



Evaluation of different blood culture media in neonatal sepsis

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Blood drawn from neonatal patients is available in only limited amounts for blood cultures. The BACTEC Pediatrics (PEDS) Plus aerobic nonradiometric blood culture bottle was designed to aid the diagnosis of pediatric bacteremia. To assess the value of PEDS Plus blood culture medium for neonatal patients, we prospectively compared the PEDS Plus blood culture medium with the standard BACTEC aerobic medium (NR6A). From January to December 1999, 192 pairs of PEDS Plus and NR6A blood culture bottles were collected by the pediatric microbiology laboratory of Taipei Veterans General Hospital. Seventeen (8.85%) isolates were considered to be clinically significant microorganisms. Isolation rate of the PEDS Plus culture bottles was significantly higher than that of the NR6A culture bottles ($p < 0.001$). Six isolates were detected at least 1 day earlier by using the PEDS Plus culture bottles ($p < 0.001$). Among those patients who were under antibiotic therapy, the PEDS Plus culture bottle showed more significant growth than the NR6A culture bottle ($p < 0.001$). After weighing their benefits, we suggest substituting PEDS Plus bottles for NR6A bottles when culturing blood from neonatal patients or from those who are receiving antibiotic therapy.

Key words: Bacteremia, neonates, PEDS Plus blood culture medium

Blood cultures are routinely obtained for the evaluation of possible sepsis. Isolation of microorganisms from pediatric patients has become increasingly important from both a diagnostic and prognostic point of view. However, blood drawn from pediatric patients, especially neonates, is only available in limited amounts for blood cultures. Some published articles have pointed out that the volume of blood cultured is a critical factor in the detection of bacteremia [1,2]. BACTEC Pediatrics Plus aerobic nonradiometric blood culture bottle was designed to aid in the diagnosis of pediatric bacteremia. To assess the value of PEDS (pediatrics) Plus blood culture medium for neonatal patients, we prospectively compared the PEDS Plus blood culture medium with the standard BACTEC aerobic medium (NR6A).

Materials and Methods

Patients

All newborn infants in the neonatal intensive care unit of the Taipei Veterans General Hospital from January to December 1999 suspected of being infected were

included in the study.

Obtaining blood specimens

Puncture sites were disinfected with 70% isopropyl alcohol followed by 10% povidone-iodine solution before venipuncture. The septa of blood culture bottles were disinfected with 70% isopropyl alcohol and allowed to dry. Equivalent blood volumes from a single venipuncture were inoculated into each of the two bottles: the PEDS Plus blood culture medium and the NR6A aerobic medium. Blood volume inoculated varied from 0.5 mL to 1 mL.

Blood culture systems

Blood samples were inoculated into both PEDS Plus and NR6A broth media for processing with the BACTEC NR 730 nonradiometric blood culture system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD, USA). NR6A bottles contained 30 mL of soybean-casein digest broth with 0.035% sodium polyanetholesulfonate (SPS). PEDS Plus bottles contained 20 mL of soybean-casein digest broth with 0.025% SPS. In addition, nonionic adsorbing resins, cationic exchange resins, and yeast extract were included in the PEDS Plus bottles. The atmosphere of both NR6A and PEDS Plus bottles contained 2.5% CO₂ in 97.5% oxygen.

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Table 1. Isolates from BACTEC PEDS Plus and NR6A blood culture bottles

Microorganisms		No. of isolates	PEDS Plus only	NR6A only	Both PEDS Plus and NR6A	<i>p</i> ^a
Aerobic gram-positive cocci						
Catalase-positive	<i>Staphylococcus aureus</i>	2	1	0	1	NS
	Coagulase-negative staphylococci	1	0	0	1	NS
Catalase-negative	Group B streptococcus	1	0	0	1	NS
Aerobic gram-negative bacilli						
Enterobacteriaceae	<i>Enterobacter</i> spp.	5	2	0	3	NS
	<i>Escherichia coli</i>	1	0	0	1	NS
	<i>Klebsiella pneumoniae</i>	1	1	0	0	NS
Aerobic gram-negative bacilli						
Nonenterobacteriaceae, nonfermentative	<i>Pseudomonas aeruginosa</i>	2	1	0	1	NS
	<i>Acinetobacter</i> spp.	1	1	0	0	NS
	<i>Chryseobacterium meningosepticum</i>	1	0	0	1	NS
Yeasts	<i>Candida</i> spp.	2	1	0	1	NS
Total number		17	7	0	10	< 0.001

Abbreviations: PEDS = pediatrics; NS = non-significant

^a*p* value compares the "PEDS Plus only" with the "NR6A only".

Identification of isolates

We reviewed all blood cultures showing positive results. Positive cultures were considered not to be contaminants if the patient had symptoms and signs of bacteremia or had two or more bottles positive for the same microorganism.

Statistical analysis

The statistical significance was analyzed by Student's *t*-test, Fisher's exact test, and Chi-square analysis. A *p* value less than 0.05 was considered as statistically significant.

Results

For a period of 1 year, 192 pairs of PEDS Plus and NR6A blood culture bottles were collected in the pediatric microbiology laboratory. Of these, 19 (9.89%) showed microorganism isolates, and two (1.04%) were

sought as contaminants. Therefore, 17 (8.85%) isolates were considered to be clinically important microorganisms. Among these 192 patients, 108 (56.25%) were male and 84 (43.75%) were female; 125 (65.1%) preterm and 67 (34.89%) term babies with a mean age of 12 days old were noted (age ranged from 1 -to 31 days).

