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The Effects of Sepsis Management Protocols on Time to Antibiotic Administration in the Emergency Department

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THE EFFECTS OF SEPSIS MANAGEMENT PROTOCOLS ON TIME TO ANTIBIOTIC ADMINISTRATION IN THE EMERGENCY DEPARTMENT

by

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ABSTRACT

Sepsis is one of the leading causes of death in U.S. hospitals, resulting from organ dysfunction caused by an inappropriate inflammatory reaction to an infection. Timely treatment with empiric antibiotics in the emergency department is crucial to facilitate positive patient outcomes. The Surviving Sepsis Campaign (SSC) recommends initiating empiric antibiotic therapy within one hour of presentation to the emergency department. Some emergency departments have implemented sepsis management protocols to guide care and ensure timely treatment. The purpose of this study is to determine the effect of a formal sepsis protocol in the emergency department on the time to antibiotic administration. A literature review was conducted using CINAHL, Cochrane Database, Health Source: Nursing/Academic Edition, and MEDLINE. Results from one systematic review, eight quasi-experimental studies, and four quality improvement projects suggested that implementation of a sepsis management protocol in an emergency department may decrease the time to antibiotic administration. (< 10 = spell out) Eleven of the 13 articles reported decreased time to antibiotic administration by as much as 8-193 minutes compared to pre-protocol. One study met the SSC goal of 1 hour and reported a median administration time of 17 minutes. Time to antibiotics was influenced by protocols based on published sepsis guidelines, inclusion of antibiotic guidelines, nurse-initiated treatment, and education for emergency clinicians regarding sepsis management. Emergency departments should implement sepsis protocols adapted to their local institution to decrease time to antibiotic administration and reduce mortality of sepsis patients. Further research on how sepsis protocols affect antibiotic administration time is needed.

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INTRODUCTION

Sepsis is one of the leading causes of death worldwide, with the mortality rate in the United States reaching up to 25% (Beardsley et al., 2016). Sepsis is defined as a dysregulated systemic reaction to infection that leads to organ failure; and its effects can quickly become life threatening (Donnelly, Safford, Shapiro, Baddley, & Wang, 2017). Research has shown that timely diagnosis and prompt and aggressive treatment of sepsis can greatly improve patient outcomes and mortality (MacRedmond et al., 2010). The Surviving Sepsis Campaign (SSC) has published guidelines for the treatment of sepsis as well as time-based care "bundles" to help guide clinician decision making (Rhodes et al., 2017). However, compliance with these guidelines remains low and the SSC reports that only two-thirds of sepsis patients receive all recommended interventions (McKinley et al., 2011). Protocolized management of sepsis, or sepsis care guided by evidence-based protocols, may help facilitate compliance with these guidelines. According to a survey of over 400 U.S. hospitals, more than half reported using protocols for the treatment of sepsis but significant practice variation still remains (Durthaler, Ernst, & Johnston, 2009).

BACKGROUND AND SIGNIFICANCE

The SSC was developed by the Society of Critical Care Medicine to educate healthcare professionals about sepsis and to provide clinical practice guidelines for the care of sepsis patients (Rhodes et al., 2017). Clinical practice guidelines are "systematically developed statements" meant to aid clinicians in making appropriate clinical decisions (National Center for Complementary and Integrative Health, 2017). An interdisciplinary committee of experts in critical care medicine updated these guidelines in "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016" (Rhodes et al., 2017). These guidelines provide best practice recommendations for assessment and treatment of sepsis as well as provide updated definitions for sepsis (Rhodes et al., 2017).

The SSC defines sepsis as "life threatening organ dysfunction caused by a dysregulated host response to infection" (Machado et al., 2017). The SSC updated this definition and eliminated the term "severe sepsis" in 2016 to help standardize the language used in practice as well as reduce the confusion between sepsis and severe sepsis (Machado et al., 2017). Septic shock is defined as sepsis with accompanying circulatory, cellular, and metabolic abnormalities that are predictors of higher mortality rates, such as organ failure (Machado et al., 2017).

