using 5.0% B/b; thus, 99.2% of all staphylococcal isolates were detected within 48 h by the PF procedure, while only 63.3% were detected by the FA procedure within this period. This observation suggests that a significant reduction in the turnaround time is possible, and supports a decision to take 48 h as the time limit for stopping antibiotic treatment in the PICU population. For staphylococci, the diagnostic yield of the PF procedure was not improved by prolonging the incubation period to > 72 h.

Staphylococci are currently the major causative organisms of nosocomial sepsis in neonatal and paediatric ICUs [14,15]. Child mortality from central nervous system sepsis in neonatal and incubation period to > 72 h.

The results of this study indicate that 2.5% B/b (the PF procedure) is more appropriate for use in PICUs than the 5.0% B/b (FA procedure), because it results in the shortest TTD for staphylococci and a smaller blood volume is required.

REFERENCES


RESEARCH NOTE

Routine antimicrobial susceptibility testing of coagulase-negative staphylococci isolated from blood cultures: is it necessary?

A. U. Chandran1,2 and R. Rennie1,3

1Medical Microbiology Laboratory, University of Alberta Hospital, 2Medical Microbiology Residency Training Program and 3Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

ABSTRACT

The clinical significance of discontinuing routine antibiotic susceptibility testing (AST) of coagulase-negative Staphylococcus (CNS) isolates from blood cultures was investigated. Prospectively,
AST was requested primarily for patients with serious underlying illnesses. Antibiotic use did not change significantly when AST was not performed routinely. Laboratory cost savings were 75% if AST was not performed, but more specimens were submitted from these patients. Oxacillin resistance in coagulase-negative staphylococci from blood cultures has remained >70% since implementation of this protocol, while annual vancomycin utilisation has shown only small, incremental increases. Therefore, it is suggested that routine AST of CNS isolates from blood culture is not essential.

**Keywords** Antibiotic susceptibility testing, bacteraemia, blood culture, coagulase-negative staphylococci, skin contamination, vancomycin usage

**Original Submission:** 8 September 2004; **Revised Submission:** 3 May 2005; **Accepted:** 9 June 2005

*Clin Microbiol Infect* 2005; 11: 1037–1040
10.1111/j.1469-0691.2005.01278.x

Coagulase-negative staphylococci are the leading cause of nosocomial bloodstream infections, especially in intensive care settings [1,2], but, as part of the normal skin flora, they are also common contaminants of blood cultures [3]. Antibiotic susceptibility testing (AST) may be of little clinical value, and there is no consensus regarding the significance of coagulase-negative *Staphylococcus* (CNS) isolates obtained from blood cultures. This report describes a pilot study in which routine AST of CNS-positive blood cultures was discontinued. Susceptibility testing was performed only upon request. Outcome measures evaluated were: (1) trends of empirical therapy with vancomycin; and (2) the financial savings to the laboratory. Vancomycin usage and antibiotic resistance patterns for coagulase-negative staphylococci were examined. Morbidity and mortality were not measured.

All inpatients and outpatients with at least one CNS-positive blood culture between 15 May 1999 and 14 September 1999 from the University of Alberta Hospital or the W.W. Cross Cancer Institute were included. For adults, a single specimen collection comprised three blood culture vials: an aerobic and anaerobic vial from one body site, plus a single aerobic vial from a second site. A bacteraemic episode was defined as at least one positive vial from a single specimen collection. For paediatric patients (aged <17 years), a single aerobic vial was collected.

Samples were taken following cleansing of the skin with an alcohol 70% v/v swab at the venipuncture site. Standard procedures were followed for the inoculation of BACTEC blood culture vials (Becton Dickinson Diagnostic Systems, Sparks, MD, USA), and specimens were incubated in the BACTEC 9240 automated system (Becton Dickinson Diagnostic Systems). Positive vials with an initial Gram’s stain suggesting *Staphylococcus* spp. were subcultured on blood and chocolate agar plates. Gram’s stain, colony morphology, a positive catalase result, a negative tube coagulase result and bacitracin resistance were used to identify CNS. Susceptibility testing was performed with the Vitek automated system GPS-SV cards (bioMérieux, Hazelwood, MO, USA). Oxacillin susceptibilities were determined by disk-diffusion, using the breakpoints for coagulase-negative staphylococci available at the time of the study [4]. Once the initial Gram’s stain had been examined, the responsible clinician was informed of the positive blood culture. There was no difference in procedure for any patient group. In the prospective part of the study, clinicians were notified that AST would be performed if requested.

