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Brief report

Ventilator-associated pneumonia due to extensive drug-resistant *Acinetobacter baumannii*: Risk factors, clinical features, and outcomes

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Acinetobacter baumannii is characterized by a rapid development of resistance to the commonly used antimicrobial agents. We investigated the risk factors, clinical features, and outcomes in ventilator-associated pneumonia (VAP) caused by extensive drug-resistant *Acinetobacter baumannii* (XDRAB). Clinical parameters and overall in-hospital mortality rates were compared between the VAP with and without XDRAB infection groups. This study showed that VAP caused by XDRAB was not associated with in-hospital mortality. However, it was related to high Simplified Acute Physiology Score II scores and increasing durations of hospital stays.

Acinetobacter baumannii is a gram-negative coccobacillius that is particularly associated with ventilator-associated pneumonia (VAP) in intensive care units (ICU). VAP is a very important infection associated with an increased length of stay in ICUs, high mortality rate, and high cost of health care.[1,2]

To the best of our knowledge, *A baumannii* is characterized by a rapid development of resistance to the commonly used antimicrobial agents. This characteristic makes the treatment of infection particularly difficult and is the main reason for *A baumannii* spread. Recently, various studies have shown that longer periods of hospitalization, longer time on mechanical ventilation, and prior use of antibiotics are the recognized factors increasing the risk of VAP because of multidrug-resistant (MDR) *Acinetobacter* infection. MDR Acinetobacter is related to high morbidity and mortality. A few studies reported that *A baumannii* has emerged as a MDR organism moving toward panresistance.[2-6]

However, data about clinical findings and mortality of *A baumannii* (extensive drug-resistant *Acinetobacter baumannii* [XDRAB]) infection in VAP are limited. Therefore, we investigated the risk factors, clinical parameters, and outcomes in patients with VAP caused by XDRAB.

MATERIALS AND METHODS

Study participants

A retrospective cohort study was performed in a 40-bed, medical-surgical, adult ICU at the Medical School of Mersin University in Turkey. Our hospital is a 402-bed, tertiary care, general hospital in Mersin. Patients with VAP because of *Acinetobacter* reported by the computerized online infectious disease surveillance and control system from June 2006 to June 2010 were retrospectively reviewed.

Definitions

We included all patients who had been hospitalized in the ICUs for more than 48 hours during the study period. The patients were enrolled consecutively and followed until VAP diagnosis, death, or discharge from the ICU. VAP was considered in the presence of a new or persistent ($\geq$48 hours) and progressive radiographic infiltrate, consolidation, cavitation, or pleural effusion, plus at least 2 of the following: (1) temperature of $\geq$ 38°C or $<$ 35°C; (2) purulent tracheal secretions or a change in characteristics of sputum; or (3)

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Table 1
Demographic and clinical characteristics of the patients

Sex (M/F), n	79/55
Age, y*	53.2 ± 21.0
Admission SAPS II score*	32.8 ± 15.1
Comorbidity, Charlson index*	2.6 ± 2.0 (1-9)
Origin of patients, %	
Medical	60.4
Surgery	39.6
Reintubation VAP, %	19.0
Days of mechanical ventilation before VAP*	11.1 ± 8.0
Hospital-days before VAP*	17.9 ± 11.6
Length of stay in the ICU, days*	24.4 ± 14.5
Length of stay in the hospital, days*	31.2 ± 16.0
Mortality, n (%)	113 (84.3)

ICU, intensive care unit; *SAPS II*, Simplified Acute Physiology Score II; *VAP*, ventilator-associated pneumonia.
*Values are presented as mean ± standard deviation.

leucocytosis (>10,000 white blood cells/mm^3) or leucopenia (<4,000 white blood cells/mm^3). The diagnosis was confirmed by positive microbial cultures of sputum or tracheal aspirate: (1) nonprotected bronchoscopic specimen cultures $\geq 10^6$ colony-forming units (cfu)/mL, (2) specimen cultures obtained by transbronchial aspirate $\geq 10^5$ cfu/mL, and (3) protected bronchoscopic lavage cultures $\geq 10^4$ cfu/mL.[1]

MDR was defined as nonsusceptibility to 3 or more of the following antimicrobials or groups of antimicrobials: aminoglycosides, antipseudomonal-penicillin-β-lactamase inhibitor combinations, antipseudomonal carbapenems, antipseudomonal fluoroquinolones, trimethoprim-sulfamethoxazole, cephalosporins, ampicillinsulbactam, polymyxins, or tetracyclines. XDR was defined as nonsusceptibility to all the above antimicrobials except polymyxins and tigecycline.[7] Bacterial isolation and antimicrobial susceptibility testing were performed in accordance with Clinical and Laboratory Standards Institute methodology.[8]

Data about demographics, diagnoses of the patients on admission, duration of mechanical ventilation before VAP, length of ICU and hospital stay, survivors, nonsurvivors, Simplified Acute Physiology Score II (SAPS II) score at admission,[9] Charlson comorbidity index, bacterial etiology and culture results, and in-hospital mortality were collected. Clinical parameters, microbiologic data, and overall in-hospital mortality were compared between the VAP with and without XDRAB infection groups.

