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AN EVALUATION OF THE BD BACTEC™ FX AUTOMATED BLOOD CULTURE SYSTEM IN PRETORIA, SOUTH AFRICA

Microbiology

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ABSTRACT

The high mortality associated with blood stream infections (BSI) calls for improved and timely diagnosis. This will ensure early initiation of appropriate antimicrobial agents as advocated by several international bodies including the surviving sepsis campaign. Blood culture remains the most important diagnostic method for detection of BSI. The study sought to evaluate a new automated blood culture monitoring system from BD (BD BACTEC™ FX). Twenty commonly isolated microorganisms including fungi and anaerobes were inoculated into blood culture bottles containing 10mls of sheep blood. Both the BD BACTEC™ FX and BacT/Alert™ systems were loaded with their respective blood culture bottles for comparison. The BD BACTEC™ FX system generally shows earlier time to detection of microbial growth than the BacT/ALERT™ system. Time to positivity was clearly defined with the BD BACTEC™ FX system. The BD BACTEC™ FX instrument was found to be as user friendly as the current BacT/ALERT™ system. Although the workflow was more efficient with the BD BACTEC™ FX instrument. The shorter time to positivity may improve patient morbidity and mortality as it may facilitate early initiation of appropriate antimicrobial agent. This ability to influence patient care by the BD BACTEC™ FX means that it may be the better of the two systems. However, a larger study utilizing clinical specimen is required to confirm this.

KEYWORDS

Continuous blood culture monitoring instrument, bloodstream infections, evaluation of blood culture instrument, BacT/ALERT, BD BACTEC FX, verification, validation

INTRODUCTION:

There has recently been an increase in the incidence of infectious disease, particularly bacteremia with multidrug resistance organisms. Worldwide, the mortality associated with nosocomial blood stream infection (BSI) remains high and varies from 30 to 55 % [1-2]. Blood cultures remain the most important diagnostic tool for the detection of BSI. The surviving sepsis campaign guidelines advocate for early initiation of antimicrobial agents to improve survival [3].

Other studies have also found that early initiation of appropriate antimicrobial agents based on *in vitro* susceptibility decrease morbidity and mortality [4]. The manual blood culture is cumbersome and does not lead to improved turn-around times [5]. The automated system provides continuous monitoring of bottles (every 10-25 min), so microbial growth is detected more rapidly [5].

The BacT/Alert™ system is based on the colorimetric detection of carbon dioxide (CO_2) concentrations by means of a sensor internally attached to the bottom of each blood-culture bottle. A membrane permeable only to CO_2 separates the sensor from the fluid contents of the bottle. Microbial growth results in CO_2 concentration increase in the medium which diffuses to the sensor; causing acidification and change in color of the sensor from green to yellow.

The BACTEC™ 9000 series systems detect CO_2 production with fluorescent sensors attached to the bottom of each bottle instead of a colorimetric sensor used in the BacT/Alert™ system. Flayhart and colleagues [6] demonstrated that BACTEC™ system was superior to the BacT/Alert™ system in recovering gram-positive and gram-negative bacterial pathogens in the presence of β-lactam antibiotics, gentamicin/penicillin, and vancomycin. This is an important factor given the high level of antimicrobial use in most centers [4].

The BD (Becton Dickinson) BACTEC™ FX builds on the proven superior fluorescence detection technology, exceptional media performance and instrument reliability of the BD BACTEC™ 9000 blood culture systems [7]. The principle of the test is fluorescence. When microorganisms are present in the cultured vials, they metabolize nutrients in the culture medium, releasing CO_2 into the medium. A dye in the sensor at the bottom of the culture bottles will react with CO_2. This modulates the amount of light that is absorbed by a fluorescent material in the sensor. The instrument's photo detectors measure the level of fluorescence, which corresponds to the amount of CO_2 released by the organisms. Then the measurement is interpreted by the system according to preprogramed positivity algorithms.

Added benefits include the most efficient workflow for reduced hands-on time, compactness which allows efficient laboratory space utilization [7].

Cutting-edge data management with enhanced blood culture observation in and out of the laboratory for reduced workflow interruptions and optimized communication of preliminary or final results to caregivers are additional benefits [7]. The aim of this study was to evaluate a new automated blood culture monitoring system from BD (BD BACTEC™ FX).

