The influence of the severity of community-acquired pneumonia on the usefulness of blood cultures

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The value of blood cultures in community-acquired pneumonia (CAP) has been questioned. At issue is the potential for blood cultures to change management. We prospectively studied the yield and impact of blood cultures in patients admitted with CAP. Two hundred and nine subjects had at least two blood cultures prior to receiving antibiotics. The severity of CAP was graded using the Pneumonia Severity Index (PSI). Twenty-nine patients (13% to 9%) had a pathogen identified by blood culture. The yield of blood cultures increased with PSI grade (I—5% to 3%, II—10% to 2%, III—10% to 3%, IV—16% to 1%, V—26% to 7%), as did the likelihood of blood cultures changing antibiotic therapy (I to III 0%, IV—9% to 7%, V—20% to 0%). One hundred and seventy-nine (85% to 6%) patients received a quinolone, limiting the impact of pathogens resistant to β-lactams. Four of 16 patients (25% to 0%) with a culture (blood or sputum)-guided change in antibiotic therapy died, compared to five of 31 patients (16% to 1%) who had an empiric change. Blood cultures are of minimal value in mild to moderate CAP, and should be limited to patients with PSI grade IV or V CAP unless a specific risk factor for pathogens resistant to the empiric therapy is present.

Key words: community-acquired pneumonia; blood cultures.

Introduction

Blood cultures have a long established role as part of the investigation of a patient admitted for treatment of community-acquired pneumonia (CAP). Although recently their usefulness has been questioned (1–4), most physicians continue to order blood cultures on all patients with CAP severe enough to require hospitalization. This is largely due to the possibility of a positive culture having a significant impact on patient care.

In most major epidemiological studies of CAP, the yield of blood cultures has ranged been between 4% and 18% (5). Bacteremia is an independent predictor of adverse outcome (6), it is not surprising that the yield of blood cultures is highest in epidemiological studies of severe community-acquired pneumonia (7–9).

The current cost conscious healthcare climate has forced physicians to re-evaluate the cost benefit of many investigations. Identifying subgroups of patients in whom a diagnostic test will have a high yield and a high likelihood of altering management is one method of improving the cost–benefit equation, provided that there is no detrimental effect on the outcome of patients in whom the test is withheld.

The Pneumonia Severity Index (PSI) developed by Fine et al. (10) is one method of classifying patients with CAP into low risk or high risk categories based on demographic, clinical, laboratory and radiological features at admission. Since the mortality rate of PSI grades I–III is significantly less than 1% (10), we hypothesized that blood cultures would only have a significant impact on patient management in patients in PSI grades IV and V. We tested this hypothesis in an ongoing prospective cohort study of CAP in a large private hospital system.

Methods

Subjects

Subjects were recruited into a prospective cohort study of CAP at Methodist Healthcare between October 1998 and June 2000. To be included in the study patients had to be 18 years or older, have symptoms and signs consistent with a lower respiratory tract infection and have a new radiological infiltrate consistent with pneumonia as determined by a radiologist or pulmonary/critical care physician. For the purpose of this analysis, patients were only included if...
they had at least two blood cultures taken prior to receiving antibiotics, including oral antibiotics. Subjects were excluded if they were non-ambulatory nursing home patients, had received chemotherapy in the past 30 days, had been hospitalized within the past 30 days, had AIDS as defined by the Center for Diseases Control criteria (11) or were receiving immunosuppressant therapy for any reason (including corticosteroids ≥20 mg day⁻¹ of prednisone).

This study was approved by the Institutional Review Board of Methodist Healthcare, Memphis, U.S.A.

DATA COLLECTION

Demographic data, the initial antibiotic treatment, culture results, subsequent modification of treatment, complications and outcome were recorded. Clinical data sufficient to calculate both the Acute Physiological and Chronic Health Evaluation (APACHE) II score (12) and the PSI score (10) were also obtained.

A change in management was defined as any change in the dose of antibiotic, or the addition or discontinuation of one or more antibiotics. The reason for any management change was obtained from the documentation in the patient chart with clarification as necessary from the treating physician.

STATISTICAL ANALYSIS

Statistical calculations were performed using the InStat Statistical Software Package Version 3.01 (GraphPad Software Inc., U.S.A.). Variables are expressed as mean ± standard deviation unless otherwise stated. Differences in continuous variables were compared using a two-tailed Student’s t-test after ensuring normal distribution. Differences in categorical variables were calculated using Fisher’s Exact Probability Test. A P < 0.05 was considered significant.

Results

Two hundred and nine subjects met the criteria for review during the study period. There were 109 female (52.2%) and 100 male (47.8%) subjects with a mean age of 59.3 years (range 18–98). Twenty-two subjects died (10.5%).

