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Major article

Application of a modified microbiologic criterion for identifying pediatric ventilator-associated pneumonia

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Background: Prevention of ventilator-associated pneumonia (VAP) is a major patient safety goal, but accurate identification of VAP in pediatric patients remains challenging.

Methods: We performed a retrospective cohort study to demonstrate feasibility of endotracheal culture and Gram's stain to support VAP diagnosis. Pediatric intensive care unit and cardiac intensive care unit patients with ≥1 endotracheal specimen having growth of ≥1 organism in conjunction with moderate/many polymorphonuclear leukocytes (ie, the modified microbiologic criterion) were included. Medical records were reviewed for presence/absence of clinical and radiographic Centers for Disease Control and Prevention (CDC) criteria for VAP. Antimicrobial use data were collected before and after culture results were known.

Results: Of 102 patients meeting inclusion criteria, 28% (n = 28) also met both clinical and radiographic CDC criteria for VAP (ie, diagnosis of PNU2). An additional 63% (n = 64) met clinical (36%; n = 37) or radiographic (27%; n = 27) criteria, but not both. Ten patients (9%) had neither clinical nor radiographic criteria for VAP. The majority (63%; n = 64) were receiving antibiotics at time of endotracheal specimen collection. Culture identification resulted in altered antimicrobial therapy in 66% of patients (n = 67).

Conclusions: Our study demonstrates the feasibility of endotracheal Gram's stain and culture for diagnosis of pediatric VAP that could potentially standardize accurate surveillance and management of pediatric VAP.

Ventilator-associated pneumonia (VAP) is an important health care-associated infection due to resultant high morbidity, mortality, and excess financial burdens.[1] VAP is the second most common nosocomial infection occurring within intensive care units (ICUs), with the national pooled mean VAP incidence rate of 2.3 per 1,000 ventilator days during the period 2006-2008.[2] However, the validity of this rate is limited by the wide variation in diagnostic criteria used for defining VAP at individual institutions. The clinical influence of VAP is significant. Multiple studies have demonstrated that patients with VAP have prolonged length of stay in ICUs, with an average attributable duration of 5-11 additional ICU admission days.[3,4] Although it is difficult to accurately assess attributable mortality rate due to VAP because of multiple confounding factors such as age and severity of underlying illness,[5] a number of matched case studies have estimated that the attributable excess mortality rate due to VAP ranges from 15%-50%.[3,6,7] Several studies have estimated that patients with VAP incur on average an additional $12,000 in attributable costs per case.[3,8]

Prevention of VAP is a major patient safety initiative nationwide. During the prior decade, several evidence-based preventive measures have been recommended, including strict hand hygiene practices, minimizing endotracheal (ET) intubation, reducing duration of mechanical ventilation, and implementing aspiration prevention strategies.[9] However in clinical practice, application of these recommended preventive measures remains a challenge in pediatric patient populations.

As of 2007, the Centers for Disease Control and Prevention (CDC) redefined VAP as pneumonia that occurs in a patient receiving mechanical ventilation at the time of or within 48 hours before the onset of the event.[2] The CDC PNU2 algorithm for identification of

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VAP includes a combination of specific radiographic, clinical signs/symptoms, and laboratory (ie, microbiologic) criteria. Radiographic criteria include 2 or more serial chest radiographs with at least 1 of the following: new or progressive and persistent infiltrate, consolidation, cavitation, or pneumatoceles in infants aged ≤1 year. For patients without underlying pulmonary or cardiac disease, 1 chest radiograph is acceptable. Clinical signs/symptoms criteria require the presence of at least 1 of the following signs: fever >38°C (>100.4°F) without other recognized cause, leukopenia (<4,000 white blood cells/mm^3), or leukocytosis (≥12,000 white blood cells/mm^3). One clinical sign must be accompanied by 2 of the following grouped respiratory symptoms: new-onset purulent sputum, change in character of sputum, or increased respiratory secretions or suctioning requirements; new-onset worsening cough or dyspnea or tachypnea; rales or bronchial breath sounds; or worsening gas exchange, increased oxygen requirements, or increased ventilator demand. Laboratory (ie, microbiologic) criteria include at least 1 of the following: positive blood culture; positive pleural fluid culture; positive quantitative culture from minimally contaminated lower respiratory tract specimen (eg, bronchoalveolar lavage [BAL] or protected brush specimen); >5% BAL-obtained cells containing intracellular bacteria on direct microscopic exam; or histopathologic exam showing abscess formation, positive quantitative culture of lung parenchyma, or evidence of lung parenchyma invasion by fungal hyphae.

