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Original Article

Pathogens and drug-resistance of hospital-acquired pneumonia in an EICU in Tianjin, China

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Abstract: Objective: Observing the pathogens and drug-resistance within hospital-acquired pneumonia (HAP) in an emergency intensive care unit (EICU) to provide a reference for clinically reasonable use of antibiotics. Methods: Sixty-two patients with HAP in Tianjin Medical University General Hospital from January 2017 to May 2019 were analyzed retrospectively. Bacterial identification and susceptibility were reviewed. Results: One hundred and thirty-seven strains of pathogenic bacteria were isolated from 62 patients, with 97.1% Gram-negative and only 2.9% Gram-positive. There were also six fungal isolates. The most common pathogens were Acinetobacter baumannii, accounting for 30.8% of all isolates, followed by Klebisella spp, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, and Escherichia coli. Acinetobacter baumannii was poorly susceptible to piperacillin-tazobactam, cefepime, Amoxicillin+clavulonic acid, ciprofloxacin. However, the isolates were sensitive to Tigecycline, so as the isolates of Klebisella spp. Pseudomonas aeruginosa was mostly sensitive to Amikacin, followed by Tobramycin. All of the isolates of Staphylococcus aureus were susceptible to Linezolid, Tigecycline and Vancomycin. Conclusions: Gram-negative bacteria especially Acinetobacter baumannii, are the main pathogens for HAP in the observed EICU. The variety of pathogens should be monitored at regular intervals to improve resistance issues and therapeutic effect.

Keywords: Hospital-acquired pneumonia, pathogens, drug resistance, EICU

Introduction

Hospital-acquired pneumonia (HAP) is an infection of the pulmonary parenchyma caused by pathogens that are present in hospital settings [1], and it is associated with substantial morbidity and mortality [2]. HAP develops in patients admitted to the hospital for >48 h and usually the incubation period is at least 2 days [3]. It is the most common infection acquired in the hospital, with the highest prevalence in intensive care units (ICUs). It develops in patients admitted to the hospital for >48 h and usually the incubation period is at least 2 days. Among hospital-acquired pneumonias, ventilator-associated pneumonia (VAP) develops in ICU patients who have been mechanically ventilated for at least 48 h. The clinical spectrum of lower respiratory tract infections potentially affecting patients managed in the ICU includes different diseases with peculiar epidemiological, clinical and microbiological aspects [4]. The incidence of nosocomial infections in EICU is three-fold higher than other wards [3].

Physicians struggle to control these infections, which have a wide spectrum of bacterial pathogens and worsening of resistance issues According to the recent review of pneumonia, gram-negative bacillin like Escherichia coli, Pseudomonas Aerugenosa, Acinetobaceter, and Enterobacter were popular. As for gram-positive bacillin, staphylococcus aureus was in the first place [5].

As a result, better knowledge of HAP microbial etiologies might allow better identification of patients at high risk of infection caused by problematic pathogens, such as multi-drug resistant (MDR), and consequently, better selection of initial antibiotics, while avoiding overuse of broad-spectrum antibiotics. A better understanding of the pathogens involved in this environment could allow us to reassess our current

Table 1. Causes of HAP in EICU

	Pathogens	Strain (constituent ratio %)
Gram-negative bacterium	Baumanii	44 (30.8)
	Klebsiella pneumoniae	29 (20.3)
	Pseudomonas aeruginosa	22 (15.4)
	Stenotrophomonas maltophilia	10 (13.3)
	Escherichia coli	7 (0.5)
	Serratia marcescens	3 (0.2)
	The others	18 (12.6)
Gram-positvie bacterium	MRSA	2 (50.0)
	Staphylococcus aureus	2 (50.0)
Fugus	Candida albicans	3 (50.0)
	The others	3 (50.0)

treatment approaches and identify better treatment options.

The aim of this study was to investigate prevalence of bacterial pathogens isolated from patients with HAP in EICU and reveal drug-resistant rates in order to get local data to direct treatment in that one hospital.

Methods

Study design and patients

We conducted a retrospective cohort study in the EICU of Tianjin Medical University General Hospital from January 2017 to May 2019. All adults patients (aged >18 years) consecutively admitted with HAP, and whose cultures of respiratory specimens were positive and associated with HAP were included. The following patients were excluded from this study: a) Patients with pneumonia before admission, b) The results of respiratory tract specimen culture of HAP patients were negative.

After gargling with normal saline for 3 times, samples of lower respiratory tract secretions were collected with sterile sputum collector or fiberoptic bronchoscope and collected into a disposable sterile sputum collector. Clinically significant values for quantitative culture were considered squamous epithetial cells <10/LP and multinuclear leukocytes >25/LP. The drug sensitivity test was determined by paper diffusion method, according to the decision result of Clinical and Laboratory Standards Institute (NCCLS). The same bacteria which was isolated from one patient is considered as from the same strain.

