Developing Adult Sepsis Protocol to Reduce the Time to Initial Antibiotic Dose and Improve Outcomes among Patients with Cancer in Emergency Department

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Objective: Sepsis is a common cause of noncancer-related deaths among oncology patients. Delay in the initiation of efficient antimicrobial therapy will decrease the survival rate. This study aims to develop a sepsis protocol for adult oncology patients to decrease the time needed to receive the initial dose of antibiotic in an emergency department (ED), improve the early recognition of sepsis, and decrease the in-hospital mortality rate due to sepsis. Methods: A quasi-experimental research design was used. A total of 168 participants were assigned into pre- and post-intervention groups (n = 85) and (n = 83), respectively. The quick Sequential Organ Failure Assessment screening tool was used to screen patients in the triage room. Results: There was a significant difference in the proportions of receiving the initial antibiotic dose whether ≤1 h or >1 h between pre- and post-intervention groups. The results also showed that 89.4% of the postintervention group received their initial antibiotic dose in <1 h compared with 10.8% of the preintervention group. The median time needed for administering the initial antibiotic dose was decreased from 95 min to 45 min. The results of the changes in mortality rates are promising as it decreased 11.7% after applying the adult sepsis protocol. Conclusions: Applying an adult sepsis protocol in the ED significantly decreased the time needed to initiate antibiotic treatment. It is recommended to utilize a multidisciplinary and systematic approach in screening and treating sepsis.

Key words: Antibiotic, emergency department, oncology, protocol, quick Sequential Organ Failure Assessment screening, sepsis

Introduction

Sepsis is a life-threatening condition caused by overactive and toxic response to infection, which can lead to organ dysfunction.1 As a possible oncologic emergency situation, sepsis occurs in a continuum beginning with infection.1,2 Lack of knowledge and undertreatment of sepsis may cause a progression to septic shock and death.3 Septic shock is defined as “a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to increase mortality substantially,”

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ABSTRACT

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whereby the patient requires vasopressor support.\textsuperscript{[1]} About 10\%–75\% of patients with cancer approached the emergency department (ED) because of infectious complications as a consequence of cancer-related treatments, which are the most common causes of noncancer-related deaths among oncology patients.\textsuperscript{[4]}

The number of sepsis cases is escalating worldwide, thus the treatment should be evidence-based and timely.\textsuperscript{[5]} Delay in the initiation of efficient antimicrobial therapy during the first 6 h could decrease the survival rate by 7.5\%\textsuperscript{[6]} Applying some standardized strategies for screening and evaluating sepsis in the ED may enhance early recognition, allow proper management, and prioritize patients’ care plan.\textsuperscript{[6]}

Setting up international best practices for the assessment and management of early sepsis with bundled interventions and protocols decreases sepsis-related morbidity and mortality in many patient populations.\textsuperscript{[4]}

The application of a sepsis protocol includes educating both nursing and physicians staff on the use of the protocol and screening tool, as well as a general review of sepsis diagnosis and management.\textsuperscript{[9]} The nurses in the ED could utilize reliable and valid screening tools such as quick Sequential Organ Failure Assessment screening (qSOFA) and Systemic Inflammatory Response Syndrome (SIRS) to detect the early signs of sepsis and alert the health-care team immediately.\textsuperscript{[7,8]}

There are few clear written structured guidelines or protocols for those patients diagnosed with sepsis and approached the ED.\textsuperscript{[9]} Based on the extensive review of literature and to the authors’ knowledge, there are no published articles in Jordan exploring the effect of applying a sepsis protocol in EDs for patients with sepsis.

Therefore, the goals of conducting this study were to develop a sepsis protocol to be used in the ED for adult oncology patients in order to decrease triage-to-antibiotic time (time needed from the first encounter in triage to the time to receive the initial dose of antibiotic) for patients with sepsis, and improve early recognition of sepsis as well as to decrease the in-hospital mortality rate due to sepsis.

