Usefulness of routine pairing of anaerobic with aerobic blood culture bottles and decision making on antimicrobial therapy

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Abstract

Objectives: To evaluate the growth concordance in paired aerobic/anaerobic bottles, and the impact of the anaerobic growth on patients' antimicrobial management.

Method: This is a prospective multicenter study which was conducted in three hospitals, with total beds of 750 beds and 52 ICU beds. Prospectively, laboratory blood cultures logbooks were daily reviewed and patients from whom blood cultures were ordered were followed, their charts were reviewed. Entries on antimicrobial therapeutic changes were noted for all paired bottles. Clinicians were blinded to the study, though they were informed about culture results via the usual work protocol in each hospital.

Results: Collected Blood culture bottles totaled 2492; 172 single bottle were excluded, and 1160 paired bottles were analyzed,1046 were concordant; 79 paired bottles had bacterial growth and 967 paired bottles had no bacterial growth. 114 paired bottles were discordant; growth in 97 aerobic bottles, 13 in anaerobic, and 4 in both bottles. The proportion of agreement for the concordant paired growth bottles was 90.2%. The composite proportion of agreement for bottles with any growth (N = 193, composite proportion of agreement = 56%, 95% C.I., 34% - 48%). Cohen kappa composite agreement, measured for the total analyzed paired bottles (N = 1160, **K**= .52, SE = .038. 95% C.I., .447 - .595). The odds of modifying antimicrobial regimen were for total and subgroups intent to treat odds, based on paired bottles showed that one modification took place in one anaerobic growth bottle (N = 1160, Odds = 0.0008), the odds for all

bottles with any growth (N = 193, odds = .005), and based on any anaerobic bottles (79 concordant, 13 anaerobic, and 4 discordant) with bacterial growth (N = 96: odds = 0.010).

Conclusion: The study demonstrates that the proportion of agreement among paired bottles were high, and needless to include anaerobic bottles in routine blood culture collection. Also the decision-making of anti-infective treatment on patients based on anaerobic blood culture growth was not evident.

Keyword: Aerobic –anaerobic culture, Antimicrobial trearment

Introduction

Until now, using blood culture for the evaluation of febrile patients suspected of having sepsis is an important helpful tool used in laboratory medicine [1]. It remains the standard of care for the diagnosis of blood stream infections, though several other short turnaround time tests were developed with the same objectives. Some tests identify gram-positive and gram-negative bacteria as well as fungi in separate lots like Gene Xpert MRSA/SA, Verigene gram-positive blood culture (BC-GP), Verigene gram-negative blood culture (BC-GN), and T2 Candida, while other tests detect the clinically important microorganisms; gram-positive and gram-negative lumped together as in Quick FISH test. Other nucleic acid-based methods for the detection of bacterial pathogens are also utilized [2, 3]. Recent developments could identify microorganism directly from growing blood culture bottles, or directly from a drawn blood specimen, like MALDI-TOF, PNA-FISH, Film Array blood culture identification and Light Cycler Septi Fast. However, these tests are labor intensive, need infrastructure, trained personnel and costly [2, 4, 5, 6].

Pending widely available new methodologies, current routine blood cultures bottles will remain the standard of care in clinical laboratories. Blood cultures are routinely ordered in paired bottles i.e. aerobic and anaerobic bottles. Though some earlier studies questioned the value of routine pairing of anaerobic bottles with the aerobic ones, claiming that no added information gained from this combination,in few cases of anaerobic syndromes, growth was clinically suspected without utilizing the anaerobic bottles, with their ensuing cost, extra blood volume, and higher risk of contamination [7], a study examined pairing of two aerobic bottles and found 6 % added microbiological diagnosis [8]. While other studies addressed the importance of routinely employing anaerobic blood culture bottles and its outcome on antimicrobial treatment [9], especially when used in some risk groups; for that some clinically important microorganisms may only grow anaerobically [10].

Our aim is to evaluate if a growth in an anaerobic bottle would have an impact on patients' antimicrobials regimen, and growth concordance in paired blood culture agents. The information gained from this study may explain why we need to reevaluate the routine use of anaerobic bottles, thus avoiding added cost, extra blood volume collected,

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higher chance of blood culture contamination, and procedure complexity.

