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Major Article

Reducing blood culture contamination using an initial specimen diversion device

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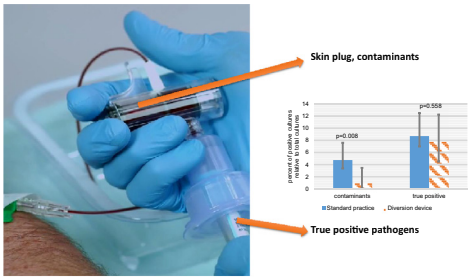

Key Words:
False positive culture
Subcutaneous colonization
Inpatient

Objectives: False positive blood cultures result from contamination, consuming laboratory resources and causing unnecessary antibiotic treatment and prolonged hospital stay. Skin disinfection reduces contamination; however, bacteria colonizing human skin are also found in tissues deep into the skin surface. A diversion device diverts the initial 1-2 mL of blood to remove any potentially contaminated skin plug. This study investigates the effect of the device on culture contamination in hospitalized patients.

Methods: In this prospective controlled pragmatic study, blood cultures were obtained using an initial specimen diversion device, either via integrated needle or attachment to a newly placed intravenous catheter. Cultures taken using standard methods served as the control.

Results: Six hundred seventy-one blood cultures were obtained. Two hundred seven cultures were taken using an initial specimen diversion device, with 2 (1.0%) contaminated cultures. Four hundred sixty-four cultures were taken without the device, with 24 (5.2%) contaminated cultures ($P < .008$). No significant difference was shown in the rate of true-positive cultures.

Conclusions: The use of a diversion device was associated with reduced culture contamination in hospitalized patients over a 6-month period, without concomitant reduction in true-positive cultures. This intervention may result in a reduction in costs, antibiotic use, and duration of hospital stay.

Bloodstream infections cause significant morbidity and mortality and their prompt identification is an essential part of modern medicine. Blood cultures, first described in the latter part of the 19th century,[1] are an essential element of the diagnosis and treatment of patients with such infections. However, as with all medical testing, false-positive results occur and can cause delays in diagnosis, inappropriate treatment, and significantly added expenses.[2,3] False-positive results in blood cultures have been described for as long as there have been such cultures and are primarily owing to contaminants.[1,2] It has been estimated that up to 50% of positive blood cultures represent contamination.[2,3] These false-positive cultures, at the microbiological laboratory level, require significant additional resources for examination. In addition, and perhaps more importantly, these false-positive cultures may result in unnecessary antibiotic treatment as well as prolonged hospital stay, causing needless harm to patients. These result in an

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estimated additional cost of $4,385-$8,720 per false positive blood culture in the United States.[3-6]

Various methods have been implemented to reduce blood culture contaminants. Overall, combined interventions have proven effective in attenuating blood culture contamination, and many institutions have successfully reduced blood culture contamination to the currently recommended rate of <2%-3%, with the highest achieving institutions obtaining rates as little as 0.6%.[4,7] However, it has been shown that the bacteria that colonize the human skin are found not only on the surface but in deeper tissues as well. It has further been shown that these bacteria cannot be completely removed, even under ideal conditions.[7,8] Thus zero, or near zero, blood culture contamination using current methods may be impossible, even with perfect technique. Therefore, it is reasonable to seek techniques beyond skin disinfection and improved adherence to further reduce the rate of blood culture contamination.

Recently, a new device was developed that diverts the initial 1-2 mL of blood to remove any potential skin plug with contaminants from entering the blood culture bottle. The SteriPath device (Magnolia Medical Technologies, Seattle, WA) is a closed-system, sterile blood collection system that diverts 1-2 mL of the initial venipuncture blood into an isolated diversion chamber, and then allows venous blood to flow into culture bottles (Fig 1). This initial specimen diversion device has been tested in some initial studies and has been shown to reduce blood culture contamination without reducing sensitivity to true bloodstream infection. A recent study showed the use of this device in an emergency department setting.[9] However, this study was conducted over a short period of time, did not evaluate inpatients, and used paired cultures rather than a pragmatic design. Thus, this study was designed as a pragmatic trial to evaluate the use of the diversion device in reducing blood culture contamination over the period of approximately 6 months in an inpatient population.

