Low Risk of Bacteremia in Children With Febrile Seizures

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Objective: To evaluate the risk of bacteremia in children with febrile seizures treated as outpatients.

Methods: A retrospective cohort study was performed involving 379 children aged 2 to 24 months presenting to an urban tertiary care children’s hospital emergency department with a febrile seizure between February 1, 1993, and May 31, 1996.

Results: The mean patient age was 15.9 months, and 217 (57%) were male. In 40 patients (10.6%), the use of oral antibiotics before initial emergency department evaluation was reported. Bacteremia occurred in 8 (2.1%) of 379 children studied. None of the children with bacteremia had received previous antibiotics. The causative organisms were Streptococcus pneumoniae in 7 cases and group A Streptococcus in 1 case. There were 5 contaminated cultures (1.3%). Although 2 of the 8 children with bacteremia ultimately required admission, there were no serious adverse outcomes. Six of 7 episodes of S pneumoniae bacteremia were caused by serotypes included in the pneumococcal conjugate vaccine, which was not available at the time of this study.

Conclusions: Children 2 to 24 months of age with febrile seizures are at similar risk for occult bacteremia as those with fever alone. Widespread use of the pneumococcal conjugate vaccine may further decrease the incidence of bacteremia in this population.

Arch Pediatr Adolesc Med. 2002;156:469-472

FEBRILE SEIZURES are a common pediatric problem, occurring in 2% to 5% of all children.1 The examination of children who present to the emergency department (ED) with a febrile seizure is controversial. Although numerous authors have examined the issue of whether these children should have lumbar punctures, only a few have examined the role of blood cultures in the evaluation of such children.2-6

In 1976, Lewin et al7 noted that bacteremia was present in 4 (6.7%) of 61 children with febrile seizures. These findings led to their recommendation that a complete blood cell count and blood culture be performed on all children presenting with febrile seizures. Lewis et al8 identified a specific viral cause in 46 (63.0%) of 73 children with febrile seizures. However, 2 children (2.7%) in their study had bacteremia associated with significant morbidity: one with Haemophilus influenzae type b meningitis and the other with Escherichia coli endocarditis. In a study by Chamberlain and Gorman,9 5 (4.3%) of 115 children with febrile seizures who were treated in the outpatient setting had bacteremia. Streptococcus pneumoniae was identified in each case. The repeated blood culture was negative in all 5 children, and only 3 had been treated with antibiotics after the original culture had been obtained. In a prospective study of children between 6 months and 5 years of age with febrile seizures, McIntyre et al10 found bacteremia in 12 (4.3%) of 282 children. All 12 children were younger than 2 years, and the organisms isolated were S pneumoniae (7 cases), H influenzae type b (3 cases), Neisseria meningitidis (1 case), and Salmonella enteritidis (1 case). These studies evaluated the incidence of bacteremia in children with febrile seizures in the pre-H influenzae type b vaccine era and included children beyond the age usually identified as being at risk for occult bacteremia.

Since the introduction of the H influenzae type b vaccine, the rates of bacteremia in febrile children have apparently decreased.7-8 In the first study of children with febrile seizures since the introduction of the H influenzae type b vaccine, Teach and Gelil7 studied 206 children younger than 6 years. The incidence of bacteremia was 2.9%. Streptococcus pneumoniae was identified in...
PATIENTS AND METHODS

STUDY DESIGN AND SETTING

This retrospective cohort study included children 2 to 24 months of age with a febrile seizure who had blood cultures drawn in the ED of an urban tertiary care children’s hospital between February 1, 1993, and May 31, 1996. A subset of this cohort was included within a larger study population previously described. During the study period, the ED saw approximately 54,000 children annually.

Standard practice during the study period was to obtain blood cultures on children 2 to 24 months of age with temperatures of 39.0°C or more but did not include routine complete blood cell counts. The decision to obtain blood cultures on children with febrile seizures who did not meet the previous criteria was made by the examining physician on the basis of clinical examination. Lumbar puncture was performed on the basis of clinical assessment by the examining physician and was not part of a standard protocol for children with febrile seizures within this age range.

