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EDITORIAL COMMENTARY

Procalcitonin in Childhood Pneumonia

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(See the original article by Stockmann et al, on pages 46-53.)

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Management of community-acquired pneumonia (CAP) in children remains a challenge [1]. Although most cases of CAP in childhood are caused by a virus, most children with CAP receive antimicrobial therapy [2]. This treatment approach stems, in part, from difficulty in distinguishing viral from bacterial causes in routine clinical practice. In contrast to other common pediatric infections, such as urinary tract infection or streptococcal pharyngitis, no single test or group of tests can consistently and accurately identify the etiology of CAP in a timely manner. Furthermore, the presence of a viral infection does not preclude bacterial coinfection [3].

In this issue of the *Journal of the Pediatric Infectious Diseases Society*, Stockmann et al [4] report on their evaluation of the utility of procalcitonin in identifying children with CAP who are at low risk for typical bacterial pathogens such as *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Staphylococcus aureus*. Biomarkers such as C-reactive protein can be helpful in assessing patient response to therapy in proven cases of bacterial CAP but are neither sufficiently sensitive nor sufficiently specific to prove or disprove a bacterial cause. Procalcitonin, a thyroid hormone calcitonin precursor expressed in response to severe bacterial infection, sepsis, and organ dysfunction, provides greater diagnostic accuracy than C-reactive protein in distinguishing pneumonia from asthma or other noninfectious respiratory diagnoses in adults [5, 6]. A procalcitonin-based algorithm was used to guide antibiotic therapy in adults with CAP when antibiotics were discouraged for those with a procalcitonin level of <0.25 ng/mL [7]. This algorithm was associated with less antibiotic exposure and no significant differences in mortality rates or treatment failure compared with those of standard care (ie, clinician decision). In children, studies that used procalcitonin to classify etiology have found conflicting results as a result of heterogeneous methods and various etiologic reference standards (eg, blood culture versus polymerase chain reaction testing [PCR]) [8]. One study that incorporated comprehensive methods for pneumococcal detection (eg, PCR, acute and convalescent pneumococcal serologies) found that a procalcitonin concentration of ≤0.5 ng/mL ruled out pneumococcal CAP in >90% of cases with a negative likelihood ratio of 0.08. Similarly, a procalcitonin concentration of ≥1.5 ng/mL with negative viral testing results had a positive likelihood ratio of 7.39 for ruling in pneumococcus [9].

Stockmann et al [4] used data from children enrolled in Centers for Disease Control and Prevention's Etiology of Pneumonia in the Community (EPIC), a prospective multicenter population-based study of children with radiographically confirmed CAP. Typical bacteria were identified in 10% (54 of 532) of the children; atypical bacteria (15%) and viruses alone (66%) were identified more commonly, and in only 9% of the children were no pathogens identified. Children with typical bacterial pathogens (with or without viruses or atypical bacteria) had a higher median procalcitonin value (6.10 ng/mL; interquartile range, 0.84–22.79 ng/mL) than children in all the other groups. Low procalcitonin values were very accurate in excluding typical bacterial infections. Among 120 children (23% of cohort) with a procalcitonin concentration of <0.1 ng/mL, the authors detected a typical bacterial pathogen in none of them (negative predictive value, 100% [95% confidence interval, 94%–100%]), but the specificity of this cutoff value was only 20%. Procalcitonin values were also consistently higher in children with more severe illness, regardless of cause. However, 20% of children with a procalcitonin concentration of <0.1 ng/mL required admission to an intensive care unit.

The study must be considered in the context of some limitations. Children with empyema that required pleural drainage were classified as having bacterial infection only if a bacterial etiology was identified. It is not clear how many of the 34 children with empyema were classified as having bacterial infection; 25 (73%) of these children had bacteria identified by culture or PCR of pleural fluid, but it is unclear whether the remaining 9 had any positive bacterial testing result. However, at least 75% of them had a

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procalcitonin value of >0.7 ng/mL, which makes it unlikely that many of the children with empyema would have been classified as being at low risk for bacterial infection. In addition, procalcitonin was measured once at the time of admission. Therefore, the peak procalcitonin concentration in the blood, the pattern of decline in response to therapy, and, consequently, the role of sequential measurements in distinguishing those with from those without bacterial infection are not known.

Nevertheless, this study has important implications. First, the high negative predictive value suggests that omitting antibiotics for children with pneumonia and a low procalcitonin value might be a viable strategy for curbing antibiotic use and its associated patient and societal consequences. Second, the low specificity indicates that most children with a higher procalcitonin value also do not have typical bacterial infection, which highlights the need for better tools for discriminating bacterial from viral infection at the point of care. Last, the high rate of intensive care unit admissions among children with a relatively low procalcitonin value suggests limited utility of this biomarker in predicting illness severity.

The quest for suitable and timely diagnostic tests that can accurately distinguish between viral and bacterial etiologies continues. The study by Stockmann et al takes us a step closer to that goal by suggesting that procalcitonin can be used to alter antibiotic management strategies for pediatric CAP, particularly if the patient's procalcitonin concentration is <0.1 ng/mL [4]. It is important also to recognize that no biomarker should completely supplant clinical judgment; rather, biomarkers should be used to augment and focus conclusions derived from clinical examination. Given the conflicting results of previous studies and paucity of definitive data, additional research is needed to clarify and replicate these results and continue to examine the use of procalcitonin and other biomarkers in clinical practice.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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