BRIEF REPORT

Overprescription of antibiotics in patients with community-acquired pneumonia in the intensive care unit

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Access this article online

Website: www.avicennajmed.com

DOI: 10.4103/ajm.AJM_189_18

Quick Response Code:

ABSTRACT

Purpose: We aimed to assess factors associated with therapy failure in patients with community-acquired pneumonia in the intensive care unit (ICU). **Methods:** Electronic charts of patients with *International Classification of Diseases*, *Ninth Revision*, codes of pneumonia who were admitted to the ICU at a tertiary academic medical center in Southern Arizona were reviewed. **Results:** Antipseudomonal coverage and anti-methicillin-resistant *Staphylococcus aureus* (MRSA) coverage were often prescribed (58.4% and 54.1%, respectively). Antipseudomonal coverage was rarely necessary as pseudomonal pneumonia was found in only one case (0.9%). Antipseudomonal and anti-MRSA coverage was not associated with improved outcomes. **Conclusion:** Overprescription of antibiotics in this population remains a significant problem. More work is needed to further limit unnecessary antibiotic use.

Key words: Antimicrobials, incentive care unit, outcomes, overuse, respiratory infection

INTRODUCTION

Around 53–63% of patients with community-acquired pneumonia (CAP) are hospitalized every year.[1] There has been a growing concern for an increase in methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia. Traditionally MRSA was a concern for nosocomial pneumonia, but as the rate of MRSA has increased in the community setting, this organism is now starting to be seen in patients without risks for healthcare-associated pneumonia.[2-4] In addition, MRSA isolates carrying Panton–Valentine leukocidin genes were associated with severe pneumonia resulting in death.[2] The Infectious Disease Society of America recently recommended adding vancomycin to the standard antibiotic coverage (respiratory fluoroquinolones or a beta-lactam plus a macrolide) for patients admitted with CAP severe enough to warrant intensive care unit (ICU) admission.[5] Often times, due to the severity of illness and need for ICU admission, many physicians also prescribe antibiotics to cover *Pseudomonas aeruginosa* despite the absence of structural lung disease. The objective of the study was to evaluate the prevalence of MRSA and *P. aeruginosa* and factors associated with failure of therapy.

METHODS

Electronic charts of patients with *International Classification of Diseases*, *Ninth Revision* (ICD 9) codes of pneumonia who were admitted to the Medical and Surgical ICU at Banner University of Arizona Medical Center (Tucson

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Cite this article as: Hooten R, Luis Marquez J, Goldlist K, Urcis R, Adams M, Matthias KR, *et al*. Overprescription of antibiotics in patients with community-acquired pneumonia in the intensive care unit. Avicenna J Med 2019;9:107-10.

Campus), a tertiary medical center, from November 2013 through December 2016 were reviewed by the research team. Inclusion criteria included patients who were aged 18 years or older and admitted to the ICU in the first 48 hours of presentation to the hospital with a diagnosis of pneumonia. Patients were excluded if they had risk factors for healthcare-associated pneumonia, including residence in a nursing home or extended care facility, home infusion therapy, chronic dialysis within the last 30 days, home wound care, immunosuppressive disease or therapy, or hospitalization in the last 90 days. Patients who were pregnant, incarcerated, or ventilator dependent were also excluded. The protocol was approved by the University of Arizona Institutional Review Board.

The entire population was used to evaluate factors associated with MRSA pneumonia and poor outcome. Failure was defined as death attributed to pneumonia, patient intubated more than 48 hours after admission to ICU, need for antibiotic escalation, or readmission attributed to pneumonia. "Any failure" was defined as all-cause mortality, patient intubated more than 48 hours after admission to ICU, need for antibiotic escalation, or readmission for any reason. Factors evaluated for association with poor outcome included demographics, signs and symptoms including chest X-ray findings, and medical history (chronic obstructive pulmonary disease [COPD], diabetes, prior antibiotic exposure within 30 days, history of MRSA or pseudomonal infection, or positive MRSA nasal swab within 90 days). The populations of MRSA pneumonia (case and control) were composed of a subset of the entire population. MRSA case subjects had a respiratory culture positive for MRSA during their hospital stay. Subjects included in the MRSA control group had to have a respiratory specimen available that was negative for MRSA and/or a negative MRSA nasal swab. The case and control groups were used to assess potential factors associated with MRSA pneumonia. A similar process was planned for *P. aeruginosa* pneumonia except the absence of a surrogate marker comparable to the MRSA nasal swab.