Blood cultures were obtained by ED nurses using sterile techniques and inoculated into pediatric blood culture bottles (Pedi-BacT; Organon Teknika Corp, Durham, NC). A single bottle containing supplemented brain-heart infusion broth with 0.02% sodium polyanethol sulfonate was inoculated for each blood culture ordered. Standard procedure in the ED was to inoculate 0.5 to 1.0 mL. Through a pneumatic tube delivery system, blood cultures were routinely received in the laboratory within an hour of when they were taken and were immediately loaded into the blood culture instrument. The microbiology laboratory used a microbial detection system (BacT/Alert; Organon Teknika Corp) to process all blood cultures. The system monitored carbon dioxide production within each bottle every 10 minutes, 24 hours per day. Bottles identified as positive were immediately removed from the instrument, 24 hours per day, and an aliquot was taken for gram stain and subculture. The ED was notified immediately of the positive culture and given information from the gram stain. Bacterial isolates were identified by conventional procedures. Only information from the gram stain, however, was available at the time of initial report of positive culture to the ED. Routine protocol included contacting families of all children with positive blood cultures for reevaluation.

PARTICIPANTS

Patients were included if they were diagnosed as having a simple or complex febrile seizure, had a blood culture obtained during the initial ED evaluation, and were discharged to home after evaluation. Patients were excluded if during initial ED evaluation they (1) were diagnosed as having a central nervous system disorder that predisposed them to seizures (eg, meningitis, static encephalopathy, seizure disorder); (2) were known to have an underlying condition that predisposed them to bacteremia (eg, sickle cell anemia, oncologic disease, immunodeficiency, indwelling central catheter); (3) underwent lumbar puncture; (4) had an illness requiring hospitalization; or (5) died during initial ED evaluation.

MEASURED OUTCOMES AND PROTOCOL

Bacteremia was defined as a blood culture obtained from a patient at initial ED presentation that was positive for pathogenic bacteria. Bacteria that were considered pathogenic included the following: S pneumoniae, Staphylococcus aureus, group A Streptococcus, Enterococcus species, N meningitidis, Enterobacteriaceae, Salmonella species, Moraxella catarrhalis, Pseudomonas species, H influenzae, Campylobacter species, and Escherichia coli. Bacteria that were considered contaminants included coagulase-negative Staphylococcus species, alpha-hemolytic Streptococcus, Micrococcus species, Clostridium species, Corynebacterium species, and Neisseria species other than N meningitidis or Neisseria gonorrhoeae. Time to positive culture was measured in hours and tenths of hours. Serious adverse outcome was defined as meningitis or death within 2 weeks of the date that the blood culture was obtained.

All children with blood cultures obtained during the study months were identified by means of microbiology laboratory data from the microbial detection system. These data indicated the patient’s name, medical record number, and final result of blood culture. Additional information collected included age of the patient, date of blood culture collection, disposition (admission or discharge), and time in hours to positive culture and identification of bacteria. The medical records of patients were abstracted for medical history, previous antibiotic use, ED discharge diagnoses, maximum fever documented in the ED, and antibiotic treatment or prescription. Charts of patients with blood cultures positive for pathogenic or contaminant bacteria were abstracted for additional data, including follow-up visit site, date, and time; diagnosis and disposition at follow-up visit; maximum temperature documented at follow-up visit; results of repeated blood culture, complete blood cell count, chest x-ray, spinal fluid assessment, urinalysis, and urine culture; and antibiotic treatment or prescription.

STATISTICAL METHODS

Continuous variables were described with means, SDs, and 95% confidence intervals (CIs). Discrete variables were described with counts and percentages, with binomial exact 95% CIs. Continuous variables were analyzed with the Wilcoxon 2-sample test. Categorical variables were analyzed with the chi-square test or Fisher exact test. Relative risks with exact 95% CIs were calculated. Statistical significance was determined a priori as P < .05.

