Effects of Blood Volume Monitoring on the Rate of Positive Blood Cultures from the Emergency Room

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Background: Blood cultures are essential in diagnosing and treating sepsis. There are several factors that affect the diagnostic yield of blood cultures such as the number of blood sampling episodes, the incubation period, the type and volume of culture media, and the amount of blood drawn. This study aimed to elucidate whether monitoring the volume of blood drawn with an educational intervention could affect the diagnostic quality of blood cultures.

Methods: We implemented quality monitoring for the blood volume drawn during blood culture testing for adults in an emergency room. We instructed the nurses in the emergency room to draw the optimal amount of blood and to reduce the number of blood culture sets from three to two. We analyzed and compared the amount of blood drawn, the rate of positive blood cultures, the contamination rate, and time to positivity (TTP) between 908 patients pre-intervention and 921 patients post-intervention.

Results: The amount of blood drawn increased from 0.7±0.3 mL per bottle (pre-intervention) to 6.5±1.7 mL per bottle (post-intervention) (P<0.0001). The rate of positive blood culture post-intervention (12.14%) was higher than that pre-intervention (6.65%) (P<0.0001). The contamination rate post-intervention (1.82%) was also significantly greater than that pre-intervention (0.60%) (P<0.0001). Except for anaerobes, there was no significant difference in the distribution of microorganisms between the pre- and post-intervention periods. The TTP for anaerobe bottles post-intervention was significantly shorter than that of pre-intervention (16.1±16.3 versus 18.6±18.3 h).

Conclusion: This study suggests that continuing education about adequate blood volume and aseptic techniques is needed to increase the rate of positive blood cultures and reduce the contamination rate of blood cultures. (Ann Clin Microbiol 2016;19:70-76)

Key Words: Blood culture, Bloodstream infection, Blood volume monitoring, Rate of positive blood culture

INTRODUCTION

Blood culture is a critical tool for the diagnosis and treatment of bacteremia, which is a major cause of morbidity and mortality [1]. Increasing the identification accuracy of true pathogens that cause bacteremia by reducing false negatives can prevent mortality among patients. Potential causes of false-negative blood cultures include inadequate blood volume or insufficient number of collected sets, collection of samples after antibiotic therapy, and infections caused by microorganisms that are not readily recovered using routine blood culture methods.

Since the bacterial density in the blood of most patients with a bloodstream infection is very low, drawing an optimal volume of blood is the single most important parameter for maximizing the detection rate of true pathogens [2,3]. Several clinical studies have reported that the yield of microorganisms increases in direct proportion to the blood culture volume [4,5]. In a comparison between standard-volume (mean, 8.7 mL) and low-volume (mean, 2.7 mL) blood cultures, the detection rate of standard-volume cultures was substantially higher than that of low-volume cultures (92% vs. 69%) [6]. Therefore, the detection rate of cultured blood could be maximized with an adequate inoculation volume.

We recently discovered that, in the emergency room (ER) at...
Our hospital, blood culture specimens were drawn at less than 1 mL per blood bottle. Our findings highlighted the need to improve the blood culture techniques used in the ER. A quality improvement intervention was conducted in April 2016 to establish the procedures for an adequate blood culture volume. Subsequently, the volume of blood specimens submitted from the ER for blood culture was monitored using an automated system. In addition, we evaluated the effects of our quality improvement intervention on improving blood culture yields in the clinical setting.

MATERIALS AND METHODS

We analyzed the data of patients in the ER who were over 18 years of age and had blood cultures ordered by attending physicians between 1 January 2016 and 30 June 2016. Blood culture data from 1 January 2016 to 30 March 2016 were used as the baseline data (pre-intervention data). In our hospital, phlebotomy for blood culture is carried out by nurses, not by dedicated phlebotomy teams. Therefore, initially, the educational intervention was conducted for a head nurse of ER, and then the head nurse took responsibility to educate the intervention to all ER nurses who conduct phlebotomies during last week of March. Following the intervention, all adult blood cultures in the ER were obtained by the trained nurses during a 3-month period from 1 April 2016 and 30 June 2016 (post-intervention) according to the new protocol, which emphasized the importance of an optimal volume for blood culture. For each venipuncture, we recommended a total collection of 20 mL of blood to be divided into aerobic and anaerobic blood culture bottles (BD BACTEC Plus Aerobic/F and BD BACTEC Plus Anaerobic/F; Becton Dickenson, Sparks, MD, USA). In addition, the protocol called for two sets of blood cultures instead of the routine three.