Laboratory data were collected from computer records. Clinical information was obtained by chart review. Fisher’s exact test was used to calculate two-sided p values (InStat; GraphPad Software Inc., San Diego, CA, USA), with p < 0.05 considered to be significant.

During phase 1 (15 May 1999–14 July 1999), 12.5% (426/3414) of blood cultures were positive, compared with 14.9% (496/3338) during phase 2 (15 July 1999–14 September 1999). Overall, CNS

**Table 1. Patient demographics and blood culture data**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Phase 1 (%)</th>
<th>Phase 2 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48 (57.8%)</td>
<td>55 (64.7%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Female</td>
<td>35 (42.2%)</td>
<td>30 (35.3%)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median, years</td>
<td>52</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>7 days–92 years</td>
<td>1 day–90 years</td>
<td></td>
</tr>
<tr>
<td>Underlying situation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult critical care</td>
<td>26 (31.3%)</td>
<td>27 (31.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>PICU/NICU</td>
<td>10 (12.0%)</td>
<td>8 (9.4%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>8 (9.6%)</td>
<td>14 (16.5%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Haematological/ oncology</td>
<td>5 (6.0%)</td>
<td>6 (7.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Blood culture collection*</td>
<td>43 (26.1%)</td>
<td>43 (26.1%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Peripheral venipuncture</td>
<td>47 (33.8%)</td>
<td>43 (26.1%)</td>
<td></td>
</tr>
<tr>
<td>Central site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVC</td>
<td>62 (44.6%)</td>
<td>63 (38.2%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Permcath</td>
<td>24 (17.3%)</td>
<td>39 (23.6%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Broviac</td>
<td>6 (4.3%)</td>
<td>21 (12.7%)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

*Data for those specimens for which information was available. PICU/NICU, paediatric intensive care unit/neonatal intensive care unit; CVC, central venous catheter.*
isolates were obtained from 68.5% (632/922) of positive specimens from 168 patients. Patients in the two phases of the study were similar with regard to age, gender and underlying conditions (Table 1). Significantly more blood culture specimens were drawn from Broviac catheters in the second group (p 0.014).

During phase 1, there were 151 CNS isolates from 83 patients and 128 bacteraemic episodes. Nineteen patients had two or more bacteraemic episodes. Vitek detected 109 (72.2%) isolates that were oxacillin-resistant; one additional oxacillin-resistant isolate was detected by disk-diffusion. Initially, 35 (27%) of 128 isolates were considered to be skin contaminants; of these, 65 (50.8%) were left untreated (Table 2).

During phase 2, 189 CNS isolates were recovered from 85 patients; 28 patients had multiple bacteraemic episodes. AST was requested and performed for 54 isolates. Reasons included a deteriorating clinical status, repeatedly positive blood cultures (whether or not antibiotic therapy had been initiated), and the presence of an indwelling central venous catheter with associated soft tissue inflammation. Of these 54 isolates, Vitek detected 40 (74.1%) that were oxacillin-resistant; disk-diffusion detected one additional oxacillin-resistant isolate. All isolates were susceptible to vancomycin.

Of the 148 bacteraemic episodes in the second group, 38 (25.7%) were considered initially to be skin contamination; however, 68 (45.9%) were not treated with antibiotics (p 0.47). Of the remaining 80 episodes, 17 (21.3%) were treated with a β-lactam agent; of these, ten (58.8%) were proven subsequently to be oxacillin-resistant or were not tested. Of the 54 susceptibility tests performed during the prospective phase, three included specimens with more than one morphotype (three with two types; one with three types). These 50 episodes represented 37 patients, 22 of whom had blood cultures from which CNS isolates were obtained on at least two occasions. Of the 50 patients who yielded CNS isolates for which AST was performed, 25 were treated with vancomycin, and seven with a β-lactam. Seventeen patients were not given antimicrobial agents, and one was given clindamycin; empirical use of vancomycin did not differ significantly (p 0.77). Oxacillin resistance has remained at >70% among tested blood culture CNS isolates since 2000 (70.2–90.1% resistant; 96–178 isolates tested annually). Total vancomycin usage has increased annually since the protocol change (from 9701 g in 1999 to 12 142 g in 2004).

Analysis of laboratory costs for labour and materials for AST of CNS-positive blood culture isolates indicated estimated annual savings of >8000 US $ (6500 Euro). Misinterpretation of CNS-positive blood culture specimens is a major laboratory and clinical expense. False-positive results account for the greatest proportion of the cost, because of the extra laboratory work and excess antibiotic usage, especially of vancomycin [5].