RESULTS

Blood cultures were obtained in 379 children with febrile seizures examined and discharged from the ED. The
mean age was 15.9±4.7 months (median, 16.0 months; range, 2-24 months). Most patients were older than 12 months (76.0%), and only 8 (2.1%) were younger than 6 months. The majority of patients were male (57.3%). The mean temperature was 39.9±0.8°C, and 38 (10.0%) of 379 children had a maximum temperature of less than 39.0°C recorded in the ED. Forty patients (10.6%) reported the use of oral antibiotics before initial ED evaluation. Seventy-three percent of the patients were given an associated discharge diagnosis from the ED. The most common associated discharge diagnoses from the initial ED visit included acute otitis media (64.1%), viral syndrome or upper respiratory tract infection (23.2%), and pneumonia (6.2%) (Table 1).

The prevalence of bacteremia was 2.1% (95% CI, 0.9%-4.1%). *Streptococcus pneumoniae* was the pathogen in 7 cases and group A *Streptococcus* in 1 case. Six (85.7%) of 7 cases of *S pneumoniae* bacteremia were caused by serotypes currently included in the pneumococcal conjugate vaccine, which was not available at the time of the study. The rate of contamination was 1.3% (95% CI, 0.4%-3.0%). Chest radiographs were obtained more frequently in patients who were later identified to have bacteremia (62.5%) than in those with negative or contaminated cultures (28.3%), but this difference did not reach statistical significance (relative risk, 0.97; 95% CI, 0.92-1.01). No patient with bacteremia was diagnosed as having pneumonia. There were no statistically significant differences in age, sex, temperature, or receipt of oral antibiotics before ED visit between patients who were later identified to have bacteremia and those who had negative or contaminated cultures (Table 2). A complete blood cell count was obtained in 36.1% of patients. There was no statistically significant difference in white blood cell count between patients who were later identified to have bacteremia (14.3×10³±5.9×10³/µL) and those with negative or contaminated cultures (18.6×10³±8.9×10³/µL; *P*=.32). Although cultures with pathogenic bacteria became positive in less time (13.4±1.3 hours) than contaminated cultures (16.5±5.4 hours), this difference did not reach statistical significance (*P*=.27).

All 8 patients with pathogenic bacteria isolated from blood cultures had documented follow-up in the ED (Table 3). Six of these patients were afebrile and were discharged after reevaluation. Five of the 6 patients underwent second blood cultures, all of which were negative. No other studies were performed in those patients. Patients 1 and 4 were still febrile and were hospitalized after reevaluation. The white blood cell counts at the time of reevaluation were 13.0×10³/µL and 30.5×10³/µL, respectively. Blood cultures were repeated in both patients and were negative. Patient 4 also underwent lumbar puncture when reexamined, and the results were unremarkable. None of the patients were diagnosed as having meningitis or had other serious adverse outcome.

Occult bacteremia is defined as the presence of pathogenic bacteria in the blood of a well-appearing febrile child without an identifiable focus of infection. Previous studies have identified age 2 to 24 months as a risk factor for occult bacteremia.7,8 In the post-*H influenzae* type b era, the prevalence of occult bacteremia in this age group is 1.6% to 2.6%.7,9 The risk of bacteremia in children presenting with febrile seizures has been less well defined. McIntyre et al10 noted bacteremia in 4.3% of children with febrile seizures; however, the majority of those patients were hospitalized. Outpatient studies of children with febrile seizures report rates of bacteremia ranging from 2.7% to 6.7%, but these studies include children up to 7 years of age, a population at low risk of bacteremia.5,6,11,12 The prevalence of bacteremia in this study, while lower than that reported in other studies of children with febrile seizures, is similar to recent reports of the prevalence of occult bacteremia by Alpern et al7 (1.9%; 95% CI, 1.5%-2.3%) and Lee and Harper9 (1.6%; 95% CI, 1.3%-1.8%).