**Literature review**

A comprehensive search was conducted in January 2016 using the electronic databases of PubMed, CINAHL, and Ovid for research-based articles published between 2006 and 2016 to explore the effect of applying a sepsis protocol and the best practices in sepsis management. The following keywords were used in different combinations to search the electronic databases: sepsis, emergency department, and severe sepsis. Studies were included if they were; (1) Research-based articles; (2) on human subjects; (3) cover sepsis management in the ED; (4) focused on adult oncology populations; and (5) published in English.

Sepsis and septic shock are medical emergencies requiring immediate treatment and resuscitation.\textsuperscript{[2]} In a study conducted by Francis et al., the researchers reviewed the charts of the patients screened for sepsis 3 months before and after implementing the ED protocol, it was revealed that the sepsis protocol and compliance with guidelines reduced time-to-initial-antibiotic-administration from 163 to 79 min (84 min’ total reduction) among the ED patients. Additionally, implementing the sepsis protocol has been shown to improve the percentage of patients who received the appropriate treatment by 26\%\textsuperscript{[6]}

In a large study conducted in Europe, the United States, and South America 28,150 patients with sepsis were evaluated retrospectively to find the relationship between the time of antibiotic administration and mortality rate. The results showed that the delay in initial antibiotic has led to an increase in mortality rate.\textsuperscript{[10]}

Nurses are in a unique position to promote the early recognition and play a key role in providing care for patients with sepsis. Bruce et al. retrospectively studied the effect of a nurse-initiated ED sepsis protocol on time to initiate the first antibiotic dose. The nurse-initiated ED sepsis protocol implementation significantly improved the time to initial antibiotic dose from 135 to 108 min before and after implementation, respectively. While, there was no change in the rates of in-hospital mortality.\textsuperscript{[11]}

Several tools can be used to screen for sepsis such as SIRS and qSOFA. Recent investigations were conducted to find the preferences and advantages of each tool to be used in clinical settings. The Third International Consensus (Sepsis-3) recommended the use of qSOFA as it is more sensitive in identifying sepsis and promoting early treatment compared to the other tools, as well as decreasing the mortality rate.\textsuperscript{[11]} One of the specialized cancer centers developed an evidence-based algorithm utilizing qSOFA to show the pathway that health-care teams should follow to provide proper management for oncology patients with different stages of sepsis.\textsuperscript{[12]}

International guidelines for sepsis management were created in 2004 and reviewed in 2016. Moderate to high levels of evidence exist for initiating key “bundled interventions” for patients with possible sepsis. The four cornerstones of sepsis bundled strategies are (a) early screening and completion of diagnostic studies, (b) source evaluation, (c) timely administration of appropriate antibiotics, and (d) aggressive management of perfusion.\textsuperscript{[2]}

**Methods**

**Design**

A quasi-experimental research design was used to examine the effect of developing adult sepsis protocol in the
ED on early detection and management of sepsis among adult patients with cancer.

Sample

All patients with cancer who were visiting the ED and suspected to have sepsis were the target population for this study. Convenience sampling was used to recruit patients suspected to have sepsis in this study. The following inclusion criteria were applied; (1) adult patients aged 18 years or older; (2) diagnosed with cancer; and (3) admitted for sepsis treatment in the ED.

The sample size for this study was determined based on power analysis using a medium effect size of 0.5 and an alpha of 0.05. Thus, the minimum sample size of 128 was determined for the two groups. However, 168 patients were recruited to overcome the attrition rate. Preintervention data were collected for the 83 participants (preintervention group) who received the conventional care and treatment, and 85 participants were enrolled and monitored after applying the ED adult sepsis protocol (postintervention group) who were managed by following the instructions of the developed adult sepsis protocol.