According to the Centers for Disease Control and Prevention (CDC), approximately 250,000 people die from sepsis every year in the U.S.; and sepsis is associated with 1 of every 3 deaths in a hospital (Centers for Disease Control and Prevention, 2017).There are more than 1.5 million new cases of sepsis per year (Centers for Disease Control and Prevention, 2017), and an additional 1 million cases per year is projected due to the aging population (Palleschi, Sirianni,

O'Connor, Dunn, & Hasenau, 2014). In 2013, the healthcare costs associated with sepsis was $23.7 billion (Novosad et al., 2016). The high incidence and high mortality rate associated with sepsis makes the diagnosis and treatment of sepsis and septic shock a paramount health issue.

In an effort to standardize care and improve patient outcomes, the SSC released sepsis management guidelines in 2004 (Rhodes et al., 2017). These guidelines were revised to reflect the latest research and were most recently updated in 2016 (Rhodes et al., 2017). The SSC guidelines are specific recommendations covering every step of treatment, including but not limited to: initial resuscitation, screening, antimicrobial therapy, vasoactive medications, blood products, mechanical ventilation, and goals of care (Rhodes et al., 2017). The SSC has stated that the guidelines do not overrule clinical decisions by the provider but are recommendations to help guide care (Rhodes et al., 2017).

The SSC has also developed sepsis management bundles, which are specific sets of interventions that are effective on their own but have more benefit when grouped together (Barochia et al., 2010). Some examples are the 3-hour and 6-hour bundles that provide interventions to be implemented within a certain time period. The 3-hour bundle states that within 3 hours of presentation of sepsis, clinicians should: 1) measure lactate level, 2) obtain blood cultures before administering antibiotics, 3) administer broad-spectrum antibiotics, and 4) infuse 30 ml/kg of crystalloid fluids for hypotension or lactate above 4mmol/L (Society of Critical Care Medicine, 2015). The SSC defines time of presentation of sepsis as either the time of triage in the emergency department or the time that a patient screens positive for sepsis in a different care setting (Society of Critical Care Medicine, 2015).

In addition to the elements included in the 3-hour bundle, the 6-hour bundle directs clinicians to: 1) administer vasopressors to maintain mean arterial pressure (MAP) greater than or equal to 65 mmHg; 2) re-assess volume status and tissue perfusion in cases of persistent hypoperfusion; and 3) re-measure lactate if initial measurement was elevated.

Bundles are meant to help change clinical practice and promote adoption of the SSC guidelines (Ferrer & Artigas, 2011). Bundles published by the SSC have been adopted by the U.S.-based National Quality Forum and have been the foundation of improvement programs intended to enhance sepsis management (Rhodes et al., 2017). Compliance with 3-hour or 6-hour sepsis bundles has been associated with a 36-40% reduction in mortality (Rhodes et al., 2017). Evidence suggests implementation of sepsis management protocols based on these bundles may improve patient outcomes. Using evidenced-based sepsis protocols have been shown to standardize care, reduce cost, and promote patient safety (Campbell, 2008).

One of the factors that make sepsis so deadly is its rapid and insidious progression. Every minute counts; and every hour that sepsis goes untreated is associated with a measurable rise in mortality (Beardsley et al., 2016). Providing treatment within 6 hours of presentation to the emergency department can reduce mortality by 16% (Dugan, 2011). Timely antibiotic administration is a key component of the SSC sepsis bundles and of sepsis treatment. Delays in antibiotic administration are associated with higher rates of acute kidney injury, acute lung injury, and mortality (Rhodes et al., 2017).

The SSC states antibiotic administration should begin within one hour of sepsis presentation (Rhodes et al., 2017), which has been shown to reduce mortality rates by 30-50%

(Lopez-Bushneil, Demaray, & Jaco, 2014). There are many barriers to timely administration of antibiotics, which include obtaining blood culture samples before starting antibiotics (Rhodes et al., 2017), and delays in communication between the provider, pharmacist, and nurse. The SSC suggests it is appropriate for a unit to stock pre-mixed antibiotics for emergent situations to expedite this process (Rhodes et al., 2017). The use of standardized order sets for treatment of patients with sepsis is also recommended due to their association with improved time to initial antibiotic therapy (Lopez-Bushneil et al., 2014).