All blood cultures in pre- and post-intervention periods underwent standard incubation and processing using the BACTEC FX system (Becton Dickenson). Each blood culture was kept in the system until microbial growth was detected, for a maximum of 5 days (at which time samples were classified as “negative”). A blood culture was considered positive if a microorganism was isolated from at least one media of each set. All positive cultures were identified using the VITEK2 microbial ID/AST testing system (bioMérieux, Inc., Hazelwood, MO, USA). To monitor blood volume, we used the BACTEC FX blood system, which analyzed samples in batches of 25 Aerobic/F media bottles [7]. The culture processing and identification of microorganism were conducted identically between pre-and post-intervention periods.

Total positive rates, true positive rates, contamination rates, and time to positivity (TTP) were evaluated by comparing the period before intervention with the period after intervention (post-intervention). The total positive rate was determined by dividing the total number of positive blood culture sets by the total number of cultured sets. The identification of contaminant bacteria among the positive blood culture sets was in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (2007) [8]. Blood cultures were considered to be contaminated when microorganisms from common skin flora, such as Corynebacterium spp., Bacillus spp., Propionibacterium spp., Micrococcus spp., and coagulase-negative Staphylococcus spp. (CoNS), were identified. Because CoNS might represent a true infection, cultures with two or more positive sets were not considered to be contaminated with CoNS. The contamination rate was determined by dividing the number of culture sets that were considered to be contaminated by the total number of cultured sets. The true positive rate was calculated by subtracting the contamination rate from the total positive rate. The TTP, which is the length of time from the beginning of incubation to the detection of bacteria growth, was calculated by the BACTEC FX system. Statistical analysis included comparing proportions by the Chi-square test, Student’s t-test, and Mann-Whitney test. A P-value less than 0.05 was considered statistically significant.

RESULTS

In the preliminary inspection, we analyzed inoculated blood volumes of blood cultures requested from each department in our hospital from January to March 2016. During the study period, the volume of 5,481 aerobic blood culture bottles was analyzed, and 49% of those bottles were submitted from the ER. The overall mean volume during the period was 2.4±1.5 mL. The ER department had the lowest mean volume, at 0.7±0.3 mL (Table 1). Based on these preliminary results, we focused the intervention on the ER department, which submitted the highest number of blood cultures and collected the lowest blood volume. To improve blood culture quality, we carried out an educational intervention for ER nurses who conduct phlebotomies. Following the intervention, we analyzed the data of all adult blood cultures submitted from the ER in the 3 months both pre- and post-intervention.
From January to June 2016, 4,741 blood culture sets were drawn from 1,829 patients in the ER at our hospital. The mean blood culture volume in the aerobic bottles was significantly increased from 0.7±0.3 mL/bottle pre-intervention to 6.5±1.7 mL/bottle post-intervention (P<0.0001) (Fig. 1). The mean number of blood culture sets per person was 3.09 pre-intervention and 2.10 post-intervention.

Of the 2,813 blood cultures collected before the566 intervention, 6.65% were identified as positive. Post-intervention, the total positive culture rate was 12.14%, which was a significant increase (P<0.0001) (Table 2). Although the contamination rate also increased from 0.60% to 1.82% (P<0.0001), the true positive rate significantly increased from 6.04 to 10.32% (P<0.0001).

Because the TTP in blood cultures can be influenced by the volume of blood drawn, the TTP values of aerobic and anaerobic blood bottles were compared pre- and post-intervention (Table 3). The TTP of anaerobic bottles at post-intervention was significantly shorter than that of those at pre-intervention (18.6±18.3 vs. 16.1±16.3 h; P<0.037). The difference in mean TTP of aerobic bottles between pre- and post-intervention was not statistically significant (18.8±15.2 vs. 22.7±22.3 h; P=0.528).

