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Retrospective analysis of antibiotic susceptibility patterns of respiratory isolates of Pseudomonas aeruginosa in a Turkish University Hospital

Ugur Gonlugur*[1], Mustafa Zahir Bakici[2], Levent Ozdemir[3], Ibrahim Akkurt[1], Serhat Icagasioglu[4] and Fusun Gultekin[4]

Address: [1]Department of Chest Diseases, Cumhuriyet University Medical School, Sivas, Turkey, [2]Department of Microbiology, Cumhuriyet University Medical School, Sivas, Turkey, [3]Department of Public Health, Cumhuriyet University Medical School, Sivas, Turkey and [4]Department of Internal Medicine, Cumhuriyet University Medical School, Sivas, Turkey

Email: Ugur Gonlugur* - gonlugur@e-kolay.net; Mustafa Zahir Bakici - mzahirbakici@yahoo.com; Levent Ozdemir - lozdemir@cumhuriyet.edu.tr; Ibrahim Akkurt - iakkurt@cumhuriyet.edu.tr; Serhat Icagasioglu - dilara@cumhuriyet.edu.tr; Fusun Gultekin - ygultek@cumhuriyet.edu.tr

* Corresponding author

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Abstract

Background: Lower respiratory tract infections due to Pseudomonas aeruginosa have a high mortality rate. Antibacterial activity of various antibiotics against P. aeruginosa isolated from each hospital depends on the variety or amount of antibiotics used in each hospital.

Method: A total of 249 respiratory isolates of Pseudomonas aeruginosa in Sivas (Turkey) were included between January-1999 and January-2002. Isolates were tested against 14 different antibiotics by a disc diffusion method or standardized microdilution technique.

Results: Organisms were cultured from the following specimens: sputum (31.3%), transtracheal/endotracheal aspirates (37.8%), and bronchial lavage (30.9%). Isolates in bronchial lavage were highly susceptible to cefoperazone and aminoglycosides. Resistance to ampicillin/sulbactam was 98.8%, ticarcillin 40.1%, ticarcillin/clavulanic acid 11.2%, piperacillin 21.8%, aztreonam 66.6%, cefotaxim 75.4%, ceftriaxone 84.2%, cefoperazone 39.0%, ceftazidime 50.8%, gentamicin 57.5%, tobramycin 58.4%, amikacin 25.4%, ciprofloxacin 16.1%, and imipenem/cilastatin 21.6%. The term multidrug-resistant P. aeruginosa covered resistance to imipenem, ciprofloxacin, ceftazidime, gentamicin, and piperacillin. 1.2% of isolates were multidrug-resistant.

Conclusions: These findings suggest that amikacin resistance increases progressively in Turkey. Piperacillin and ticarcillin/clavulanate were the most active agents against both imipenem- and ciprofloxacin-resistant isolates in our region.

Background

Pseudomonas aeruginosa is primarily a nosocomial pathogen and the most common gram-negative bacillus causing hospital-acquired pneumonia. Despite therapy, the mortality from hospital-acquired pseudomonal pneumonia is approximately 70 percent [1]. Unfortunately, there are no specific measures to prevent nosocomial pseudomonal infections. Despite the availability of a variety of effective antimicrobial agents, treatment of pseudomonal pneumonia is often challenging. The aim of this study was to

Table 1: Resistance rates (percentages) of Pseudomonas aeruginosa to antibiotics

Antibiotic	Site of isolation			
	MIC 50/90	Sputum n = 78	Tracheal aspirates n = 94	Bronchial lavage n = 77
Ampicillin/sulbactam	8/32	96.6	100	100
Ticarcillin	16/128	50.0	55.2	15.2
Ticarcillin/clavulanic acid	16/>64	7.3	15.1	15.0
Piperacillin	16/128	22.7	20.9	21.6
Aztreonam	2/>16	70.0	79.1	49.2
Cefotaxim	8/>32	76.1	89.5	60.0
Ceftriaxone	16/64	86.9	100	66.1
Cefoperazone	16/64	56.4	55.5	4.2
Ceftazidime	1/>16	54.0	67.4	27.6
Gentamicin	4/>8	68.8	86.0	11.7
Tobramycin	4/>8	63.1	79.3	29.3
Amikacin	16/64	25.3	40.9	6.6
Ciprofloxacin	1/4	16.6	18.1	13.1
Imipenem/cilastatin	4/>8	19.2	28.4	15.1

reveal the antibiotic susceptibility patterns of Pseudomonas aeruginosa isolated airway samples in Sivas, Central Anatolia.

