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Research Article

Ventilator associated pneumonia caused by extensive-drug resistant *Acinetobacter* species: Colistin is the remaining choice

Ahmed Hasanin [a,*], Ahmed Mukhtar [a], Akram El-adawy [a], Hossam Elazizi [a], Ahmed Lotfy [a], Heba Nassar [a], Doaa Ghaith [b]

[a] *Department of Anesthesia, Faculty of Medicine, Cairo University, Egypt*
[b] *Department of Clinical Pathology, Faculty of Medicine, Cairo University, Egypt*

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KEYWORDS

Acinetobacter spp.;
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Abstract *Introduction:* Ventilator-associated pneumonia [VAP] is associated with increased morbidity and mortality especially when caused by extensive drug resistant [XDR] pathogens. Till now, little is known regarding the exact pathogenesis of XDR Acinetobacter baumannii [XDR-AB] infection. The aim of the present study was to identify prevalence and risk factors for VAP caused by XDR-AB in our intensive care unit, and to test the susceptibility pattern of tigecycline, carbapenems, and Colistin among the isolates.

Methods: A prospective cohort study was conducted to enroll patients who developed VAP over 18-month period. All possible risk factors were documented as well as patient outcome. Susceptibility testing for the isolates was performed using inhibitory concentrations [MICs] determined by Epsilometer tests (E-tests) to Carbapenems, Tigecycline, and Colistin.

Results: Among 544 consecutive patients admitted to our ICU during 18 months, Forty-seven patients developed VAP. The prevalence of XDR-AB was 63.8% (30 patients). No specific factor was associated with increase of the risk of acquisition of AB-VAP in our cohort either by univariate or by multivariate analysis. Carbapenems showed poor activity against all isolates [MIC range 10–128 mg/L]. Tigecycline showed good activity against only 15 isolates [MIC range 0.25–2 mg/L]. Colistin demonstrated potent in vitro activity against all isolates of AB [MIC range 0.016–1 mg/L].

Conclusions: XDR AB-VAP is endemic in our ICU without a definite factor associated with increased risk of infection. Given that almost half of the strains are also resistant to tigecycline, colistin appears to be an appropriate first-line antimicrobial drug in critically ill patients developing VAP based on invitro results.

* Corresponding author at: 28 Alarkam Ibn Abi Alarkam Street, Almeeraj, Almaadi, Cairo, Egypt. Tel.: +20 1112737771.
E-mail address: ahmedmohamedhasanin@gmail.com (A. Hasanin).

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1. Introduction

Ventilator-associated pneumonia [VAP] is associated with prolonged mechanical ventilation, increased intensive care unit [ICU] length of stay, and substantially increased mortality [1]. Furthermore, the risk of mortality associated with VAP increased when VAP is caused by one of multidrug-resistant (MDR) pathogens [2].

Acinetobacter species [*Acinetobacter* spp.] is a non-fermentative, aerobic, gram-negative coccobacilli, non-lactose-fermenting and oxidase negative microorganism. Multiple mechanisms have been implicated in the resistance of *Acinetobacter* spp. and it is considered one of the most virulent MDR pathogens. *Acinetobacter* has been isolated in food and inanimate objects and may colonize humans and survive on dry or moist environment [3–5].

Carbapenems were considered for many years the mainstay of therapy of VAP caused by *Acinetobacter* spp. [6]. However, recent outbreaks of carbapenem-resistant Acinetobacter infection have raised the interest in colistin, an 'old' antibiotics introduced in 1959 and was abandoned in the 1970s after introduction of aminoglycosides [7,8]. However, the ability of colistin to penetrate the lung tissue is a debatable issue and moreover, it demonstrated dose-dependent neurotoxicity and nephrotoxicity [9]. On the other hand, tigecycline is a newer relatively safe broad spectrum tetracycline and displays inhibitory activity against *Acinetobacter* spp. [10].