Despite the danger to patients and the financial burden that sepsis poses to hospitals and patients, in a study conducted by Durthaler et al. (2009), only 49% of hospitals had implemented formal sepsis protocols in their ICUs as the SCC recommends; and only 55.6% had adopted a standardized screening tool for identification of sepsis. Similar data are not available for sepsis protocol implementation within emergency departments.

Critical care nurses have a significant role in implementing sepsis protocols (Campbell, 2008). Perhaps this is because nurses have the most patient contact of any healthcare professional and nurses are often present to detect changes in a patient's condition (Durthaler et al., 2009). In addition, nurses are usually responsible for administering initial antibiotics in a timely manner, which is crucial to sepsis treatment.

The low percentage of patients that receive antibiotic treatment within the 1-hour recommended by the SSC is a serious cause for concern (McKinley et al., 2011). Research suggests that implementation of nurse-driven protocols may play a role in lessening the time to initial treatment (Bruce, Maiden, Fedullo, & Kim, 2015). Implementation of a protocol in the

emergency department based on SSC recommendations has been shown to lessen the time to initial antibiotic therapy by as much as 84 minutes (Bruce et al., 2015). The implementation of sepsis management protocols based on SSC guidelines may be key to improving bundle compliance and improving patient outcomes.

PURPOSE

The purpose of this literature review is to determine the effect of formal sepsis management protocols on time to antibiotic administration in the emergency department. This review will also explore which other factors influence timely antibiotic administration as well as individual components of these protocols, and the role of the nurse in executing these protocols.

METHODS

A literature review was conducted using the CINAHL, MEDLINE, and Cochrane Database of Systematic Reviews databases. Search terms included sepsis, septic*, severe sepsis, or septic shock, and protocol* or bundle*, and hospital* or ward* or inpatient* or unit* and antibiotic* or antimicrobial*. Search terms excluded child* or ped* or neonat*. Additional inclusion criteria consisted of peer reviewed research articles, hospitalized adults with sepsis, sepsis protocols, and primary or secondary outcomes of time to antibiotic administration. Articles were excluded if they were published before 2004 to reflect the first release of sepsis guidelines by the SSC. Articles were evaluated for quality of evidence using a table adapted from Fineout-Overholt that included the criteria of: study design, sample, major variables, measurement of variables, statistical analysis, major findings, and worth to practice (Fineout-Overholt & Johnston, 2007). A total of 13 articles were included in this literature review (See Appendix A). These articles included one systematic review, eight quasi-experimental studies, and four quality improvement projects.

RESULTS

Eleven of the thirteen articles reported implementation of a sepsis management protocol resulted in a statistically significant reduction in time to antibiotic administration in the emergency department (See Appendix) (Bruce et al., 2015; Crowe, Mistry, Rzechula, & Kulstad, 2010; De Miguel-Yanes et al., 2009; Francis, Rich, Williamson, & Peterson, 2010; McColl et al., 2017; McLaughlin, Scott, Koenig, & Mueller, 2017; Palleschi et al., 2014; Rehmani, Memon, & Al-Gammal, 2014; Seoane et al., 2013; Sweet et al., 2010; Tromp et al., 2010). The study performed by Papali et al. (2017) reported a reduction in time to administration from 173.5 minutes to 110 minutes; but the data were not statistically significant.

McLaughlin et al. (2017) conducted the only study with results that indicated compliance with the SSC guidelines that recommend antibiotic therapy be started as soon as possible or within 1 hour of presentation of sepsis (Rhodes et al., 2017). In this study, the protocol included order sets for cephalosporin antibiotics to be administered by intravenous push route. The quickest administration time decreased from 30 minutes pre-intervention to 17 minutes post-intervention (McLaughlin et al., 2017). Many other articles reported administration times close to the 1-hour goal recommended by the SCC, most notably the study performed by Sweet et al. (2010). In this study, a comprehensive education program accompanied a protocol based on Early Goal-Directed Therapy (EGDT). The median time to antibiotic administration decreased by 192 minutes, from 253.2 to 60.6 minutes (Sweet et al., 2010). Three other articles reported times close to 1 hour such as 68, 70.5, and 72 minutes (McColl et al., 2017; Rehmani et al., 2014; Seoane et al., 2013).

