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CLINICAL STUDY

Do we really need blood cultures in treating patients with community-acquired pneumonia?

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Abstract: *Objectives:* Positive blood cultures (BC) are considered a gold standard specific test for diagnosing and managing patients with community-acquired pneumonia (CAP). The aims of this study were to determine the positivity rate of BCs performed in patients with CAP, empirically started antibiotic regimens and conformity of the empirically started antibiotics with the results of BCs.
Methods: Patients with the diagnosis of CAP with started empiric antibiotic treatment and performed BC test were included in the study. The BC set consisting of aerobic/anaerobic bottles was obtained from a single draw. Co-morbidities of patients, empirically started antibiotics and BC results were noted. Empiric antibiotics were checked as to whether they conform to BC results.
Results: The study included 262 patients with CAP. Majority of BC sets (195) revealed no bacterial growth. Of the total 262 sets of BCs, 67 (25.6 %) sets displayed growth of organism and only 30 sets (11.5 %) represented significant isolates. Commonly isolated microorganisms were Escherichia coli, Streptococcus species and Staphylococcus species. Ampicillin/Sulbactam and Fluoroquinolone combination was the leading antibiotic regimen chosen for the treatment (54.2 %). The majority of patients had at least one co-morbidity. Ninety-six patients (37 %) had a pulmonary disease, 74 (29 %) had a malignancy, 74 (29 %) had heart failure and 67 (26 %) suffered from diabetes.
Conclusion: Significantly positive results are rare (11.5 %) and majority of blood cultures revealed negative results. BC tests may not be performed in all patients with CAP *(Tab. 3, Ref. 11)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: community-acquired pneumonia, blood culture, empiric antibiotic.

Community-acquired pneumonia (CAP) continues to be a serious health problem worldwide. Its incidence ranges from 3 to 5 cases per 1000 inhabitants among adults, and the mortality in hospitalized patients is in range of 5–15 %. CAP is the number one cause of death from infectious diseases (1). Most patients hospitalized for CAP respond satisfactorily to treatment but approximately 10–15 % of patients develop treatment failure and almost 6% may manifest a rapidly progressing and life-threatening pneumonia. It has been shown that death from CAP occurs primarily in patients with therapeutic failure, i.e. in 40 % of this population (1, 2).

Positive blood cultures are considered a gold standard specific test for diagnosing and managing patients with bacterial infections. However, with the exception of a few infectious foci such as endocarditis or meningitis, their low sensitivity usually limits their diagnostic utility. Several hospital-based studies have indicated that blood cultures are typically positive in less than 10 % of bacterial pneumonias, soft tissue infections, and urinary tract infections, and as a result, their performance may not be cost-effective (3). Blood cultures are recommended as part of the diagnostic workup for patients with CAP who are admitted to hospital for treatment and their positivity rate fluctuates around 11 % (2, 4). Nevertheless, there is some uncertainty about the role of blood cultures in patients who are seen in emergency rooms (ER) with pneumonia and are well enough to be sent home. The published American Thoracic Society Guidelines for the management of adults with community-acquired pneumonia do not mention blood cultures as part of the recommended testing for patients with CAP managed out of hospital (5).

One study identified that the yield of blood cultures obtained at emergency department was lower in those selected for outpatient care as compared to hospital care (6). However, such a distinction may not be relevant today due to healthcare restructuring performed over the past decade which has seen a shift toward care of sicker patients in the community (3).

The aims of this study were to determine the positivity rate of blood cultures performed in patients with community-acquired pneumonia, empirically started antibiotic regimens and conformity of the empirically started antibiotics with the results of blood cultures.

Methods

Study Design

This was a prospective study of patients with confirmed pneumonia admitted between June 1, 2007 and May 31, 2008. The

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study was conducted at the Marmara University Hospital, Department of Emergency Medicine, Istanbul, Turkey. Our ED sees a volume of 36,000 patients per year. The study was approved by the local Medical Ethics Committee, and informed consent was obtained from each patient.

Study Setting and Population

Community-acquired pneumonia was defined as a new infiltrate on chest X-ray (for which there is no other explanation) plus at least two of the following symptoms or signs: cough, sputum production, temperature >38 °C or <35 °C, auscultatory findings consistent with pneumonia, labored breathing (including altered breath sounds and rales), pleuritic chest pain, leucocytosis or leucopenia (>10.000 U/l, <4.000 U/l or >10 % rods in leukocyte differentiation).

