Comparison of BACTEC Automated Blood Culture System and Conventional System in Hospitalized Pediatric Patients

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Abstract

A prospective study in pediatric patients compared the BACTEC system, an automated blood culture system using Bactec Ped Plus/F broth media, with the conventional system using Brain Heart Infusion broth media. Each single blood sample drawn for culture from hospitalized children was evaluated by both systems simultaneously. Of 244 pairs of blood samples, 44 (18%) were positive for microorganisms. Of these isolates, 24 (55%) were detected by both systems, 10 (23%) were detected by the BACTEC system only, and 10 (23%) were detected by the conventional system only. The mean turn around time of the BACTEC system (0.56±0.34, range 0.08-1.55 days) was significantly shorter than that of the conventional system (3.36± 2.72, range 1-7 days, $p<0.001$). Seven isolates strongly suspected to be due to contaminants grew out after 5 days of incubation and were detected by the conventional system only. In this study the BACTEC system and the conventional system were equally effective in detecting microorganisms in the patients' blood samples even if antibiotic therapy had been previously administered. However, the results from the BACTEC system were available much sooner and less likely to be contaminants.

Key word : Blood Culture, Automated System, Bacteremia

Blood culture is one of the most common microbiological tests performed in hospitalized patients. Decisions about therapy are based on the results of blood culture in many illnesses. Conventional blood culture systems have been in use for many decades and are laborious and slow, although they are inexpensive. Recently, automated blood culture systems have been developed to overcome those draw-backs. With the new systems, bacterial growth is continuously monitored. The monitoring

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systems are computerized and give an alarm signal on detection of any growth. The automated systems are convenient and timely, but are quite expensive especially for developing countries. The enriched broth with resin used in the new automated systems may also be better in promoting growth of organisms in patients' blood samples.

Our hospital has been using the BACTEC automated system with the fluorescent test system for detection of carbon dioxide production alongside the conventional system since early 1995. This study aimed to compare the two systems in terms of timeliness and sensitivity in detecting microorganism growth in blood samples from pediatric patients. The results may help determine the cost-benefit of the new system.

MATERIAL AND METHOD

This study was performed prospectively in pediatric patients in Siriraj Hospital, Bangkok, from January 1996 to June 1997. The study blood samples were collected from patients who had blood culture requested by attending physicians. Blood samples collected from each blood drawn were inoculated in equal amount (1-3 ml.) into 2 vials of the different blood culture mediums. One was the standard blood culture media used in the conventional blood culture system, and the other was Bactec Peds Plus/F,® for the BACTEC system. The order of inoculation to each vial was not specified i.e. by randomization. Each pair of blood culture vials were sent to the laboratory room at the same time. The results of growth and turn around time, i.e. interval between the time of blood drawn and the time of result availability, were recorded. The patients' history of prior antibiotic therapy, clinical presentations, diagnosis and the result of the initial complete blood count were also recorded for further analysis.

Conventional Blood Culture System

The conventional system is a manual blood culture system. The standard culture media used in the conventional system was Brain Heart Infusion broth with 0.1 per cent agar (Difco Co., Ltd., Detroit, Michigan, U.S.A.). The volume of broth in each vial was approximately 50 ml. The inoculated bottles were incubated at 35°C. The vials were inspected twice daily for evidence of bacterial growth e.g. turbidity, hemolysis or gas production, and if such evidence was found further gram stain or subculture was carried out for identification. Blind gram stain and subculture on the agar plate were routinely performed after 6-18 hours of incubation and at the end of 7 days if no growth of organism had been detected earlier. The vials were discarded after 7 days if no organism growth was detected in general cases and after 14 days in cases of suspected endocarditis. Any growth of organisms detected from the broth medium or the agar plate before the specimens were discarded was reported as positive.