Numerical variables were statistically analyzed using frequency analysis in descriptive analysis, where he mean age of the patients was analyzed using mean ± standard deviation. All statistical analyzes were performed using the statistical software SPSS version 22.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013.

Results

General information statistics

In the observed period, 62 patients admitted to the EICU developed HAP according to predefined criteria. Mean patient age was 74.92± 11.73 years. 58.1% of the patients (n=36) were males, and 41.9% of the patients (n=26) were females. The most common primary condition for the patients was chronic heart disease (82%), such as coronary heart disease or rheumatic heart disease. Twenty-eight patients were diabetic and 14 had digestive system diseases, especially gastrointestinal bleeding. What's more, 27.4% of them have COPD or interstitial lung disease.

Culture results of respiratory specimens

In the majority of patients, two pathogens (n=22; 35.5%) were present, while 32.3% had three pathogens, whereas a single pathogen was isolated from only 24.2% of the patients. Three patients were sources of five simultaneous pathogens. Isolates from patients with HAP are shown in **Table 1**. Gram-negative bacteria were the dominant agents (93%) isolated from the 143 positive cultures. The most common pathogen was Acinetobacter baumannii, accounting for 31% of isolates. Other common Gram-negatives included Klebsiella spp, P. aeruginosa, Stenotrophomonas maltophilia, and Escherichia coli.

Table 2. Drug-resistant rate of the most common causative agents of HAP in the EICU (%)

Antibiotics	Baumanii	Klebsiella pneumoniae	Pseudomonas aeruginosa	Escherichia coli	Stenotrophomonas maltophilia
CPZ-SBT	34.1	24.1	18.1	28.6	60
TAZ	93.2	34.5	31.8	57.1	/
CFM	90.1	55.2	27.2	85.7	/
AZT	97.7	44.8	45.5	100	/
AMC	90.1	24.1	68.2	71.4	/
CZP	93.2	20.7	9	100	/
TOB	72.7	20.7	4.5	85.7	/
TYGACIL	0	10.3	100	0	/
IMP	88.6	13.8	27.2	14.3	/
LEV	86.4	31	9	71.3	/
AMK	45.5	10.3	0	14.3	/
SMZCo	79.5	79.3	100	71.4	20

CPZ-SBT cefoperazone-sulbactam, TAZ piperacillin-tazobactam, CFM cefepime, AZT aztreonam, AMC Amoxicillin+clavulonic acid, CZP ciprofloxacin, TOB Tobramycin, TYGACIL tigecycline, IMP imipenem, LEV levofloxacin, AMK amikacin.

Results of drug sensitivity tests for major detected bacteria

The results of susceptibility testing for the top four Gram-negative bacilli (GNB) that most frequently caused HAP are shown in **Table 2**. According to these results, isolates of A. baumannii showed high resistance rates against piperacillin-tazobactam (93.2%), ciprofloxacin (93.2%) and amikacin (90.1%). Although they showed low degree of susceptibility to cefepime (90.1%), the susceptibility to cefoperazone-sulbactam was higher. However, they were totally sensitive to tigecycline.

Isolates of Klebisella spp were resistant to SMZCo (79.3%), followed by cefepime (55.2%), yet susceptible to amikacin (10.3%) and tigecycline (10.3%). Most isolates of Klebisella spp from patients with HAP and VAP were MDR (65.5%).

For isolates of P. aeruginosa, his highest level of sensitivity was retained toward amikacin, followed by tobramycin. And they were highly susceptible to ciprofloxacin and levofloxacin, which drug-resistant rates were below 10%.

Other Gram-negative bacteria also showed low rate of susceptibility to the tested antibiotics, except to cefoperazone-sulbactam.

The only Gram-positive bacteria isolated was S. aureus (4 isolated from HAP). The frequency of methicillin-resistant S. aureus (MRSA) was 50%. All the isolates of S. aureus were susceptible to linezolid, tigecycline and vancomycin.