Materials and Methods

This is a prospective multicenter observational study; it started in early January 2015 till the end April 2015.The study was held in Amman, Jordan, it was conducted in three hospitals; two teaching; the Specialty and Jordan hospitals, and one community service hospital; Al Khalidi Medical Center, with total beds of 750 beds and 52 ICU beds. The internal review boards in the two teaching hospitals and the medical administrator of the community hospital approved the study.

Study teams included a microbiologist, clinical pharmacist and medical residents. Prospectively, laboratory blood cultures log books were daily reviewed. Patients from whom blood cultures were ordered were followed up by members of the study team (medical residents and clinical pharmacists), and their in-patient chart were reviewed. Entries on whether clinicians have had made antimicrobial therapeutic decisions based on the anaerobic blood culture bottles were noted, microorganism grown from concordant and discordant bottles were considered. Clinicians were informed about culture results through the usual work protocol in each hospital. During the conduct of the study, only the study teams were aware of the microbiological and clinical data collection, and the treating physicians were blinded to the ongoing study.

Study Conduct

Microbiologists ensured daily monitoring of all processed in-patients blood cultures. Blood volume sampled from patients was 5 ml per each blood culture bottle for adults and 2 ml for pediatric bottles in the Specialty and Al Khalidi hospitals (BD BACTEC 9120), and 0.1 ml blood for pediatric and 0.5 ml blood for adults in Jordan hospital

(Versa trek).Growth in any bottle is considered a panic value and the attending physician(s) are informed. Paired aerobic/anaerobic bottles results were verified for analysis. Results on paired blood cultures bottles with or without microorganisms' growth were collected and communicated to the clinical study teams. The clinical teams review patients' charts from which blood cultures were collected; monitor the results of blood culture paired bottles, screen patients' charts and record data on whether the attending physician decided to make changes on anti-infective agents based on information provided by the anaerobic blood culture bottles. Uninformed changes on anti-infective therapy by the attending or medical staff for concordant or discordant blood cultures bottles were not considered clinical decision-making.

Outcome Measure:

The main outcome measure is to evaluate if a growth in an anaerobic bottle would have an impact on patients' antimicrobials regimen, and growth concordance in paired blood culture bottles. The information gained from this study may explain why we need to reevaluate the routine use of anaerobic bottles, thus avoiding added cost, extra blood volume collected, higher chance of blood culture contamination, and procedure complexity.

Inclusion and Exclusion Criteria

All paired blood culture bottles were included; for all age groups, both genders, all stages of sepsis or suspected septic patients, that required blood cultures as judged by the attending clinician, and the corresponding patients require antimicrobial therapy. Also included, paired blood cultures (aerobic and anaerobic bottles), whether there was growth in both bottles or no growth (concordant), and single bottle growth or dual growth of different microorganisms in both bottles (discordant). Bottles from the automated blood culture machines were considered for the study if

they were processed by: BD BACTEC 9120 (Becton, Dickinson and company Franklin Lakes, NJ, USA)in Al Khalidi and the Specialty hospitals and Versa trek (Part of Thermo Fisher Scientific, 1 Thermo Fisher Way, Oakwood Village, OH 44146, USA) in Jordan hospital. Excluded from analysis were all single blood culture bottles.

Statistical analysis

Total numbers of blood cultures bottles; paired, concordant and discordant growth bottles were considered for analysis. Single blood culture bottles were excluded. The inter-rater agreement of bacterial growth/no growth for aerobic versus anaerobic culture bottles were calculated by Cohen kappa (**K**). Absolute counts and odds were calculated for different denominators to reveal the impact of anaerobic growth in paired bottles on modifying the antimicrobial therapy. Proportion were calculated for the agreement of the paired growth bottles; same bacteria grew in both bottles or no growth in both bottles (concordant) and the composite proportion of agreement in paired aerobic/anaerobic bacterial growth was calculated. Confidence intervals for proportions were calculated according to the Wilson efficient-score method, corrected for continuity. P value is considered significant if< .05 .Statistical analysis was done by SPSS version 20.

