Procalcitonin Helps Detect Bacterial Infections in Febrile Infants

Procalcitonin May Help Detect Serious Bacterial Infections in Febrile Infants CME

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Complete author affiliations and disclosures, and other CME information, are available at the end of this activity.

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Learning Objectives

Upon completion of this activity, participants will be able to:

1. Describe the test performance of procalcitonin for detecting serious bacterial infections in febrile infants up to 90 days of age without apparent bacterial source.
2. Report the optimal cutoff value of procalcitonin to identify febrile infants up to 90 days of age at low risk for serious bacterial infections.

Authors and Disclosures

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Disclosure: Brande Nicole Martin has disclosed no relevant financial information.

October 6, 2008 — Use of procalcitonin was effective in detecting serious bacterial infections (SBIs) in young febrile infants according to the results of a prospective, observational study reported in the October issue of Pediatrics.

"Procalcitonin has been shown to be an accurate discriminator between viral and bacterial infections for older children and adults," write Vincenzo Maniaci, MD, from Children's Hospital Boston and Harvard Medical School in Boston, Massachusetts, and colleagues, "This is the first prospective study to evaluate the performance of a high-sensitivity procalcitonin assay for febrile infants <3 months of age."

The study goals were to evaluate the test performance of procalcitonin for identifying SBIs in febrile infants not older than 90 days of age without an identifiable bacterial source and to determine the optimal cutoff value to identify infants at low risk for SBIs.
In 234 febrile infants not older than 90 days of age (median age, 51 days) who presented to an urban, pediatric emergency department, an automated high-sensitivity assay was used to measure serum procalcitonin levels. To optimize sensitivity and negative predictive value for the detection of SBIs, the investigators selected an optimal procalcitonin cutoff value. Infants were classified as having definite, possible, or no SBIs.

Of 30 infants (12.8%) with definite SBIs, 4 had bacteremia, 2 had bacteremia with urinary tract infections (UTIs), and 24 had UTIs. Of 12 infants (5.1%) with possible SBIs, 5 had pneumonia and 7 had UTIs.

Compared with mean procalcitonin levels in infants with no SBI (0.38 ± 1.0 ng/mL), mean procalcitonin levels for definite SBIs (2.21 ± 3.9 ng/mL) and definite plus possible SBIs (2.48 ± 4.6 ng/mL) were significantly higher.

For definite SBIs, the area under the receiver operating characteristic curve was 0.82 compared with 0.76 for definite and possible SBIs. A cutoff value of 0.12 ng/mL had a sensitivity of 95.2%, specificity of 25.5%, negative predictive value of 96.1%, and negative likelihood ratio of 0.19 for identifying definite and possible SBIs. This cutoff value accurately identified all cases of bacteremia.

"Procalcitonin has favorable test characteristics for detecting [SBIs] in young febrile infants," the study authors write. "Procalcitonin measurements performed especially well in detecting the most serious occult infections."

Limitations of this study include its small sample size, the small number of patients with SBIs, an inability to analyze subgroups, a lack of data on duration of fever, and a higher rate of definite SBIs compared with previous prevalence studies.

"The performance of procalcitonin as a single clinical marker of infection approaches that of popular strategies that incorporate various laboratory studies and clinical impression scores," the study authors conclude. "However, the future utility of procalcitonin likely depends on its combination with other clinical data; better discrimination of infants with bacterial and viral infections could potentially lead to more focused evaluations of febrile infants."

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**Pediatrics. 2008;122:701-710.**

**Learning Objectives for This Educational Activity**

Upon completion of this activity, participants will be able to:

1. Describe the test performance of procalcitonin for detecting serious bacterial infections in febrile infants up to 90 days of age without apparent bacterial source.

2. Report the optimal cutoff value of procalcitonin to identify febrile infants up to 90 days of age at low risk for serious bacterial infections.

**Clinical Context**

The prediction of SBIs in febrile infants without apparent source by examination remains challenging. In the November 2003 issue of *Pediatrics*, Galetto-Lacour and colleagues reported that a white blood cell count cutoff value of 15,000 cells/µL had a sensitivity of 52% and specificity of 78% in the identification of serious bacterial infection in febrile infants aged 7 days to 36 months. C-reactive protein has higher sensitivity of 78% and specificity of 91% for detecting SBI in febrile infants, according to Pulliam and colleagues in the December 2001 issue of *Pediatrics*.

Procalcitonin is a new biomarker that is being studied as a diagnostic tool to detect infection. In the August 2007 issue of the *Pediatric Infectious Disease Journal*, Andreola and colleagues found that the area under receiver operating characteristic curve was better for procalcitonin (0.82) and C-reactive protein (0.85) than for white blood cell count (0.71) and absolute neutrophil count (0.74).