Fisher exact test was used to identify factors associated with outcomes or pneumonia type. Classification factors associated with *P* values <0.2 were further evaluated using multivariate logistic regression. To be retained as a predictive factor, the *P* value in the final model was needed to be <0.05.

Statistical analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC). Procedure FREQ was used to evaluate differences in proportions with the Fisher option. A *t* test or Wilcoxon test was used to evaluate differences in age, ICU length of stay, and follow-up times. Logistic regression was performed with factors identified ($P < 0.2$) by the univariate results. Both forward and backward stepwise procedures were used to ensure model stability.

RESULTS

A total of 1065 charts were identified using ICD 9 codes for pneumonia and admission to the ICU. Of these, only 209 patients met appropriate inclusion criteria. The cohort consisted of 104 (49.8%) males and 105 (50.2%) females, predominately white (79.5%) and non-Hispanic (69.7%).

Comorbidities, clinical presentation, microbiology, radiology, and antibiotics prescribed are presented in Table 1. The most common comorbidity was COPD (31.1%). Dyspnea was the most common presenting symptoms (83.4%). A total of 117 patients (56%) had a respiratory specimen performed [Table 1], out of which 39 were positive (33.3%). A total of 60 nasal swab MRSA polymerase chain reaction (PCR) tests were performed and only 11 had positive results (18.3%). The most common bacterial cause of pneumonia was *Streptococcus pneumoniae*. Only seven patients had MRSA (five from sputum and two from tracheal aspirate) and one patient had *P. aeruginosa* (from tracheal aspirate). Notably only three patients had MRSA bacteremia with no cases of *P. aeruginosa* bacteremia. A total of 124 cases had negative respiratory specimen and/or MRSA nasal swab (control cases). There were seven cases of MRSA pneumonia. A total of 113 patients (54.1%) received anti-MRSA therapy, 122 (58.4%) received antipseudomonal therapy, and 164 (78.5%) received atypical coverage.

Independent factors associated with MRSA pneumonia on the univariate analysis ($P < 0.2$) included history of MRSA ($P = 0.053$), positive blood culture ($P = 0.083$), fever ($P = 0.045$), necrotizing pneumonia ($P = 0.104$), effusion ($P = 0.0741$), and ICU length of stay ($P = 0.047$) [Table 1]. Only effusion ($P = 0.001$) and fever ($P = 0.002$) were associated with MRSA pneumonia in the multivariate logistic regression.

A total of 69 patients developed failure (33.0%) and 105 had any failure (50.2%). Table 2 shows independent variables associated with these primary outcomes. Positive blood culture ($P = 0.019$), effusion ($P = 0.100$), receipt of antibiotics over 48 hours ($P = 0.080$), and receipt of antibiotics against atypical organisms ($P = 0.033$) were all associated with failure on the univariate analysis. Only positive blood culture ($P = 0.010$) was associated with failure on the multivariate logistic regression. Similarly, positive blood culture ($P = 0.002$) was the only independent factor associated with any failure on multivariate logistic regression.

Table 1: Comorbidities, clinical presentation, microbiology, and antibiotic prescription (*N* = 209)