Material and methods

The antibiotic susceptibility patterns of 249 respiratory isolates of Pseudomonas aeruginosa were retrospectively analyzed. Data between 01.01.1999 and 01.01.2002 was obtained in microbiology laboratory of University of Cumhuriyet and processed to eliminate duplicate registrations. The isolates were identified conventional or automatized (Api) techniques. Isolates collected from the same specimen source of the same patient within 7 days were excluded. Organisms were cultured from the following specimens: sputum (31.3%), transtracheal/endotracheal aspirates (37.8%), and bronchial lavage (30.9%). All consecutive isolates were accepted, as we did not attempt to distinguish the actual pathogens from colonizing strains.

Susceptibility to 14 antimicrobial agents was confirmed at the central laboratory by disk diffusion according to the National Committee for Clinical Laboratory Standards guidelines [2]. Inoculated plates were incubated aerobically at 35°C and estimated after 18 h. For quality control of the disk diffusion tests E. coli ATCC 25922 and S. aureus ATCC 25923 strains were used. Disk diffusion method was used until November 1999 in our microbiology laboratory, and later antibiotic resistance patterns were analyzed by a co-ordinating laboratory that determined minimal inhibitory concentrations of these 14 antimicrobial agents using a standardized microdilution technique (Sceptor system, Becton Dickinson Microbiology System).

The results of the susceptibility testing were classified into two categories. The category "susceptible" was defined as identification of a strain as susceptible by the disk diffusion method or microdilution technique. All resistant and intermediate isolates of the species were classified under the definition "resistant".

The significance of differences in resistance was evaluated using EpiInfo software (version 5.0). Susceptibility and resistance were calculated as percentages with 95% confidence intervals. The X^2 test with Yates correction or Fisher's exact two-tailed test was used to assess the association of selected variables with the prevalence of resistant isolates. The analysis was performed on the cross-tabulated values of the presence of the resistant/susceptible isolates, according to the categories of the selected variable. A p-value of <0.05 was considered statistically significant.

Results

The antibiotic resistance patterns of isolates are presented in Table 1. Compared to those in sputum or tracheal aspirates, isolates in bronchial lavage were more susceptible to ticarcillin, aztreonam, cefoperazone, ceftriaxone, ceftazidime, gentamicin, tobramycin, amikacin ($p < 0.01$), and cefotaxim ($p < 0.05$). Isolates in tracheal aspirates were more resistant to ceftriaxone ($p < 0.01$), gentamicin ($p < 0.01$), tobramycin ($p < 0.05$), and amikacin ($p < 0.05$) than in sputum.

The term multidrug-resistant P. aeruginosa covered resistance to imipenem, ciprofloxacin, ceftazidime, gentamicin, and piperacillin. Among the 249 isolates, 3 (1.2%) were designated as being multidrug-resistant.

Table 2: Resistance rates (percentages) of imipenem-, gentamicin-, piperacillin-, and ciprofloxacin-resistant isolates

Antibiotic	All isolates n = 249	Imipenem-resistant n = 49	Gentamicin-resistant n = 137	Ciprofloxacin-resistant n = 40	Piperacillin-resistant n = 43
Aztreonam	66.6	79.4	89.7	100	83.3
Cefoperazone	39.0	68.0	68.4	72.7	57.7
Cefotaxim	75.4	90.9	94.7	96.1	82.1
Ceftazidime	50.8	77.0	73.5	79.5	76.9
Ceftriaxone	84.2	93.7	95.3	93.5	89.7
Ciprofloxacin	16.1	32.6	21.1	100	18.6
Imipenem	21.6	100	29.9	45.5	21.4
Tobramycin	58.4	74.5	88.5	78.9	69.0
Amikacin	25.4	49.0	41.2	28.9	30.2
Gentamicin	57.5	77.5	100	75.0	64.3
Piperacillin	21.8	20.6	27.9	27.6	100
Ticarcillin	40.1	74.0	67.1	66.7	68.2
Ticarcillin/clavulanic acid	11.2	13.0	11.6	23.8	33.3

The antibiotic resistance patterns of imipenem-, gentamicin-, and ciprofloxacin-resistant isolates are presented in Table 2. Compared to the entire group, ciprofloxacin-resistant strains were more resistant to five classes of anti-pseudomonal agents (aminoglycosides, extended-spectrum cephalosporins, carboxypenicillins, monobactam, and carbapenem), whereas gentamicin-resistant strains (aminoglycosides, extended-spectrum cephalosporins, carboxypenicillins, monobactam) and imipenem-resistant strains (aminoglycosides, extended-spectrum cephalosporins, carboxypenicillins, quinolones) more resistant to four classes of anti-pseudomonal agents ($p < 0.05$). Imipenem-resistant strains were more susceptible to aztreonam than ciprofloxacin-resistant strains, and to tobramycin than gentamicin-resistant strains ($p < 0.05$). Piperacillin and ticarcillin/clavulanate were the most active agents against both imipenem- and ciprofloxacin-resistant strains.