METHODS

Study design

This prospective, controlled, pragmatic study was conducted in the Shaare Zedek Medical Center, a 1,000-bed university-affiliated general hospital in Jerusalem, Israel. The hospital includes all major departments and services, including 4 medical and 2 geriatric wards, hematology and oncology, pediatrics, a surgical division including a vascular surgery unit, gynecology and obstetrics, cardiothoracic surgery, urology, orthopedics, plastic surgery, ophthalmology, otorhinolaryngology, neurosurgery and several intensive care units. The study was conducted in the 6-month period from March 2017 to August 2017, in 1 of the departments of medicine (Medicine B) at our institution.

Our institutional protocol mandates skin disinfection followed by venipuncture using a butterfly needle or a newly placed intravenous catheter. Blood is then inoculated directed into blood culture bottles. Cultures are obtained in preference by phlebotomy teams (the full institutional protocol is provided in Appendix A). These interventions have been shown in multiple studies to reduce the rate of blood culture contamination.[2,6] Cultures not obtained by phlebotomy teams are taken frequently by resident physicians. Despite these protocols, prior to initiation of the current study, the culture contamination rate in the department studied was approximately 4%, which is higher than recommended by guidelines. This study was initiated to reduce that rate.

During the study, blood cultures were obtained using the initial specimen diversion device, either via an integrated needle, or in cases of intravenous line placement, by attaching the device to the newly placed intravenous catheter in patients in 1 medical department. The control group consisted of blood cultures taken using the standard practice—skin disinfection followed by cultures obtained via standard devices—Vacuette Holdex (Greiner Bio-One, Kremsmünster, Austria) attached to either a butterfly needle or to a newly placed peripheral intravenous catheter. In accordance with our standard practice, blood cultures were not obtained from existing peripheral lines. In either method, blood was inoculated into BD BACTEC Plus Aerobic/F in addition to Plus Anaerobic/F culture bottles (BACTEC, Franklin Lakes, NJ). An automated blood culture system, BD BACTEC FX (BACTEC) was used to process the blood cultures. Relevant characteristics of the blood culture, including date of culture and site of blood collection, were recorded. Isolates were identified using MALDI-TOF (VITEK MS, bioMérieux, Marcy l'Etoile, France) and standard biochemical methods.

During the first month of the study, observers provided technical support to ensure proper use of the device by the users—whether

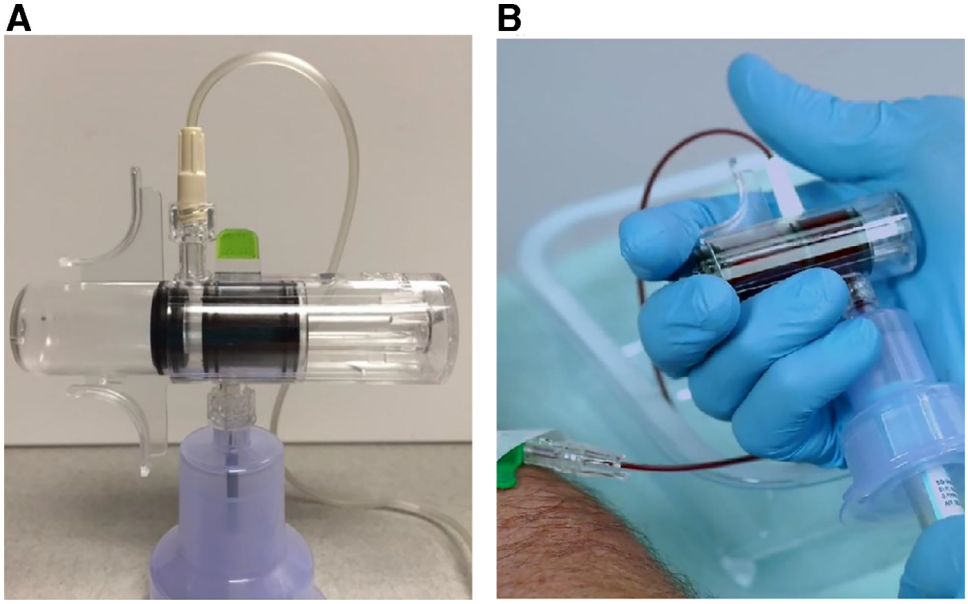

Fig 1. Diagram and function of initial specimen diversion device. (A) Shows the device prior to use. (B) Shows the device in use. The phlebotomist is squeezing the device to let blood into the diversion chamber. After the chamber is filled the blood continues to the culture bottle (bottom right).

phlebotomists or physicians. The observers did not provide direct assistance in blood culture collection. For the remaining 5 months of the study, the device was used without observer presence. During the entire period, blood cultures were collected according to the clinical discretion of the treating physician.