Parameter	All Subjects	MRSA—case/control populations		
	(*N* = 209)	MRSA case (*n* = 7)	MRSA control (*n* = 124)	*P* value
Age—mean (SD)	61.5 (17.5)	54.1 (15.1)	61.5 (17.5)	>0.2
Sex (female)	104/209 (49.8%)	3/7 (42.9%)	65/124 (52.4%)	>0.2
Ethnicity (Hispanic)	63/208 (30.3%)	1/7 (14.3)	39/124 (31.5%)	>0.2
Race (white)	163/205 (79.5%)	6/7 (85.7%)	102/123 (82.9%)	>0.2
Recent influenza	3/209 (1.44%)	0/7 (0.00%)	2/124 (1.61%)	>0.2
Recent antibiotics	26/206 (12.6%)	1/7 (14.3%)	17/123 (13.8%)	>0.2
Diabetes	29/191 (15.2%)	1/6 (16.7%)	17/116 (14.7%)	>0.2
COPD	61/196 (31.1%)	2/6 (33.3%)	40/118 (33.9%)	>0.2
History of MRSA	1/209 (0.48 %)	1/7 (14.3%)	0/124 (0.00%)	0.0534
Respiratory specimen				
BAL	21 (10.1%)	0 (0.00%)	21 (16.9%)	
Sputum	71 (34.0%)	5 (71.4%)	64 (51.6%)	>0.2
Trach aspiration	25 (12.0%)	2 (28.6%)	20 (16.1%)	
Not available	92 (44.0%)	0 (0.00%)	19 (15.3%)	
Positive MRSA nasal swab	11/60 (18.3%)	4/4 (100%)	0/49 (0.00%)	—
Positive blood culture	30/202 (14.9%)	3/7 (42.9%)	18/123 (14.6%)	0.0831
Coccidioidomycosis	8/112 (7.14%)	1/6 (16.7%)	3/69 (4.35%)	>0.2
Positive respiratory PCR panel	13/104 (12.5%)	0/1 (0.00%)	10/72 (13.9%)	>0.2
Positive influenza PCR	14/117 (12.0%)	0/2 (0.00%)	12/78 (15.4%)	>0.2
Cough	133/204 (65.2%)	3/7 (42.9%)	80/120 (66.7%)	>0.2
Fever	63/203 (31.0%)	5/7 (71.4%)	39/122 (32.0)	0.0452
Hypotension	45/200 (22.5%)	3/7 (42.9%)	28/120 (23.3%)	>0.2
Dyspnea	171/205 (83.4%)	5/7 (71.4%)	104/122 (85.2%)	>0.2
CXR—necrotizing pneumonia	3/209 (1.44%)	1/7 (14.3%)	1/124 (0.81%)	0.104
CXR—effusion	57/209 (27.3%)	4/7 (57.1%)	30/124 (24.2%)	0.0741
CXR—multilobular	105/209 (50.2%)	5/7 (71.4%)	68/124 (54.8%)	>0.2
Antibiotics > 48 h	197/207 (95.2%)	7/7 (100%)	119/123 (96.8%)	>0.2
Anti-MRSA antibiotic	113/209 (54.1%)	6/7 (85.7%)	70/124 (56.5%)	>0.2
Antipseudomonal antibiotic	122/209 (58.4%)	6/7 (85.7%)	73/124 (58.9%)	>0.2
Atypical coverage	164/209 (78.5%)	6/7 (85.7%)	102/124 (82.3%)	>0.2
Readmission	63/208 (30.3%)	3/7 (42.9%)	34/124 (27.4%)	>0.2
Readmission d/t pneumonia	27/205 (13.2%)	2/7 (28.6%)	17/123 (13.8%)	>0.2
CDI within 6 months	8/208 (3.85%)	0/7 (0.00%)	5/124 (4.03%)	>0.2
Intubation after 48 h	16/207 (7.73%)	0/7 (0.00%)	12/124 (9.68%)	>0.2
Antibiotic escalated	17/208 (8.17%)	1/7 (14.3%)	12/124 (9.68%)	>0.2
Death	29/207 (14.0%)	1/7 (14.3%)	18/123 (14.6%)	>0.2
Death due to pneumonia	20/207 (9.66%)	0/7 (0.00%)	13/123 (10.6%)	>0.2
ICU length of stay (days)	3 (0–50)	7 (3–15)	3 (2–7)	0.0471
Follow-up duration (days)	180 (1–180)	180 (84–180)	180 (17–180)	>0.2

MRSA = methicillin-resistant *Staphylococcus aureus*, ICU = intensive care unit, COPD = chronic obstructive pulmonary disease, BAL = bronchoalveolar lavage, CXR = chest X-ray, CDI = *Clostridium difficile* infection, SD = standard deviation, PCR = polymerase chain reaction

DISCUSSION

In our study, we found that overprescription of antibiotics in the ICU for patients with CAP remains a significant problem. Antipseudomonal coverage and anti-MRSA coverage were often prescribed in this population (58.4% and 54.1%, respectively). Antipseudomonal coverage was rarely necessary as pseudomonal pneumonia was found in only one case (0.9%). This patient did not have history of COPD or bronchiectasis. MRSA was found in only 6.0% of the cases. We found that lack of antipseudomonal and anti-MRSA coverage was not associated with higher rates of primary outcomes (failure or any failure).

Our study does not support the routine use of antipseudomonal and anti-MRSA therapy for patients with CAP in the ICU given low prevalence. It may be necessary to use anti-MRSA therapy in selected patients (e.g., with hypotension, necrotizing pneumonia, and positive nasal swab MRSA PCR).[5,6] Recent data were published regarding the negative predictive value of a negative nasal swab MRSA PCR. Two studies by Dangerfield *et al*.[7] and Giancola *et al*.[6] have shown that a negative nasal swab MRSA PCR indicates the absence of MRSA pneumonia in patients with low MRSA incidence and this test might be used to deescalate antibiotics in cases of negative culture.

