Evaluation of a Nurse-Initiated Sepsis Protocol in the Emergency Department

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Abstract

The aims of this study were to evaluate the impacts of a nurse-initiated sepsis protocol on compliance with sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign and to identify predictors of patient mortality. A retrospective chart review was conducted among patients admitted with severe sepsis or septic shock to two emergency departments at a university-affiliated medical center in southern California from October 2011 to May 2012, which included 78 and 108 patients for pre- and postintervention groups, respectively. There were no statistically significant differences between two groups in sepsis resuscitation bundle compliance ($p > 0.05$). The compliance rate for administration of broad spectrum antibiotics within three hours of ED admission declined slightly from pre- to postintervention group (80.8% to 76.7%), even though the mean time to the first antibiotic administration improved numerically by 21 minutes in the postintervention group ($p > 0.05$). The increased oxygen requirement to keep oxygen saturation > 90%, elevated bilirubin level (> 4.0), prolonged INR (> 1.5) or aPTT > 60 sec, and use of vasopressors were significant positive predictors of patient mortality whereas body weight was the negative predictor. In conclusion, the implementation of a nurse-initiated sepsis protocol had no significant impacts on compliance with sepsis resuscitation bundle guidelines. Other strategies to improve the compliance need to be explored.

Keywords: sepsis, predictors, mortality, protocol, nurse

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Chapter One: Introduction

Sepsis occurs in 1 out of 100 persons every year and is estimated to increase each year, with an estimated in-hospital mortality range from 14.7% to 29.9% (Gaieski et al., 2013). Sepsis is the 10th leading cause of death in the United States and an estimated 740,000 patients are hospitalized annually. Frequently, sepsis goes unrecognized or untreated because key elements in prevention of sepsis progression are not implemented in a timely manner (Mikkelsen et al., 2010; Sweet et al., 2010; Tromp et al., 2010). Currently sepsis is treated on the presumption of an infectious state, however many beneficial interventions are omitted due to the absence of an individualized order set. In order to meet the challenges of sepsis and to improve diagnosis and management, the Surviving Sepsis Campaign® (SSC) revised the clinical practice guidelines which include treating extremely labile sepsis or septic shock patients (Dellinger, et al., 2013). Key recommendations of the guidelines include early recognition of sepsis, goal-directed resuscitation of the septic patient during the first six hours after recognition, and endorses very early antibiotic therapy be started within one hour of recognition of severe sepsis and septic shock (Dellinger, et al., 2013). Timelines begin upon triage in the Emergency Department (ED), where the admitting nurse is the first line of defense for identifying septic patients.

Pertinent nursing recommendations highlight improved recognition of deteriorating patients, increased early initiation of resuscitation, and use of early warning signals to identify patients at risk for further deterioration (Kleinpell, et al, 2013). It is the nurses' responsibility to screen patients to include in the sepsis resuscitation bundle, recognize priorities, and start the trend of aggressive treatment of sepsis (Tromp, et al., 2010). The nurses' crucial role in identifying and initiating treatment for septic patients may be hastened if nurses are empowered by comprehensive education and guided by a specific treatment protocol which initiates life-saving interventions to decrease mortality and untoward outcomes.

Chapter Two: Review of Literature

Sepsis is the number one cause of death in the intensive care units (ICUs) and the incidence of severe sepsis is expected to double over the next 25 to 30 years ("Surviving Sepsis Campaign," n.d.). Early Goal Directed Therapy (EGDT) was introduced that included aggressive fluid resuscitation, early antibiotics, invasive monitoring, and management of hemodynamics in septic patients. (Rivers, et al., 2001). Subsequently, in 2008, the Society of Critical Care Medicine published international evidence-based practice guidelines that were adopted by the Surviving Sepsis Campaign (SSC) for treatment of patients diagnosed with sepsis in the ED (Dellinger, et al., 2008). Implementing EGDT in EDs has shown mortality reduction from 8%-18% in some studies when EGDT was initiated as soon as possible on patients meeting the severe sepsis or septic shock criteria (Crowe et al., 2010; Focht et al., 2009; Jones, et al, 2007; Lin, et al., 2006; Micek et al., 2006). In a randomized controlled trial among 233 patients in severe sepsis and septic shock, there was a statistically significant reduction in mortality among those treated with EGDT (p=0.009) (Rivers, et al., 2001).

