Original Article

Assessment of the Intensive Care Unit Treatment of Pneumonia at a Veterans Affairs Facility

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ABSTRACT

Introduction: Pneumonia is a common cause of morbidity and mortality in the critically ill. Clinicians use a range of duration for antibiotic treatment from 7 to 14 days or longer. Failure to de-escalate antimicrobial therapy in a timely manner may lead to increased antimicrobial resistance, increased risk of side effects, and increased cost.

Objective: To investigate potential methods to improve treatment of pneumonia for patients in 4 intensive care units (ICUs).

Methods: A retrospective descriptive chart review was conducted at the Veterans Affairs North Texas Health Care System (VANTHCS). Veterans aged 18 to 90 years admitted to the ICU with a diagnosis of pneumonia were included. Descriptive statistics were used to interpret the data. Current management was reviewed to identify markers such as length of antibiotic therapy, ICU length of stay, and inpatient mortality. Secondary objectives included appropriateness and accuracy of the empiric regimen.

Results: Of the 1,854 Veterans admitted, 107 met inclusion criteria. Antibiotic choices for positive cultures were appropriate in 45 out of 46 (98%) patients, with an average length of therapy of 8.6 ± 6.3 days. De-escalation of antibiotics based on sensitivity data occurred in 73% of positive cultures.

Conclusions: Pneumonia in the VANTHCS ICUs is initially treated with empiric antibiotics. Empiric antibiotic therapy for pneumonia was appropriate and accurate over this time period. Opportunities exist for de-escalation in patients with or without positive cultures. The procalcitonin assay is now being utilized at VANTHCS to optimize patient care.

Key Words—antibiotics, de-escalation, pneumonia

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According to the Infectious Disease Society of America's (IDSA) guidelines for the management of adults with hospital-acquired (HAP), ventilator-associated (VAP), and health care-associated pneumonia (HCAP), bacterial pneumonia is the second most common nosocomial infection associated with high rates of morbidity and mortality.¹ This is especially true for critically ill patients. Pneumonia in this population can extend the hospital course by an average of 7 days and sometimes longer.¹ Common

pneumonia pathogens include aerobic gram-negative bacilli, such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and the *Acinetobacter* species. Infections due to gram-positive cocci, such as *Staphylococcus aureus* and particularly methicillin-resistant *S. aureus* (MRSA), are increasing in specific populations with comorbid conditions such as diabetes mellitus. Multidrug-resistant (MDR) pathogens have also dramatically increased in hospitalized patients.¹ HAP, HCAP, and VAP are

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commonly caused by the organisms listed previously; for patients admitted to the intensive care unit (ICU) for community-acquired pneumonia (CAP), the most common organisms are *Streptococcus pneumoniae* and *Haemophilus influenzae* in addition to those listed previously.¹ Empiric antimicrobial therapy, as defined by the IDSA guidelines, is based on whether or not the clinician suspects the patient is at risk for an MDR pathogen. Appropriate empiric therapy usually includes double coverage with an anti-pseudomonal β -lactam/cephalosporin/ carbapenem plus an anti-pseudomonal fluoroquinolone/aminoglycoside for gram-negative organisms plus vancomycin/linezolid for MRSA coverage.¹ Currently, empiric antibiotic therapy is selected by the provider with respect to a partially restricted formulary. Typical empiric coverage at the Veterans Affairs North Texas Health Care System (VANTHCS) consists of vancomycin, piperacillin/tazobactam, and levofloxacin.

Optimal length of antimicrobial therapy for pneumonia has been inconsistent in published medical literature and is therefore not standardized in most facilities. Several researchers have studied 8-day versus 15-day therapy, whereas others have looked at 5-day therapy.²⁻⁴ Clinicians are also using varied lengths of antibiotic therapy, ranging from 7 to 14 days or longer, if medically indicated. The IDSA recommends a 7-day course of therapy for HAP or VAP provided that the patient is clinically improving and the organism is not *P. aeruginosa*.¹

Previous data have shown that shorter courses of therapy may be beneficial with regard to patient outcome with no effect on clinical success.²⁻⁴ A study by Chastre and colleagues sought to determine whether 8 days was as effective as 15 days of antibiotic treatment for VAP. Results showed no difference between the groups with regard to mortality or recurrence of infection; the patients treated for 8 days versus 15 days had more mean [SD] antibiotic-free days (13.1 [7.4] vs 8.7 [5.2] days; $P < .001$).² In addition to selecting the proper empiric therapy, failure to de-escalate antimicrobial therapy in a timely manner may lead to increased antimicrobial resistance and increased health care-related costs.^{2,3,5} Diagnostic tools such as the clinical pulmonary infection score (CPIS) or procalcitonin levels are available and could potentially be utilized by the institution.