The distribution of microorganisms detected pre- and post-intervention is shown in Table 4. The five most common microorganisms during pre-intervention were Escherichia coli, coagulase-negative staphylococcus (CoNS), Klebsiella spp., Staphylococcus aureus, and anaerobes. The most common microorganisms post-intervention were E. coli, CoNS, Klebsiella spp., Streptococcus spp., and other Enterobacteriaceae. Except for anaerobes, there was no significant difference in the distribution of microorganisms pre-intervention versus post-intervention. The detection frequency of anaerobes between pre- and post-intervention was significantly different (P=0.009).

**DISCUSSION**

ER patients with a suspected underlying infection should be evaluated for the presence of bloodstream infection using blood cultures. Patients with positive blood culture results should be treated with adequate antibiotics to reduce morbidity and mortality. False negative results caused by an inadequate blood culture technique can have devastating consequences for patients with bacteremia. Therefore, blood cultures should be performed according to the protocols of an effective quality control program to avoid false negatives.

Blood culture volume is the most important factor for reducing false negative results. Several studies have reported that the sensitivity of detecting bacteria in blood cultures can be volume-dependent [4,6]. Although the CLSI recommends blood draw volumes of 20 mL per set for adult patients, incidences of low-volume blood draws still exist in the clinical setting. A survey conducted by Shin et al. showed that the mean blood draw volume per set for adults among nine university hospitals in South Korea was 7.7 mL [9]. In comparison, the mean volume
Table 2. Comparison of the true positive rate and contamination rate in bottles submitted for blood culture pre- and post-intervention

<table>
<thead>
<tr>
<th>Period</th>
<th>Total No. of blood culture sets</th>
<th>No. (%) of</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Positive culture sets</td>
<td>Contaminant culture sets</td>
<td>True positive culture sets</td>
</tr>
<tr>
<td>Pre-intervention</td>
<td>2,813</td>
<td>187 (6.65)</td>
<td>17 (0.60)</td>
<td>170 (6.04)</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>1,928</td>
<td>234 (12.14)</td>
<td>35 (1.82)</td>
<td>199 (10.32)</td>
</tr>
</tbody>
</table>

Table 3. Comparison of the time to positivity (TTP) values between pre- and post-intervention

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aerobic bottles</th>
<th>An aerobic bottles</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
<td>P-value*</td>
<td>Pre-intervention</td>
</tr>
<tr>
<td>TTP of total positive (h)</td>
<td>18.8±15.2</td>
<td>22.7±22.3</td>
<td>0.5283</td>
<td>18.6±18.3</td>
</tr>
<tr>
<td>TTP of contaminant (h)</td>
<td>43.5±22.4</td>
<td>32.8±22.5</td>
<td>0.0487</td>
<td>60.8±36.4</td>
</tr>
</tbody>
</table>

*Calculated by the Mann-Whitney test.

Table 4. Distribution of microorganisms isolated from blood culture-positive patients pre- and post-intervention

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>No. of patients with positive results (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>31 (36)</td>
<td>60 (38)</td>
<td>0.656</td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em> spp. (CoNS)</td>
<td>10 (12)</td>
<td>28 (18)</td>
<td>0.197</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>9 (10)</td>
<td>18 (12)</td>
<td>0.800</td>
</tr>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td>5 (6)</td>
<td>11 (7)</td>
<td>0.711</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>9 (10)</td>
<td>8 (5)</td>
<td>0.121</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp.</td>
<td>0 (0)</td>
<td>4 (3)</td>
<td>0.135</td>
</tr>
<tr>
<td>Other <em>Enterobacteriaceae</em></td>
<td>3 (3)</td>
<td>10 (6)</td>
<td>0.336</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>8 (9)</td>
<td>3 (2)</td>
<td>0.009</td>
</tr>
<tr>
<td><em>Candida</em> spp.</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0.669</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>0.100</td>
</tr>
<tr>
<td>Others</td>
<td>7 (8)</td>
<td>12 (8)</td>
<td>0.902</td>
</tr>
<tr>
<td>Total</td>
<td>86 (100)</td>
<td>156 (100)</td>
<td></td>
</tr>
</tbody>
</table>

