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(RESEARCH ARTICLE)

A novel Colorcult hemoculture in early diagnosis of blood stream infection: A boon in meagre resources

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Abstract

Blood stream infections (BSIs) account for major cause of morbidity and mortality. Conventional hemoculture methods are time consuming, with poor sensitivity and high risk of contamination. Automated blood culture systems are highly sensitive but are overpriced. Hence, it is not suitable for resource poor settings. In this background, this study was done to analyze the sensitivity of novel non automated chemical sensor-based blood culture and to compare the time to detection of both conventional and colorimetric method of blood culture. Blood specimens were collected from 50 study participants, admitted with suspected sepsis, inoculated into the colorcult & conventional culture media and processed as per CLSI guidelines. Culture positive by both conventional and colorcult method was six (12%). Most of the study isolates were Gram negative bacteria (83.4%). The isolates were detected at the earliest within 96 hours by colorcult, whereas by conventional method only three (50 %) were detected within 96 hours and another three (50%) after seven days only. Owing to the escalation in BSIs associated morbidity and mortality, early diagnosis by a simple, cost effective, highly sensitive and specific method is an absolute necessity in resource poor settings. The performance of colorcult is superior to conventional method but cost effective than automated methods and can be used as an alternative method in the diagnosis of BSIs.

Keywords: Colorcult; Hemoculture; Bloodstream infections; Blood stream

1. Introduction

Blood stream infections (BSIs) account for major cause of morbidity and mortality. The incidence of BSIs has been estimated around 48.9 million with the mortality of 11 million which contributes to almost 20% of all global deaths [1]. Changing epidemiology, non-standardized antibiotic guidelines and paucity of rapid diagnostic facilities are the prime determinants leading to mortality in patients with BSIs. Every hour of delay in the diagnosis decreases the survival rate by 8 % [2,3]. Hence prompt treatment initiation hinges upon rapid diagnosis and possible targeted antimicrobial therapy. Last few decades had dramatic improvements in the diagnosis of BSIs by various biomarkers, yet blood culture remains the gold standard method [4]. Conventional blood cultures are time consuming, poor sensitivity and high risk of contamination. Automated blood culture systems are highly sensitive but are overpriced. Hence, it is not suitable for resource poor settings.

In this background, this study was done to analyze the sensitivity of novel non automated chemical sensor-based blood culture and to compare the time to detection of both conventional and colorimetric method of blood culture.

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2. Materials and methods

A total of 50 blood samples were collected from patients admitted in tertiary care teaching hospital with clinical signs and symptoms suggestive of sepsis. Written informed consent was obtained. Institutional ethics committee clearance was obtained before starting the study. Blood sample was collected under aseptic precaution before the initiation of antibiotics. If they were already on antibiotics, sample was collected prior to the next dose of antibiotics. 10 ml of blood was inoculated into the colorcult (non automated chemical detector-based culture vial with sodium polyanethol sulphate & resins) and conventional culture media using BHI (Brain Heart Infusion) broth, incubated at 37ºC for 14 days.

Subcultures were made into nutrient agar, mac Conkey agar and blood agar after 24 hours. Repeat subcultures were done after seven days. Identification was done by standard microbiological techniques and antibiotic sensitivity was done as per CLSI guidelines. The colorcult bottles were observed for changes in the colour of chemical sensor. The chemical sensor present at the bottom of the bottle changes the color if growth is present, from light blue or green to bright yellow.

2.1. Inclusion criteria

All clinically suspected cases of BSIs

2.2. Exclusion criteria

Neonatal sepsis

3. Results

Of the 50 patients, 20 (40%) were female and 30 (60%) were male. Among them, 23(46%) had no prior antibiotic treatment. Culture positive by both conventional and colorcult method was six (12%) (Table 1). Of these, four (8%) had prior antibiotic treatment. Organisms isolated were *Acinetobacter baumanii* was 16.7%, *Klebsiella* Spp is 50%, Methicillin Sensitive *Staphylococcus aureus* was 16.7%, *Pseudomonas aeruginosa* was 16.7%. All the isolates were detected at the earliest within 96 hours by colorcult, whereas by conventional method only three (50 %) were detected within 96 hours and another three (50%) after seven days only. *Staphylococcus* was sensitive to cefoxitin, linezolid, erythromycin, clindamycin, gentamicin, tetracycline, cotrimoxazole, vancomycin and resistant to penicillin. *Pseudomonas aeruginosa* was sensitive to amikacin, gentamicin, cetazidime, meropenem, piperacillin tazobatum. *Acinetobacter baumanii* was resistant to amikacin, gentamicin, cetazidime, meropenem, piperacillin tazobatum. *Klebsiella* was sensitive to amikacin, gentamicin, ceftazidime, ceftriaxone, cefotaxime, ceftazidime clavulanic acid, meropenem, ciprofloxacin, co trimoxazole and resistant to amoxicillin.

Table 1 Distribution of blood culture positive among study population

Age	Male	Female	Culture positive Number (%)	TTP Colorcult (Mean±SD) (Hours)	TTP Conventional (Mean±SD) (Hours)
<20 years	NIL	NIL	NIL	NIL	NIL
21-40 years	06	4	NIL	NIL	NIL
41-60 years	11	15	4	72±19.5	90±53.3
61-80 years	13	1	2	36±16.9	36±16.9
Total	30	20	6(12)		

*TTP-time to positivit

4. Discussion

BSIs are challenging, difficult to treat and life-threatening public health problem. Rapid, prompt and correct diagnoses are the key elements in the management and outcome of these BSIs. Blood culture abides as the critical and gold standard method in the diagnosis of BSIs, even with many limitations. The sensitivity of blood culture has been reported to be 35-90% [5].