Thirty-eight subjects (18.2%) had at least one positive blood culture. The organism cultured in nine subjects was considered to be a contaminant (Staphylococcus epidermidis — six, Diptheroids—three). Twenty-nine patients (13.9%) had a total of 31 pathogens identified from blood cultures (Streptococcus pneumoniae—20, S. viridans—three, Haemophilus influenzae—one, Staphylococcus aureus—one, Enterobacter agglomerans—one, Eschericia coli—one, Streptococcus group B—one, Streptococcus group D—one, Streptococcus group G—one, Acinetobacter lwoffi—one). In five patients, the same organism was isolated from sputum (all S. pneumoniae), and in one patient with pneumococcal bacteremia, H. influenzae was also isolated from sputum. Of the 20 S. pneumoniae isolated, seven had penicillin minimal inhibitory concentrations (MICs) between 0.0625 μg ml⁻¹ and 1.0 μg ml⁻¹ and three had MICs for penicillin ≥2 μg ml⁻¹; seven had MICs for cefotaxime between 0.5 μg ml⁻¹ and 2.0 μg ml⁻¹ and one isolate had an MIC for cefotaxime of 4 μg ml⁻¹; 11 isolates were resistant to erythromycin and all isolates were fully sensitive to levofloxacin and vancomycin.

Table 1 summarizes both the yield of blood cultures and their impact on management by the severity of pneumonia as classified by the PSI. The trend towards an increasing yield of pathogens from blood cultures with increasing PSI grade was statistically significant (P=0.02).

Twelve of the 29 (41%) patients had a management change based on the blood culture results. In seven (PSI grade V—five, PSI grade IV—two) antibiotic therapy was intensified (add vancomycin—five, add ampicillin/sulbactam—one, add both vancomycin and ampicillin/sulbactam—one), four of whom subsequently died. In only one patient, who subsequently died, was a change in therapy chosen (group D Streptococcus resistant to levofloxacin). In

<table>
<thead>
<tr>
<th>Pneumonia Severity Index Grade</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>19</td>
<td>59</td>
<td>39</td>
<td>62</td>
<td>30</td>
<td>209</td>
</tr>
<tr>
<td>Subjects with at least one positive culture</td>
<td>2 (10.5%)</td>
<td>7 (11.9%)</td>
<td>4 (10.3%)</td>
<td>14 (22.6%)</td>
<td>11 (36.7%)</td>
<td>38 (18.2%)</td>
</tr>
<tr>
<td>False positive cultures</td>
<td>1 (5.3%)</td>
<td>1 (1.7%)</td>
<td>0 (0%)</td>
<td>4 (6.5%)</td>
<td>3 (10.0%)</td>
<td>9 (4.3%)</td>
</tr>
<tr>
<td>Subjects with pathogen identified by culture</td>
<td>1 (5.3%)</td>
<td>6 (10.2%)</td>
<td>4 (10.3%)</td>
<td>10 (16.1%)</td>
<td>8 (26.7%)</td>
<td>29 (13.9%)</td>
</tr>
<tr>
<td>Subjects where culture changed management</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>6 (9.7%)</td>
<td>6 (20.0%)</td>
<td>12 (5.7%)</td>
</tr>
</tbody>
</table>
In a prospective study of patients with CAP, we have shown that the yield of blood cultures increases significantly with the severity of pneumonia, and that positive cultures only impacted on the management of patients with PSI grade IV and V pneumonia. The very clear correlation between the severity of pneumonia, as measured with PSI grade IV and V pneumonia, confirmed our hypotheses. This suggests that blood cultures do not need to be performed routinely on all cases of CAP and can safely be limited to specific patient subgroups.

Our overall mortality of 10.5% is consistent with other recent studies of patients hospitalized with CAP (13–16). The positive yield of 13.9% for blood cultures in our study is close to the most favorable sensitivities reported (5). This high yield is probably explained by our exclusion of patients who did not have blood cultures taken prior to the commencement of antibiotic therapy, since prior antibiotic therapy substantially reduces the likelihood of a positive culture (17,18).

The finding that pathogens identified by blood culture were resistant to the empiric antibiotic regimen chosen in only one case was surprising. The main reason appears to be the choice of a quinolone as part of the initial empiric therapy regimen in 85.6%, which negated the problem of penicillin and cephalosporin resistant pneumococci. That physicians chose to increase antibiotic therapy in some cases despite culture results indicating the current antibiotic choices to be appropriate was also interesting. As the subsequent mortality rate in these patients demonstrates (57%), these patients were clearly critically ill and not responding to therapy.

Based on our data, we would recommend that blood cultures not be ordered routinely on patients with PSI grade I to III CAP. Some patients, particularly those with chronic suppurative lung disease (9,19), are at greater risk of having drug resistant or unusual pathogens. Although most of these patients will fall into PSI grades IV or V if they develop pneumonia, continuing to order blood cultures in patients with mild to moderate CAP when a specific risk factor for drug resistant or unusual pathogens is probably justified.