A majority of the studies complied with the SSC 3-hour bundle (Bruce et al., 2015; Francis et al., 2010; McColl et al., 2017; McLaughlin et al., 2017; Palleschi et al., 2014; Rehmani et al., 2014; Seoane et al., 2013; Sweet et al., 2010; Tromp et al., 2010). It should be noted that seven of these nine studies were already in compliance with this bundle prior to their investigation as their control or comparison groups had antibiotic administration times less than 3 hours (See Appendix A).

Most of the studies included in this literature review set a goal for antibiotic administration time of 1-6 hours following implementation of a protocol (Bruce et al., 2015; Crowe et al., 2010; De Miguel-Yanes et al., 2009; Francis et al., 2010; McColl et al., 2017; McLaughlin et al., 2017; Palleschi et al., 2014; Papali et al., 2017; Rehmani et al., 2014; Seoane et al., 2013; Tromp et al., 2010). McLaughlin et al. (2017) was the only study that met its 1-hour time goal. Papali et al. (2017) and Seoane et al. (2013) both had 2-hour time goals and achieved them as well, although the data gathered by Papali et al. (2017) were not statistically significant. Three studies achieved their 3-hour time goals (Bruce et al., 2015; Palleschi et al., 2014; Tromp et al., 2010).

Most of the studies that did not meet goal for antibiotic administration had set goals of 1-hour (Francis et al., 2010; McColl et al., 2017; Rehmani et al., 2014).These studies showed significant improvements in time to antibiotic administration following the implementation of a protocol and were close to reaching their goal, with post-intervention times of 79, 70.5, and 68 minutes respectively. The intervention by De Miguel-Yanes et al. (2009) did not meet the time goal of 3 hours; but these researchers reported a significant improvement in time to antibiotics, decreasing from 360 minutes in the control group to 228 minutes in the intervention group.

The studies that reported the greatest decrease in antibiotic administration time were Sweet et al. (2010), which reduced the time by 192.6 minutes in the intervention groups, and De Miguel-Yanes et al. (2009), which reduced the time by 132 minutes.

DISCUSSION

This literature review sought to understand the effects of sepsis management protocols on the time to administration of antibiotics in the emergency department. Analysis of the data suggests implementation of sepsis management protocols decreases the time to antibiotic administration. The data also suggest that sepsis management protocols may help emergency departments comply with the SSC 3-hour bundle that recommends antibiotic administration within 3 hours of presentation to the emergency department (Society of Critical Care Medicine, 2015). It remains unclear whether sepsis management protocols can reduce the time to antibiotic administration enough to comply with the SSC guideline that recommends antibiotics be administered as soon as possible or within 1 hour of presentation (Rhodes et al., 2017).

All of the articles included in this literature review implemented unique sepsis management protocols within an emergency department; and most of them were successful in improving timely antibiotic administration. However, each of these protocols contained varying elements, was based on different guidelines or research, and/or was implemented in differing ways.

Basis of Protocols

Each of the studies included in this literature review designed customized sepsis protocols based on relevant research or guidelines. Due to differing elements and designs, protocols may vary in their effectiveness. The SSC offers general guidelines for the management of sepsis as well as sepsis management bundles that help clinicians apply these guidelines to their practice (Society of Critical Care Medicine, 2015). Nine of the 13 articles based their sepsis

protocols on the SSC guidelines or bundles (See Appendix B) (Bruce et al., 2015; De Miguel-Yanes et al., 2009; Francis et al., 2010; McColl et al., 2017; McLaughlin et al., 2017; Palleschi et al., 2014; Rehmani et al., 2014; Seoane et al., 2013; Tromp et al., 2010).