per set in our hospital was less than 2 mL in the ER. The total rate of bacteria-positive blood draws was 8.0% among the nine South Korean university hospitals in the Shin et al. study [9], and the CLSI suggests that an adequate positive rate is 6-12%. In our hospital, the data from the 3-month period before intervention revealed a total positive rate of 5.49-6.44%, which was lower than average. Following intervention, the total positive rate of the ER was increased to 12.14%. As blood volume was increased, the total positive rate increased, and the rate was higher than the average of the nine South Korean university hospitals in the Shin et al. study. The data demonstrated that the detection yield of microorganisms that cause bloodstream infection was higher when the blood culture volume was increased, thus confirming the importance of blood volume monitoring as part of our quality control program.

To measure the blood volume in the sample-collection bottles, previous studies have used methods that subtract the unused bottle weight (or media level) from the full bottle weight (or media level) [10,11]. These manual monitoring methods are labor-intensive and time-consuming. Recently, a virtual blood volume monitoring method using the BACTEC FX system, which is based on the metabolism of red blood cells, was introduced, and it demonstrated a linear correlation with manual blood volume measurements [7]. The BACTEC FX system provides reliable estimates of the blood volume in blood culture bottles, with a mean error of 0.2 mL. The method is very convenient for the monitoring of blood volume; thus, we used the virtual monitoring method in this study. However, a potential limitation of the
Despite this increased contamination rate during the post-intervention period, the contaminant rate also increased. In our study, however, as the volume of the cultures in adequate blood volume were prone to growth of contaminants. To ensure adequate blood volumes for blood culture would be important in improving the true positive rate and the identification of microorganisms that cause bloodstream infections which is a major cause of morbidity and mortality.

In conclusion, blood volumes were previously obtained in a suboptimal amount, and the results of the present study demonstrates how the intervention increased the true positive rate of blood cultures from the ER. A continuous-monitoring system to ensure adequate blood volumes for blood culture would be important in improving the true positive rate and the identification of microorganisms that cause bloodstream infections which is a major cause of morbidity and mortality.

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REFERENCES

=국문초록=

응급실에서 혈액배양 채혈량 모니터링이 혈액배양 양성률에 미치는 효과

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소민경1, 정혜선1, 김충종2, 최희정2, 이미애1

배경: 혈액배양은 균혈증 진단과 치료에 필수적인 검사이다. 혈액배양 양성률에 영향을 미치는 인자로는 혈액배양량, 채혈횟수, 배양기간, 사용한 배지의 종류, 배지의 양 등이다. 본 연구는 응급실에서 혈액배양 질관리 교육 후 혈액배양 채혈량의 모니터링을 실시하여 그에 따른 효과에 대하여 알아보고자 한다.

방법: 본 연구는 응급실에서 성인 혈액배양 검사를 대상으로 혈액배양 질관리 교육 후 혈액배양 채혈량의 질관리 모니터링을 하였다. 질관리 중재로는 채혈량을 늘려 채혈하도록 교육하였으며, 채혈량 증가에 따라 채혈 횟수는 3쌍에서 2쌍으로 줄여 채혈하도록 하였다. 질관리 중재 전후에 혈액배양 양성률, 오염률, time to positivity (TTP)를 비교하여 분석하였다.

결과: 혈액채혈량은 질관리 중재 전 병당 0.7±0.3 mL에서 중재 후 병당 6.5±1.7 mL로 증가하였다 (P<0.0001). 환자당 채혈 횟수는 중재 전 3.09회, 중재 후는 2.10회였다. 중재 전후 혈액배양 양성률은 6.65%에서 12.14%로 증가하였으며 통계적으로 유의한 차이를 보였다 (P<0.0001). 혈액배양 오염률은 혈액체취량의 질관리 중재 이후 0.60%에서 1.82%로 상승하였다 (P<0.0001). 두 군간의 균종은 혼성균주를 제외하고는 통계적 유의한 차이는 없었다. TTP는 중재 전 후를 비교했을 때 트러미배지에서 18.6±18.3시간에서 16.1±16.3시간으로 통계학적으로 중재 후 유의하게 단축되었다.