The argument in favor of performing blood cultures is both clinical and epidemiological. From a clinical perspective, proponents argue that a positive blood culture may reveal a pathogen not being covered by the antibiotic regimen, or that the antibiotic sensitivity of the organism identified will allow the physician to narrow the spectrum of antibiotic therapy. Two studies have shown that initial inappropriate antimicrobial treatment is an independent

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**Table 2. Initial empiric antibiotic therapy**

<table>
<thead>
<tr>
<th>Antibiotic regimen</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinolone*</td>
<td>126 (60.3%)</td>
</tr>
<tr>
<td>Quinolone* + cephalosporin†</td>
<td>16 (7.7%)</td>
</tr>
<tr>
<td>Quinolone* + other</td>
<td>16 (7.7%)</td>
</tr>
<tr>
<td>Cephalosporin† + macrolide‡</td>
<td>12 (5.7%)</td>
</tr>
<tr>
<td>Quinolone* + macrolide‡</td>
<td>10 (4.8%)</td>
</tr>
<tr>
<td>Other β-lactum#</td>
<td>6 (2.9%)</td>
</tr>
<tr>
<td>Quinolone* + cephalosporin† + other</td>
<td>6 (2.9%)</td>
</tr>
<tr>
<td>Quinolone* + cephalosporin† + macrolide‡</td>
<td>5 (2.4%)</td>
</tr>
<tr>
<td>Cephalosporin†</td>
<td>5 (2.4%)</td>
</tr>
<tr>
<td>Macrolide‡</td>
<td>4 (1.9%)</td>
</tr>
<tr>
<td>Other β-lactum# + other</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>209</td>
</tr>
</tbody>
</table>

* Levofloxacin or trovafloxacin;
† cefotaxime or ceftriaxone;
‡ erythromycin, clarithromycin or azithromycin;
# ampicillin, ticarcillin or piperacillin.

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**Table 3. Change in antibiotic therapy and subsequent mortality**

<table>
<thead>
<tr>
<th>Blood culture status</th>
<th>Survived</th>
<th>Deceased</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in antibiotics</td>
<td>8 (66.7%)</td>
<td>4 (33.3%)</td>
<td>12</td>
</tr>
<tr>
<td>No change in antibiotics</td>
<td>13 (76.5%)</td>
<td>4 (24.5%)</td>
<td>17</td>
</tr>
<tr>
<td>Change in antibiotics</td>
<td>31 (86.1%)</td>
<td>5 (13.9%)</td>
<td>36</td>
</tr>
<tr>
<td>No change in antibiotics</td>
<td>135 (93.8%)</td>
<td>9 (6.2%)</td>
<td>144</td>
</tr>
</tbody>
</table>
adverse risk factor in patients with CAP, with the risk of death increased between five (20) and 20-fold (19). However, in patients with CAP failing to respond to initial antibiotic therapy, Sanyal et al. (16) found no difference in mortality between patients in whom antibiotics were changed empirically and in those who had a change in therapy guided by a positive microbiological study. Our findings are similar, with a mortality of 16-1% (5/31) in patients with a blind change in antibiotic therapy compared to 25-0% (4/16) in patients with a microbiologically (blood and sputum)-guided change in therapy. Although this appears counter intuitive, Austrian and Gold's original work in pneumococcal pneumonia found that antibiotics have no demonstrable impact on outcome in the first 3 days after commencing therapy (21). Any change in antibiotic therapy based on culture results is also unlikely to have any impact on outcome for several days. Allowing sufficient time for a change in therapy to have an influence on outcome, the identification of a pathogen not covered by the initial empiric antibiotic regimen will not have a beneficial effect on outcome for 5–6 days after admission. By this time, the ultimate outcome of most patients has already been determined.

Narrowing antibiotic therapy may certainly be beneficial, both as a cost-saving measure and by potentially reducing the likelihood of antibiotic resistance. However, we have previously shown that physicians are reluctant to use narrow antibiotic therapy even when culture results indicate this is appropriate (4). As the length of hospital stay is proportional to the severity of pneumonia, the decision to discharge a patient with mild CAP is also frequently made before antibiotic sensitivity results are known. This further reduces the impact of blood cultures in these patients.

Accurate local epidemiological data on the microbiological etiology of CAP is critical to physicians in making decisions about initial empiric antibiotic therapy. However, taken in isolation, blood cultures are likely to give a skewed view of the etiology of pneumonia. Mycoplasma pneumoniae and Chlamydia pneumoniae are not detected by blood culture and the vast majority of Legionella infections also remain undetected (22). As invasive pneumococcal isolates are also less likely to be antibiotic resistant than non-invasive isolates (23), antibiotic resistance data based only on blood cultures will also be biased. So although providing critical epidemiological information, the results of blood cultures can only be evaluated in the context of a comprehensive microbiologic study (including sputum culture, urinary antigen testing and serological studies).

In summary, in the clinical setting of mild to moderate community-acquired pneumonia, blood cultures had a low yield and no impact on management. While the yield of blood cultures is higher in patients with more severe pneumonia, there was no evidence that a change in antibiotic therapy based on a positive blood culture result led to an improved outcome. We recommend that blood cultures be used routinely only for patients with severe community-acquired pneumonia (PSI grades IV and V) or in patients with specific risk factors that predispose to pathogens not typically covered by standard empiric therapy regimes. While useful epidemiologically, blood cultures results alone are misleading unless interpreted in the context of a comprehensive microbiological survey of etiology.

References