Table 1 shows blood isolates detected from the Bactec PEDS Plus and NR6A blood culture bottles. Of the 17 clinically significant isolates, seven (41.2%) isolates were detected in the PEDS Plus bottles only and none was detected in the NR6A bottles only. The remaining 10 (58.8%) isolates were detected in both PEDS Plus and NR6A bottles. Staphylococci, aerobic gram-negative bacilli, and yeasts showed more growth within the PEDS Plus media than in the NR6A culture media, but individually, this growth difference was not statistically significant. However, when considering all

Table 2. Comparison between BACTEC PEDS Plus and NR6A blood isolate recovery time

Microorganism	Reported on the same day	PEDS Plus first	NR6A first	<i>p</i> ^a
Aerobic gram-positive cocci (n = 3)	1	2	0	NS
Aerobic gram-negative bacilli:				
Enterobacteriaceae (n = 4)	1	3	0	NS
Nonenterobacteriaceae, nonfermentative (n = 2)	2	0	0	NS
Yeasts (n = 1)	0	1	0	NS
Total number of isolates	4	6	0	< 0.001

Abbreviations: PEDS = pediatrics; NS = non-significant

^a*p* value compares the numbers of positive results detected first from PEDS Plus or NR6A culture bottles.

Table 3. Comparison between BACTEC PEDS Plus and NR6A blood isolates in antibiotic therapy

	PEDS Plus only	NR6A only	p^a
Patients received/receiving antibiotics	5	0	< 0.001
Patients never received antibiotics	2	0	NS
Total number	7	0	

Abbreviations: PEDS = pediatrics; NS = non-significant

^a p value compares the numbers of positive results detected first from PEDS Plus or NR6A culture bottles.

of these differences as a group, PEDS Plus culture bottles showed more efficient in the detection of bacteremia than the NR6A culture bottles ($p < 0.001$).

Table 2 compares the recovery time between the PEDS Plus and NR6A blood cultures. Among the 10 organisms isolated from both bottles, four (40%) isolates were detected on the same day. The remaining six isolates were detected at least 1 day earlier by using the PEDS Plus culture bottles ($p < 0.001$).

Table 3 compares the antibiotic effect on microorganism recovery rate between the two culture media. We reviewed the medical records and categorized those who were receiving antibiotics during blood culture collection or had received antibiotics before blood culture collection. Among those patients receiving antibiotics or had received antibiotics, PEDS Plus culture bottles showed more significant growth than NR6A culture bottles ($p < 0.001$). On the other hand, there was no statistical difference between the two culture media in patients who never received antibiotics.

Discussion

Early and accurate recovery of microorganisms is important in severe neonatal infection. In the past 20 years, marked improvement has been made in both blood culture media and culture equipment. However, the volume of blood that can be drawn safely from sick neonates often limits neonatal blood cultures. As Li *et al* previously pointed out, the amount of blood volume inoculated is significantly correlated with the positive culture rate of each culture system [1]. Therefore, an important question is whether or not there is a way to increase the culture rate in neonates?

In the present study, by using a Bactec nonradiometric system, we focused on neonatal infections. The amount of blood inoculated into each culture bottle was limited to 1 mL or less. Due to individualized health consideration, we were unable to draw exact amount of blood from each patient. However, our results showed that PEDS Plus culture media provided a significant increase in yield of

pathogens when compared to aerobic NR6A media. This result is compatible with the results published by others [3].

PEDS Plus bottle content is different from NR6A in broth volume, addition of resins and yeast extract, and SPS. Broth volume is reduced from 30 mL in NR6A bottles to 20 mL in PEDS Plus bottles. Since the standard dilution of blood in culture broth varies from 1:10 to 1:20 [4], this reduction of broth volume may help blood not to become diluted in broth which would then lead to a lack of growth of bacteria in the culture bottle [5]. Results of the present study were compatible with this hypothesis in that the culture rate of the PEDS Plus bottles was significantly higher than that of the NR6A bottles.

Addition of nonionic absorbing resin and cationic exchange resin in the PEDS Plus bottle was also important in regards to patients receiving antibiotics. Several reports have suggested that resin-containing medium is more efficacious than traditional aerobic medium in detecting microorganisms during antimicrobial therapy [6-8]. As shown in our study, the positive culture rate of the PEDS Plus bottles was significantly higher than that of the NR6A bottles in patients receiving antimicrobial therapy.

Another difference between PEDS Plus and NR6A bottle content is the concentration of SPS. Even though SPS is generally beneficial in increasing positive blood culture rate, it can inhibit the growth of *Neisseria meningitides* [9]. This organism is not rarely seen in pediatric bacteremia [10]. SPS concentration of the PEDS Plus bottles is decreased from 0.035% to 0.025%. In the present study, no *N. meningitides* was isolated, so we were unable to address the effect of the change of SPS concentration on culture rates.

Since both PEDS Plus and NR6A are aerobic media, no anaerobic data was available in this study. In the past 20 years, there has been a decline in the percentage of positive blood cultures yielding anaerobic organisms from 18% to less than 4% [11-13]. Our previous study also showed that routine use of anaerobic blood culture may not be necessary for pediatric patients [14].

Many efforts have been made to increase the blood culture rate in neonatal sepsis, including multiple site blood cultures and different culture media [15,16]. In the present study, we have shown that PEDS Plus bottles are superior to NR6A aerobic bottles in both positive culture rate and recovery time. The suggested price of PEDS Plus and NR6A bottles are NT\$100 and NT\$67 respectively. Weighing the benefits and costs, we recommend substituting PEDS Plus bottles for NR6A bottles when culturing blood from neonatal patients or from those who are currently under antibiotic therapy.

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