Despite these well-defined criteria, identification of VAP in pediatric patients remains problematic due to lack of the feasibility of applying these criteria (particularly the requirement for BAL) in this population.[10-13] Therefore, studies of VAP in pediatric populations are few and findings from these studies are limited by differences in surveillance methods and application of diagnostic criteria. Available studies often involve a single center with unmatched data and a small number of highly selected patient populations.[10] A recent systematic review of 48 studies in the pediatric literature from 1947-2010 focused on the optimal diagnostic strategies for VAP in this population[13] and concluded that suboptimal diagnostic methods remain the primary difficulty in achieving a gold standard.

For the purpose of surveillance using the PNU2 definition, CDC/National Healthcare Safety Network recommends using quantitative minimally contaminated BAL or protected specimen brush specimen cultures. However, these procedures are invasive, costly, require skilled personnel, and are associated with unacceptably high risk in pediatric patients, limiting their use in clinical practice.[13,14] Alternatively, although ET aspirates could potentially be associated with lower specificity (particularly if few or no polymorphonuclear [PMN] cells are present), they are more cost-effective, feasible, and safer compared with BAL. Not surprisingly, ET aspirate and culture has become the most common practice used for clinical diagnosis of VAP, although its validity as a substitute for more invasive methods remains controversial.[15] A recently released CDC paradigm for surveillance and diagnosis of VAP in adults[2] supports the use of either BAL or ET aspirate as acceptable sources for quantitative or semiquantitative culture and/or Gram's stain. The relative importance of microbiologic criteria over radiographic criteria is highlighted in the new paradigm by the fact that radiographic criteria are now eliminated.[16]

It is evident that there is a need for additional studies in pediatric populations to develop the most appropriate case definitions and diagnostic methods for VAP. Herein, we describe a cohort of pediatric patients at a free-standing children's hospital with the goal of assessing the contribution of ET aspirate culture and Gram's stain as a modified microbiologic criterion to identify VAP and to measure the effect of ET culture on antimicrobial agent use.

METHODS

Study population

Our study was reviewed and approved by the Institutional Review Board of Children's National Medical Center. ET aspirate cultures yielding ≥1 organism from patients hospitalized at the Children's National Medical Center pediatric or cardiac ICUs from July 2008-September 2009 were identified using the institutional microbiology laboratory data repository (Sunquest Laboratory Information System, Sunquest, Inc, Tucson, Ariz). Patients were only included if their ET specimen also had moderate or many PMN leukocytes present on Gram's stain. We called this criterion the modified microbiologic criterion.

Data collection

A retrospective review of electronic medical records for patients meeting inclusion criteria was performed, specifically to assess the presence or absence of CDC-defined PNU2 criteria for VAP, including clinical signs/symptoms, laboratory results, and chest radiograph findings. Antimicrobial agent use data for each patient before and after results of ET culture was known were collected. Additional data elements collected included age, gender, admission date, underlying disease, unit location at time of ET specimen collection, and organism isolated.

Statistical analysis

Descriptive analyses were performed to describe the study cohort with regard to the distribution of age, gender, underlying disease, and clinical outcome, as measured by length of ICU stay and mortality. Overall VAP rate per 1,000 ventilator days was calculated. The number and percentage of patients receiving antimicrobial therapy before ET specimen collection, as well as the number and percentage of patients for whom antimicrobial therapy was altered following culture results, was assessed.

RESULTS

One hundred two patients with a total of 121 ET culture specimens meeting inclusion criteria (ie, presence of an ET culture with moderate to many PMNs and growth of ≥1 organisms) were identified. Of 102 patients meeting the modified microbiologic inclusion criterion, 28% (n = 28) also met both clinical and radiographic CDC criteria for VAP. An additional 63% (n = 64) of patients fulfilled either clinical (n = 37; 36%) or radiographic criteria (n = 27; 27%) but not both. Ten patients (9%) had neither clinical nor radiographic criteria for VAP at the time of ET specimen collection (Fig 1).

Cultures yielded gram-negative bacterial pathogens in 70% of specimens (n = 85 out of 121), gram-positive bacterial pathogens in 22% of specimens (n = 26 out of 121), and yeast in 8% of specimens (n = 10 out of 121). The most common gram-negative bacteria isolated were *Pseudomonas aeruginosa* (31%; n = 38 out of 121), *Enterobacter* spp (10%; n = 12 out of 121), *Moraxella catarrhalis* (6%; n = 7 out of 121), *Serratia marcescens* (3%; n = 4 out of 121), and *Stenotrophomonas maltophilia* (3%; n = 4 out of 121). The most common gram-positive bacteria isolated were *Staphylococcus aureus* (16%; n = 19 out of 121) and *Streptococcus* spp (4%; n = 5 out of 121). Eighteen patients (15%) had polymicrobial growth (Fig 2). None of the patients underwent BAL nor had pleural fluid specimens sent. None of the patients who had blood cultures performed had positive blood cultures.