BACTEC,® Automated System

The system used was the BACTEC 9240 (Becton Dickinson Diagnostic Instrument Systems, Sparkes, Maryland, U.S.A.). The inoculated blood culture vials were incubated at 35°C in an agitated automated incubator which is connected to the computerized system for continuous monitoring of the bacterial growth by carbon dioxide detection. The carbon dioxide produced by metabolism as the organisms reacts with a sensor dye at the bottom of the vials. The reaction modulates the amount of light that is absorbed by the fluorescent material in the sensor and is detected by photo detectors for fluorescence. A reading for carbon dioxide is made every 10 minutes. The positive culture vials are flagged by an indicator light in front of the incubator and also displayed in the monitor. If carbon dioxide production was not detected by 7 days, the specimens were blindly subcultured before being discarded.

The culture media used for the BACTEC system was Bactec Peds Plus/F,® (BPP)[1] (Becton Dickinson, Maryland, U.S.A.) which is an enriched soybean-casein digest broth containing nonionic absorbing resins and cationic exchange resins to help removal of any antibiotics in the blood samples. BPP also contains 0.06 per cent yeast extract and only 0.025 per cent sodium polyanethol sulfonate (SPS), less than the usual concentration of 0.035 per cent which is present in standard broth media. The volume of broth in each vial was approximately 40 ml.

Analysis of data

The turn around time required for each system was compared by the student *t*-test. The efficacy of organisms detection by each system was compared by the Mc Nemar's test especially among those patients who had received antibiotics prior to blood being drawn. The type of organism detected

by each system was also compared. All p values were two-tailed.

RESULTS

Two hundred and forty-four pairs of blood samples from 244 patients were collected from January 1996 to June 1997. Organism growth was detected in 44 (18%) of the blood samples. Of these, 24 (54%) were detected by both systems, 10 (23%) were detected by the BACTEC system only and 10 (23%) were detected by the conventional system only (Table 1). Of the samples with discordant results, 6 isolates were gram-positive cocci and 4 were gram-negative bacilli detected by BACTEC. This was not different from 7 gram-positive cocci and 3 gram-negative bacilli isolates detected by the conventional system. The most common organism which grew out in blood culture was coagulase-negative staphylococci (19/44, 43%). The mean turn around time for the BACTEC system (0.56± 0.34 days, range 0.08-1.55 days) was significantly shorter than that of the conventional system (3.36± 2.72 days, range 1-7 days) ($p<0.001$).

From review of the patients records, at least 7 out of 10 isolates which were identified in the conventional system only (5 coagulase-negative staphylococci and 2 nonfermentative gram-negative rods) were suspected to be contaminants. The presence of these bacteria did not fit the clinical pictures and subsequent cultures were negative without antibiotic treatment. The mean turn around time for these 7 blood samples was 6.6 days (range 5-7 days). If the 7 suspected contaminating isolates were excluded, BACTEC system would be significantly more sensitive than the conventional system at detecting bloodstream pathogens ($p=0.04$).

Medical records revealed that 153 (62.7%) blood samples had been collected from patients who were receiving antibiotic therapy and 30 (19.6%) of these samples had organism growth. The BACTEC and conventional systems were equally effective in detecting organism growth in blood samples of patients who had received antibiotic therapy (26/30 *vs* 25/30).

DISCUSSION

Blood culture is the most important microbiological test for bacteremia and fungemia. Most blood culture results influence therapeutic decisions. If microorganisms are not isolated, then antibiotic sensitivity tests to guide antibiotic choices of treatment cannot be carried out.

Many factors affect blood culture yield, such as the amount of the microorganism present in the blood stream (which could be <1-10 cfu/ml), the presence of antimicrobial agents in the blood, the volume of the blood sample drawn for culture, the ratio of the blood to broth media, the type of broth media, the length of incubation, and the incubation atmosphere. Children usually have a higher amount of microorganism due to their immature immune defense mechanism. However, they have a

Table 1. The pathogens detected from blood culture by each system.