A retrospective descriptive chart review was conducted to determine the most common approaches to the treatment of pneumonia in a critically ill patient population to determine how to optimize care. Optimizing patient care includes proper patient diagnosis,

determining whether or not the patient needs empiric antibiotic therapy, and de-escalation of empiric therapy. Timely de-escalation of antibiotics for a patient with a low likelihood of pneumonia will help decrease antibiotic resistance and provide cost-saving measures to the VA health care system.

OBJECTIVES

The primary purpose of this study was to investigate methods for improving the treatment of pneumonia for patients in the ICU. Current management was reviewed to identify markers such as the length of antibiotic therapy needed in patients with pneumonia, ICU length of stay, and inpatient mortality.

Secondary objectives included appropriateness and accuracy of the empiric antibiotics used to treat pneumonia. Appropriate de-escalation based on culture results was also assessed to determine whether a process for early discontinuation using either CPIS or procalcitonin levels would be beneficial.

METHODS

This retrospective descriptive chart review was conducted at the VANTHCS and included 4 ICUs (medical, cardiac, surgical, and thoracic). The local institutional review board committees approved the design of the study. Veterans were enrolled if they were between 18 and 90 years old, were admitted to an ICU between August 1, 2010 and July 31, 2011, and had a diagnosis of pneumonia upon admission to the ICU or during their ICU stay based on ICD-9 codes.

Data were collected from the patients' charts using the VA's electronic medical records (CPRS and *Essentris*). The following variables were collected for interpretation: age, gender, daily markers of infection (including temperature, white blood count [WBC] with differential, sputum analysis, microbiological culture data, and chest radiograph), antibiotics and length of antibiotic therapy, respiratory medications, dates of admission to the hospital and ICU (if not the date of admission), date of discharge, and date of death. Descriptive statistics were used to interpret the data.

DEFINITIONS

Pneumonia was defined in this study by the investigators as having an infiltrate on chest radiograph (CXR), fever of 100.5°F or higher, and a WBC $\geq 10.5 \times 10^3$ cells/mm³ or higher, or bands greater than 6%. This definition is similar to that of the IDSA guidelines minus purulent secretions.¹ The authors

chose to not include purulent secretions, as there was not a way to accurately and consistently interpret them in the current documentation systems. Appropriate antimicrobial coverage was defined as an empiric antimicrobial regimen that would cover all suspected organisms based on suspected site of infection, regardless of susceptibility data.³ Inappropriate antimicrobial coverage was defined as the absence of a particular anti-infective agent targeting a specific class of microorganisms likely causing the infectious process. Accuracy was defined as an empiric antimicrobial regimen that was susceptible to the isolated pathogen(s) and was only assessed for positive cultures.³ De-escalation was defined as antibiotics discontinued after 48 hours of no signs or symptoms of pneumonia (negative CXR, negative cultures, afebrile, no leukocytosis) or antibiotics not needed based upon sensitivity of cultured organisms.³

RESULTS

A total of 1,854 patients were admitted to the ICU during the study period. After patients were screened based on primary and secondary diagnoses, 107 patients met inclusion criteria (**Figure 1**). In **Table 1**, patient characteristics for the study are taken

at the time admitted to the ICU. The mean age of our patients was 66 years and 99% were male. Several patients were admitted to the ICU more than once during their hospital admission, thus accounting for 116 total occurrences. The median ICU length of stay was 7 days (mean, 11 ± 14 days; range, 1-90) with the median hospital length of stay of 12 days (mean, 21 ± 28 days; range, 2-181). There was a 26% inpatient mortality rate. The majority of the diagnoses were HCAP, with 20% (24/116) of the occurrences, and 18% (21/116) of occurrences were HAP. There were non-pneumonia diagnoses that were also prominent, including chronic obstructive pulmonary disease (COPD), acute congestive heart failure (CHF) exacerbation, and other pulmonary diseases.

With respect to culture-positive versus culture-negative patient characteristics, ICU length of stay was 5 days longer for the culture positive group. Hospital length of stay was 6 days longer in the culture-positive group and inpatient mortality was 10% higher in the culture-positive group.