McColl et al. (2017) developed a protocol named Sepsis Treatment Early Protocol (STEP) using the recommendations from SSC and expert opinion. STEP included many of the elements of the SSC management bundles but added elements such as obtaining a chest x-ray and an ECG. Alternatively, Palleschi et al. (2014) based their protocol directly on the SSC 6-hour bundle and focused their investigation on improving compliance with the first 3 elements, which included: 1) measuring serum lactate; 2) obtaining blood cultures before beginning administration of antibiotics; and 3) administering antibiotics within 3 hours (Palleschi et al., 2014). Although both studies reported reduced antibiotic times, McColl et al. (2017) was more successful and achieved results closer to the 1-hour goal recommended by the SSC.

This suggests developing a protocol to fit a particular institution may be more successful than applying the SSC bundle elements without modification. Rogers (2003) developed a theory for understanding diffusion of innovations that included discussion regarding implementation of sepsis protocols into clinical practice. Some important factors that affect the adoption of new ideas are “compatibility” and “trialability” (Sanson-Fisher, 2004). For a sepsis protocol to be “compatible” clinicians must believe that it is a good fit and meets the needs of their institution (Sanson-Fisher, 2004). “Trialability” refers to the ability for clinicians to test and change aspects of the protocol as they see fit (Sanson-Fisher, 2004). For sepsis protocols to be most widely adopted, they should be tailored to be compatible with the institution in which they are implemented as well as adaptable to change. The SSC supports this claim by stating that

developing a customized protocol to better meet the needs of a particular institution is imperative when applying the bundles to practice (Society of Critical Care Medicine, 2017).

Another basis for some of the protocols was Early Goal-Directed Therapy (EGDT), first developed by Rivers et al. (2001). Crowe et al. (2010) and Sweet et al. (2010) both borrowed the concepts of EGDT to create their protocols, with mixed results. The goal of EGDT is hemodynamic resuscitation and the original algorithm does not address antibiotic administration directly (Rivers et al., 2001). Due to this, Crowe et al. (2010) created a protocol that focused on interventions to achieve hemodynamic stability, such as the insertion of a central line and periodic sampling of central venous blood to measure oxygen saturation. A 6-hour goal for antibiotic administration was included in the protocol and was achieved in 97.7% of patients; however, when compared to the SSC recommendation of starting antibiotics within 1 hour, this goal may be inadequate to obtain positive patient outcomes (Crowe et al., 2010). This suggests protocols based on EGDT might not focus as much on early antibiotic administration. Sweet et al. (2010) achieved significant reduction in antibiotic administration time, but because their protocol was also based on EGDT, they had no antibiotic administration time goal. EGDT focuses on hemodynamic resuscitation; but protocols based on EGDT should also include specific time goals for antibiotic administration to reflect the most recent evidence.

Papali et al. (2017) is the only study that based its protocol on the World Health Organization – Integrated Management of Adult Illness (WHO-IMAI) sepsis management guidelines. These guidelines were developed for use in resource-limited countries such as Haiti, the setting for this study (Papali et al., 2017). The WHO recommends antimicrobial therapy, including antibiotics, antimalarials, and influenza-specific antivirals, be started within 2 hours

(Reference). This study did not report a statistically significant change in time to antibiotic administration but attributed this to lack of resources, such as intravenous therapy supplies, rather than to the protocol itself (Papali et al., 2017).

Antibiotic Guidelines

Five of the 13 articles utilized antibiotic guidelines as part of their sepsis protocols to help guide care (See Appendix B) (Francis et al., 2010; McColl et al., 2017; McLaughlin et al., 2017; Rehmani et al., 2014; Seoane et al., 2013). Antibiotic guidelines are empiric antibiotic administration suggestions offered to providers as part of a sepsis management protocol that helps guide their choice of antibiotics for a patient with sepsis. Analysis of the articles included in this literature review revealed a relationship between successful studies and the use of antibiotic guidelines within their sepsis management protocols.