There was not significant difference in the susceptibility to ureidopenicillins in imipenem-, gentamicin-, and ciprofloxacin-resistant strains compared to the entire group. Piperacillin-resistant strains were more resistant to aztreonam, ceftazidime, ticarcillin, and ticarcillin/clavulanate than the entire group. Piperacillin-resistant strains were more susceptible to cefotaxim and tobramycin but, more resistant to ticarcillin/clavulanate than gentamicin-resistant strains ($p < 0.05$).

Discussion

Resistance of gram-negative aerobic bacteria to aminoglycoside antibiotics differs by region and country. Resistance to aminoglycosides was higher in Southern Europe than in Central and Northern Europe. Reports of the susceptibility of P. aeruginosa to gentamicin and tobramycin have ranged from as low as 49.8% and 77.7%, in Greece, to as high as 96.6% and 99.2%, respectively, in the United Kingdom [3]. It was reported that 54% of gram-negative bacilli in Turkey are resistant to gentamicin, 35% to tobramycin, and only 0.9% to amikacin in 1988 [4]. Consistent to this finding, resistance to amikacin (25.4%) of P. aeruginosa was still lower than to gentamicin (57.5%) or tobramycin (58.4%). However, this data suggests that resistance to amikacin increases progressively in Turkey.

Isolates in tracheal aspirates were highly resistant whereas isolates obtained from bronchial lavage fluids were relatively quite susceptible. In our hospital, tracheal aspiration is generally a procedure performed in intensive care units or the patients with critical illness. Consequently, our isolates in tracheal aspirates may reflect nosocomial strains. On the other hand, bronchoscopy, a lesser invasive procedure, was generally performed to newly hospitalised patients. The variations of antibiotic resistance for different locations may be due to the isolation procedures.

Resistance to imipenem was 14% in Spain [5], 19.3% in Italy [6], and 68% in Saudi Arabia [7]. Our result is similar to Latin America (SENTRY Antimicrobial Surveillance Program, 1998), 21.6% and 21%, respectively [8]. Resistance to ciprofloxacin of our isolates was 16.1%, whereas this rate 23% in Spain [5], 31.9% in Italy [6], and 26.8% in Latin America [8]. Contrary to ciprofloxacin, our isolates were highly resistant to ceftazidime (50.8%). Resistance to ceftazidime was 15% [5], 13.4% [6], and 22% [8] in other site of the World. Resistance to piperacillin was higher like ceftazidime. This rate was 10% in Spain, 12% in Italy, 14% in Latin America, 21.8% in our study. Resistance rates of anti-pseudomonal antibiotics were quite low in United Kingdom: 5% for ceftazidime, 7% for piperacillin, 10% for ciprofloxacin, and 11% for imipenem [9].

Isolates that were resistant to one class of antibiotics were also resistant to at least one other class of antibiotics except resistance to piperacillin. This finding suggests that piperacillin resistance occur independently and specifically in our isolates compared to other anti-pseudomonal agents. One hundred isolates were resistant to ticarcilin but 81 of them were susceptible to ticarcillin-clavulanate, which suggests that the production of β-lactamase may be the major mechanism of resistance in these organisms.

Gaynes and Culver demonstrated that resistance was more common among P. aeruginosa isolated from the respiratory tract, patients in intensive care units, and in teaching hospitals [10]. In spite of this knowledge, it was found only three multidrug-resistant isolates in 3-year survey. We think that our rate of multidrug-resistance (1.2%) was reasonable.

Conclusions

Because of high resistance rates to extended-spectrum cephalosporins and the progression of amikacin resistance, a national strategy on the limited and prudent use of anti-pseudomonal agents is urgently needed in Turkey.

Authors' contributions

UG had primary responsibility for study design, collection of data, and writing the manuscript. LO performed the final data analyses. IA had intellectual contribution as well as the writing of manuscript. MB, SI, and FG had intellectual contribution.

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