Pathogens	Detected by both systems	Detected by BACTEC only	Detected by conventional only	Total (%)
Coagulase-negative staphylococci	9	4	6*	19 (43.2)
S.aureus	2	1	0	3 (6.8)
S.pneumoniae	1	1	0	2 (4.5)
Viridans streptococci	2	0	0	2 (4.5)
Beta hemolytic streptococci	0	0	1	1 (2.3)
Salmonella species	1	2	0	3 (6.8)
K.pneumoniae	1	1	0	2 (4.5)
E.cloacae	1	0	0	1 (2.3)
E.coli	2	0	1	3 (6.8)
Nonfermentative gram-negative rods	0	0	2*	2 (4.5)
P.aerugenosa	2	0	0	2 (4.5)
Candida species	3	1	0	4 (9)
Total	24 (54%)	10 (23%)	10 (23%)	44 (100%)

*7 isolates (5 coagulase-negative staphylococci and 2 nonfermentative gram-negative rods) were probably contamination.

higher chance of receiving antibiotic therapy at the time the blood is drawn. In the present study more than 60 per cent of blood samples were collected while the patients were on antibiotic therapy. Culture medium containing an antibiotic removal device is therefore helpful for pediatric patients. Resin is an antibiotic removal device which has been shown to improve the culture yield[2]. In this study, however, BPP did not detect more cases of bacteremia than conventional medium among patients who were receiving antibiotics. Many substances contained in blood such as complement, lysozyme, and white blood cells may also inhibit organism growth *in vitro*. Therefore, the use of an appropriate amount of blood and the dilution of the blood in the broth media are crucial for the best yield [3-5]. In general, dilution between 1:5 to 1:20 is acceptable. In this study the volume of BPP was less than the volume of standard conventional media. Consequently, the ratio of blood to broth in the ACTEC system was somewhat more than the conventional system. We did not see any effect on organism growth with difference in dilution in this range.

A further difference between conventional broth and BPP was the concentration of sodium polyanethol sulfonate (SPS). SPS has anticomplementary, antiphagocytic activity and inactivates some antibiotics but may inhibit growth of some fastidious bacteria such as *Neisseria* species[2,6,7]. BPP contains less SPS than conventional broth, and therefore, may give a better yield for *Neisseria*. However, it may not support the growth of *Enterobacteriaceae* well due to the greater availability of complement[8]. Such an effect was not significant enough to be seen in this study.

The conventional manual system and the media which has been used for decades are still very useful, cheap and flexible, although the methodology is laborious and slow. Inspection for evidence of organism growth is insensitive and requires skill. Many new systems have been invented to overcome such problems. The principle of automated systems is to detect microorganism growth as soon as possible, by continuous monitoring, with few or no manual steps to minimize skill dependency and work load. All new commercial automated systems are similar in many features such as self-contained modular incubation, agitation, computerized detection unit, and all monitor growth continuously. The main difference among these systems is the method of microorganism growth detection. For example, the BACTEC used in this study detects carbon dioxide production from organism growth by using a fluorescent sensor while the BacT/Alert detects the pH change from carbon dioxide production by using a colorimeter. The ESP system detects change in pressure due to gas production from organism growth. The new systems are comparable in terms of performance and are better than the conventional manual system[9-11]. The major drawback of these automated systems has been the cost, especially for developing countries where the conventional system is much cheaper to use. However, the cost of the new system may be worthwhile if it brings a better outcome for the patients due to more sensitive and timelier blood culture results.

Our hospital has been using the BACTEC with BPP system since 1995 for those patients who can afford the cost. This study has shown that the BACTEC performed as well as the conventional system in detecting organisms and provided results two days faster. All the results by the BACTEC were reported within 3 days. This could affect the decision and outcome of the treatment. Moreover, knowing that all positive cultures will show up in 3 days, antibiotics could be discontinued after 3 days of no growth instead of 7 days by the conventional system. The cost saving from this application is enormous particularly if expensive antibiotics are used.