All of the studies that utilized antibiotic guidelines were successful in achieving low antibiotic administration times, with all 5 studies reporting times of 79 minutes or less (Francis et al., 2010; McColl et al., 2017; McLaughlin et al., 2017; Rehmani et al., 2014; Seoane et al., 2013) Francis et al. (2010) developed empiric antibiotic guidelines in collaboration with infection disease consultants and included them as part of their sepsis protocol. These guidelines were based on suspected infection site and susceptibility patterns of pathogens in the community in which the study was conducted. Guidelines tailored to specific communities and institutions may help not only reduce the time to administration, but also encourage more appropriate antibiotic choices.

Rehmani et al. (2014) recognized that there is an important role pharmacy plays in antibiotic administration time. Hospital pharmacies are responsible for mixing the antibiotics in a timely manner once the provider has placed the order. Not only did they have guidelines for empiric antibiotic selection, but the pharmacy had instructions to mix certain antibiotics within 30 minutes so that the administration process may be expedited (Rehmani et al., 2014).

Both McLaughlin et al. (2017) and Seoane et al. (2013) utilized antibiotic guidelines in their sepsis management protocols that were not based on suspected or known site of infection. McLaughlin et al. (2017) employed antibiotic guidelines that only apply to cephalosporin antibiotics. In this study, providers were encouraged to order cephalosporin antibiotics via the intravenous push route in an effort to make administering intravenous antibiotics quicker and easier for nurses. This method did not have any adverse effects and did not pose any safety threats when compared to the traditional IV infusion method (McLaughlin et al., 2017). This effort was very successful and McLaughlin et al. (2017) reported antibiotic administration times as low as 17 minutes from ED admission. Seoane et al. (2013) also had restrictive guidelines for antibiotics, and required that piperacillin/tazobactam, ciprofloxacin, and vancomycin be administered consecutively for each patient with sepsis presenting to the emergency department. Vancomycin was replaced with linezolid if the patient was transferred to the ICU to reduce risk for renal deficiency in critically ill patients (Seoane et al., 2013). Although using antibiotic guidelines that limit the choice of antibiotics for providers may expedite the administration of these drugs, using the same antibiotics for all sepsis patients may pose risks. The SSC guidelines warn against inappropriate empiric antibiotic choice due to possible resistance or recent use of a specific antibiotic, which might decrease its effectiveness (Rhodes et al., 2017).

Nurse Involvement

Nurses play a pivotal role in decreasing the time to antibiotic administration (Bruce et al., 2015). All articles included in this review, with the exceptions of Crowe et al. (2010) and De Miguel-Yanes et al. (2009), involved ensuring nurses received education about sepsis protocols and management (See Appendix B). In five of the 13 articles, nurses played a role in developing their unit specific sepsis management protocol (Bruce et al., 2015; McColl et al., 2017; McLaughlin et al., 2017; Seoane et al., 2013; Sweet et al., 2010).

In some studies, implementation of the sepsis protocol provided nurses with additional responsibilities. In the study performed by Bruce et al. (2015), nurses performed the Systemic Inflammatory Response Syndrome (SIRS) screening and also had the responsibility of initiating the protocol if the patient screened positive. McColl et al. (2017) involved nurses even more in the protocol and included a nurse-implemented medical directive. Nurses initiated fluid resuscitation and obtained blood samples for culture and other tests before provider assessment if the patient screened positive for sepsis. The SSC recommends that blood cultures be drawn before administration of antibiotics (Rhodes et al., 2017) and many protocols include this important element. Tromp et al. (2010) included a similar element in their protocol in which nurses could immediately draw blood for labs and culture. Nurses obtaining blood cultures without the need for an order from a provider can expedite the antibiotic administration process. When nurses have the autonomy to obtain blood cultures when appropriate, they can ensure that it is performed early and antibiotic administration can ensue without delay.

Education

All of the studies included in this review provided education to the ED staff concerning sepsis care or sepsis management protocols. Ten of the twelve studies included in this review provided either face-to face or computer-based education to ED staff before the initiation of the sepsis protocol on the unit (See Appendix B). The study conducted by Seoane et al. (2013) was the only study that implemented education after the initiation of the sepsis protocol. In the systematic review, four of the seven studies provided education regarding sepsis care before initiation of the protocols (Turi & Von Ah, 2013).