METHODS:

The following ATCC control strains were used: *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumonia, Streptococcus viridans ,Enterococcus faecalis, Streptococcus pyogenes, Streptococcus agalactiae, Corynebacterium spp., Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Salmonella spp., Pseudomonas aeruginosa, Acinetobacter baumannii, Haemophilus influenzae, Candida albicans, Candida glabrata, Cryptococcus neoformans, Peptostreptococcus anaerobius, Bacteroides fragilis.*

To simulate patient conditions and to support the growth of fastidious bacteria 10ml of sheep blood was inoculated into adult blood culture bottles (aerobic and anaerobic) and 2ml in paediatric bottles. The numbers of organisms placed in each bottle approximated those found in cases of septicaemia. Serial dilutions of the organisms were prepared to achieve approximately 5 to 30 colony forming unit (CFU) per bottle. Colonies of each test strain were inoculated into separate tubes containing sterile saline to achieve a 1 McFarland Standard (equivalent to ~3 x 10^8 CFU/ml). The Vitek densitometer was used to prepare a suspension with the correct turbidity. From 1 McFarland

suspensions, dilution series were prepared and individually calculated volumes of the appropriate dilution of each strain were added to sheep blood to produce final concentrations of 100 and 10 CFU/mL in blood. Each test (BACTEC™ FX) and reference (BacT/ALERT™) blood culture vial (inoculated with 10ml sheep blood for adults and 2ml for paediatrics) were inoculated with 0.1ml of the final dilution of each test organism. To determine the CFU count, 0.1ml of the final dilution was inoculated onto the agar medium appropriate for each organism, using the spread plate technique. *Haemophilus influenzae* was inoculated onto a chocolate agar plate, *Streptococcus pneumoniae* onto a blood agar plate and *Peptostreptococcu*s and *Bacteroides* onto blood agar plates and immediately into an anaerobic jar. Uninoculated sterility control vials, vials with added sheep blood and no organism of both the test (BACTEC™ FX) and reference (BacT/ALERT™) blood culture vials were included. Processing of isolates was performed on different days.

RESULTS:

The time to growth detection was recorded for both systems. Time to positivity of BacT/ALERT™ and BD BACTEC™ FX blood culture monitoring instruments is demonstrated in table 1. The BD BACTEC™ FX system generally shows earlier time to detection of microbial growth than the BacT/ALERT™ system. The BD BACTEC™ FX system detected 95% of the microorganisms. According to Clinical Laboratory Improvement Amendments (CLIA), sensitivity and specificity are not applicable for validation/verification of blood culture systems [8]. The detection of growth and the time to positivity are used as variables for performance measurement, and the BD BACTEC™ FX system performed better than the BacT/ALERT™ system. They are also used as determinants for reproducibility with both systems identifying similar organisms, albeit at differing times.

Table 1. Comparison of the time to detection of microbial growth with different inoculums.

Microorganisms	Inoculum (CFU/ml)	Time to detection (hours) BD BACTEC™ FX	Time to detection (hours) BacT/ALERT™
Gram positives	10	8-76	10->120
	100	3-23	5-23
Gram negatives	10	5-13	7-24
	100	2-13	4-17
Anaerobes	10	89->120	24->120
	100	10->120	14->120
Yeasts	10	11-18	14-72
	100	8-36	10-44

User friendliness and efficiency

Six laboratory personnel working with both systems were given questionnaires to assess software, maintenance and workflow efficiencies. The BD BACTEC™ FX instrument was found to be as user friendly as the current BacT/ALERT™ system. Although the BD BACTEC™ FX requires that the vial's barcode be scanned when the vial is removed from the instrument, this was found not to be a problem by the laboratory personnel. It was found to assist in preventing removal of vials that have not flagged positive as sometimes happens with BacT/ALERT™ which does not require scanning of the vial's barcode. Table 2 demonstrates software, maintenance and workflow efficiencies of both systems. The BD BACTEC™ FX system was found to be comparable to the BacT/ALERT™ system as far as the maintenance and user friendliness was concern. The workflow was slightly more efficient with BD BACTEC™ FX system, although this was not statistically significant. The system also give interpretation of whether there is actual growth or not (positive or negative) which make it easy for even a less-trained person to know what instrument flag means. Furthermore, the system gives the exact time to positivity which may be useful in the diagnosis of catheter associated blood stream infection (CABSI)/central line associated blood stream infection (CLABSI). Figures 1 and 2 are the result screen shots of BD BACTEC™ FX and BacT/ALERT™ systems respectively.

Table 2. Software, maintenance and workflow efficiency assessment (Average scores).

	Bactec FX	BacT/Alert
1.Work flow efficiency		
1.1 reduced hands on time	3.3	3
1.2 ease of operation	3.3	2.6
1.2 ease of accessing data	3.5	2
1.2 ease of visualizing the status of the machine	3.6	3
2. Maintenance		
2.1 Ease of maintenance	3	3.3
3.Software		
3.1 User friendliness	3.3	3.3
3.2 Ease of troubleshooting errors	3.5	3

Scores 1-4 (Poor – Excellent)

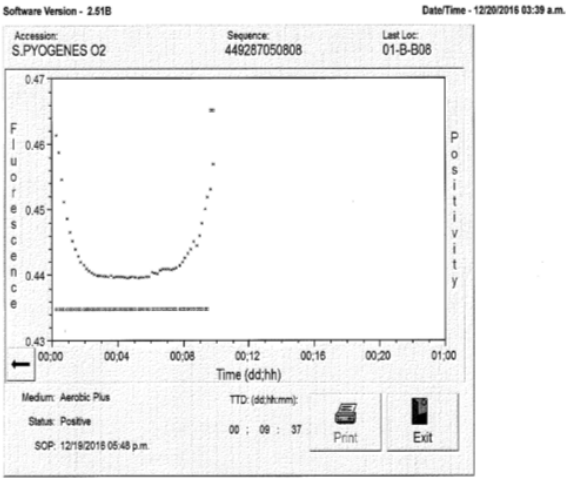

Figure 1. BD BACTEC™ FX results interface.