Results

Collected Blood culture bottles totaled 2492; 172 single bottle were excluded, and 1160 paired bottles were analyzed, 1046 were concordant; 79 paired bottles had bacterial growth and 967 paired bottles had no bacterial growth. While 114 paired bottles were discordant; growth was observed in 97 aerobic bottles, 13 in anaerobic, 4 in both bottles, and 193 bottles had any growth **(Table 1)**.

The proportion of agreement for the concordant

Table 1. Characteristics ofthe Collected Blood Culture Bottles; For the Total bottles and those included in Analysis.

Blood Culture Bottles	Number (%)
Total collected	2492
Excluded unpaired	172
Total analysis included paired	1160 (100)
Paired with no growth	967 (83.4)
Paired with growth	79 (6.8)
Concordant	1046 (90.2)
Discordant	
Aerobic	97 (8.4)
Anaerobic	13 (1.2)
Discordant paired growth	4 (.3)
Concordant and discordant with growth	83 (7.1)
Total aerobic growth	101 (8.7)*
Total anaerobic growth	17 (1.5)*
With any growth	193 (16.6)#

* The proportion difference between aerobic and anaerobic growth rates is highly significant (p <.0001) by McNemar Test
# Including Paired Bottles with Growth (n = 79), and Discordant Sets (n =114).

paired bottles (N = 1046) was 90.2 %. The composite proportion of agreement in concordant and discordant aerobic/anaerobic bacterial growth(N = 193, composite proportion of agreement =56%, 95% C.I., 34% - 48%). Cohen kappa composite agreement, measured for the total analyzed paired bottles; for bacterial growth/no growth in paired bottles (N = 1046), 79 concordant aerobic growth, anaerobic growth N = 17 and aerobic growth N = 101 (4 discordant bacterial growth pairs were counted with both aerobic and anaerobic bottles, N = 1160, **K** = .52, SE = .038. 95% C.I.,.447- .595).

The odds that a treating attending decide to change or modify an already prescribed antimicrobial regimen were calculated based on several denominators. Intent to treat for the total and subgroups odds showed that the antimicrobial regimes were not changed or modified based on concordant and discordant growth except

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for one anaerobic growth bottle (N =1160, Odds = 0.0008),the odds for all bottles with any growth (N =193, odds = .005), and based on any anaerobic bottle with bacterial growth (N = 96:79 from concordance, 13 anaerobic, and 4 from the discordant bottles cultures, odds = 0.010) **(Table 2)**.

Discussion

The usual trend is to use paired aerobic/anaerobic bottles for blood culture collection. This routine tendency is practiced undisputed for its anticipated usefulness; neverthelessone would seriously revise this concept [11].Especially, aerobic blood culture bottles collected more than once at several time points increase sensitivity, 73.2% one blood culture, 93.9% with two, 96.9% with three, and 99.7% with four blood culture bottles [12].Our study

Table 2. Odds for the Impact of Anaerobic Blood Culture Bottles Growth on Modifying the Anti-infective Agents.

Blood CulturesBottles	Number	Odds of The Clinical Decision
Total Paired bottles Analyzed	1160 (87.1%)	.0008*
Anaerobic bottles with Growth	96	.010&
All bottles with Any Bacterial Growth	193 (16.6%)	.005#