Sepsis resuscitation bundle includes seven interventions that should be completed immediately upon diagnosis of severe sepsis with a goal to perform every task for each diagnosed patient within the first 6 hours of triage. These elements, which are based on EGDT, are built around best practices that qualify as high levels of evidence as outlined by the GRADE system approach from the 2008 Surviving Sepsis Campaign Guidelines ("Severe Sepsis Bundles," n.d.). Tasks include obtaining serum lactate level, blood cultures prior to antibiotic administration, broad spectrum antibiotic administration within 3 hours of an ED admission, and within 1 hour of diagnosis outside the ED, fluid resuscitation of 20mL/kg with vasopressors initiated with unresponsive MAP, and maintain adequate CVP and ScvO2 with a goal CVP of >8mm Hg and goal ScvO2 >70%. SSC guidelines recommend that each institution develop a

sepsis management protocol (Dellinger et al., 2008).

Francis et al. (2010) reported that implementation of ED sepsis protocol decreased time to antibiotics of 163 minutes to 79 minutes, a reduction of 84 minutes (95% confidence interval [CI] 42 to 126 min). Another study that implemented a severe sepsis protocol in the ED and stocked antibiotic in the ED decreased time to antibiotics from 2.7 hrs to 1.4 hrs (*p=0.06*) and an additional decrease in mortality from 51.4% to 27.0% (absolute risk reduction=24%, 95% CI 3% to 47%) (MacRedmond, et al., 2010). Other studies showed that simply initiating a sepsis protocol in the ED improves time to antibiotics (Sweet, et al., 2010; Tromp, et al., 2010). Kumar and colleagues (2006) showed that delay in antibiotics for each hour in patients with septic shock and hypotension over the first 6 hours was associated with an average decrease in survival of 7.6%.

Numerous studies that compare pre- and postimplementation of a sepsis protocol focused on EGDT therapy and modified the guidelines only slightly to accommodate differences in settings and populations. Despite slight differences in sepsis protocol inclusion criteria, many showed positive outcomes in decreasing mortality (Crowe, et al., 2010; Focht, et al., 2009; Francis, et al., 2010; MacRedmond, et al., 2010; Nguyen, et al., 2007; Talmor, et al., 2008). Therefore the focus of the protocol may instead be centered on methods of implementation and strength of nursing education to ensure increasingly positive patient outcomes. Tromp and colleagues (2010) reported a study based on a solely nurse initiated sepsis protocol among 731 patients, showing overall in-hospital mortality rate reduction of 6.3% to 5.5% after implementation of the nurse-driven sepsis protocol. . These results demonstrated that training and performance feedback by nurses can significantly improve mortality rates

Theoretical Framework

The Iowa model of evidence-based practice to promote quality care was followed to guide this evidence-based practice improvement. Triggers are found identifying a problem, other facilities are

benchmarked, and process improvement data and risk management data are presented which lead to problem identification (Titler, et al., 2001). Literature including national guidelines and evidence-based data were reviewed and the topic of implementing a sepsis protocol became a priority for the organization and a task force was formed to assemble research and related literature. The literature was researched and other facilities protocols were assessed. After appraising the studies, a pilot protocol was developed and implemented, and outcomes desired were outlined. Baseline data was collected to compare to postintervention data and evaluated for improvement of care. Data found by comparing pre- and postintervention periods will guide modification of practice and hopefully identify and barriers or areas that need improvement. Continuing evaluation will be done to improve quality of care in the environment, with staff, and patients and family.

