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Brief report

Microbiologic isolates and risk factors associated with antimicrobial resistance in patients admitted to the intensive care unit in a tertiary care hospital

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This study reviewed the clinical and microbiologic data for patients admitted to the intensive care unit with hospital-acquired infections. In the multivariate analysis, AIDS and previous antibiotic use were associated with the emergence of multiresistant bacteria. Hematologic diseases, length of stay, number of days on central venous catheter, antimicrobial use, and presence of multiresistant bacteria were associated with death. The previous use of antibiotics and the length of the hospital stay contribute to the development of infections caused by multiresistant gram-negative bacteria.

Antimicrobial selective pressure is a major risk factor for antimicrobial bacterial resistance in critical and noncritical wards. Twenty-five percent to 40% of patients are exposed to these drugs during hospital stays.[1,2] Patients in intensive care units (ICUs) have other risk factors that impact antimicrobial resistance in bacteria, such as multiple comorbidities, more severe disease, invasive procedures, longer hospital stays, exposure to antimicrobial selection pressures, and inappropriate use of antimicrobial drugs.[3]

The present retrospective case-control study evaluated the risk factors for hospital-acquired infections (HAI) caused by multiresistant bacteria and the relationship between multiresistant bacteria and mortality in a cohort of patients admitted to the adult ICU of a tertiary care teaching hospital.

METHODS

Microbiologic isolates classification

We retrospectively studied microbiologic isolates from all patients identified with infections after ICU admission in a tertiary care hospital. Demographic and clinical information from patients >18 years old admitted to the ICU with an established diagnosis of HAI from January 2008 to December 2009 were assessed by chart review.

The identification of bacterial species was performed according to the protocols of the clinical laboratory, and the results of susceptibility tests using the disk-diffusion method were interpreted according to the recommendations of the Clinical and Laboratory Standards Institute. We considered only the results for the first microbiologic isolate, irrespective of the body site from which the specimen was obtained or the antimicrobial susceptibility pattern. We have considered respiratory infections as laboratory-defined pneumonia. Isolates from patients with diagnoses of community-acquired infections or colonization or from surveillance procedures were excluded.

Based on the diagnostic criteria of the Centers for Disease Control and Prevention, the Infection Control Committee nurse classified HAI.[4] Bacterial multiresistance was classified according to the Centers for Disease Control and Prevention recommendations and the Infection Control Committee criteria.[5]

Statistical analysis

Data were analyzed with SPSS 14.0 (SPSS Inc, Chicago, IL). Statistical significance was defined as $P < .05$. Multivariate analysis was performed using logistic and Poisson regression, and the results are presented as odds ratios (95% confidence interval). The variables analyzed were those with $P < .20$ in the univariate

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analyses. All tests were 2-sided, and a P value <.05 considered indicative of statistical significance. SPSS 14.0 (SPSS Inc) was used for all statistical analyses.

RESULTS

As shown in Table 1, a total of 685 microbiologic samples from 394 patients (males, 54%; mean age, 59 years) infected with multiresistant bacteria were included. Characteristics of the patients included a mean of 16 days stay in the ICU and 46 days of hospitalization; 67% of patients underwent surgical procedure; 55%, 51%, and 88% of the patients used antibiotic in the ward, ICU, and combined, respectively; 88% of the patients had urinary catheter with a mean of 10 days duration; 69% of the patients had a central venous catheter (CVC) with a mean of 10 days duration; 77% of the patients were on mechanical ventilation with a mean of 7 days duration; and 58% of the patients infected with multiresistant bacteria died within 4 weeks after ICU admission.

The risk factors associated with the emergence of multiresistant bacteria according to the univariate analysis were the Acute Physiology and Chronic Health Evaluation (APACHE) II score ($P = .07$), AIDS ($P < .01$), hospital outcome (discharge or death) ($P < .01$), number of days in the hospital ($P < .01$), previous hospitalization (6 months prior to this hospital stay) ($P < .01$), number of days in the ICU ($P < .01$), diabetes ($P = .02$), cardiovascular disease ($P < .01$), gastrointestinal tract disease ($P = .05$), surgical procedure ($P = .10$), use of mechanical ventilation ($P = .03$), days on mechanical ventilation ($P < .01$), days of use of CVC ($P < .01$), and days on urinary catheter use ($P < .01$). There was an association between multiresistant bacteria and patients who had previously used antimicrobials of the following types for more than 48 hours in the wards: sulfonamides, third-generation cephalosporins, fourth-generation cephalosporins ($P < .01$), vancomycin ($P < .01$), lincosamides ($P = .20$), aminoglicosydes ($P < .01$), macrolides ($P = .08$), carbapenems ($P < .01$), quinolones ($P < .01$), penicillins ($P = .03$), and penicillin/β-lactamase inhibitor ($P < .01$). The factors associated with hospital mortality included multidrug-resistant bacteria ($P < .01$) and methicillin-resistant *Staphylococcus aureus* ($P = .09$).

In the multivariate analysis, AIDS; previous hospital stay during the last 6 months; and previous antibiotic use including aminoglycosides, quinolones, and carbapenems were associated with the emergence of bacterial resistance. Fluoroquinolone and carbapenem use in wards and the ICU were independently associated with bacterial multiresistance (Table 2).