Exclusion criteria were as follows: patients younger than 18 years, pregnancy, hospital-acquired pneumonia (development of symptoms 48 hours following the admission or discharge from an acute care facility, two weeks prior to admission), immunosuppression [systemic steroid use at admission (prednisone equivalent >20 mg/daily for more than 3 days)]; and pulmonary embolism.

Study Protocol

A blood culture set consisting of aerobic/anaerobic bottles was obtained from a single draw. Inoculated bottles were immediately placed in the instrument and incubated at 37 °C. A significant isolate was defined as the growth of a pathogenic organism from at least one set of blood cultures. At least two positive sets of blood cultures within a 48-hour period were required to classify the common contaminants as significant. Significant isolates were identified and tested for antimicrobial susceptibility according to the guidelines of National Committee for Clinical Laboratory Standards. Co-morbidities and other relevant patient characteristics were identified to address factors related with the etiology of CAP. The definitions of co-morbidities were based on the presence of conditions for which the patient was under active medical supervision or was receiving treatment at the time of hospital admission. The evaluated co-morbidities included pulmonary diseases (chronic obstructive pulmonary disease or treated asthma), congestive heart failure, diabetes (both, type I and type II) and malignancy.

Data Analysis

Analyses were performed with SPSS version 11.0 (SPSS Inc., Chicago, IL); Pearson chi-squared test was performed to compare the parameters. The data are given within 95 % confidence intervals (CI). In the analysis, $p<0.05$ is considered statistically significant.

Results

The study included 262 patients with pneumonia (116 females and 146 males). The mean age was 63.1±15.4 for female patients, and 64.6±14.9 for male patients. There was no statistically significant difference between genders (p=0.45). Characteristics of the patients are shown in Table 1.

Tab. 1. Demographics and co-morbidities of 262 patients with community-acquired pneumonia.

Characteristic	n	%
Age (Years)		
65<	164	62.6
65>	98	37.4
Gender		
Female	116	44.3
Male	146	55.7
Co-morbidities		
Pulmonary disease	96	37
Heart failure	74	29
Diabetes	67	26
Malignancy	74	29
Pulmonary	23	
Lymphoma	12	
Multiple myeloma	10	
Leukemia	8	
Prostate	5	
Colon	4	
Breast	4	
Meningioma	2	
Larynx	2	
Renal	2	
Gastric	1	
Eusophagus	1	

Note: Total percentage for the number of co-morbidities exceeds 100% because most of the patients had more than one disease at the same time.

Tab. 2. The rate and etiology of positive blood cultures.

Microorganism	n	%
Escherichia coli	6	20
Streptococcus pneumoniae	5	16.6
Methicillin sensitive staphylococcus aureus	5	16.6
Klebsiella pneumonia	3	10
Alpha hemolytic Streptococcus	2	6.6
Pseudomonas aeroginosa	2	6.6
Methicillin resistant staphylococcus aureus	2	6.6
Haemophilus influenzae	2	6.6
Staphylococcus hemolitycus	1	3.3
Staphylococcus warneri	1	3.3
Salmonella enteritidis	1	3.3
Total	30	100.0

During the study period, 262 sets of blood cultures (BC) were drawn from all patients. Majority of BCs, namely 195 BC sets yielded no bacterial growth. Of the total 262 sets of BCs, 67 (25.6 %) displayed growth of organisms and only 30 (11.5 %) of these were deemed to represent significant isolates. The grown microorganisms were Escherichia coli, Streptococcus species, Staphylococcus species, Klebsiella pneumoniae, Pseudomonas auroginosa, Haemophilus influenzae and Salmonella enteritidis. The microorganisms were isolated from four aerobic BC bottles,

Tab. 3. Empirically started antibiotic regimens.

Empirically started antibiotics	n	%
Ampicillin/Sulbactam + Fluoroquinolone	142	54.2
Fluoroquinolone	75	28.6
Piperacillin/sulbactam + Fluoroquinolone	32	12.2
Cephalosporin + Macrolide	7	2.7
Macrolide	5	1.9
Cephalosporin	1	0.4
Total	262	100

8 anaerobic BC bottles and 18 combined aerobic and anaerobic sets. The rate and etiology of positive BCs are shown in Table 2. The remaining 37 sets of BC results were interpreted as "contamination".

All 262 patients had been started on empiric antibiotic regimens. Ampicillin/Sulbactam and Fluoroquinolone combination was the leading antibiotic regimen chosen for treatment (54.2 %); it was followed by Fluoroquinolone (28.6 %), Piperacillin/sulbactam and Fluoroquinolone combination (12.2 %); Cephalosporin and Macrolide combination (2.7 %); Macrolide (1.9 %) and Cephalosporin (0.4 %). Empirically started antibiotic regimens are shown in Table 3.