Aims

The aims of this study were to evaluate the impact of a nurse-initiated sepsis protocol on compliance with sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign and to identify predictors of mortality among patients admitted with severe sepsis or septic shock to the emergency departments (EDs) of a tertiary care, university-affiliated medical center. The sepsis resuscitation bundle compliance end points were: (a) measuring serum lactate, (b) obtaining blood cultures prior to administration of antibiotics, (c) administration of broad spectrum antibiotics within three hours of ED admission, (d) fluid resuscitation within 1 hour in the event of hypotension and/or serum lactate > 4 mmol; and (e) administration of vasopressors for hypotension not responding to initial fluid resuscitation to maintain a MAP of ≥ 65 mmHg.

Chapter Three: Methods

Design

A pre- and postintervention pilot study using a retrospective chart review method was conducted among patients admitted with severe sepsis or septic shock to the EDs from October 2011 to May 2012. A nurse-initiated sepsis protocol was developed as a guide for nurses and physicians to implement evidence-based sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign. The nurses and physicians in both emergency departments participated in a mandatory online educational session on the sepsis protocol. A convenience sample of patients admitted with severe sepsis or septic shock to the emergency departments within four months before and after the initiation of the nurse-initiated sepsis protocol was chosen and a retrospective chart review using electronic medical records was conducted for data collection.

Setting and sample

This study was carried out at two EDs in a university-associated tertiary medical center. The first ED had 24 beds and treated approximately 36,000 patients per year and the second ED had 11 beds and treated about 16,000 patients per year. These EDs account for more than 30% of the Medical Center's admissions.

The inclusion criteria were: (a) age of 18 years or older; (b) male or female; (c) ICD-9 code of severe sepsis or septic shock as either a primary or secondary admitting diagnosis to the emergency department. ICD-9 stands for International Classification of Disease, 9th edition and serves as a coding system to identify diseases processes in the US and internationally. Patients included in the study met triggers as having severe sepsis or septic shock, based on the 2008 Surviving Sepsis Campaign definitions for severe sepsis and septic shock (Dellinger et al., 2008).

The triggers included any two of the SIRS criteria (Table 1). Patients were excluded if they were not initially admitted through the ED, or if they developed severe sepsis or septic shock during hospitalization.

Table 1: Screening Criteria

1: Any Two of the Following **(At least 2 are required**):

___Temp: >38.3C (100.9F) OR <36.0C (96.8)
___Heart Rate: >90/minute
___Respiratory Rate >20 Breaths per Minute
___**If Immune Compromised: Temp >38 C (100.4F)

AND

2: Evidence of Hypoperfusion **(At least 1 is required):**

___MAP <65 mmHg
___SBP <40 mmHg below baseline
___Acute Altered Mental Status
___Oxygen Saturation <92%
___Capillary Refill >3sec
___Diminished Pulses
___Mottled Extremities

AND

3. Suspected Infection Source
___Urosepsis
___Meningitis
___Soft Tissue
___Community Acquired Pneumonia
___Healthcare Associated Pneumonia
___Abdominal or Pelvic
___Other

Note. From University of California San Diego Medical Center Sepsis Protocol, with permission.

Nurse-initiated sepsis protocol

The sepsis protocol was developed by multidisciplinary healthcare members from departments of emergency medicine, critical care, pharmacy, infectious disease, performance

improvement, and senior nursing staff. The final protocol was based on the sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign completed in December 2011 (Dellinger et al., 2008). Following internal review, the protocol was approved for use in the EDs at the beginning of February 2012.