Setting

This study was conducted at a nongovernmental, nonprofit cancer center and the only specialized setting for providing a comprehensive care for patients with cancer. It is an accredited and well‑equipped facility with a bed capacity of 352 beds. At the center, there are 22 beds in the ED, which serve more than 60 patients on daily basis.[13]

Ethical approval

This study was approved by the Institutional Review Board, complete confidentiality was granted and the anonymity was assured for the participants by numerically coding the data collection sheets to identify the participants. A locked file cabinet to store all data was used.

Procedure

Developing the adult sepsis protocol

After extensively reviewing the literature, and based on the global guidelines and evidence to manage sepsis in adult patients,[1,2,12] the sepsis protocol was developed by a consensus from a taskforce committee. This committee included a consultant intensivist, an ED consultant, a clinical pharmacist, an ED direct care nurse, and an ED nurse manager. The developed protocol was approved by the Centre’s medical board.

The adult sepsis protocol provides a clear and structured practice bundle and an order set of assessment, diagnoses, and finally management. This order set was formulated on the center’s electronic system to standardize the practice and management in the ED, and to allow for ED physicians to request the order set immediately after the initial diagnosis of sepsis.

The order set consists of five main categories; (1) nursing sepsis order; (2) laboratory order; (3) radiology order; (4) medication order; (5) intensive care unit (ICU) adult consultation. Each category has suborders to be checked if needed. The nursing sepsis order consists of; (1) hourly vital signs through cardiac monitor; (2) oxygen administration through nasal cannula or a simple face mask to maintain oxygen saturation >92%; (3) one or two peripheral access (large bore cannula is preferred); (4) urinary catheter if not contraindicated. The second category in the sepsis order set is the laboratory order, which contains a laboratory sepsis order such as peripheral blood culture and central if available, lactic acid, urine analysis and culture, complete blood count, chemistry profile, arterial blood gases, and other laboratory tests if indicated. The third category is the radiology order of chest X‑ray. The fourth category is the medication order, which provides clear instructions about the intravenous fluids bolus dose, maintenance dose, time, rate, as well as the recommended time for administering the initial dose of antibiotic. Finally, the fifth order is an ICU consultation based on the mean arterial pressure (MAP) if it is <65 mmHg, to consider starting vasopressors.

In the medication order and after collecting blood culture and lactic acid, the instruction is to administer the initial antibiotic dose within 1 h from diagnosis if possible. However, if collecting the blood culture and lactic acid are difficult, it is important to administer the antibiotic immediately to decrease mortality rate.

In addition, for all patients with sepsis and their MAP < 65 mmHg, an intravenous fluid is administered at 30 ml/kg over 3 h as bolus, then the staff nurse should assess the vital signs and inform the ED physician about blood pressure and lactic acid results, then a maintenance dose of intravenous fluid should be started.[21]

Staff awareness

Awareness was provided for all ED physicians and nurses in a period of 2 months (August–September 2016) using in-service educational sessions through monthly journal clubs and one-on-one education about using the newly developed protocol, as well as using the qSOFA tool to screen for sepsis. The ED nurses received the education and training by the primary investigator and the clinical resource nurse of the unit. The ED physicians also received several educational sessions by a consultant intensivist. The educational sessions started by awareness about sepsis assessment and management in general, and how to utilize the newly developed protocol and the adopted screening tool for assessing and managing sepsis in the ED. The
surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016 and the third international consensus definitions for sepsis and septic shock (sepsis-3) were used as guides for the content of the provided education and training.[1,2]

Data collection
The researchers used the qSOFA tool to screen patients for sepsis in the triage room. The study was conducted over a 7-month period (May–December 2016). A demographics’ data sheet was used to collect the participants’ characteristics and electronic medical records were used to elicit information about the time needed for triage-to-physician assessment (time needed from the first encounter in triage to initial physician assessment), triage-to-blood sampling (time needed from the first encounter in triage to the time of collecting the ordered blood samples), triage-to-fluid resuscitation (time needed from the first encounter in triage to the time of receiving the intravenous fluids), and triage-to-antibiotic (time needed from the first encounter in triage to the time to receive the initial dose of antibiotic) were measured in minutes for patients in the pre- and post-intervention groups.

