Respiratory Medicine 111 (2016) 84–90

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Clinical characteristics of patients with hemodialysis-associated pneumonia compared to patients with non-hemodialysis community-onset pneumonia

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ARTICLE INFO

Article history:
Received 19 July 2015
Received in revised form
14 December 2015
Accepted 22 December 2015
Available online 25 December 2015

Keywords:
Pneumonia
Hemodialysis
End-stage renal disease
Antibiotics
Mortality

SUMMARY

Background: The 2005 ATS/IDSA guidelines included hemodialysis-associated pneumonia (HDAP) as a category of healthcare-associated pneumonia (HCAP). However, the clinical epidemiology of HDAP has been not well established. This study aimed to evaluate the clinical and microbiological characteristics of HDAP patients compared to community-acquired pneumonia (CAP) or other HCAP except HDAP (O-HCAP).

Methods: We conducted a retrospective observational study on HDAP patients who were admitted between January 2012 and December 2014. We compared clinical features, distribution of microorganisms, antibiotic regimens, and clinical outcomes among the three groups.

Results: A total of 914 patients, comprised of 595 patients with CAP, 24 with HDAP, and 295 with O-HCAP, were evaluated. The median PSI score of the HDAP group was higher than that of the CAP group and similar to that of the O-HCAP group. The major pathogens of the HDAP group were *Staphylococcus aureus* and *Klebsiella pneumoniae*. The isolation rate of multidrug-resistant (MDR) pathogens and total in-hospital mortality of the HDAP group was similar to those of the CAP group (8.3% vs. 6.8%, $p = 1.000$ and 4.1% vs. 7.5%, $p = 0.821$, respectively). Otherwise, the isolation rate of MDR pathogens and total in-hospital mortality rate in the O-HCAP group were at 15.2% and 16.9%, respectively, and were the highest among the three groups.

Conclusions: Based on microorganisms and clinical outcomes, the HDAP group was clinically more similar to the CAP group than the O-HCAP group. Therefore, the 2005 ATS/IDSA guidelines that include HDAP as a category of HCAP might be reassessed.

1. Introduction

Hemodialysis-associated pneumonia (HDAP) is defined as a diagnosis of pneumonia developing in patients who had received chronic hemodialysis within 30 days [1]. HDAP is the most common infectious cause of death in hemodialysis patients, with a mortality rate of pneumonia that is 14–16 times higher in dialysis patients with end-stage renal disease (ESRD) compared to the general population as reported by the United States Renal Data System (USRDS) registry and the National Center for Health Statistics (NCHS) [2].

In 2005, the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) released guidelines for the management of healthcare-associated pneumonia (HCAP) patients whose clinical epidemiology was similar to those developed for hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia [1]. The guidelines recommend that HCAP patients should be treated empirically with broad-spectrum antibiotics to cover multidrug-resistant (MDR) pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa* [1]. According to these guidelines, HDAP was included as within the definition of HCAP [1]. However, because HCAP consists of heterogeneous populations, individual analysis for each group is needed. Among the HCAP subgroups, nursing home-acquired pneumonia (NHAP) has been the most widely studied [3], but there have been only a few reports regarding the clinical characteristics of HDAP [4].

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http://dx.doi.org/10.1016/j.rmed.2015.12.009
0954-6111/

To determine whether the initial HCAP-guidelines concordant with antibiotic therapy in HDAP patients are appropriate, it is important to identify the distribution of MDR pathogens. Two recent retrospective studies reported low rates of *P. aeruginosa* isolates ranging from 1.6% to 2.9% and MRSA ranging from 3.2% to 27.5% in HDAP patients [4,5].

As the number of patients with dialysis has been increasing worldwide [6], the incidence of HDAP patients will also increase; therefore, it is essential to understand the clinical features and impact on outcomes for HDAP patients. The aim of the current study was to define the clinical characteristics and outcomes of HDAP patients compared to community-acquired pneumonia (CAP) and other healthcare-associated pneumonia (O-HCAP) except HDAP patients. We evaluated the isolation rate of MDR pathogens and total-in hospital mortality in HDAP patients, especially.

2. Methods

2.1. Study design

We conducted a retrospective observational study of patients that were ≥18 years of age admitted with pneumonia and hospitalized at the Jeju National University Hospital (a 600-bed community hospital in Jeju City, Jeju, South Korea) between January 2012 and December 2014. We categorized the study patients into CAP, HDAP, and O-HCAP groups, and compared baseline characteristics, disease severity, identified pathogens, antibiotic regimens, and clinical outcomes among the groups. The Ethical Review Committee approved the study protocol. Informed consent was waived because of the retrospective nature of the study.

