

AAEM Clinical Practice Statement

Does Early and Appropriate Antibiotic Administration Improve Mortality in Emergency Department Patients with Severe Sepsis or Septic Shock? (9/6/2015)

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Introduction

Management of emergency department (ED) patients with severe sepsis and septic shock focuses on early identification, hemodynamic resuscitation, and appropriate antibiotic administration.[1] The 2012 Surviving Sepsis Campaign guidelines for the management of patients with severe sepsis and septic shock recommend that antibiotics be administered within the first hour of recognition of severe sepsis or septic shock.[1] In contrast, a 2010 Cochrane Database Systematic Review concluded that there was no Level I evidence to support the use of early, pre-intensive care unit administration of antibiotics for patients with severe sepsis.[2] The objective of this AAEM Clinical Practice Guideline is to summarize current evidence and provide guidance to emergency providers on the timing and selection of antimicrobial therapy in patients with severe sepsis and septic shock.

Executive Summary

A systematic search of PubMed yielded 267 articles over the last 10 years that evaluated antibiotic administration in adults with severe sepsis or septic shock. For the purpose of this review *appropriateness* was defined as antibiotic medications for which an isolated pathogen was susceptible, while *early timing* was relative, trial-specific, and never defined *a priori*. Only articles that assessed early timing or appropriateness of antibiotic therapy with respect to patient-centered outcomes (i.e., mortality) in patients with severe sepsis or septic shock were included.[2-16] Fourteen articles were chosen; eight retrospective trials, four prospective cohort studies, one randomized controlled trial, and one Cochrane Systematic Review.

Eight of the thirteen independent studies reported on timeliness of antibiotics, whereas six studies reported on antibiotic appropriateness. Seven of the eight studies on antibiotic timing concluded that earlier antibiotics improved mortality. The evidence demonstrating benefit of early antibiotics was strongest for patients with septic shock. Five of six articles that addressed appropriateness of antibiotics reported significant associations with mortality. There were no studies that suggested patient harm associated with early or appropriate antibiotics. However, no data was reported with regards to resistance patterns or inappropriate antibiotic administration in patients who are

ultimately found not to have sepsis.

A landmark publication by Kumar, et. al, found that for every hour delay in effective antibiotic therapy, in-hospital mortality increased by 7.6% during the initial six hours of treatment. A subsequent study by the same authors reported a 28-day mortality benefit when septic shock patients with positive blood cultures were treated initially with a beta-lactam antibiotic plus a fluoroquinolone, macrolide, or aminoglycoside antimicrobial. This combination therapy was also associated with fewer intensive care unit days, ventilator days, and days receiving a vasopressor.

Gaieski, et. al. found that ED patients with sepsis who received early goal directed therapy and antibiotics within one hour from triage had a significantly lower mortality. In a preplanned analysis of a randomized controlled trial, Puskarich, et al found a significant mortality benefit if antibiotics were given before the onset of shock compared to antibiotic administration after shock was recognized. More recently, Vazquez-Guillamet, et al reported that four patients with positive blood cultures needed to be treated with appropriate antibiotics to prevent one death.

In contrast, Labelle, et al found no relationship between mortality and time to appropriate antibiotic administration in a single center study of patients with septic shock. Of the remaining three retrospective and three prospective studies, four supported providing early antibiotics, three supported appropriate antibiotics and a single small retrospective report reported no outcome improvement associated with either timing or appropriateness.

Overall, 4,287 patients were included in studies that supported early antibiotics compared with 765 patients in trials that showed no benefit. There were 8,150 patients in studies that showed benefit of appropriate antibiotics and 184 patients in a single trial that showed no benefit. There were no studies that suggested any harm to patients by providing early and appropriate antibiotics.

In all studies, “appropriateness” of antibiotics was determined by culture results, which are unavailable at the time of initial antibiotic selection in the ED. Although this definition of “appropriateness” may not be practical with regards to the practice of emergency medicine., the evidence clearly illustrates that outcomes are improved when the pathogen is sensitive to the initial antimicrobials. Therefore, the emergency provider is advised to select antibiotics on the basis of the suspected source, culture history, risk factors, and the local antibiogram.

Conclusion

Current evidence supports the use of early and appropriate antibiotics for patients with severe sepsis and septic shock. The evidence to support the use of *early timing* is strongest in patients with septic shock, where administration within the first hour of recognition may be most beneficial to decrease mortality.

Recommendation

Does early and appropriate antibiotics improve mortality in emergency department patients with severe sepsis or septic shock?

Answer: Yes