* Calculated based on the intent to treat at the time of blood culture collection based on total number of bottles.
& Calculated for the anaerobe bottles with growthN = 96 (Concordant n = 79, anaerobic n = 13, and discordant n = 4).
\# Calculated based on all bottles that grow aerobic and anaerobic bacteria, i.e.,the Paired bottles with Growth (n = 79), and Discordant bottles (n =114).
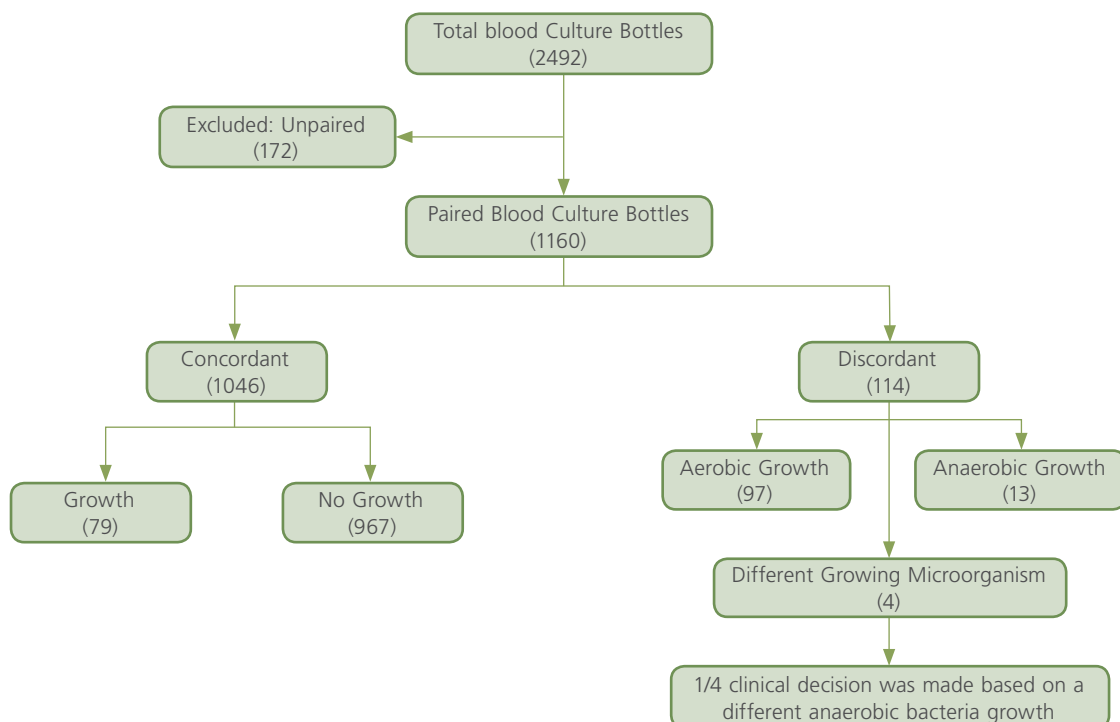

Figure 1. Flow of Blood Culture Bottles Segregated According to Concordance and Aerobic and Anaerobic Bacterial Growth.

showed that there was a total high proportion of agreement between aerobic and anaerobic bottles (92%), to a point that we may rely on aerobic bottles, this suggests obtaining frequent aerobic bottles; up to three or four, increasing sensitivity while sparing extra cost, complex blood collection methodology, samples contamination, and blood volume [12,13].

In this study, we found that when the aerobic bottles fail to grow a microorganism, anaerobic bottles fail as well in 83% of times; furthermore, discordant growing aerobic bottles were higher than the anaerobic bottles (McNemar p < .0001). In case of paired growth both bottles were concordant in 95.2% of times, and the need for anaerobic bottle is questionable. The unique microorganisms' recovery from anaerobic bottles was 17 (20.5%) of total positive cultures. Some previous studies focused on the potential benefit of keeping anaerobic bottle on board though anaerobe recoveries were not high, anticipating the growth of facultative anaerobes like staphylococci, streptococci, and some members of the family *Enterobacteriaceae*. However, it was observed that the amount of blood injected per bottle was associated with a better growth yield, this argues against the routine anaerobic bottles use, which is if the blood volume was saved for aerobic bottles [14,15]. Only one patient in the 4 discordant paired bottles grew an organism that called for intervention by a clinician.

Though the aim of the study is not to look into blood cultures sensitivity, specificity, the yield percentage, and contamination versus pathogen, however it was noteworthy to point out that the rate of any growth from the paired bottles was 193 (16.6%) bottles, which was not different from previous reports [11]. This is largely dependent on clinical scenario, threshold to order blood culture, timing of culture, sterility technique, volume of blood drawn among other lurking variables [14,15,16]

In conclusion, the clinical decision-making of anti-infective treatment based on anaerobic blood culture growth was not evident, and patient care based on utilizing aerobic blood cultures alone would do well. Also, the proportion of agreement between aerobic and anaerobic bottles was high and needless to include anaerobic bottles as a routine blood culture collection procedure.

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