The extent and intensity of the education provided varied greatly between studies. Francis et al. (2010) reported that information about the use of the protocol and sepsis management was only provided through informal "rounds sessions." In contrast, the study performed by McColl et al. (2017) introduced the campaign "Target Sepsis" that provided "extensive" education in the form of rounds, group presentations, luncheons, and posters displayed in the ED. This was arguably one of the most successful studies included in this review in regards to reducing administration time as well as almost reaching the 1-hour goal set by the SSC. The education in this study covered the sepsis protocol, care of a sepsis patient, and training for nurses in how to communicate with providers about the goal of treating sepsis patients in less than an hour. Palleschi et al. (2014) also provided more involved education in the form of professional meetings over the course of two months. The topics covered included sepsis pathology, prevalence, epidemiology, SSC guidelines, and early treatment standards such as timely antibiotics. According to these studies, extensive education about sepsis protocols and treatment

corresponds with decreased antibiotic administration times and higher compliance with SSC guidelines.

Summary

The element that correlated the most with low antibiotic administration times was the use of antibiotic guidelines in the sepsis protocol. The use of SSC guidelines to develop the protocols also contributed to decreased antibiotic administration times. The success of customized protocols suggests that tailoring protocols to be more compatible with an institution may be most effective. The use of nurse-implemented medical directives had a strong correlation with decreased antibiotic administration times as well. Educational programs that included face-to-face teaching contributed most to decreased administration times. More extensive education that formally introduced the protocol and its importance to the ED staff was the most successful.

LIMITATIONS

Little research has been conducted on how the implementation of sepsis management protocols effect the time to administration of antibiotics in the emergency department. The variation in protocol elements and implementation between studies made it difficult to compare effects on antibiotic administration time.

Most studies did not report on sepsis management knowledge of the providers, nurses, pharmacists, or staff prior to implementation of the protocol. Some studies had low antibiotic administration times in the control group before the intervention, making their change in antibiotic administration time less significant (McColl et al., 2017; McLaughlin et al., 2017).

Another limitation noted was the low level of evidence of some articles. McColl et al. (2017), Palleschi et al. (2014), Papali et al. (2017), and Seoane et al. (2013) were all quality improvement projects. Their results are less impactful than the findings of the quasi-experimental studies and systematic review included in this literature review.

PRACTICE RECOMMENDATIONS

The most up to date research and practice guidelines, such as the SSC sepsis management guidelines, should be used to create a protocol in every emergency department. However, this protocol should also be adapted to the institution in which it will be implemented. The strengths, weaknesses, and culture of the institution should be considered when developing a protocol to ensure that it will be accepted and integrated into the emergency department in which it is implemented (Sanson-Fisher, 2004).

Recommendations for Practice

Nurses play a pivotal role in the time to antibiotic administration. In addition to often being the first clinicians whom assess and identify signs of sepsis, they have the responsibility of obtaining blood cultures before antibiotic therapy and administering antibiotics within an hour of presentation to the emergency department. Nurse-implemented medical directives should be established and included in protocols to allow for the timely collection of blood cultures by nurses. Early completion of blood culture collection will expedite antibiotic administration. Antibiotics guidelines should also be used in sepsis protocols.

Recommendations for Education

The pharmacy plays an important role in the treatment of sepsis patients. Pharmacists should be educated about sepsis management and the importance of timely antibiotic administration. They should also be included in the sepsis management protocol implemented in the emergency department so they may prepare antibiotics faster if they are intended for a patient with sepsis. The management of sepsis requires the collaboration of multiple disciplines and

including pharmacists in sepsis protocols will help expedite the process of antibiotic administration.

Multidisciplinary collaboration is key to successful implementation of a sepsis protocol. All of the staff in the ED must be educated about sepsis management and clinicians must work together to achieve optimal care. Education should include training about how to communicate concerns and recommendations surrounding the protocol. Nurses should be educated to quickly recognize the signs and symptoms of sepsis; and they should encourage timely prescription of antibiotics and ensure compliance with sepsis protocols once the patient is identified as having a higher likelihood of having sepsis.