Statistical analysis

SPSS 16.0 (SPSS Inc, Chicago, IL) was used for statistical analyses. P values of $< .05$ were considered significant. Binary logistic regression analysis was used to assess the risk factors associated with XDRAB infection in VAP. Our analysis was a binary logistic regression with the dependent variable of XDRAB infection and with independent variable of age, sex, SAPS II, diagnoses of the patients on admission, reintubation, duration of mechanical ventilation before VAP, and length of ICU and hospital stay.

RESULTS

A total of 134 patients with microbiologically confirmed VAP because of Acinetobacter was evaluated. Demographic and clinical characteristics of the patients are presented in Table 1. In general, VAP occurred after the first intubation in 81 of the participants. All participants were appropriately treated for concurrent organisms with additional antimicrobial agents that demonstrated in vitro susceptibilities.

Table 2
Comparison of clinical data for pneumonia-related characteristics in VAP patients with XDRAB and non-XDRAB

	Non-XDRAB (n = 100)	XDRAB (n = 34)	*P* value
Age, y*	54.8 ± 20.9	48.4 ± 20.9	.124
Admission SAPS II score*	31.2 ± 15.2	37.6 ± 14.2	.034†
Comorbidity, Charlson index*	2.6 ± 2.0	2.5 ± 1.9	.784
Origin of patients, %			.320
Medical	58.0	67.6	
Surgery	42.0	32.4	
Days of mechanical ventilation before VAP*	10.5 ± 7.5	12.3 ± 9.1	.311
Hospital days before VAP*	16.5 ± 10.0	20.9 ± 14.1	.078
Length of stay in the ICU (days)*	21.7 ± 11.9	30.4 ± 17.9	.005†
Length of stay in the hospital (days)*	27.8 ± 13.2	39.0 ± 18.9	.001†
Reintubation VAP, %	17.4	22.6	.586
Mortality, %	84	85.3	.858

ICU, intensive care unit; *SAPS II*, Simplified Acute Physiology Score II; *VAP*, ventilator-associated pneumonia.
*Values are presented as mean ± standard deviation.
†Statistically significant.

As seen in Table 2, 2 groups were similar with respect to age, Charlson comorbidity index, origin of patients, duration of hospitalization, and mechanical ventilation prior to the development of VAP, rate of reintubation because of VAP, and mortality. VAP caused by XDRAB was not associated with in-hospital mortality ($P = .858$). The SAPS II score was higher in the patients with XDRAB infection compared with the patients with non-XDRAB infection at ICU admission (37.6 ± 14.2 and 31.2 ± 15.2, respectively; $P = .034$). In patients with VAP caused by XDRAB, length of stay in the ICU and in the hospital increased significantly (30.4 ± 17.9 vs 21.7 ± 11.9 days, $P = .005$ and 39.0 ± 18.9 vs 27.8 ± 13.2 days, $P = .001$, respectively) (Table 2).

To assess the risk factors associated with XDRAB infection binary logistic regression analysis was used. The incidence of VAP caused by XDRAB increased with a higher length of stay in the hospital (odds ratio, 1.06; 95% confidence interval: 1.026-1.097, $P = .001$) and higher SAPS II score (odds ratio, 1.95; 95% confidence interval: 1.154-3.301, $P = .013$).

DISCUSSION

Patients with VAP caused by XDRAB had higher SAPS II scores, longer length of ICU stay, and longer hospital stay. *A baumannii* is one of the most important VAP pathogens and has the reputation of causing outbreaks in ICUs. *A baumannii*-related infection usually leads to significant morbidity and mortality. Frequent, unnecessary, or longer use of antibiotics results in a selection favoring resistant bacteria. MDR *A baumannii* has been reported worldwide and is now recognized as one of the most difficult health care-associated infections to control and treat. However, XDRAB has rarely been reported.[10,11]

Longer hospital stay, ICU stay, longer time on mechanical ventilation, exposure to antimicrobial agents, colonization pressure, invasive procedures, underlying severity of illness, and reintubation are the recognized factors increasing the risk of MDR *A baumannii* infection.[3,5,6] In patients with VAP caused by XDRAB, length of stay in ICUs and in hospital increased significantly ($P = .001$). Additionally, we found that patients with XDRAB were older and had longer duration of mechanical ventilation prior to the development of VAP and higher rate of reintubation because of VAP compared with patients without XDRAB, although the difference was not statistically significant.

In our study, patients with VAP caused by XDRAB had higher SAPS II scores at ICU admission ($P = .034$). The patients with high SAPS II scores treated with broad-spectrum antibiotics for longer

durations in ICU. It is known that use of broad-spectrum antibiotics is related with resistance.[12]

Mortality rates of 30% to 75% have been reported for nosocomial pneumonia caused by *A baumannii*, with the highest rates reported in ventilator-dependent patients. In a study of patients with VAP, mortality associated with *A baumannii* was 75%, compared with 55% for VAP caused by other organisms ($P < .05$).[13] However, mortality rates for patients with MDR *A baumannii* infections were not significantly higher from patients without MDR *A baumannii* infections in a study in hospitalized patients.[14] Our findings also showed a high hospital mortality rate in patients with *A baumannii* infections, but resistance of *A baumannii* was not associated with mortality ($P = .858$). In conclusion, XDRAB infections have occurred more frequently in patients with high SAPS II scores, exposure to an ICU, and prolonged length of hospital stay.

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