

care for septic patients. The SSC released their latest guidelines in 2012, which included statements emphasizing that antibiotics be administered to patients with septic shock (1B) or severe sepsis (1C) within an hour of recognition (5). These recommendations were largely based on a landmark retrospective cohort study that showed for every hour delay in administering antibiotics to patients with septic shock, there was a 7.6% increase in mortality over the first 6 h (6). In 2010, a Cochrane Database Systemic Review evaluated the evidence of the mortality impact of antibiotic administration to patients with severe sepsis before admission to the intensive care unit (ICU) (7). The authors found no randomized or prospective trials to answer this question. They could not provide a strong recommendation for early antibiotic administration, although they did mention it is reasonable to do, based on available evidence. The objective of this American Academy of Emergency Medicine Clinical Practice statement 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.

METHODS

This was a structured literature review using a PubMed search for articles investigating the impact of antibiotic administration on outcomes of patients with severe sepsis and septic shock. Specifically, the impact of the time to administration of antibiotics and the appropriateness of selected antibiotics in patients with severe sepsis and septic shock was evaluated. Appropriateness of the selected antibiotic was defined a priori as an antimicrobial for which a pathogen showed in vitro susceptibility on culture sensitivities. Time to administration was a relative, trial-specific definition that varied from study to study. Only articles that measured patient-centered outcomes, such as mortality, were included. Four separate searches were completed using PubMed. These searches were limited to studies published between 2005 and 2015, inclusive, involving adult humans subjects and written in English. Abstracts that met initial criteria were then independently reviewed by at least two authors to determine relevance and possible inclusion. Only studies that were randomized controlled trials, prospective trials, meta-analyses, and retrospective cohort studies were included; all review articles, case series, and case reports were not. All references of included articles were also evaluated to determine whether any additional studies should be included. The results of the search criteria can be found in Table 1.

After this, two of the authors reviewed each included article and assigned a “grade of evidence” score that reflected the study question, methodology, and design.

These results are listed in Table 2. A “quality ranking score,” designed to classify articles based on the strength of methods and design, was also performed by the authors and is listed in Table 3.

RESULTS

A total of 1522 articles were identified by the four PubMed searches that met inclusion criteria. Of these, 14 were included in the final analysis: 8 retrospective cohort studies, 4 prospective cohort studies, 1 randomized controlled trial, and a single Cochrane Systemic Review (Table 4). Of the eight studies designed to assess the impact of timely antibiotic administration, seven showed a decrease in mortality, with the greatest benefit shown for patients in septic shock. Of the six articles addressing the impact of appropriate antimicrobial therapy on mortality, five demonstrated a mortality benefit. In the 14 papers utilized in this clinical statement, 4287 patients benefited from early antibiotic administration, whereas 765 patients did not demonstrate an improvement in mortality. Furthermore, 8150 patients benefited from receiving appropriate antibiotics, whereas 184 patients did not. There was no evidence for harm to patients by providing either early or appropriate antimicrobials. Importantly, no studies showed any evidence of harm with either early or appropriate antibiotic therapy. We were unable to find any data regarding the impact on resistance patterns with inappropriate antibiotic use in patients who were ultimately found not to have sepsis.

RECOMMENDATION

Early and appropriate antibiotic administration as described in the Methods section improves mortality in ED patients with severe sepsis and septic shock.

Level of recommendation: C.

DISCUSSION

The ED management of patients with severe sepsis and septic shock is focused on the delivery of optimal and timely therapy. The goal of this clinical practice guideline is to provide emergency physicians with an evidence-based recommendation for the antimicrobial management of these patients. Defining the “appropriateness” of antibiotics can be challenging, as it is ultimately based on identifying a causative pathogen. In approximately one-third of cases, blood cultures identify a specific organism; in another one-third of patients, cultures of other sites provide necessary clinical data; whereas no organism is identified in the final one-third of patients (1,20,21). There is recent evidence that suggests that

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