The Code Sepsis Pilot Screening Tool and Protocol was benchmarked against Loma Linda Hospital and John Hopkins Hospital, and was modified to fit the patient population at current study site. It is a stage 1 (all patients who meet criteria) and stage 2 (patients with persistent symptoms) treatment protocol, beginning with sepsis assessment done by the ED triage nurse. Once the patient met criteria, the ED attending and ED charge nurse were notified and the sepsis protocol was triggered and labeled on the patient's chart. An internal Code Sepsis was called on the patient, which alerted the Pharmacist, ED charge nurse, radiology department, and House Supervisor. The nurse then initiated Code Sepsis Stage 1elements (Table 2) and if a patient had persistent hypotension after fluid resuscitation, Code Sepsis Stage 2 was immediately initiated (Table 2) with precise resuscitation goals identified and use of vasopressors such as Norepinephrine, Phenylephrine, Vasopressin, or Dopamine to maintain MAP within parameters.

Table 2: Code Sepsis Protocol

Initiates Code Sepsis Stage 1: (Standing Order Set)

Diagnostics:

Lactate, Blood Cultures x 2, CBC w Diff, PT(INR), PTT, CMP, Phos, CPK, LDH, ABG or VBG, Blood Bank Tubes, UA, CXR, ECG, Other

Interventions:

1. IV: Place 2 large bore peripheral IVs or
2. CVC: Central Venous Catheter (CVC) by MD
3. Weight: Patient's approximate weights in KG_
4. Weight Based IV Fluid Bolus Ranges run over 1st 30 minutes **(Select One)**

Under 50kg, Consult ED Attending and Record Bolus Amount Here:_
50-75kg, administer 1500mL Normal Saline (Sodium Chloride 0.9%)
76-100kg, administer 2000mL Normal Saline (Sodium Chloride 0.9%)
>101kg, administer 2500mL Normal Saline (Sodium Chloride 0.9%)

****Administer all IV Antibiotics at the same time (In Parallel). The ED Code pharmacist will review antibiotics for appropriateness, administration priority order, and Y-site compatibility**

IV ABX Start Time (Patient Triage Time, 1st RN contact): __

*Initiate Code Sepsis Stage 2:

For Persistent Hypotension (SBP <90mmHg OR MAP <65mmHg ORSBP 40mmHg below baseline) after volume resuscitation OR lactate >40:

1. Transduce to measure a CVP
2. *Consider* additional volume resuscitation (as above)
3. Start Central Venous Catheter (CVC) if not already inserted or if not contraindicated;
4. Consider ScvO2
5. Begin Vasopressor
6. Contact Nursing Supervisor (to expedite bed placement) and ICU team
7. Serial Lactate (q6h)
8. *Consider* Transfusion to hematocrit of 30
9. *Consider* Stress dose steroids

Resuscitation Goals:

A.CVP 8-12 mmHg (12-15 if intubated)
B. Mean arterial pressure >65 mmHg
C. Urine output >0.5ml/kg/hr
D. ScvO2 >65% or Lactate clearance >10%

Note. From University of California San Diego Medical Center Sepsis Protocol, with permission.

An educational program on implementation of the Code Sepsis Protocol was provided for all emergency physicians, residents, and nursing staff. This included online education in PowerPoint format for physicians and residents. Nurses in the ED were given a mandatory PowerPoint to view that was made available to all nurses posted on the ED nurses' *Ishare* account. Educational posters with the sepsis algorithm and code sepsis protocol were placed in the ED's, and sepsis reference cards were made available to all nurses. The training included the severe sepsis triggers, nurses' role in implementing the protocol, and evidence related to the Surviving Sepsis Campaign guidelines.

Instruments

An investigator-developed standardized data collection tool was utilized to collect the data (Appendix A). The information were collected regarding date and time of admission, vital signs upon admission, fluid resuscitation within one hour, fluid resuscitation within three hours, time of first antibiotic, blood cultures and lactate drawn before antibiotics, lactate level, time of vasopressor initiation, severe sepsis criteria, culture results, type of infection if identified, length of stay, and mortality. Demographics were also collected such as gender, age, weight, and site of hospitalization**.**