Ease of use of the device was evaluated using a standardized survey of phlebotomists and others involved in sample collection.

Definitions

Culture contamination was defined a priori as follows: classification of positive blood culture as contaminated was initially defined by microbiological criteria—growth of coagulase-negative staphylococci, corynebacteria, micrococci, or alpha-hemolytic streptococci. Cultures could be reclassified as true infections if such an organism was isolated from multiple blood cultures obtained by different venipuncture. All classification of cultures as positive or as true contaminant was via criteria defined prior to initiation of the study and implemented prior to unblinding of study versus control group. It should be noted that given the high sensitivity and short time to positivity of modern blood culture systems,[10] time to positivity is not an effective method of identifying culture contaminants. If a single blood culture showed growth of true infection and contaminant organisms, it was included in both categories.

Statistical analysis

Data were analyzed using Winpepi version 11.65 (JH Abramson). Proportions were compared using the χ^2 test or the Fisher exact test, where appropriate. Continuous variables were compared by the Student *t* test or the Mann-Whitney *U* test, where appropriate. Two-tailed *P* values were taken and a $P < .05$ was defined as significant.

The study was approved by the institutional review board of Shaare Zedek Medical Center.

RESULTS

In the 6 months of the study period, 671 blood cultures were obtained in the study department. Of these, 207 cultures were recorded to have been taken using the initial specimen diversion device; this population served as the study group. In 464 cultures, use of the device was not recorded; this population served as the control group. A significant difference in age was found between the control group and the study group (74 ± 1.4 vs 77 ± 2.1, respectively, $P < .004$). Otherwise no differences between the 2 groups were noted (Table 1).

Of the 464 cultures in the control group, 68 (14.7%) were positive for bacterial growth. Of those positive cultures, 24 were defined as contaminants, thus resulting in a contamination rate of 5.2%. In the study group, 207 blood cultures were obtained. Of these, 18 (8.7%) were positive for bacterial growth. Of these positive cultures, 2 were defined as contaminants, thus resulting in a contamination rate of 1.0% in the study group ($P < .008$ for the difference between the groups). Except for a single culture in the control group, which grew *Streptococcus parasanguinis*, all other contaminated cultures grew coagulase-negative staphylococci.

Table 1
Characteristics of study population

Variable	Diversion device n = 207 (%)	Standard practice n = 506 (%)	*P* value
Male	118 (57.0)	311 (61.5)	.446
Age (years) ± 95% CI	77 ± 2.1	74 ± 1.4	.004
Place of residence			
Home	148 (71.5)	385 (76.1)	.292
Assisted living	11 (5.3)	23 (4.5)	.847
Chronic care facility	48 (23.2)	98 (19.4)	.303
Hospitalized within the last year	128 (61.8)	304 (60.1)	.669
7-day mortality	36 (17.4)	77 (15.2)	.498

CI, confidence interval.

Table 2
Microbiological and clinical characteristics of positive cultures

Variable	Diversion device n = 207 (%)	Standard practice n = 464 (%)	*P* value
All positive cultures	18 (8.7)	68 (13.4)	.034
Culture contamination*	2 (1.0)	24 (4.7)	.008
CoNS	2 (1.0)	23 (4.5)	.013
Other	0 (0.0)	1 (0.2)	1.000
Contamination by age group (years)			
18-64	0 of 28 (0.0)	2 of 96 (2.1)	1.000
65-80	1 of 70 (1.4)	16 of 226 (7.1)	.081
81+	1 of 109 (0.9)	6 of 184 (3.3)	.253
True positive cultures	16 (7.7)	44 (8.7)	.558
Enterobacteriaceae	3 (1.4)	20 (4.0)	.067
Staphylococci	12 (5.8)	18 (3.6)	.312
Other	1 (0.5)	6 (1.2)	.447

CoNS, coagulase-negative staphylococci.
*Defined by growth of CoNS, corynebacteria, micrococci, or alpha-hemolytic streptococci. If such an organism was isolated from multiple cultures it was redefined as true infection.