The majority of patients had at least one co-morbidity. Ninety-six patients (37 %) had pulmonary disease, 74 (29 %) had malignancy, 74 (29 %) had heart failure and 67 (26 %) had diabetes (Tab. 1). Malignancy in male patients was significantly higher than in female patients ($p=0.019$). The microorganisms isolated in BCs did not differ between patients with or without malignancy or genders ($p>0.05$).

Discussion

This study of BCs in patients with CAP shows that BC results have low sensitivity and limit their diagnostic utility. Although our positivity rate is 11.5 %, it is similar to those in formerly published articles (7, 8). Routine microbiological tests are not recommended by most guidelines for patients managed in the community (8).

Investigations recommended for patients requiring admission include: blood cultures, sputum gram stain and culture, and thoracentesis should pleural fluid be present. About 11 % of patients with CAP will have positive blood cultures more commonly associated with severe illness (8). Although the usefulness of blood cultures for all patients admitted to hospital is questioned, investigators in one study (9) note that the survival rates improve should the results of blood cultures be obtained within 24 hours of admission. The yield of clinically useful information is greater should the culture specimen be collected before the administration of antibiotics. Nevertheless, a question arises as to what kind of circumstances specify this 24-hour period. None of the empirically started antibiotics are modified according to BC results in our study. The majority of patients in our study are treated with broad spectrum and combined antibiotics. Therefore, we did not need to modify the antibiotic regimens, but also we did not need to modify the antibiotic regimen of the patients treated with one antibiotic alone.

Antimicrobials are the mainstay of treatment for most patients with CAP. Decisions about antimicrobial treatment are guided by factors such as spectrum of activity, pharmacokinetics, efficacy, safety profile, cost, and whether or not a specific pathogen is identified (10). Until diagnostic methods improve rapidly, most patients will be treated empirically. Although some authorities propose a syndromic approach to treatment, most data indicate that the presenting clinical features are not specific enough to predict reliably the causative agent of CAP. Thus, unless there is a specific epidemiological factor, the empirical approach to initial therapy is usually based on the likelihood that one of the key pathogens is responsible for the disease.

In a study by Van der Eerden et al (11) the initial antibiotic treatment guided by the clinical and epidemiological presentation, was at least as effective as the treatment guided by the results of rapid microbiological investigations. Based on clinical criteria, patients were treated with penicillin, erythromycin, amoxicillin/clavulonate, or flucloxacillin + gentamicin. This study supports the usefulness of the clinical and epidemiological presentation for the selection of antibiotic therapy in CAP, at least when all treatment alternatives are effective against *S. pneumoniae*.

Although many pathogens have been associated with CAP, the range of key pathogens causing the majority of cases is small. The predominant pathogen in CAP is *S. pneumoniae* (pneumococcus), which accounts for about two-thirds of all cases of bacteremic pneumonia (3, 8). Gram-negative bacilli (Enterobacteriaceae and pseudomonas) are the cause of CAP in some patients who have had previous antimicrobial treatment or have pulmonary comorbidities (8, 10). The microorganisms isolated from BCs in our study match those stated in international guidelines. Thus in patients with CAP it is recommended to start with empiric antibiotics. In fact, blood cultures are typically positive in less than 10 % of all bacterial pneumonias; therefore, the start with empiric antibiotics without performing BC tests may not be totally wrong. Nevertheless, especially specific populations such as immunosuppressed patients or patients with severe pneumonia in need of intensive monitoring may present with extraordinary circumstances. The immune deficiency enables unexpected microorganisms to grow and be responsible for the development of CAP.

Limitations

Our study has several limitations. The majority of our patients have more than one co-morbidity and the choice of empiric treatment was based on broad-spectrum antibiotics, most frequently on combined therapy. The fact that the broad-spectrum empiric antibiotic choice may cover all the microorganisms potentially responsible for CAP may explain the reason why we did not need to modify the antibiotic regimens. We did not calculate the cost-effectivity in our study. Possibly, the cost-effectivity calculations may help to indicate the value of performing BCs in patients with CAP.

Conclusion

This study documents the use of blood cultures in patients with community-acquired pneumonia. Significantly positive results are rare (11.5 %) and the majority of the blood cultures revealed negative results. Blood culture tests may not be performed in all patients with community-acquired pneumonia. Further prospective studies in community-based populations are required to define which patients are likely to benefit from blood cultures.

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