Blood culture from each patient in this study was done only once. In general, one blood culture should be able to detect more than 91 per cent of bacteremia[12]. Generally, only one blood sampling is acceptable for pediatric patients. In this study, almost half of the positive results were reported by one system only. Many of these isolates could be contaminants especially the ones that grew out slowly[13]. All the suspected contamination determined by clinical data in this study grew out after 5 days of incubation and were isolated by the conventional system only. The slow growth isolates were not seen with the BACTEC system. However, some rapid growth isolates could also be contaminants but were not seen in this study. The conventional system was at greater risk of getting contamination during the procedure of blind subculture which was not done in the BACTEC system. Blind subculture was considered an indispensable step when detection of organism by direct inspection could be insensitive. The BACTEC system may also be less sensitive in detecting contaminants. It has

been shown that no one medium or system is capable of detecting all microorganisms. The BACTEC with BPP may not be able to detect some true pathogens detected by the conventional system or vice versa. However, when the suspected contaminating isolates were excluded, the likelihood of detecting pathogens in the BACTEC system was much higher than in the conventional system.

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การเปรียบเทียบระหว่างระบบแบคเท็คและระบบดั้งเดิมในการเพาะเชื้อจากเลือดในผู้ป่วยเด็ก

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รายงานนี้เป็นการศึกษาเปรียบเทียบแบบไปข้างหน้าระหว่างระบบที่ใช้ในการเพาะเชื้อจากเลือดแบบ BACTEC กับแบบดั้งเดิมในผู้ป่วยเด็กที่พักรักษาตัวในโรงพยาบาล โดยในการเจาะเลือดแต่ละครั้งจะแบ่งใส่ลงในขวดน้ำยา BACTEC Peds Plus/F ซึ่งใช้กับระบบ BACTEC และขวดน้ำยา Bain Heart Infusion ซึ่งใช้กับระบบดั้งเดิมในปริมาณเท่า ๆ กัน ขวดน้ำยาที่ใส่ตัวอย่างเลือดทั้งสองจะนำมาอบเพาะเชื้อพร้อม ๆ กัน พบว่าจากตัวอย่างเลือด 244 ตัวอย่าง มีจำนวน 44 (18%) ตัวอย่างที่พบเชื้อขึ้น โดย 24 ตัวอย่างพบเชื้อขึ้นจากทั้งสองระบบ 10 ตัวอย่างพบเชื้อขึ้นจากระบบ BACTEC เท่านั้น และอีก 10 ตัวอย่างพบเชื้อขึ้นจากระบบดั้งเดิมเท่านั้น ระยะเวลาที่ใช้ในการเพาะเชื้อจนกระทั่งได้ผลรายงานจากระบบ BACTEC ใช้เวลาเฉลี่ย 0.56 $\pm$ 0.34 วัน (ตั้งแต่ 0.08–1.55 วัน) ซึ่งสั้นกว่าระบบดั้งเดิม ซึ่งใช้เวลาเฉลี่ย 3.36 $\pm$ 2.72 วัน (ตั้งแต่ 1–7 วัน) อย่างมีนัยสำคัญ ($p < 0.001$) ในจำนวนนี้มี 7 ตัวอย่างที่น่าจะเป็นเชื้อปนเปื้อน ซึ่งเชื้อขึ้นหลังจากอบเชื้อไปแล้ว 5 วันและขึ้นโดยระบบดั้งเดิมเท่านั้น จากการศึกษานี้พบว่า ระบบ BACTEC มีประสิทธิภาพเท่าเทียมกับระบบดั้งเดิมในการเพาะเชื้อจากกระแสเลือดในผู้ป่วยเด็ก ทั้งที่ได้รับและไม่ได้รับยาปฏิชีวนะมาก่อน แต่ใช้เวลาสั้นกว่ามากและเชื้อที่เพาะขึ้นจากระบบ BACTEC มีโอกาสจะเป็นเชื้อชนิดปนเปื้อนน้อยกว่า

คำสำคัญ : การเพาะเชื้อจากเลือด, ระบบอัตโนมัติ, การติดเชื้อในกระแสเลือด

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