[Original Research]

CHEST

The Burden of Viruses in Pneumonia Associated With Acute Respiratory Failure

An Underappreciated Issue

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BACKGROUND: Pneumonia associated with mechanical ventilation (MV) results in substantial mortality and represents a leading reason for the use of antibiotics. The role of viruses in this setting is unclear. Identifying a viral cause in such instances could facilitate antibiotic stewardship.

METHODS: We performed a secondary analysis of a prospective cohort with pneumonia requiring MV. We included both cases occurring in the community and hospital-onset cases and classified patients according to the cause of the pneumonia. The prevalence of viral pathogens represented the primary end point. We identified variables independently associated with isolation of a viral organism as the sole pathogen.

RESULTS: The cohort included 364 patients, and a virus was the sole pathogen in 79 cases (21.7%). The most common viruses included rhinovirus/enterovirus (n = 20), influenza A (n = 12), and respiratory syncytial virus (n = 11). The rate of in-hospital death was high (37.2%) and did not differ from that seen in others (36.5%). The duration of MV, hospital length of stay, and 30-day readmission rates also did not differ based on the cause of pneumonia. Two variables were independently associated with recovery of a virus: an Acute Physiology and Health Evaluation II score of < 26 (adjusted odds ratio [AOR], 0.51; 95% CI, 0.28-0.93; $P = .027$) and stem cell transplantation (SCT) (AOR, 4.39; 95% CI, 2.03-9.50; $P = .001$). A sensitivity analysis excluding patients who underwent SCT did not substantially alter our observations.

CONCLUSIONS: Viruses represent a major cause of pneumonia in critically ill patients requiring MV. Identifying such subjects presents an opportunity for discontinuing antibiotics. Clinicians should consider systematically evaluating patients with pneumonia requiring MV for viral pathogens.

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KEY WORDS: acute respiratory failure; bacteria; outcomes; pneumonia; virus

ABBREVIATIONS: AOR = adjusted OR; CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; LOS = length of stay; MV = mechanical ventilation; SCT = stem cell transplantation; VAP = ventilator-associated pneumonia

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Pneumonia remains both a leading reason for mechanical ventilation (MV) and a potential complication of MV. Hence, the impact of pneumonia in the ICU remains substantial.[1,2] As such, multiple quality efforts focus on reducing the burden of pneumonia in the ICU, regardless of whether the pneumonia results in admission to the ICU or if it represents a consequence of MV.[2] Similarly, pneumonia in the setting of acute respiratory failure (ARF) continues to be a leading reason for antibiotic administration.[3,4] Appropriate and timely antibiotic administration is key to limiting morbidity and mortality in ARF and pneumonia.[5] This nexus between appropriate antibiotic therapy and outcomes has been demonstrated in diverse types of pneumonia, including severe community-acquired pneumonia (CAP), nosocomial pneumonia leading to ARF, and ventilator-associated pneumonia (VAP).[5] Because of this relationship, intensivists often are quick to prescribe broad-spectrum antimicrobial agents in suspected cases of pneumonia. However, as a consequence, many patients are likely exposed unnecessarily to agents that are not specifically indicated. This overuse of antibiotics contributes to the escalating prevalence of resistant bacteria encountered in health care and further limits the options available to treat many emerging pathogens.

One way to improve antibiotic prescribing and to increase rates of antibiotic de-escalation is to identify subjects who do not require further antibiotics because their pneumonic syndrome is caused by a viral pathogen.[6] Properly determining that the cause of a specific pneumonia is a viral pathogen can reassure the clinician that it is safe to discontinue further antibiotics (should no bacterial pathogen simultaneously be identified). In other words, better appreciating the range of pathogens encountered in pneumonia arising in or complicating ARF can foster improved antibiotic stewardship. Similarly, understanding the significance of viruses in ICU-related pneumonia could facilitate the development of both clinical decision aids and diagnostic tools that also might augment antibiotic stewardship.

The significance of viral organisms in pneumonia historically was believed to be limited to immunosuppressed and transplant populations. Several contemporary analyses, however, illustrate the significance of viruses generally as important causes of pneumonia. Jain et al,[7] for instance, in an observational study of hospitalized patients with CAP noted that viruses were a more prevalent cause of the infection than were bacteria. Similarly, investigators have implicated viral organisms as a major cause of VAP.[8,9] Hong et al[9] isolated viruses in > 20% of VAP cases.

To examine the epidemiology and outcomes associated with viral pneumonia seen in ARF, we conducted a retrospective analysis of pneumonia seen in patients undergoing MV. We hypothesized that viruses were common causes of pneumonia associated with ARF. We sought to describe the prevalence of viral organisms. We further aimed to assess the outcomes and risk factors associated with a viral cause in patients with pneumonia and respiratory failure requiring MV.

Methods

Study Overview

This study was a secondary analysis of a prospective cohort of adult patients diagnosed with pneumonia in the setting of respiratory failure requiring MV during a 1-year period at a single center (January to December 2016). Prior aspects of this analysis, particularly information regarding bacterial causes and appropriate initial therapy, have been described elsewhere.[10] Briefly, the study was conducted between January 1, 2016 and December 31, 2016. We included only adults (age ≥ 18 years) admitted to the hospital for at least 48 hours and evaluated cases of pneumonia, regardless of whether it had a community or hospital onset. All subjects had to undergo MV for at least 24 hours to be included in the study cohort. In other words, we examined suspected cases of CAP, hospital-acquired pneumonia (HAP), and VAP. We excluded subjects transferred from other health-care facilities. As this study was retrospective, the hospital's institutional review board waived any need for informed consent (IRB No. 201509075).

End Points and Definitions

The isolation of a viral organism as the sole pathogen identified served as the primary end point for the study. We defined CAP, HAP, and VAP in accordance with the American Thoracic Society/Infectious Disease Society of America position statement on nosocomial pneumonia.[11] Initially, we identified patients for a potential diagnosis of pneumonia and concurrent ARF based on the physician ordering respiratory cultures. Following case finding based on the ordering of cultures, chest imaging was reviewed by one investigator (M. H. K.) (1) to ensure that there was an infiltrate consistent with a diagnosis of pneumonia and (2) to classify the pneumonia type based on the timing of the pneumonia relative to the onset of hospitalization and MV. We further required that all cases meet at least meet two of the following criteria: fever (> 38°C or < 35°C), leukocytosis or leukopenia, and purulent respiratory secretions to ensure the presence of pneumonia.

We classified the results from respiratory cultures as demonstrating either a viral or a bacterial organism or as culture negative. Patients with both a bacterial and viral pathogen (ie, mixed infections) were classified as bacterial for purposes of our analysis given our focus on antibiotic stewardship.

Respiratory specimens obtained through various approaches (eg, sputum, tracheal aspirate, and BAL) were included. We also reviewed results from blood cultures, pleural fluid cultures, and