

Blood cultures before antibiotics- Sequence matters

Time is of the essence in the diagnosis and treatment of sepsis and other serious infections such as meningitis. Clinicians sometimes have to balance competing priorities—the need to collect blood cultures prior to antimicrobial initiation and the need to expedite administration of antimicrobials.¹⁻³ Recent studies suggest that clinicians forgo collecting pre-antimicrobial blood cultures in up to 51% of septic patients, possibly due to concerns about increasing delays to antimicrobial initiation.⁴⁻⁷

This newsletter reviews a recent trial evaluating the diagnostic sensitivity of pre- and post-antimicrobial blood cultures in patients with severe sepsis (FABLED trial).⁸

The FABLED trial

The FABLED trial was a prospective trial involving 325 patients with severe sepsis across 7 urban emergency departments in the United States and Canada. Adults presenting with severe manifestations of sepsis, including systolic blood pressure < 90 mm Hg or serum lactate \geq 4 mmol/L, were included in this trial. Patients with bleeding diathesis, severe thrombocytopenia, or an international normalized ratio > 6.0 were excluded.

Blood cultures were collected prior to and after (within 4 hours) initiation of empirical antibiotics in all study participants. 5 hospitals collected 2 sets of blood cultures prior to and after antimicrobial administration and 2 hospitals collected 2 and 1 set respectively.

Results

Notable characteristics of the study participants were a mean age of 65.6 years and relatively few chronic comorbidities (median Charlson Comorbidity Index score 1). The majority of patients received beta-lactams empirically (piperacillin-tazobactam, 60.6%; the two most common agents used in the remainder were third-generation cephalosporins, 23.4%; or carbapenems, 4.6%). The most common sources of sepsis were the respiratory (32.9%) and genitourinary tract (17.8%). The most commonly isolated pathogens were *Escherichia coli* (22.5%) and *Staphylococcus aureus* (15.7%).

Post-antimicrobial blood cultures were half as sensitive as pre-antimicrobial blood cultures in detecting bloodstream pathogens (sensitivity 52.9%, 95% CI 42.8- 62.9%).

The primary outcome of the trial was to determine the sensitivity of post-antimicrobial blood cultures. Post-antimicrobial blood cultures were less frequently positive than pre-antimicrobial cultures (63 of 325 patients; **19.4%** vs 102 of 325 patients; **31.4%**). The absolute difference in the proportion of positive pre- vs post-antimicrobial blood cultures was 12.0% (95% CI 5.4-18.6%, $p < .001$). This reduction was consistent across all time points (e.g. < 30 vs 120- 240 minutes post-antimicrobial administration), demonstrating that antimicrobial administration rapidly and significantly reduced the yield of blood cultures.

Study authors also found that combining post-antimicrobial blood culture results and culture results from other sites (e.g. sputum, urine) increased pathogen identification sensitivity from 52.9% to 67.6%. Despite this modest increase in diagnostic sensitivity, the combination of post-antimicrobial blood culture results and results from other cultures was still inferior to that of pre-antimicrobial blood cultures alone.

The findings of the FABLED trial, together with other trials, provide convincing evidence that collecting blood cultures prior to antimicrobial administration provides the best diagnostic yield.⁹⁻¹¹ These findings also support best-practice recommendations from The Surviving Sepsis Guidelines on the importance of collecting pre-antimicrobial blood cultures.¹ Blood cultures are essential for identifying pathogens and determining antimicrobial susceptibility. In the era of increasing antimicrobial resistance, these microbiological results are necessary for optimizing treatment effectiveness and safely de-escalating broad-spectrum antimicrobial agents.

Strengths and Limitations

FABLED's study design of collecting paired blood cultures in each study participant is a key strength, allowing comparison between yields of pre and post-antimicrobial blood cultures. However, 2 participating hospitals collected only 1 set of post-antimicrobial blood cultures per patient, which could have contributed to the low sensitivity of post-antimicrobial cultures.

Despite this limitation, the FABLED trial provides strong evidence that antimicrobial administration significantly reduces blood culture yield. To maximize the diagnostic yield, blood cultures should be collected prior to administering antibiotics.

Recommendations

1. Providers should obtain blood cultures prior to administering antimicrobials. The Surviving Sepsis Guideline suggests that delaying antibiotic administration for up to 45 minutes, in order to collect blood cultures, is acceptable.¹
2. Empirical antibiotics should be administered as soon as possible after blood cultures are collected.
3. In situations where pre-antimicrobial blood cultures were not collected, blood cultures should still be collected as soon as possible following antimicrobial administration.
4. Providers should tailor definitive antimicrobial therapy based on blood culture results.

References

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