Brief Report

Impact of respiratory virus molecular testing on antibiotic utilization in community-acquired pneumonia

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We compared the clinical characteristics and antibiotic therapy of community-acquired pneumonia patients who were positive on a respiratory virus molecular test (polymerase chain reaction) with those who were negative. We found that respiratory virus molecular polymerase chain reaction testing has a minimal impact on reducing antibiotic utilization among viral pneumonia patients.
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BACKGROUND

Community-acquired pneumonia (CAP) is an important cause of morbidity and mortality in the United States.[1] The specific microbiologic etiology of CAP is frequently difficult to identify, but recent studies suggest that viral pathogens account for approximately 29%-39% of total cases.[2,3] The inability to differentiate between a bacterial or viral etiology in CAP based on clinical presentation, physical findings, radiographic findings and routine microbiologic cultures makes selection of therapy difficult, and typically all cases are treated empirically for a bacterial process. Development in molecular diagnostic techniques may help to alleviate this situation. Multiplex polymerase chain reaction (PCR) technology has been recently introduced into clinical laboratories and may facilitate the identification of a panel of potential respiratory pathogens that are responsible for the cause of CAP. Respiratory viral panel (RVP) PCR–based technology can detect multiple viral pathogens and is a very sensitive and specific diagnostic tool which offers the potential of allowing physicians to make a specific diagnosis of viral pneumonia. However, it remains unclear whether this improvement in diagnostic accuracy will lead to a reduction in unnecessary antibiotic utilization in the hospitalized CAP patient. Several studies have found that viral PCR testing did not reduce antibiotic utilization in inpatient settings.[4-6] It is important to evaluate the use of antibiotic therapy in inpatients with viral pneumonia because unnecessary antibiotic therapy may foster the development of multidrug-resistant organisms and increase the risk for *Clostridium difficile* colitis.[7,8] In an effort to address these issues, we performed an analysis of antibiotic use among RVP PCR–positive versus –negative inpatients diagnosed with CAP to determine whether using this new technology has any impact on reducing antibiotic utilization in patients with viral pneumonia. In addition, we evaluated the clinical characteristics and outcomes in CAP in these 2 groups of patients.

METHODS

This multisite cohort study included hospitalized adult patients diagnosed with CAP who were tested using a PCR-based RVP during calendar year 2014. Patients who underwent RVP testing after 48 hours of admission were excluded from the study. A manual chart review was also done to identify patients with pneumonia, defined as clinical signs of pneumonia in association with lung imaging demonstrating infiltrates with or without culture growth. PCR-RVP testing was performed using the Film Array Respiratory Panel test (Biofire Diagnostics LLC, Salt Lake City, UT). The respiratory viruses tested in the panel PCR were adenovirus, coronavirus, metapneumovirus, rhinovirus, enterovirus, influenza A, influenza B, parainfluenza, and respiratory syncytial virus. The study protocol was reviewed and approval by the TriHealth Institutional Review Board.

Data were extracted through the TriHealth electronic medical record system (EPIC Systems, Verona, WI). The main outcome was utilization of antibiotic therapy after the pneumonia diagnosis. Other study outcomes included length of stay, intensive care unit days, mortality, ventilator days, and discharge disposition. Data on

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demographics, comorbidities, testing results, vitals, and laboratory and image results were collected. Treatment management was evaluated by determining the discontinuation of antibiotic therapy within 48 hours of pneumonia diagnosis.

Univariate analysis was conducted to compare outcomes and other study variables between patients who were RVP positive versus RVP negative. Logistic regression was used to examine the adjusted risk between the 2 groups and each of the significant variables. The χ^2 test and Fisher exact test, when appropriate, were used for categorical variables. For continuous variables, Student t tests and comparison of medians were used for normally and nonnormally distributed data, respectively. The significance level for all analysis was $\alpha = 0.05$. Statistical analysis was performed using SPSS for Windows version 22 (SPSS Inc, Chicago, IL).

RESULTS

Among the 190 study subjects, 108 (57%) were RVP positive for viral pathogens and 82 (43%) were RVP negative. Univariate analysis revealed that age >65 years and leukocytosis were significantly associated with a negative RVP PCR ($P = .04$ and $P = .001$, respectively). Additionally, higher white blood cell count and creatinine values on admission were significantly associated with being RVP PCR negative ($P = .003$ and $P = .01$, respectively), suggesting a bacterial etiology for pneumonia (Table 1).

Clinical outcomes were similar between the RVP-positive and RVP-negative groups. Among the patients who were RVP positive, 72% were continued on antibiotic treatment for ≥2 days after the diagnosis of pneumonia versus 90% of those who were RVP negative ($P = .002$) (Table 2).