Discussion

Several studies have shown that the majority of bacterial cases of HAP/VAP (50-80%) are caused by Gram-negative bacteria [6, 7], and our study is no exception. This research showed that the most common pathogens were Gram-negative bacteria, such as Acinetobacter baumannii, Klebisella spp, P. aeruginosa. The result is a little different from the review mentioned above [4]. Among Gram-positive bacteria, the isolates were completely S. aureus. The most common fungal infection was Candida albicans. In a lareger study in China, Acinetobacter baumannii [30.0% (183/610)], Pseudomonas aeruginosa [22.0% (134/610)], Staphylococcus aureus [13.4% (82/610)] and Klebsiella pneumonia [9.7% (59/610)] were the most common pathogens [8]. Well, a study with 10 Asian countries showed that Acinetobacter spp, P. aeruginosa, S. aureus, and K. pneumoniae are the most frequent isolates from adults with HAP or VAP in Asian countries [9]. In other ICUs like RICU, the pathogenic bacteria are Gram-negative bacteria, headed by Pseudomonas aeruginosa, and Staphylococcus aureus and Candida albicans also occupy prominent positions [21]. A study of 27 ICUs in Europe showed that the pathogens usually responsible for HAP are Enterobacteriaceae, Staphylococcus aureus, Pseudomonas aeruginosa and Ac-

inetobacter baumannii [2]. As we can see that the results of studies mentioned above are all simillar with ours.

Several prospective and retrospective studies have evaluated the prevalence of multidrug-resistant Gram-negative pathogens in HAP/VAP, and studies have shown an increased incidence of MDR Gram-negative pathogens in Europe and the United States [10-13]. Results of our study showed that 93.0% of isolates from the patients with HAP belong to Gram-negative bacteria, and most of them were come from Acinetobacter baumanniii. Acinetobacter spp. has become the first cause of nosocomial infection, which is difficult to treat so that its mortality is very high. Our research showed that isolates of Acinetobacter baumannii were completely susceptible to tigecycline. The Asian study suggested that their isolates of Acinetobacter baumannii showed a very low resistance rate to colistin (0.8%). But they showed high resistance rates to imipenem (67.3%), ciprofloxacin (80.7%), piperacillin-tazobactam (76.7%) [5], which were all lower than ours. A meta-analysis showed that a wide variation in the prevalence of multidrug-resistance among Acinetobacter baumannii causing HAP (ranging from 55% to 100%) and mortality rates (ranging from 28% to 68%), between regions and countries [14]. Therefore, continuous monitoring of drug resistance and strict infection control are recommended for the prevention and control of MDRAB in HAP [14].

Isolates of P. aeruginosa showed that the drug-resistant dates of ciprofloxacin, levofloxacin and tobramycin were all under 10%, and they were completely sensitive to amikacin. A research showed that pneumonia due to MDR P. aeruginosa was associated with longer ICU stays, prolonged mechanical ventilation, and higher mortality [15]. And a later study of ICU-acquired pneumonia showed that Multidrug-resistant P. aeruginosa was present in 34% of cases, and chronic renal disease independently predicted multidrug-resistant pneumonia in these cases [16]. Compared to previous local results with the same organism in 2010, the pathogens and resistance have changed. In 2010, HAP isolates of Acinetobacter baumannii were 41% resistant to imipenem, but risen to 88% in this study. The same thing happened to P. aeruginosa and Klebisella spp [17]. Although our study suggested that Klebisella spp was still sensitive to Imipenem, but the drug-resistant rate was higher than before (13.8% vs 7.0%). It is not surprising, since differences in antimicrobial flora and susceptibility patterns can vary considerably between regions, countries, hospitals, ICUs and specimen sources. According to Dong J et al, the isolation rate of carbapenem-resistant Klebsiella pneumoniae (CRKP) is becoming higher (42%) [18]. The predicting factors of poor prognosis to hospital acquired Klebsiella pneumoniae bloodstream infection included diabetes, infection of CRKP, and presence of a central venous catheter [18].

In our study Gram-positive bacteria were isolated from only four patients, all S. aureus and 50% of the isolates were MRSA. This urges addition of linezolid or vancomycin to empiric antibiotic regimen in such patients.

Our hospital is the largest general hospital in Tianjin, treating almost one-third of all emergency cases in the city. A large number of patients were sent to our hospital because of unsatisfied treatment, so most of them had already used antibiotics before. At the same time, our elderly EICU patients have low immunity and poor respiratory function, with more serious underlying basic diseases. Our study reminds us that MDR strains and mixed infections are important problems in our EICU.

Although extensive studies on the etiology of HAP have been conducted in various countries with varying results, but the differences in criteria, study design, diagnostic methods, and inherent epidemiological differences make it challenging to compare the results [19]. In order to initiate the most appropriate empirical antibiotic regimens, clinicians need to know locally predominant causative agents of HAP in any specific clinical setting like EICU and their drug susceptibility patterns.

In addition to this, measures to prevent HAP are also important. Measures like minimizing length of stay, contact isolation precautions, proper oral care, improving hand and equipment hygiene practices, oral and digestive decontamination with antibiotics, and precaution against aspiration may reduce the risk for HAP [20].

This study has the following shortcomings: 1. This study is a single-center study with limited subjects included; 2. This study did not consid-

er the effect of respiratory specimens collection time on the results.

Disclosure of conflict of interest

None.

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