2.2. Definition and categorization of pneumonia

Pneumonia was defined as the presence of a new infiltrate on chest radiography plus at least one of the following: fever (temperature ≥ 38.0 °C) or hypothermia (temperature < 35.0 °C), new-onset cough with or without sputum production, pleuritic chest pain, dyspnea, or altered breath sounds on auscultation. Aspiration tendency was defined as having factors predisposing to aspiration such as previous or acute cerebrovascular disorder; neurodegenerative disorder and neuromuscular disease; impaired consciousness, cognition disorder such as dementia; gastroesophageal disorder (eg, esophageal diverticulum, achalasia, systemic sclerosis, esophageal cancer, severe reflux esophagitis, post-gastrectomy); laryngeal, pharyngeal tumor; tracheostomy, nasogastric tube replacement [7]. Respiratory failure was defined when the PaO2 was 60 mmHg or less or when the PaO2/FiO2 ratio was 300 mmHg or less. Multi-lobar involvement was defined as the presence of pneumonic infiltrates in two or more lobes on chest radiograph or computed tomography [8].

We investigated total patients admitted with community-onset pneumonia including HCAP and CAP. According to the 2005 ATS/IDSA guidelines, HCAP included patients with any of the following: (1) recent history of hospitalization in an acute care hospital for ≥ 2 days within the past 90 days, (2) residence in a nursing home or long-term care facility, (3) recent outpatient intravenous therapy (such as antibiotic therapy or chemotherapy) or wound care within the past 30 days, or (4) long-term dialysis (including hemodialysis and peritoneal dialysis) within 30 days of entering the study. Among fulfilling (4), HDAP was defined as a diagnosis of pneumonia in patients with maintenance hemodialysis 3 times a week, and CAP was defined as a diagnosis of pneumonia in patients who did not meet any of the criteria for HCAP [1]. We excluded patients with continuous ambulatory peritoneal dialysis (CAPD) or additional HCAP indications in HDAP. Patients were excluded if HDAP developed after being hospitalized for >72 h, had been re-visited within 10 days of discharging from the hospital, or had been transferred in from other hospitals after admission for >48 h [9].

The clinical outcome measures evaluated included duration of antibiotic therapy, the rate of antibiotic change, the use of inappropriate antibiotics, the rate of initial antibiotic therapy failure, length of hospital stay, and total in-hospital mortality rate. Changes of antibiotic regimens were included as both escalation and de-escalation after culture sensitivities or clinical stability were identified. Escalation of antibiotic regimens was defined as a new therapy covered broader classes of pathogens, while de-escalation was defined as a new therapy covered fewer classes of bacteria. Inappropriate antibiotic therapy was defined if the empirical antibiotic treatment was not effective against the identified pathogen based on *in vitro* susceptibility testing [10]. Initial treatment failure was defined as death during the initial treatment or a change of therapeutic agent from initial agent to others after 48 h due to clinical instability such as a lack of response or worsening of fever pattern based on 38.0 °C, radiographic status, requiring mechanical ventilation, requiring aggressive fluid and/or resuscitation or vasopressors [11].

2.3. Microbiology

Microorganisms in samples obtained from sputum, tracheal aspirate, bronchial alveolar lavage fluid, or blood were investigated. Sputum samples were cultured in a semi-quantitative manner, and pathogens were identified when a predominant microorganism was detected from group 4 or 5 sputum according to Geckler's grading system [12]. Blood cultures were considered as an etiology diagnosis if there was no other infection source for a positive blood culture. For *Mycoplasma pneumoniae* or *Chlamydia pneumoniae,* serum samples were evaluated. Serum samples in which particle agglutination antibody titers were >64 or that were proven to have a 4-fold or greater increase of antibody titers in paired sera were regarded as positive. BinaxNOW® (Binax Inc., Scarborough, ME, USA) was used to detect urinary *Streptococcus pneumoniae* antigens. The BinaxNOW® Legionella Urinary Antigen Test (Binax Inc.) for *Legionella pneumophila* serogroup 1 was performed according to the clinical judgment of the attending physician. A positive urinary antigen was considered to be a bacterial infection. The antibiotic sensitivity of all isolates was determined using a disc diffusion method. According to the 2005 ATS/IDSA guidelines, Methicillin-resistant *S. aureus* (MRSA), *P. aeruginosa*, extended-spectrum β-lactamase (ESBL) producing *Klebsiella* species, *Escherichia coli*, *Acinetobacter* species, and *Stenotrophomonas maltophilia* were considered MDR pathogens [1]. Predicted theoretical susceptibility was applied for atypical pathogens including *M. pneumoniae*, *Chlamydophila* species, and *Legionella* species, which were considered to be fully susceptible to antibiotic therapy with macrolides and fluoroquinolones [13].

2.4. Statistical analyses

Data are presented as a percent or median (interquartile range) unless otherwise stated. Continuous variables were compared using the Kruskal–Wallis test to compare the median values among the groups and a post hoc Tukey's test to compare the average values between individual pairs of groups. Categorical variables were compared using the Pearson $\chi 2$ test, and the Fisher exact test used where any cell of the contingency table was expected to be below 5. A p-value < 0.05 was considered statistically significant, and the threshold for p-value significance was adjusted by a post