Limitations of blood culture include timing of sample collection, antiseptic used for skin disinfection, site of sample collection, volume and number of blood samples collected. The most suitable time for blood collection is important in making the diagnosis. Different studies suggested that blood should be collected before starting of the antimicrobials, at peak of fever, and atleast 30-60 min interval between each samples[6].

Punctilious skin preparation is utmost important to minimize the contamination rate. Alcoholic solutions are effective than non alcoholic solutions for skin preparation [6]. Contamination rate ranges from 3.4-13% when sample is collected through intravenous catheter whereas, sampling through new peripheral venipuncture produces 1.2 - 7.3% [7]. Hence, current guidelines advocated simultaneous collection of samples from both sites especially for the diagnosis of suspected central line associated BSIs (CLABSI). Blood which is drawn from the central line grows at least two hours earlier than the blood sample collected from the peripheral venipuncture. Yet, improper blood collection is associated certainly with over diagnosis of CLABSI [8].

Since the microbial density is very low in most of the patients with BSIs, the volume of blood collected for culture plays a major role in the diagnosis. It has been reported that the average bacterial concentration is less than one colony forming unit (CFU)/ ml [9]. The sensitivity was found to be 95% when 3CFU's are sampled, which indicates that at least 30 ml of blood should be cultured [10].

The solitary blood culture practice still prevails. Current guidelines approved at least 2-3 sets of blood culture with sufficient volume should be done in order to improve the sensitivity [8]. Limitation of multisampling strategy is it creates an additional opportunity for contamination. Conventional methods not only take a longer time for the detection of these infections, but are also labor intensive.

Bac T/ALERT 3D automated method detects earlier and studies recorded time to detection (TTD) by this method was 15.83 hours, but reported more contaminants compared to conventional method [11]. Major causes of false positive instrument signals include samples with leukocytosis, over - filled bottles and temperature fluctuation during incubation. [12]. False negative signals are due to pre incubation temperature and duration, type of microbe, pairing instrument and type of bottle used [4]. Samples are usually incubated for 5-7 days. It may remain negative on day 5, require prolonged incubation to 15 days or more especially when infective endocarditis is suspected [13].

Novel non automated sensor-based blood culture methods have been developed for predicting BSIs. Biosensors are analytical devices which convert biological signals into directly measurable signals using various sensing methods such as electric, electrochemical, mechanical and optical methods which have increased specificity and shorter detection time [14]

In this study, colorimetric sensing system (colorcult) was used for bacterial detection owing to their simple onsite operation. Colorcult culture media contains many proteins and other nutrients which supports the growth of micro-organisms present in the blood. A polyanionic anticoagulant SPS, deactivates many antibiotics, and also interferes with the complements, lyzozymes, and phagocytes in the clinical specimen. It has shown multiple advantages over conventional method such as rapid signal readout and naked eye that requires no external instrument or detector, cost effectiveness, portability and increased sensitivity [14].

CO_2 is produced by the growth of microorganisms, which can be detected by the chemical sensor present in the bottom of the vial. The color change is proportional to the amount of CO_2 produced by the organisms. A change in light blue or green to bright yellow color denotes positive culture report. Resins present in the vials improvise isolation of organisms from the specimens without further processing.

In this study, the incidence of BSIs based on positive blood culture among suspected cases of sepsis was 12%. Similar rate (13%) was reported by Pandey et al [15].

The colorcult method in this study detects all the isolates (100%) within 96 hours, whereas conventional method detects only 50% of isolates in 96 hours. Hence, the performance of colorcult is superior to conventional method but cost effective than automated methods.

Comparison between colorcult and automated methods was not done which is a limitation of this study. Gram negative bacilli (82%) were the commonest organisms isolated in this study, wherein *Klebsiella* species was the predominant isolate. Various studies also reported a similar predominance of *Klebsiella* isolates [16]. Gram negative bacteremia is of great concern because of their association with multidrug resistance.

In developing countries like India, there is increased incidence of BSIs because of changing epidemiology, lack of strict antibiotic stewardship program, emergence of multi drug resistant organisms and scarcity of good diagnostic facilities especially in constrained setting such as primary health care facilities and small laboratories.

Limitations

- Sample size is small
- Automated method is not included to assess its efficacy
- Detection of slow growers and anaerobes are snot evaluated

5. Conclusion

Owing to the escalation in BSIs associated morbidity and mortality, early diagnosis by a simple, cost effective, highly sensitive and specific method is an absolute necessity in resource poor settings. The performance of colorcult is superior to conventional method but cost effective than automated methods and can be used as an alternative method in the diagnosis of BSIs.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

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Authors short biography

Dr. Poongodi Santhana kumarasamy, MD (Microbiology), Professor of Microbiology, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India has more than 20 publications in various national & international journals. She is a life time member of IAMM & ACM. She has guided three STS projects under ICMR. She has done three funded projects under Tamil Nadu state research committee. She is a guide for DM (Virology) and MD (Microbiology) students.