DEM Journal Club

Article Appraisal

Article: Blood culture results before and after antibiotic administration in patients with severe manifestations of sepsis: a diagnostic study.

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Background and Study Objective(s):

Best practice sepsis care recommends drawing blood cultures prior to antimicrobial administration. However, death is associated with delayed antimicrobial therapy after septic shock starts. Forgoing blood cultures prior to antimicrobial administration may improve time to treatment and other patient-oriented outcomes. It is unclear whether delaying blood cultures until after antimicrobial administration affects test sensitivity. The objective of this study was to determine the sensitivity of blood cultures drawn after antimicrobial administration in patients with severe manifestations of sepsis.

Study Design:

This was a patient-level, single-group diagnostic study carried out in 7 emergency departments in Canada and the US. The detailed inclusion and exclusion criteria were not explicitly presented in the manuscript or supplemental material, but generally included adults > 18 years old presenting to the ED with severe manifestations of sepsis, defined as sBP < 90 or lactate >4.0. Patients with bleeding risk or disorders were generally excluded. 2 sets of blood cultures were obtained from each patient prior to antimicrobial administration and further blood cultures were obtained after.

Sensitivity of blood culture obtained within 120 minutes after antimicrobial therapy was determined with the same patient's pre-antimicrobial blood culture results used as the reference standard for the test. The authors decided to extend the time window to 240 minutes mid-study due to enrolment difficulties. A discordant result was defined as an organism present in pre-antimicrobial cultures that was not grown in the post-antimicrobial cultures. A concordant result was defined as the same, or no organisms grown in both pre- and post-antimicrobal blood cultures. The authors also determined the sensitivity of post-antimicrobial blood cultures combined with cultures of other body sources.

Results:

Cheng and colleagues enrolled 325 adults (mean age 65.6 years and 63% male) who presented to the emergency department with severe sepsis as defined by elevated lactate and/or hypotension. All enrolled received blood cultures before and after empiric antibiotic coverage. Preantimicrobial blood cultures grew at least one microbial pathogen in 31.4% of patients. Post antimicrobial cultures (obtained up to 240 minutes after antibiotics to maximize yield) grew at least one microbial pathogen in 19.4% of patients. When preantimicrobial cultures were set as the gold-standard for sensitivity, postantimicrobial culture sensitivity was 52.9%; this was comparable across all time subsets. To address their secondary outcome, results of other microbial cultures (i.e. urine, sputum, wound) were added and only increased the sensitivity of postantimicrobial cultures to 67.6%.

Validity of Results:

This study addressed a clear question with elegant methodology. Although an older definition of sepsis was used, it is still a validated means of accurately identifying septic patients. The use of preantimicrobial culture results as the gold-standard for sensitivity was reasonable and allowed for straight-forward statistical comparison of sensitivities between the same group before and after antibiotics. Low-virulent skin flora present in only one set of blood cultures were deemed contaminants and appropriately excluded from positive culture calculations.

There were some limitations to note. Only about a tenth of total screened individuals were ever included in the study and exhaustive inclusion and exclusion criteria were not readily stated within the original study. The specific method for screening patients was not included and therefore a significant number of patients may have been missed. Also, as described in methods, postantimicrobial culture number and volume varied depending on study site. Although the authors say that adequate blood volumes were drawn, potential variability and under-reporting of the true postantimicrobial culture sensitivity cannot be ruled out.

Finally, the study protocol was amended ad hoc as 16% of the patients could not get their postantimicrobial culture obtained within the originally stipulated 120 minute cut-off. While the authors appropriately calculated per-protocol and intention-to-diagnose results (both comparable), this highlights the common logistical limitations of acquiring timely blood cultures – even in departments conducting a study on that very metric.

Generalizability of Results:

This study is very generalizable to a standard adult ED population. It was designed in a pragmatic nature, allowing inter-site differences in blood culture collection and adjunct culture collection. The question of sensitivity of post-antimicrobial blood cultures compared to pre-antibiotic cultures is relevant for the time sensitive nature of quality care in patients with severe sepsis. However, given that the inclusion criteria were not strictly defined within the manuscript, it may be difficult to accurately identify patients in whom to apply this to.

The Bottom Line:

This well done diagnostic study demonstrates that the sensitivity of blood cultures drawn after antibiotic administration in patients with severe manifestations of sepsis are only 52.9% or 67% when other cultures are taken into account.

Both groups in Victoria and Vancouver agreed that this further supports current practice of timely blood cultures and antibiotic administration in best sepsis care, but that blood cultures should be routinely drawn prior to antibiotics unless there is a significant delay. There is likely a trade off between early antibiotics and false-negative blood cultures. It is not clear as to what threshold of antibiotic delay patient outcomes are altered. While this study did not address any patient outcomes, further studies may shed light on outcome differences in patients with negative cultures or who receive antibiotics prior to drawing blood cultures.