We previously reported the prevalence of extensive drug resistant gram negative bacilli in our institution [11]; in this study, we sought to conduct a prospective cohort study to identify primarily the prevalence of VAP caused by extensive drug resistant [XDR] *Acinetobacter* spp. and secondarily to test the susceptibility pattern of tigecycline, carbapenems, and colistin against VAP caused by *Acinetobacter* spp. as well as the possible risk factors.

2. Methods

A cross sectional observational study was performed in Cairo University hospitals surgical ICU admitting trauma and emergency postoperative patients over 18-month period. All consecutive patients who were clinically suspected of having developed VAP after 48 h of mechanical ventilation [MV] in our ICU were included.

Patients were assumed to have VAP when new, persistent infiltrate was seen on chest X-rays and at least two of the following were observed: a body temperature below 36 °C or above 38 °C; a white blood cell count lower than 4000/mm^3 or higher than 11,000/mm^3; and macroscopically purulent tracheal aspirate [12]. Tracheal aspirate was classified as purulent or nonpurulent after visual inspection by the clinical treatment team.

Once VAP was suspected, tracheal aspirate for quantitative culture was obtained [Day 0], before antimicrobial treatment was started (for patients not on current antimicrobial therapy). Blood cultures were obtained for patients with suspected bacteremia.

2.1. Bacteriological analysis

Tracheobronchial secretions were aseptically collected, following specimen collection guidelines, after tracheal instillation of 10 ml saline. The specimens were sent to the laboratory and cultivated within 1 h of collection. A dilution of the tracheal aspirate was prepared and inoculated with a calibrated loop on chocolate, blood and MacConkey agar. After overnight incubation in appropriate conditions, the plates were interpreted according to quantification of growth [13]. Qualitative cultures were considered positive when the growth of 10^5 colony-forming units cfu/ml or more is observed.

All non-fermentative, oxidase-negative, catalase-positive, strictly aerobic, motionless, Gram-negative coccobacilli were considered belonging to Acinetobacter genus. [Phenotype identification was completed with API 20 NEsystem, Biomérieux, France].

Susceptibility testing was performed using inhibitory concentrations [MICs] determined by Epsilometer tests [E-tests; AB.Biodisk, Sweden] for the following antibiotics: tigecycline, colistin, and Imipenem.

Extensive drug resistance was defined as resistance to all classes of antimicrobial agents except for one or two classes. Modifications to the empirical therapy were based on the results of tracheal aspirate cultures and blood cultures.

The severity of presenting illness was assessed by an Acute Physiology and Chronic Health Evaluation II [APACHE II] score calculated within 24 h of ICU admission. Other data collection included smoking status; history of congestive heart failure; history of malignancy; immunosuppression; albumin level; use of H2 antagonists; proton pump inhibitor use; corticosteroid use; and the need for dialysis, cause of ICU admission, reoperation, use of blood product, central venous catheterization, urinary tract catheterization duration of mechanical ventilation, and duration of stay in the ICU before VAP.

3. Statistical analysis

To assess risk factor status, two groups of patients were considered. AB-VAP: patients who developed VAP with *Acinetobacter* spp., and Non AB-VAP: patients who developed VAP with other pathogens. All the pre-operative variables and post-operative events were compared between the two groups using univariate and multivariate analyses. Student's *t*-test or the Mann–Whitney *U*-test was used for quantitative data and Pearson's chi-square or Fisher's exact test for categorical data. Differences were considered statistically significant when the p value is <0.2. Data were shown as mean ± SD or as median and range or as percentages. All variables significant in univariate analysis were analyzed by a multiple regression logistic model. The forward stepwise logistic strategy was applied, and variables were included in the model if the log likelihood ratio chi-square test was significant. SPSS version 15.0 for Windows [SPSS, Inc., Chicago, IL, USA] was used for statistical analyses.

4. Results

Among 544 consecutive patients admitted to our ICU during 18 months, total number of mechanically ventilated patients was 243. Forty-seven patients [19.3%] developed VAP. The prevalence of *Acinetobacter* spp. was 30 [63.8%].

Demographic and baseline data were comparable among both groups [Table 1]. There is no specific factor associated