This prospective, cohort, observational study of febrile infants up to age 90 days without identifiable source assesses the test performance of procalcitonin in the identification of SBI and the optimal cutoff value of procalcitonin that indicates low risk for SBI.

**Study Highlights**

- 435 infants who presented to an emergency department for fever of 38.0°C or higher without identifiable bacterial source were enrolled during an 18-month period.
- Exclusion criteria were immunodeficiency, chronic disease, focal bacterial infection except otitis media, vesicoureteral reflux requiring antibiotics, surgery in the prior 7 days except circumcision, and immunizations or antibiotics in the prior 48 hours.
- Routine evaluation included complete blood count with differential; blood culture; urinalysis and urine culture on catheter specimen; cerebrospinal fluid (CSF) cell count, protein, glucose, Gram stain, and culture; chest radiograph if physical examination indicated pneumonia; and stool leukocyte count and culture if indicated.
- Serum procalcitonin levels were measured with an automated high-sensitivity assay.
- Procalcitonin data were not available for 201 infants because of lack of specimen in 30 infants and hemolysis or insufficient quantity in 171 infants.
- Data were available for 234 infants.
- Median age was 51 days.
- Infants with data vs those without data differed in sex (boys, 53% vs 62%), rates of lumbar puncture (84% vs 75%), and rates of definite plus possible SBI (17.9% vs 12.5%).
- Infants were classified as having definite, possible, or no SBI.
- Definite SBI included bacteremia, defined by pathogen in blood culture; UTI, defined by at least 50,000 colony-forming units (CFUs)
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Per milliliter of single or dominant pathogen or 10,000 to 49,000 CFU/mL with positive urinalysis; bacterial meningitis, defined by pathogen in CSF culture or bacteremia with CSF pleocytosis; bacterial pneumonia, based on pleural fluid culture or chest radiograph with positive blood or sputum culture; and bacterial gastroenteritis, based on stool culture.

- Possible SBI included UTI, defined by 10,000 to 49,000 CFU/mL of single pathogen with negative urinalysis or at least 50,000 CFU/mL of multiple pathogens; bacterial pneumonia, based on abnormal chest radiograph and no positive blood, sputum, or pleural fluid culture.
- 30 of 234 infants (12.8%) had definite SBI: 4 with bacteremia, 2 with bacteremia and UTI, and 24 with UTI.
- 12 (5.1%) of 234 infants had possible SBI: 5 had pneumonia, and 7 had UTI.

Mean procalcitonin level was higher for definite SBI (2.21 ng/mL; SD, 3.89) and definite plus possible SBI (2.48 ng/mL; SD, 4.59) vs no SBI (0.38 ng/mL; SD, 1.04).
- Mean procalcitonin level for 6 bacteremia cases was 2.52 ng/mL (SD, 2.72; range, 0.25 - 7.3 ng/dL).
- Mean procalcitonin level for UTI was 2.20 ng/mL (SD, 4.3).
- Area under the receiver operating characteristic curve was 0.82 for definite SBI and 0.76 for definite plus possible SBI.
- Optimal procalcitonin cutoff level to detect definite plus possible SBI was 0.12 ng/mL (sensitivity, 95.2%; specificity, 25.5%; negative predictive value, 96.1%; and negative likelihood ratio, 0.19).
- Use of 0.12 ng/mL procalcitonin cutoff value would have detected all 6 cases of bacteremia and misclassified 2 cases of UTI as low risk.
- Study limitations included small sample size, low number of SBI cases, lack of information on duration of fever, and loss of study specimens from hemolysis caused by storage.

**Pearls for Practice**

- In febrile infants up to 90 days of age without source of the fever by examination, mean procalcitonin levels are higher in cases of definite SBIs and definite plus possible SBIs vs no SBIs.
- In febrile infants up to 90 days of age without source of the fever by examination, a cutoff procalcitonin level of 0.12 ng/mL has a sensitivity of 95.2%, specificity of 25.5%, negative predictive value of 96.1%, and negative likelihood ratio of 0.19 for the detection of definite plus possible SBIs.

Which of the following is most likely to be associated with procalcitonin levels for infectious gastroenteritis?

- Same level for definite, definite plus possible, and no SBIs
- Higher level for definite SBI than for no SBI
- Higher level for no SBI than for definite SBI
- Higher level for no SBI than for definite plus possible SBI

A 45-day-old infant has a temperature of 38.5°C and normal findings on physical examination. As part of the evaluation for SBI, a procalcitonin level is ordered. Which of the following procalcitonin levels is most likely to be the optimal cutoff value in detecting definite plus possible SBIs?

- 0.12 ng/mL
- 1.2 ng/mL
- 12.0 ng/mL
- 120 ng/mL

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**Target Audience**

This article is intended for primary care clinicians, infectious disease specialists, emergency medicine physicians, and other specialists who provide care to febrile infants up to age 90 days without identifiable source.
Goal
The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

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