwards, 2005; Fluit *et al.,* 2000; Streit *et al.,* 2004). *P. aeruginosa* is a leading cause of nosocomial infections, ranking second among the gram-negative pathogens reported to the National Nosocomial Infection Surveillance System. There are a limited number of antimicrobial agents with reliable activity against *P. aeruginosa*, including antipseudomonal penicillins and cephalosporins, carbapenems, and fluoroquinolones, particularly ciprofloxacin. Aminoglycosides are frequently used as part of combination regimens for treatment of serious pseudomonal infections but are generally not recommended as single drug (Carmeli *et al.,* 1999).

The purpose of this study was to compare

the bactericidal activity of three groups of antibiotics against *P. aeruginosa* isolates from the LRTI patients.

Materials and Methods

This cross-sectional study was conducted in the Department of Pulmonary Medicine and Microbiology Department of a tertiary care hospital, Lucknow, between September 2010 to August 2012. Sixty four patients from indoor and outdoor patient departments of pulmonary medicine, with confirmed diagnoses of lower respiratory tract infections and who did not receive either of the antibiotics in previous 72hrs, patients of ages ≥ 18 years with symptoms which were suggestive of LRTI (i.e., two or more of the following symptoms: cough, sputum production, shortness of breath, wheeze, fever during this illness, chest pain), who gave written informed consents for their participation were enrolled for the study. The study was approved by the institutional ethics committee.

Sputum and broncho alveolar lavage samples were collected in sterile, wide mouthed containers and then transferred to Microbiology Laboratory for further processing. Samples were cultured on Blood agar, Mac Conkey agar and Pseudomonas isolation agar plates (Hi-media,Mumbai). Colonies with appropriate colonial morphologies were classified presumptively as *P. aeruginosa* and they were further identified by conventional biochemical tests (Forbes *et al.,* 2007). Antimicrobial susceptibility was done by Kirby Bauer disk diffusion method as per Clinical Laboratory Standard Institute (CLSI) 2010 guidelines (CLSI, 2010). *P. aeruginosa* ATCC 27853 was used as quality control.

Results and Discussion

Out of 200 samples, 64 were confirmed as *P. aeruginosa* isolates. Data on the antimicrobial susceptibility patterns of the 8 multidrug resistant strains are shown in Table 1.

Many of the isolates were resistant to ampicillin and amoxicillin/clavulanic acid (97.0%). Table 2 shows the activity of the two carbapenems, fluoroquinolones and Cephalosporins against the 64 isolates of *P. aeruginosa.* Thirty (46.9%) isolates were susceptible to both cefepime and ceftazidime and thirty four (53.1%) resistant to both agents.

Eighty nine (89.0%) of the isolates were susceptible and two (3.2%) were resistant to both meropenem and imipenem. Minor category interpretation difference occurred with 2 (3.2%) of the 64 isolates. Three (4.6%) isolates were susceptible to imipenem and resistant to meropenem. More of the 64 isolates were susceptible to carbapenem (89%) than to Fluoroquinolones (46.9%) Cephalosporins (34.5%).

Resistance to antimicrobial agents is an increasing clinical problem and is a known public health threat. *P. aeruginosa* shows a particular tendency for the development of resistance.

The appearance of resistance in *P. aeruginosa* also limits future therapeutic choices and is associated with increased rates of mortality and morbidity and higher costs (Carmeli *et al.,* 1999). *P. aeruginosa* was most common Gram negative bacteria in LRTIs, as found by a study in North America (Hoban *et al.,* 2003). In our study, the percentages of antibiotic resistant isolates were found to be fairly high, with the exception of imipenem and pipercillin/tazobactum, which were the most effective antibiotics. The present data showed that imipenem was the efficacious antibiotic agent against *P. aeruginosa* with a

low resistant rate of just 3.2%, however Dorobˇat *et al.* reported resistance upto 28.2% to imipenem and 26.0% to meropenem in LRTI patients (Dorobˇat *et al.*, 2007). In contrast, second and third generation cephalosporins were found to be less efficacious than ***c***arbepenems. In the present study antimicrobial susceptibility of the fluoroquinolones tested ranged against *P. aeruginosa* 34.4% and 51.6% showed the reverse pattern. 95.4% of isolates were susceptible to both of the carbapenems and 53.2% to both of fluoroquinolones. quinolones may be accelerating the development of antimicrobial resistance to these agents and may be the driving force behind increases in resistance (Peña *et al.*, 1995).

Table.1 In vitro Susceptibility testing of 64 isolates of *P. aeruginosa* to be commonly used antimicrobial agents

Drugs	***Sensitive***	***Resistant***	***Intermediate***
Ampicillin	0%	3.0%	97.0%
Amikacin	69.0%	29.0%	2.0%
Amoxicillin/clavulanic acid	0.0%	97.0%	3.0%
Aztreonam	55.0%	43.0%	2.0%
Ceftriaxone	33.0%	65.0%	2.0%
Gentamycin	44.0%	51.0%	5.0%
Pipercillin/Tazobactum	83.0%	14.0%	3.0%
Tobramycin	65.0%	30.0%	35.0%

Table.2 *In vitro* activity of three antimicrobial against of drugs in 64 *P. aeruginosa* isolates 3groups-(A) Carbepenems-(Meropenem and Imipenem),(B) Fluoroquinolones-(Ciprofloxacin and Levofloxacin),(C) Cephalosporins-(Cefepime and Ceftazidime)

A.Meropenem* and *Imipenem		***No. of isolates(%)***
Susceptible	Susceptible	57(89.0)
Resistant	Resistant	2 (3.2)
Intermediate	Susceptible	2(3.2)
Resistant	Susceptible	3(4.6)
B.Cefepime* and *Ceftazidime		
Susceptible	Susceptible	30 (46.9)
Resistant	Resistant	34 (53.1)
C. Levofloxacin* and *Ciprofloxacin		
Susceptible	Susceptible	22 (34.5)
Resistant	Resistant	33 (51.6)
Intermediate	Resistant	2 (3.2)
Intermediate	Susceptible	1 (1.5)
Resistant	Susceptible	3 (4.6)
Susceptible	Intermidiate	3 (4.6)

Compared with other antimicrobials, Imipenem demonstrated enhanced activity against *P. aeruginosa* isolates. We observed that resistant to imipenem was lower than that to meropenem, ceftazidime and ciprofloxacin.

Carbapenem groups of drugs are more effective and susceptible than fluoroquinolones and cephalosporins groups of drugs against the isolates of *P. aeruginosa* from our population of LRTI patients. Based on our study carbapenem groups of agents may be of value for treatment of pulmonary exacerbation in patients with LRTI.

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