Our study has several limitations. It is retrospective in nature and was performed in one center in Southwestern United States, which limits the generalizability of our findings. In addition, only 113 patients (54%) had respiratory culture performed and 90 (43%) had a nasal swab MRSA PCR

Table 2: Association between dependent variables and primary outcomes (failure and any failure)

Characteristic	Failure present (*n* = 69)	Failure absent (*n* = 140)	*P* value	Any failure present (*n* = 105)	Any failure absent (*n* = 104)	*P* value
Sex—female	32/69 (46.4%)	71/140 (51.4%)	>0.2	51/104 (49.0%)	53/140 (50.5%)	>0.2
Ethnicity—Hispanic	18/69 (26.1%)	45/139 (32.4%)	>0.2	28/104 (26.9%)	35/104 (33.7%)	>0.2
Race—white	55/68 (80.9%)	108/137 (78.8%)	>0.2	76/102 (74.5%)	87/103 (84.7%)	>0.2
Recent influenza	2/69 (2.90%)	1/140 (0.71%)	>0.2	2/104 (1.92%)	1/105 (0.95%)	>0.2
Recent antibiotic	61/69 (88.4%)	119/137 (86.9%)	>0.2	13/103 (12.6%)	13/103 (12.6%)	>0.2
Diabetes	7/66 (10.6%)	22/125 (17.6%)	>0.2	14/96 (14.6%)	15/95 (15.8%)	>0.2
COPD	20/64 (31.3%)	41/132 (31.1%)	>0.2	24/95 (25.3%)	37/101 (36.6%)	0.0920
History of MRSA	1/69 (1.45%)	0/140 (0.0%)	>0.2	1/104 (0.96%)	0/105 (0.0%)	>0.2
Nasal MRSA	3/19 (15.8%)	8/41 (19.5%)	>0.2	6/27 (77.8%)	5/33 (84.9%)	>0.2
Blood culture positive	16/67 (23.9%)	14/135 (66.8%)	0.0193	23/99 (23.2%)	7/103 (6.80%)	0.0013
Coccidioidomycosis	1/32 (3.13%)	7/80 (8.75%)	>0.2	3/52 (5.77%)	5/60 (8.33%)	>0.2
Positive respiratory PCR	4/38 (10.5%)	9/66 (13.6%)	>0.2	6/53 (11.3%)	7/51 (13.7%)	>0.2
Positive influenza PCR	4/40 (10.0%)	10/77 (13.0%)	>0.2	5/55 (9.09%)	9/62 (14.5%)	>0.2
CXR—necrotizing	1/69 (1.45%)	2/140 (1.43%)	>0.2	2/104 (1.92%)	1/105 (0.95%)	>0.2
CXR—effusion	24/69 (34.8%)	39/140 (27.9%)	0.0997	36/104 (34.6%)	27/105 (25.7%)	0.177
CXR—multilobular	37/69 (53.6%)	72/140 (51.4%)	>0.25	52/104 (50.0%)	57/105 (54.3%)	>0.2
Cough	42/67 (62.7%)	91/137 (66.4%)	>0.2	62/101 (61.4%)	71/103 (68.9%)	>0.2
Fever	22/66 (33.3%)	41/137 (29.9%)	>0.2	29/100 (29.0%)	34/103 (33.0%)	>0.2
Hypotension	18/66 (27.3%)	27/134 (20.2%)	>0.2	27/99 (27.3%)	18/101 (17.8%)	0.129
Dyspnea	58/67 (86.6%)	113/138 (67.3%)	>0.2	87/101 (86.1%)	84/104 (80.8%)	>0.2
Antibiotics > 48 h	61/67 (91.0%)	136/140 (67.3%)	0.0803	94/102 (92.2%)	103/105 (98.1%)	0.0562
Anti-MRSA antibiotics	38/69 (55.1%)	75/140 (53.6%)	>0.2	55/104 (47.1%)	47/105 (44.8%)	>0.2
Antipseudomonal antibiotics	41/69 (59.4%)	65/140 (46.4%)	>0.2	61/104 (58.7%)	61/105 (58.1%)	>0.2
Anti-atypical organism antibiotics	48/69 (69.6%)	81/140 (57.9%)	0.0326	75/104 (72.1%)	89/105 (84.8%)	0.0294

MRSA = methicillin-resistant *Staphylococcus aureus*, COPD = chronic obstructive pulmonary disease, CXR = chest X-ray, PCR = polymerase chain reaction

performed in the previous 90 days. We did not assess timing of antibiotics, which could impact culture and nasal swab data.

Future directions include looking at a larger population subset and further defining populations needing broad-spectrum antibiotics to prevent antibiotic resistance.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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