Of the control group cultures, 44 were defined as true positives resulting in a true-positive rate of 9.5%. Of the study group cultures, 16 were defined as true positives resulting in a true-positive rate of 7.7%. Enterobacteriaceae and staphylococci were the most common causes of true bacteremia in both groups. No significant difference in the true-positive rate or in the microbiological characteristics of true-positive cultures were noted between the 2 groups (Table 2 and Fig 2).

In a survey of ease of device use, all respondents who had used the device more than once considered it slightly or moderately more difficult to use than standard practice (grade 2 or 3 of 5).

DISCUSSION

A substantial fraction of positive blood cultures represent contamination rather than true bloodstream infection,[2,3] including in the control group of our study (Fig 2), where 24 of 464 (5.2%) cultures represented contamination and 44 (9.5%) represented true infection. These false-positive cultures, at the microbiological laboratory level, require significant futile resources for examination. In addition, and perhaps more importantly, these false-positive cultures result in unnecessary antibiotic treatment as well as prolonged hospital stay, causing needless harm to patients. This results in substantial additional cost per false positive blood culture.[3-6]

In this study, we investigated the efficacy of an initial specimen diversion device in reducing the rate of blood culture contamination. We found that the device was associated with a reduction in blood culture contamination with a 5.2% (24 of 464) contamination rate in the control group and a 1.0% (2 of 207 cultures) contamination in the study group ($P < .008$). These results are consistent with those obtained in a recent study performed in an emergency department population.[9] In our study, the control group was noted to be younger than the study group.

This study suggests that use of an initial specimen diversion device can effectively reduce culture contamination among hospitalized patients without impacting the rate of true-positive cultures. Furthermore, this reduction can be maintained over a relatively extended period of time.