According to the Poisson regression in Table 2, age, number of days of hospitalization during the previous 6 months, hematologic diseases, bone marrow transplantation, length of the stay, APACHE II score, days of urinary catheterization, days on a CVC, previous antimicrobial use in the wards, and infection caused by multiresistant bacteria were independently associated with death.

Table 1
Microbiology profile of the patients hospitalized in the intensive care unit

Isolated bacteria and resistance profile		
Source of biologic material	Prevalent bacteria, n (%)	Resistant bacteria, n (%)
Respiratory tract	323 (47.2)	125 (38.7)
Staphylococcus aureus	71 (22.0)	51 (40.8)
Acinetobacter baumannii	56 (17.3)	34 (27.2)
Pseudomonas aeruginosa	49 (15.2)	7 (5.6)
Klebsiella spp	46 (14.2)	25 (20.0)
Other	101 (31.2)	8 (6.4)
Urine	137 (20.0)	37 (27.0)
Escherichia coli	46 (33.6)	8 (21.6)
Klebsiella spp	27 (19.7)	19 (51.4)
Enterococcus spp	20 (14.6)	1 (2.7)
Other	44 (32.0)	9 (24.3)
Blood culture	89 (13)	19 (21.3)
Cons	27 (30.3)	0 (0.0)
Staphylococcus aureus	13 (14.6)	3 (15.8)
Escherichia coli	10 (11.2)	3 (15.8)
Other	39 (43.8)	13 (68.4)
Ascites fluid	38 (5.5)	12 (31.6)
Enterococcus spp	9 (23.7)	1 (8.3)
Escherichia coli	8 (21.0)	2 (16.6)
Klebsiella spp	8 (21.0)	3 (25.0)
Other	13 (34.2)	6 (50.0)
Catheter	25 (3.6)	7 (28.0)
Cons	12 (48.0)	0 (0.0)
Enterobacter spp	4 (16.0)	1 (14.3)
Other	9 (36.0)	6 (85.7)
Other sites of infection	73 (10.7)	23 (31.5)

Cons, Coagulase-negative *Staphylococcus*.

Table 2
Multivariate analysis

	Odds ratio	95% CI	*P* value
Risk factors related to bacterial resistance in patients hospitalized in the intensive care unit			
AIDS	1.63	1.076-2.481	.021
Days for previous hospital stays	1.01	1.004-1.017	.001
Entire hospital antibiotic use	2.34	1.346-4.085	.003
Aminoglycoside use in the ICU	1.96	1.205-3.203	.007
Quinolone use in the ICU	1.36	1.041-1.777	.024
Quinolone use in the ward	1.29	1.004-1.650	.047
Carbapenem use in the wards and ICU	1.85	1.497-2.275	<.001
Risk factors related to death in patients hospitalized in the intensive care unit			
Age	1.01	1.006-1.013	<.001
Days of previous hospital stays	1.01	1.002-1.008	.001
Hematologic disease	1.18	1.029-1.350	.018
Bone marrow transplantation	1.39	1.000-1.924	.050
APACHE II score	1.01	1.002-1.012	.010
Length of stay	0.99	0.990-0.996	<.001
Length of use of a urinary catheter	1.00	1.002-1.003	<.001
Length of use of a CVC	1.01	1.002-1.010	.006
Antimicrobial use in the ward	1.38	1.212-1.564	<.001
Identification of resistant bacteria	1.18	1.055-1.319	.004

APACHE, Acute Physiology and Chronic Health Evaluation; *CVC*, central venous catheter; *CI*, confidence interval.

DISCUSSION

Multivariate analysis to identify the risk factors for nosocomial infections caused by multiresistant bacteria among patients in the ICU in our study revealed that previous hospitalization for a prolonged length of time and previous antimicrobial use during the whole hospitalization period (ward plus ICU), including the use of aminoglycosides, fluoroquinolones, and carbapenems, were significant independent risk factors. In addition, our study found that other factors, such as AIDS and number of previous days of hospitalization during the 6 months preceding the current hospitalization, were independently associated with the emergence of infections caused by multiresistant bacteria. The previous use of antibiotics and the length of the hospital stay are factors that have been shown to contribute to the development of infections caused by multiresistant gram-negative bacteria, especially in the ICU setting.[6–8]

Mortality related to nosocomial infections remains significant in ICUs.[6] In our study, previous use of antimicrobials in the ward, infections caused multiresistant bacteria, and hematologic disorders were significant factors associated with higher hospital mortality in the ICU. Mainardi et al[9] have highlighted the association of high mortality with the previous use of antimicrobials in immunocompromised patients with hematologic disorders.

Recently, Michalopoulos et al demonstrated that critically ill patients with multiresistant gram-negative bacteria-related primary bacteremia exhibit significant mortality that is primarily associated with age and multiorgan failure.[10]

Other studies have evaluated the association between nosocomial infections and invasive devices.[11] Our study evaluated the association between invasive devices and the emergence of multiresistant bacteria and found that the longer use of a central venous or urinary catheter was a statistically significant risk factor for mortality without a significant size effect (odds ratio). Other studies have shown higher hospital mortality rates with the development of sepsis associated with older CVCs.[12,13]

In summary, our study attempted to identify significant clinical factors associated with nosocomial infections caused by multiresistant bacteria in the ICU. The continued monitoring and evaluation of risk factors such as previous and continuing antibiotic use, especially in immunocompromised patients associated with hospitalization for a prolonged period of time, are important measures that can decrease the mortality rate.

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