Table 2 represents the antibiotic data. Seventy-one (60%) patients had a negative culture or no cultures were drawn. Of the remaining 36 patients, there were 46 positive cultures, meaning that some patients

Figure 1. Flow diagram of the patients included or excluded in this study. CABG = coronary artery bypass graft; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; s/p = status post.

Table 1. Demographic and clinical characteristics of the study patients

	Total patients (N = 107; occurrences 116)	Culture positive	Culture negative
Age, mean $\pm$ SD years	66 $\pm$ 8.7	65 $\pm$ 8.6	66 $\pm$ 8.7
Sex, % male	99	99	99
Temperature, °F mean $\pm$ SD	—	99.3 $\pm$ 1.1	99 $\pm$ 1
WBC, $\times 10^3$ cells/mm ³ mean $\pm$ SD	—	13.9 $\pm$ 6.9	12.6 $\pm$ 7.0
Infiltrate on chest X-ray, n/N (%)	65/116 (56%)	33/46 (71%)	32/71 (45%)
ICU length of stay, days median (range)	7 (1–90)	10 (1–90)	5 (1–42)
Readmissions to the ICU, n	9	4	5
Hospital length of stay, days median (range)	12 (2–181)	15 (2–137)	9 (1–181)
Inpatient mortality, %	26	30	20
Diagnosis ^a			
HCAP	24	12	12
HAP	21	11	10
VAP	12	10	2
CAP	19	7	12
COPD exacerbation	18	2	16
Aspiration PNA	7	2	5
Other ^b	12	2	10

Note: CAP = community-acquired pneumonia; COPD = chronic obstructive pulmonary disease; HAP = hospital-acquired pneumonia; HCAP = health care-associated pneumonia; ICU = intensive care unit; PNA = pneumonia; VAP = ventilator-associated pneumonia; WBC = white blood cell count.

^aPatient may have had multiple episodes during hospital stay.

^bPostobstructive pneumonia (3), necrotizing pneumonia (2), transfusion-related acute lung injury (2), congestive heart failure exacerbation (1), atelectasis (1), asthma (1), left lower lobe empyema (1), viral vs legionella vs metapneumonia (1).

Table 2. Antibiotic therapy based on culture data

	Appropriateness of antibiotics		Average length of therapy (SD)
	Yes	No	
Positive cultures (n = 46)	45	1	8.6 (6.3) days
Negative cultures (n = 39)	35	4	6.8 (4.2) days
No cultures (n = 32)	32	0	7.1 (5.4) days
Accuracy of antibiotics (positive cultures only)	44	2	—
De-escalation (positive cultures only)	34	12	—

had more than 1 organism present in the culture or multiple cultures were taken during their ICU admission. Empiric antibiotic choices for positive cultures in the ICUs were appropriate in 45 of 46 (98%) cases. The average length of antibiotic therapy was 8.6 $\pm$ 6.3 days. Based on the positive cultures, the accuracy

of empiric antibiotics was 95%. De-escalation of empiric antibiotics based on sensitivity data occurred in 73% of positive cultures. Appropriateness of empiric antibiotics for negative cultures was 35/39 with an average length of therapy of 6.7 $\pm$ 4.2 days. For patients with no cultures, the appropriateness

of empiric antibiotics is 100% based on the suspected type of pneumonia, with an average length of therapy of 7.1 ± 5.4 days.

DISCUSSION

In examining the primary purpose of this study, those patients with positive cultures had a longer length of antibiotic therapy, increased ICU length of stay, and increased inpatient mortality (Table 2) as compared to those with negative or no cultures. These results show that, at the VANTHCS, pneumonia may increase ICU length of stay as well as increase patient mortality. Length of antibiotic therapy was longer in these patients when there was an actual organism isolated, thus driving duration of antibiotic therapy.

With respect to the secondary objectives, our study found that empiric antibiotic selection in the ICUs was appropriate and accurate based on the isolated microorganism. The 2 cultures that were not accurate for antibiotic therapy were due to *Candida* spp. and mycobacterium, which are not included in the typical empiric coverage at our institution.

In looking at the culture-positive versus culture-negative results, fever incidence and WBC count were very similar between the 2 groups. An infiltrate on CXR was noted in 71% of patients in the culture-positive group compared to less than 50% in the culture-negative group. In addition, there were cultures not drawn in 33% of patients. This may have been due to an order not being written, an order not being completed by nursing, or cultures not received by the lab and not re-drawn.