CONCLUSION

The implementation of sepsis protocols in the emergency department was associated with decreased antibiotic administration time. Elements of these protocols that influenced antibiotic administration time included adherence to sepsis guidelines, inclusion of antibiotic guidelines, increased nurse involvement, and education for ED staff. Nurses play an important role in developing and applying sepsis protocols and should encourage multidisciplinary collaboration to decrease antibiotic administration time in the emergency department.

APPENDIX A

Table 1: Antibiotic Administration Times

Table 1: Antibiotic Administration Times

Article	**Median Time to Antibiotic Administration**		**Difference (min)**	**Significance**
	Control (min)	**Intervention (min)**		
(Bruce et al., 2015)	135	108	-27	p = 0.02
(Francis et al., 2010)	163	79	-84	95% CI [64, 94]
(McLaughlin et al., 2017)	31	23	-8	p < 0.0001
	42	30	-12	p = 0.0064
	42	28	-14	p < 0.0001
	30	17	-13	p = 0.0007
(Papali et al., 2017)	173.5	110	-63.5	p = 0.72
(Seoane et al., 2013)	140	72	-68	p < 0.001
(Sweet et al., 2010)	253.2	60.6	-192.6	95% CI [-286.2, -117.6]
(Tromp et al., 2010)	145	Period 1: 125	-20	No data
		Period 2: 105	-40	
	Mean Time to Antibiotic Administration			
	Control (min)	**Intervention (min)**		
(De Miguel-Yanes et al., 2009)	360	228	-132	p = 0.001
(McColl et al., 2017)	100.5	70.5	-30	p < 0.0001
(Palleschi et al., 2014)	182.09	92.6	-89.49	No data
(Rehmani et al., 2014)	140	68	-72	p = 0.0001
	Other Antibiotic Administration Time Data			
(Crowe et al., 2010)	Antibiotics started in first 6 hours (360 min) in 97.7% of patients			95% CI [96%, 100%]
(Turi & Von Ah, 2013)	Improvement range of 72 minutes to 3 hours (180 min)			No data

APPENDIX B

Table 2: Elements of Protocols

Table 2: Elements of Protocols

Article	Basis of Protocol	Antibiotic Guidelines	Nurse Involvement	Methods of Education
(Bruce et al., 2015)	Surviving Sepsis Campaign	None	Protocol development, performed SIRS screening	Online modules
(Crowe et al., 2010)	Early Goal-Directed Therapy	None	Minimal	Method Not Specified
(De Miguel-Yanes et al., 2009)	Surviving Sepsis Campaign	None	Minimal	Face to face meeting
(Francis et al., 2010)	Surviving Sepsis Campaign	Yes, empiric guidelines based on site of infection	Minimal	Informal rounds sessions
(McColl et al., 2017)	Surviving Sepsis Campaign	Yes, based on site of infection	Protocol development, nurse-implemented medical directive	Formal rounds sessions, group presentations
(McLaughlin et al., 2017)	Surviving Sepsis Campaign	Yes, focused on Intravenous Push cephalosporin antibiotics	Protocol development	Face to face meetings
(Palleschi et al., 2014)	Surviving Sepsis Campaign	None	Minimal	Online modules, face to face meetings
(Papali et al., 2017)	World Health Organization Algorithm	None	Minimal	Lectures
(Rehmani et al., 2014)	Surviving Sepsis Campaign	Yes, based on site of infection	Minimal	Lectures
(Seoane et al., 2013)	Surviving Sepsis Campaign	Yes	Protocol development	Online modules, lectures
(Sweet et al., 2010)	Early Goal-Directed Therapy	None	Protocol development	Online modules, lectures
(Tromp et al., 2010)	Surviving Sepsis Campaign	None	Protocol development, ability to draw blood cultures autonomously	Face to face meeting
(Turi & Von Ah, 2013)	Not Specified	None	Minimal	Methods Not Specified

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