In a period of 3 months (May–July 2016) before implementing the developed adult sepsis protocol, data were collected for all participants who approached the ED and were suspected to have sepsis (n = 83), those were the patients who received the conventional care provided in the ED. After applying the developed adult sepsis protocol in the ED, data were collected for a period of 3 months (October–December 2016) (n = 85). There was no direct contact with the patients, the researchers recorded the following timelines: triage-to-physician assessment, triage-to-blood sampling, triage-to-fluid resuscitation, and triage-to-antibiotic on the data collection sheet only before and after applying the developed protocol.

The mortality rate for all patients in the current study was monitored for 1 month after admission with a confirmed diagnosis of sepsis.

Instruments
Demographic characteristics
This form was developed by the researcher to capture the following demographic and clinical variables; age, gender, and type of cancer. As well as the information about the time needed for triage-to-physician assessment, triage-to-blood sampling, triage-to-fluid resuscitation, and triage-to-antibiotic were obtained from the medical record.

Triage screening tool (quick Sequential Organ Failure Assessment screening)
qSOFA was used to screen for adult patients suspected to have sepsis. The qSOFA consists of three clinical signs; altered mental status from baseline, systolic blood pressure of ≤100 mm Hg, respiratory rate of ≥22/min. The qSOFA score ranges from 0 to 3 with one point given for each presented sign, a score ≥2 means a positive result and indicates immediate assessment by a physician to confirm the diagnosis and to make the decision to start using the protocol.[1,14]

Statistical analysis
Analysis was performed using statistical analysis system (SAS) version 9.4 (SAS Institute Inc, Cary, NC). A significance criterion of P < 0.05 was used in the analysis. Descriptive statistics was used to describe the variables based on the level of measurement. χ² test was used for differences in proportions.

The sepsis-related mortality rate was measured using the formula (the number of patients who died from sepsis among sepsis-diagnosis admissions via the adult ED in a month/number of sepsis-diagnosis admissions via the adult ED in a month ×100) in pre- and post-intervention periods.

Results
A total of 168 patients enrolled in the study, divided into two groups: a preintervention group who received the conventional care (n = 83), and a postintervention group (n = 85) who were assessed and managed based on the developed adult sepsis protocol. The patients’ age ranged between 19 and 80 years with a standard deviation of 13.2. Males (53.5%) were more than females (46.5%). Breast, lymphoma, and leukemia were the most common (17.2%) types of cancer among participants, followed by colon and lung cancer (8.9% and 8.3%, respectively) [Figure 1].

Table 1 shows the differences in proportions in terms of the time needed from the first encounter with patients and performing the triage assessment by a registered nurse until the initial dose of antibiotic was administered for the preintervention and postintervention groups. The results reveal that there is a significant difference in the proportions of receiving the initial antibiotic dose whether ≤1 h or >1 h between pre- and post-intervention groups. The results also reveal that of the patients in the postintervention group, 76 (89.4%) had less delay than nine (10.8%) patients in the preintervention group in receiving the initial antibiotic dose in <1 h.

Table 2 shows the median time duration (time needed) for triage-to-physician assessment, triage-to-blood sampling, triage-to-fluid resuscitation, and triage-to-antibiotic. The results show that after applying the developed adult sepsis protocol, the median time needed (min) had decreased as follows; the first encounter in triage to perform a physician assessment (20 min to 6 min), collect blood sampling (44 min to 20 min), fluid resuscitation (53 min to 20 min), and administering the initial antibiotic dose (95 min to 45 min).
The results of the changes in mortality rates are promising as it decreased 11.7% after applying the adult sepsis protocol in the ED.

Discussion

Many adult patients with cancer arrived to the ED complaining of sepsis and septic shock, in which early identification and appropriate treatment can improve patient outcomes by preventing deterioration.[9] However, sepsis frequently goes unrecognized or undertreated in EDs. Working with a multidisciplinary team in oncology ED would allow all staff to focus on standardizing sepsis management to rapidly and efficiently treat sepsis cases.