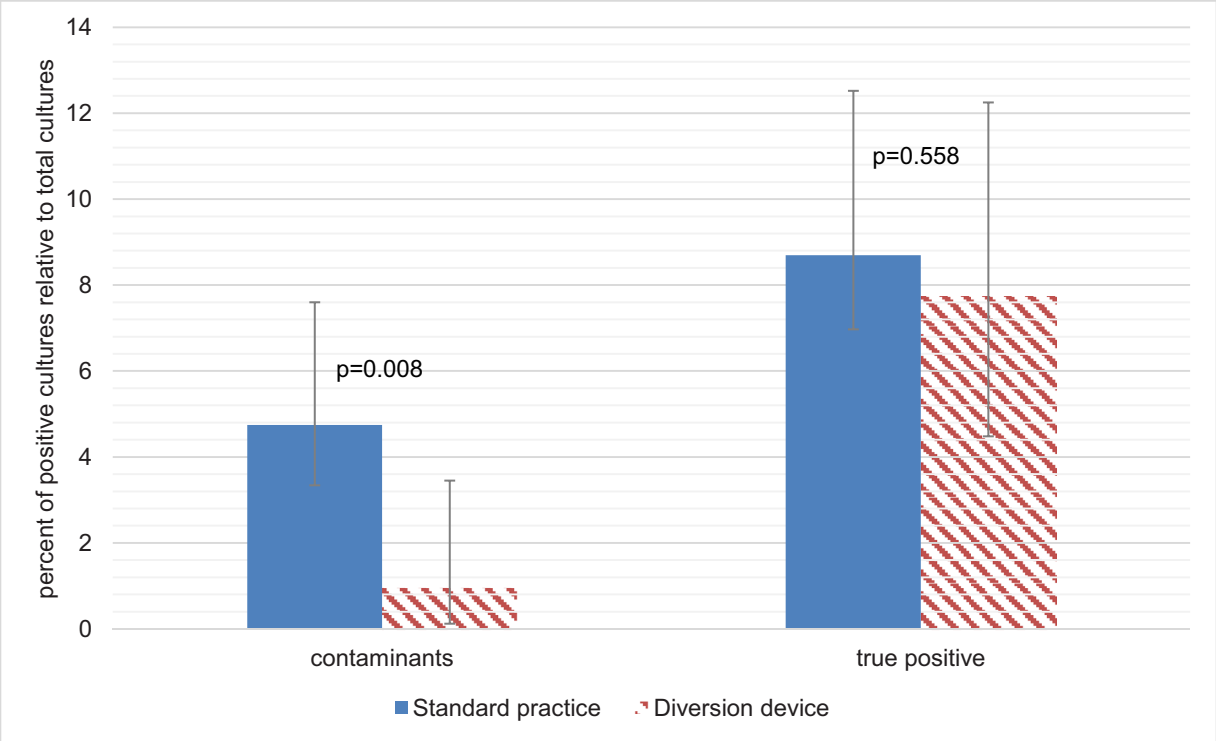

Fig 2. Positive culture rate for both contaminated and true-positive cultures.

The study has several limitations. First, although this study was controlled, a pragmatic design, rather than a randomized control, was employed. Such a study is limited in controlling for confounders related to selection of sample. Indeed, the study population was older than that of the control, although no other significant differences were noted (Table 1). Additionally, this study was a single-center study with a relatively small study population. As such, results should be interpreted cautiously.

CONCLUSIONS

This study found that use of an initial specimen diversion device was associated with a reduction in blood culture contamination in hospitalized patients over a 6-month period, from 5.2% (24 of 464) in the control group to 1.0% (2 of 207, $P < .008$) in the study group, without a concomitant reduction in true-positive cultures. This is an intervention that may result in a reduction in costs, unnecessary antibiotic use and, hospital length of stay.

Acknowledgments

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APPENDIX A

Institutional protocol of the Shaare Zedek Medical Center for the collection of blood cultures in hospitalized adult patients.

8.1.1 Frequency and timing of collection.

8.1.1.1 A blood culture set includes a Bactec+ Aerobic bottle and a Bactec+ Anaerobic bottle.

8.1.1.2 At least 2-3 sets should be obtained prior to beginning treatment, with an hour interval between each sample.

8.1.1.3 In urgent cases, where due to the patient's condition treatment cannot be delayed, such as sepsis, meningitis, or pneumonia, two sets can be taken simultaneously from both arms.

8.1.1.4 Three sets are **required** in patients where SBE, FUO, Brucella, or fungus infection are suspected.

8.1.1.5 In patients already on antibiotic treatment, cultures should be obtained while antibiotic concentration is at trough levels (immediately prior to administration of the next dose of antibiotic).

8.1.2 Collection of the correct volume.

8.1.2.1 It is advisable to obtain 8cc-10cc of blood per bottle during each collection. Obtainment of the correct volume is essential for increasing microorganism detection.

8.1.3 Mode of collection and adherence to sterility at collection.

* Standard precautions should be adhered during patient treatment *

8.1.3.1 Collection of the sample shall be done at the patient bedside.

8.1.3.2 Paste the barcode sticker containing patient details on the test order form. Complete the test order form including date, time of collection, location of collection (peripheral line, central line, etc.), and the physician questionnaire.

Special requests such as: fungi, Brucella, SBE, etc. must be indicated on the form with emphasis.

In the case of Brucella this also must be prominently marked on the top of the bottles.

8.1.3.3 Paste the label with patient details, date and location of collection on the bottle. (Please avoid placing the label on the bottle barcode).

8.1.3.4 Choose a different collection site for each set, preferably from a peripheral vein.

8.1.3.5 Do not obtain blood from a vein with an indwelling intravenous catheter.

8.1.3.6 Disinfect the site of collection with 70% alcohol in a circular motion outward.

8.1.3.7 Allow to dry (for 30 seconds), avoid contact with the disinfected area.

8.1.3.8 Remove bottle cap, disinfect the cap with an alcohol swab; allow to dry.

8.1.3.9 Obtain the sample from the patient, first collect sample in to the aerobic bottle in order to remove the air, and then in to the anaerobic bottle.

8.1.3.10 Mix the bottles to prevent blood clotting.

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