There was no difference in the frequency with which chest radiographs were obtained; however, 17 patients with negative or contaminated cultures and no patients with bacteremia were diagnosed as having pneumonia. Variables found to be associated with occult bacteremia in other studies, such as temperature and white blood cell count,5,6,9 were not significantly different between patients with and without bacteremia in this study. The low rate of bacteremia and, thus, small sample size may underestimate potential differences between these 2 groups.
Approximately 10% of children in this study received antibiotics before ED evaluation. If children who received antibiotics before evaluation are at lower risk of bacteremia, the overall risk of bacteremia may have been underestimated. In addition, the American Academy of Pediatrics practice parameter urges clinicians to “strongly consider” a lumbar puncture in the child younger than 12 months who presents with febrile seizures. Since children undergoing lumbar puncture were excluded from this study, these younger children may be underrepresented in our population. However, the population presented in this study most accurately represents children who a practitioner may most worry are at risk for occult bacteremia and, therefore, consider examining with a blood culture alone.

Since our study was a retrospective evaluation of a cohort of patients with febrile seizures evaluated by blood culture, we might expect that physicians would have obtained blood cultures on those children they considered to be at highest risk for bacteremia. This may have led to a prevalence rate that overestimated that of all-comers but closely estimates that in clinical practice.

The detection of bacteremia and prevention of serious complications are important goals in the examination of febrile young children. The data in this study indicate that children 2 to 24 months of age with febrile seizures and without clinical indication for lumbar puncture are at similar risk of occult bacteremia as those with fever alone. Since most cases of bacteremia in this study were due to \textit{S pneumoniae}, widespread use of the pneumococcal conjugate vaccine may decrease the incidence of occult bacteremia in this population even further.

Accepted for publication January 11, 2002.

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Table 3. Characteristics of Patients With Febrile Seizures and Bacteremia*

<table>
<thead>
<tr>
<th>Patient/Sex/Age, mo</th>
<th>Additional Diagnoses</th>
<th>Antibiotic Treatment†</th>
<th>Organism</th>
<th>Serotype</th>
<th>Time to Growth, h</th>
<th>Admitted‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/24</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{Group A Streptococcus}</td>
<td></td>
<td>14.2</td>
<td>Yes</td>
</tr>
<tr>
<td>2/F/19</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{Streptococcus pneumoniae}</td>
<td>14</td>
<td>14.0</td>
<td>No</td>
</tr>
<tr>
<td>3/M/11</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{S pneumoniae}</td>
<td>23F</td>
<td>14.5</td>
<td>No</td>
</tr>
<tr>
<td>4/M/22</td>
<td>Viral syndrome</td>
<td>No</td>
<td>\textbf{S pneumoniae}</td>
<td>4</td>
<td>13.8</td>
<td>Yes</td>
</tr>
<tr>
<td>5/M/18</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{S pneumoniae}</td>
<td>6A</td>
<td>11.2</td>
<td>No</td>
</tr>
<tr>
<td>6/F/12</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{S pneumoniae}</td>
<td>14</td>
<td>11.7</td>
<td>No</td>
</tr>
<tr>
<td>7/M/17</td>
<td>Otitis media</td>
<td>Yes</td>
<td>\textbf{S pneumoniae}</td>
<td>19F</td>
<td>14.5</td>
<td>No</td>
</tr>
<tr>
<td>8/M/17</td>
<td>Sinusitis</td>
<td>Yes</td>
<td>\textbf{S pneumoniae}</td>
<td>6B</td>
<td>13.5</td>
<td>No</td>
</tr>
</tbody>
</table>

*No patients received pretreatment with antibiotics.
†Indicates whether oral antibiotic therapy was prescribed after initial blood culture was obtained.
‡Indicates whether patient was admitted to the hospital after reevaluation.

In the post-\textit{H influenzae} type \textit{b} era, the prevalence of occult bacteremia in febrile children aged 2 to 24 months is 1.6% to 2.6%. The risk of bacteremia in children presenting with febrile seizures is less well defined. The data in this study suggest that well-appearing children 2 to 24 months of age with febrile seizures are at similar risk for occult bacteremia as those with fever alone. Furthermore, the majority of cases of bacteremia in this study were due to \textit{S pneumoniae}, and there were no serious adverse outcomes. The widespread use of the pneumococcal conjugate vaccine may decrease the rate of bacteremia even further.

REFERENCES