Table 1
Patient characteristics and clinical findings

Characteristics	RVP PCR negative (n = 82) n	RVP PCR negative (n = 82) %	RVP PCR positive (n = 108) n	RVP PCR positive (n = 108) %	P value
Male sex	36	43.9	37	34.3	.18
Age >65 y	46	56.1	44	40.7	.04
White	64	78.0	82	75.9	.73
Comorbidities					
Leukocytosis	48	63.2	40	38.8	.001
Acute kidney injury	15	18.3	16	14.8	.52
Acute respiratory failure	14	17.1	17	15.7	.81
Hypokalemia	9	11.0	20	18.5	.15
Anemia	13	15.9	11	10.2	.24
Hypoxia	6	7.3	16	14.8	.11
COPD	7	8.5	14	13.0	.34
Sepsis	8	9.8	10	9.3	.91
Steroid use	30	36.6	47	43.5	.34
Chest radiograph					.89
Unilateral	39	52.7	48	50.5	
Bilateral	23	31.1	33	34.7	
Interstitial	6	8.1	6	6.3	
Not clear	5	6.8	5	5.3	
Laboratory values	Mean	SD	Mean	SD	P value
Oxygen saturation (%)	89.3	12.1	92.0	6.9	.08
Temperature maximum (°F)	100.2	1.6	100.3	1.7	.80
Laboratory values median	Median	IQR	Median	IQR	P value
WBC (K/μL)	12.0	8.8-16.3	9.7	6.8-13.7	.003
Creatinine (mg/dL)	1.2	1.0-1.5	1.0	0.8-1.3	.01
AST (U/L)	24	20-44	32	22-45	.34

AST, aspartate aminotransferase; *CAP*, community-acquired pneumonia; *COPD*, chronic obstructive pulmonary disease; *IQR*, interquartile range; *PCR*, polymerase chain reaction; *RVP*, respiratory viral panel; *WBC*, white blood cell.

Table 2
Patient treatment and outcomes

Treatment and outcomes	RVP PCR negative (n = 82)	RVP PCR positive (n = 108)	P value
Treatment			
Antibiotics, n (%)	81 (98.8)	103 (95.4)	.24
Antibiotics ≥2 d, n (%)	74 (90.2)	78 (72.2)	.002
Duration of inpatient antibiotic treatment, median (IQR)	4.0 (3.0-5.0)	3.0 (2.0-6.0)	.56
Outcomes			
ICU transfer, n (%)	6 (7.3)	9 (8.3)	.80
Ventilator, n (%)	29 (35.4)	34 (31.5)	.57
Mortality, n (%)	3 (3.7)	2 (1.9)	.65
Length of stay (days), median (IQR)	5.0 (3.0-9.0)	5.0 (3.0-9.0)	.80

CAP, community-acquired pneumonia; *ICU*, intensive care unit; *IQR*, interquartile range; *PCR*, polymerase chain reaction; *RVP*, respiratory viral panel.

DISCUSSION

We found that patients with a positive RVP result were less likely to be treated with >48 hours of antibiotic therapy versus patients with a negative RVP result. However, there was no significant difference in the median total duration of antibiotic therapy between these 2 groups of patients, which is consistent with previous studies.[7,8] Our study suggests that physicians hesitate to discontinue antibiotic therapy even when patients are found to have viral pneumonia using a highly sensitive and specific PCR methodology. The clinical challenge in the syndrome of viral pneumonia is the issue of coinfection with bacterial pathogens, which has been reported to occur in 14%-40% of cases.[9] The decision to continue antibiotic therapy despite microbiologic evidence for a viral etiology depends on multiple clinical factors, including severity of illness, radiographic imaging results, laboratory studies including white blood cell count, and comorbidities. Our study revealed that leukocytosis and age >65 years were significantly associated with RVP PCR–negative cases, suggesting that application of additional clinical and laboratory markers combined with RVP PCR testing may assist physicians in identifying which patients may be appropriate for discontinuing antibiotics. Procalcitonin (PCT) is a biomarker which has been found to be valuable in differentiating between bacterial and viral pneumonia in the clinical setting.[10] Low serum PCT levels argue against a bacterial etiology for CAP. Combining the results of RVP PCR testing and PCT testing may reassure physicians that patients with viral pneumonia do not have a bacterial superinfection, which in turn should result in decreasing antibiotic overutilization. Studies evaluating the use of antibiotic therapy in CAP patients where both RVP PCR and PCT testing are used would be beneficial.

CONCLUSIONS

We found that RVP PCR testing in CAP patients has only a minimal impact on antibiotic utilization. Additional interventions will be necessary to significantly reduce antibiotic overutilization in viral pneumonia.

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