In addition to the graphical demonstration of *S. pyogenes* growth, the system also shows status as positive and time to detection (TTD) as 9 hours and 37 minutes.

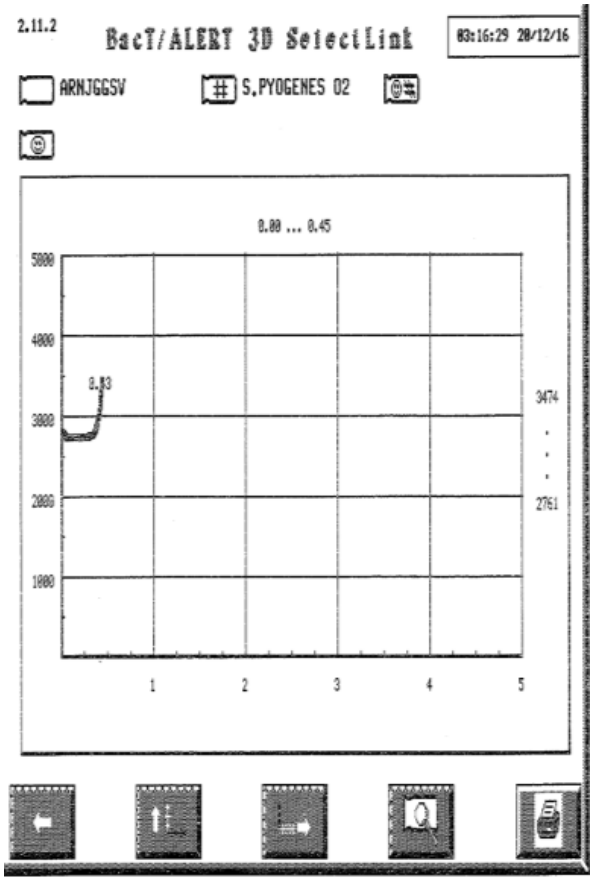

Figure 2. BacT/ALERT™ results interface

The time is represented in days on the X-axis. The time to detection of *S. pyogenes* growth requires the operator to estimate and the system transmits TTD to the laboratory information system in fixed hours.

DISCUSSION:

The study demonstrated that BD BACTEC™ FX blood culture monitoring system detect microbial growth generally earlier than the BacT/ALERT™ blood culture monitoring system. This is on average two hours earlier time to positivity. This early time to positivity may improve patient morbidity and mortality as it may facilitate early initiation of appropriate antimicrobial agent. Rosa and Goldani found that each increase of 1 hour in the time to antibiotic administration raised the risk of mortality within 28 days by 18% [9]. Multivariate analysis found delayed treatment to be an independent predictor of infection-related mortality (odds ratio, 3.8; 95% confidence interval, 1.3–11.0; P = .01) and associated with a longer hospital stay than early treatment (20.2 days versus 14.3 days; P = .05). These findings support the notion that delay of therapy has deleterious effects on clinical outcomes, and efforts should be made to ensure that appropriate therapy is initiated promptly [10].

Although BD BACTEC™ FX system detected anaerobic bacterial growth on average 48 hours later than the BacT/ALERT™ system, the significant of this is not clear. No *Peptostreptococcus anaerobius* growth was detected by the BD BACTEC™ FX system, while BacT/ALERT™ system detected growth. This could not be explained by the concentration of sodium polyanethol sulfonate (SPS) which is known to inhibit growth of certain microorganisms such as *P. anaerobius*. The BD BACTEC™ broth contains SPS concentration of 0.035% w/v while BacT/ALERT™ broth contains concentration of 0.05% w/v.

Lytic agents like saponin, release phagocytised organisms present in clinical specimens [11]. The significance of saponin in BD BACTEC™ broth needs clinical samples to assess appropriately.

CONCLUSION:

The BD BACTEC™ FX has demonstrated the ability to detect microbial growth in blood specimens. Its shorter time to positive identification of commonly isolated microorganisms suggests that it can positively influence patient care. The system was also found to give reproducible results compare to BacT/ALERT™ system. A larger study with clinical samples is required to determined which of the two instruments better influence patient care.

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