The number of bacteraemic episodes treated with antibiotics did not differ significantly between the two phases. Vancomycin was the agent used most commonly, with or without susceptibility results, and its use did not increase significantly. During phase 2, AST was performed primarily for patients with serious underlying illnesses, and those with multiple positive specimens from different sites. Although there were significantly more blood cultures drawn from Broviac sites in the second group, this does not suggest that these patients were more ill than those in phase 1, as the overall proportions of specimens collected from central sites were similar.

There was a 75% decrease in laboratory AST costs although, initially, more blood culture specimens from patients with a blood CNS isolate were sent to the laboratory, and there were more CNS-positive cultures, which may have offset a small portion of these savings. Clinicians may use multiple positive blood cultures as a major criterion in their decision to treat a patient actively, even though this may not be a reliable measure of true infection or contamination [6–11]. There is no standard for laboratory and clinical decisions regarding CNS-positive blood cultures. Most specimens are collected from patients who are symptomatic and have underlying risk-factors. Therefore, it may be difficult to distinguish true infection from skin contamination on a clinical basis [8,9,12–15].

---

**Table 2. Treatment decisions before and after discontinuation of routine susceptibility testing of coagulase-negative staphylococci isolated from blood culture**

<table>
<thead>
<tr>
<th></th>
<th>No treatment</th>
<th>VAN</th>
<th>ERY/CLI</th>
<th>β-Lactam</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Phase 1 (n = 128)</td>
<td>65 (50.8)</td>
<td>56 (43.8)</td>
<td>0 (0)</td>
<td>7 (5.5)</td>
</tr>
<tr>
<td>Phase 2 (n = 148)</td>
<td>68 (45.9)</td>
<td>60 (40.5)</td>
<td>3 (2.0)</td>
<td>17 (11.5)</td>
</tr>
<tr>
<td>p value</td>
<td>0.57</td>
<td>0.77</td>
<td>0.50</td>
<td>0.22</td>
</tr>
</tbody>
</table>

VAN, vancomycin; ERY/CLI, erythromycin and/or clindamycin.

* Number of bacteraemic episodes. Some patients had more than one CNS isolate per episode.

© 2005 Copyright by the European Society of Clinical Microbiology and Infectious Diseases, CMI, 11, 1035–1047
In the present study, the clinician decided whether the CNS isolate represented a true bacteraemic episode. This did not change treatment decisions, or disrupt patient care. There was no evidence for increased resistance trends, nor did vancomycin utilisation increase more than would be expected, since there were also more patients with central venous catheters, more foreign body-related infections, and more infections overall caused by CNS, Enterococcus spp. and methicillin-resistant Staphylococcus aureus. Increased vancomycin use cannot, therefore, result solely from the absence of routine AST of blood culture CNS isolates. Ongoing review has validated this practice and it is now laboratory policy. The laboratory is now also performing AST validated this practice and it is now laboratory policy. The laboratory is now also performing AST only upon request for CNS isolates from central venous catheters in the same patient populations.

ACKNOWLEDGEMENTS

The authors thank the staff of the Bacteriology Laboratory of the University of Alberta Hospital Microbiology Laboratory for their diligent work, T. Heffner, L. Douglas and S. Shokoples for their assistance with data collection and management, and M. Gray for vancomycin utilisation data. The results of this study were presented, in part, at the 100th Annual General Meeting of the American Society for Microbiology (Los Angeles, CA, USA, 2000).

REFERENCES


RESEARCH NOTE

Activity of five quinolones, three macrolides and telithromycin against 12 Haemophilus influenzae strains with different resistance phenotypes

G. A. Pankuch, G. Lin and P. C. Appelbaum

Department of Pathology, Hershey Medical Center, Hershey, PA, USA

ABSTRACT

Gemifloxacin MICs for 12 Haemophilus influenzae strains with different resistance phenotypes were 0.001–0.015 mg/L. Gemifloxacin was bactericidal against all 12 strains after 24 h at 2 × MIC. Ciprofloxacin, levofloxacin, gatifloxacin and

Corresponding author and reprint requests: P. C. Appelbaum, Hershey Medical Center, PO Box 850, Hershey, PA 17033, USA E-mail: pappelbaum@psu.edu

© 2005 Copyright by the European Society of Clinical Microbiology and Infectious Diseases, CMI, 11, 1035–1047