Applying Adult Sepsis Protocol in ED for patients with cancer produced significant reduction in the mean from the time of first encounter with the triage nurse to the time of receiving the initial antibiotic dose. The results of the current study showed that the time needed to administer the initial dose of antibiotic was decreased 50 min in total after applying the protocol. The application of Adult Sepsis Protocol in the ED changed nursing and physicians’ practice and allowed for early detection and recognition of sepsis signs by using a well-known screening tool as well as using a systematic approach to providing management. This was consistent with similar studies conducted in EDs.[6,11]

Nurse staff plays a critical role in the early recognition and screening for sepsis by utilizing the qSOFA tool. The tool can be swiftly scored by nurses without the need for blood sampling tests. This facilitates the rapid identification for the signs of sepsis, and the need for further assessment by physicians, as well as improves the treatment outcomes. Using the qSOFA tool is in line with the recommendations of the third international consensus definitions for sepsis and septic shock.[1]

The mortality rate showed marked decrease in the incidence rate after applying the protocol. However, no analysis was performed to infer causality, but the percentage of mortality rates after applying the protocol was promising compared to the preintervention rates.

These results are similar to those reported by Wang et al.,[15] as they revealed that the in-hospital mortality rate was decreased after applying a sepsis bundle strategy to improve the outcomes of patients with sepsis in China.

However, the current results are incompatible with the results of the studies by Bruce et al.,[11] Ferrer et al.,[10] and ProCESS investigators[16] as they reported that there were no significant differences in mortality rates after using a protocol-based therapy for sepsis. This inconsistency could be related to the small sample size and convenient selection in our study, as well as the differences in populations between the studies.

Applying the adult sepsis protocol in the ED showed several benefits such as the decrease in the overall time needed to perform the initial assessment until receiving the initial dose of antibiotic, as well as decreasing the time needed for performing blood sampling and fluid resuscitation. Using a systematic approach to assess and manage patients with sepsis increased the compliance rate and eliminated any unnecessary delays. Also, applying such protocol will enhance the multidisciplinary approach in assessing and managing patients with sepsis.[10]

The limitations for our study included the inability to infer causality in the relationship between using the adult sepsis protocol and in-hospital mortality rates. The convenient selection for the sample size is considered a limitation as well. The effect of the education provided for the nurses and physicians as well as the compliance rate were not evaluated. However, this can be estimated by the improvement in the response time for screening and requesting orders which was measured in minutes in this study. This study did not explore if there were patients diagnosed with sepsis after admission.

Figure 1: The percentage of cancer types for all participants. ca: cancer

Table 1: Time from the first encounter in triage to receive the initial antibiotic dose

| Value                  | Preintervention (n=83), n (%) | Postintervention (n=85), n (%) | χ² | P       |
|------------------------|------------------------------|--------------------------------|----|---------|
| Time from triage to antibiotic (h) |                             |                                |    |         |
| ≤ 1                    | 9 (10.8)                     | 76 (89.4)                      | 103.71 | 0.000   |
| > 1                    | 74 (89.2)                    | 9 (10.6)                       |     |         |
Conclusion

Immediate screening and management of sepsis for patients with cancer in the ED can minimize the risk of sepsis deterioration. The findings of the current study revealed that applying an adult sepsis protocol in the ED significantly decreased the time needed from the first encounter with the patient in the triage until the initiate antibiotic treatment. Furthermore, it was shown that the mortality rate was decreased after applying the protocol. It is highly recommended to utilize the multidisciplinary and systematic approach in screening and treating sepsis. Adding sepsis educational interventions to nurses’ training will improve awareness and recognition of the importance of early identification and treatment of sepsis. This project demonstrates that utilizing a systematic approach could improve and initiate changes in practice and improve patients’ outcomes.

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Conflicts of interest

There are no conflicts of interest.

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