Opportunities exist to improve the use of de-escalation strategies and early discontinuation of antibiotics. De-escalation did not occur for 27% of the positive cultures. Upon examining the sensitivity reports, it was found that several cultures were for MSSA. Vancomycin was the empiric antibiotic choice, but it was not de-escalated to a more narrow-spectrum antibiotic with known culture results. An example worth noting is that of a patient on piperacillin/tazobactam for a fully susceptible *Citrobacter koseri*. The antibiotic coverage could have been de-escalated for this patient, but the patient remained on the piperacillin/tazobactam. A possible reason de-escalation did occur was that the patient had a second infection and a broader agent would cover both infections.

Results of “no” for appropriateness of antibiotics means that the patient was not empirically started on broad-spectrum antibiotics to cover all suspected organisms. For example, the patient was only

started on a piperacillin/tazobactam, which lacks MRSA coverage, and the patient then grew MRSA from their sputum culture.

Tools such as the use of the CPIS or procalcitonin levels that are not currently utilized at our institution may have helped guide therapy by decreasing the length of therapy in patients without cultures or cultures without positive growth. A study by Singh and colleagues⁶ investigated short-course empiric antibiotic therapy in the ICU using the CPIS. The CPIS incorporates 6 readily accessible clinical variables to determine the likelihood that the patient’s clinical findings are due to VAP, with a score of 6 and below suggesting a low likelihood of pneumonia. The 6 components are temperature, WBC, tracheal secretions, PaO₂/FiO₂, culture of tracheal aspirate, and CXR. Patients were evaluated at 3 days; if the CPIS score remained 6 or less, then antibiotics were discontinued. This study showed no difference in mortality or ICU length of stay.

The CPIS score is not practical to use at VANTHCS due to the software that is used to collect the data. It would be difficult for the computer system to transfer the CXR data and tracheal secretions to get a CPIS score. It would require the nurse to manually enter this information into the software program, which would increase the workload of the nursing staff.

A diagnostic tool being utilized more often in certain settings is procalcitonin. Procalcitonin levels rise in response to pro-inflammatory stimuli specifically of bacterial origin and is usually used as a marker of severe sepsis. This assay is perceived to be a fairly specific marker for severe bacterial infection and may be used as an antibiotic discontinuation tool. Based on the PRORATA trial, procalcitonin concentrations were defined for discontinuation and continuation of antimicrobial therapy.⁷ Studies have also shown that using procalcitonin levels to guide antimicrobial therapy may help reduce antibiotic treatment by 2.5 to 3 days.⁷

A 2012 meta-analysis of procalcitonin-guided antibiotic therapy algorithms showed that there were a decreased number of antibiotic days as well as no change in mortality when this test was used.⁸ As shown in our data, about 60% of the patients had no cultures taken or had cultures without positive growth. By integrating the procalcitonin assay into an admission order set for suspected pneumonia, we could more accurately diagnose and start appropriate empiric antibiotic therapy. This would help the VANTHCS decrease the number of antibiotic days and

help guide treatment. As a result of these data, VAN-THCS has since acquired the procalcitonin assay and is currently using it in-house as both a diagnostic and antibiotic stewardship tool. Ongoing studies are examining the effectiveness of this tool and will hopefully lead to the development of a protocol to optimize patient care by decreasing antibiotic exposure and thus decreasing antimicrobial resistance.

There are several limitations to this study. It was a retrospective descriptive chart review. Whereas *CPRS* and *Essentris* are useful tools for patient care, it is sometimes difficult to retrieve patient data for research purposes. This was a single-center study, which could prevent its generalizability to other VA hospitals, other hospitals in general, or the ICU population as a whole. Different resistance patterns exist throughout the nation and, at times, are different even across different units within the same institution. In addition, we only reviewed data on patients with positive sputum cultures. This may have led to an underestimation of the pneumonia incidence due to the exclusion of patients not having any sputum production to send for culture.

Several patients included in this study had non-pneumonia diagnoses. These patients were included, as they were initially diagnosed with pneumonia and that was the reason for admission to the ICU. These patients may have received empiric antibiotics inappropriately, as 10 out of 12 patients were culture-negative (Table 1). This may have also falsely elevated the average length of therapy in the “negative culture” group as seen in Table 2.

CONCLUSION

The treatment of pneumonia in the VAN-THCS ICUs is initially treated with empiric antibiotics. Empiric antibiotic therapy for the treatment of pneumonia at our institution is appropriate and accurate. There are opportunities to improve the de-escalation of antibiotics. Using the procalcitonin assay as a diag-

nostic tool may prove to be useful at the VAN-THCS and help to optimize patient care through decreasing health care-related costs, antibiotic exposure, and antimicrobial resistance.

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