Data collection procedures

This study was approved by the Institutional Review Boards at the medical center and the university (Appendice B & C). Informed consent was waived as this retrospective chart review could be not practically carried out without the waiver of information consent form study participants. To identify study participants, all patients admitted through the ED with an ICD-9 code of severe sepsis or septic shock as either a primary or secondary diagnosis were further screened via electronic medical records for inclusion criteria including vital signs and evidence

of organ dysfunction from October 1, 2011 to January 31, 2012 for preintervention group and from February 1, 2012 to May 31, 2012 for the postintervention group. A blinded code was assigned to each participant to protect the patient identity. ICU nurses completed data entry into Excel spreadsheet from the data collection tool

Data analyses

Data in Excel spreadsheet were transferred into SPSS database and analyzed (Version 20.0, SPSS Inc, Chicago, Illinois) and the level of statistics were set at p value <0.05 for all data analyses. Descriptive statistics of frequency, percentage, median, and range were calculated to compare sample characteristics and the main outcomes of pre- and postintervention groups. The main outcomes for this study included compliance with sepsis resuscitation bundle, length of hospital stay, and mortality. Non-parametric tests of chi-square tests for categorical variables and Mann-Whitney tests for continuous variables were employed**.**

In order to identify the potential predictor variables for patient mortality, the bivariate correlation procedures with Kendall Tau test were first used between the dichotomous independent variables and patient mortality. All statistically significant variables from the bivariate correlations were then entered into the multivariate logistic regression models to identify the potential predictors of mortality. Non-significant variables were eliminated backwards.

Chapter Four: Results

Sample characteristics

Demographic and clinical characteristics of the patients are shown in Table 3. Data were collected from 181 patients, 78 from the pre- and 103 from the postintervention groups. In general, the two groups were well balanced without any significant differences ($p > 0.05$). The average age of the entire sample was 61 years old and the majority was male (57.5%) and from one site (71.8%). About two thirds of the patients presented with either urinary tract infection (30.9%) or pneumonia (33.1%). For severe sepsis criteria required for eligibility, the majority of patients presented with hypotension (63.5%) and either low urinary output (35.4%) or acute altered mental status (33.7%). Approximately half of the patients were in septic shock.

Table 3 Sample characteristics

Characteristics	Total (*N*= 181)	Pre-intervention (*n*= 78)	Post-intervention (*n*= 103)	*p* value
Age, median (range), yr	61.0 (20-92)	61.5 (22-92)	61.0 (20-92)	0.472
Gender				
Male	104 (57.5)	39 (50)	65 (63.1)	0.095
Female	77 (42.5)	39 (50)	38 (36.9)	
Body weight, median (range), Kg	77 (34-147)	78 (44-147)	75 (34-138)	0.480
Site				1.000
Site A	51 (28.2)	22 (28.2)	29 (28.2)	
Site B	130 (71.8)	56 (71.8)	74 (71.8)	
Infections				
Urinary Trach Infection	56 (30.9)	25 (32.1)	31 (30.1)	0.871
Pneumonia	69 (33.1)	28 (35.9)	32 (31.1)	0.526
Gastrointestinal infection	17 (9.4)	11 (14.1)	6 (5.8)	0.073
C Diff infection	7 (3.9)	4 (5.1)	3 (2.9)	0.466
Abscess	3 (1.7)	1 (1.3)	2 (1.9)	1.000
Endocarditis	4 (2.2)	1 (1.3)	3 (2.9)	0.635
Cellulitis	10 (5.5)	5 (6.4)	5 (4.9)	0.747
Peritonitis	7 (3.9)	1 (1.3)	6 (5.8)	0.242
Cather-associated bloodstream infection	10 (5.5)	2 (2.6)	8 (7.8)	0.191
Other/unknown	18 (10.0)	6 (7.7)	12 (11.6)	
Severe sepsis criteria				
Systolic blood pressure <90, or MAP < 65	115 (63.5)	51 (65.4)	64 (62.1)	0.755
Increased O2 requirement to keep Sat >	18 (9.9)	5 (6.4)	13 (12.6)	0.213
90%	64 (35.4)	27 (34.6)	37 (35.9)	0.877
Urine output < 0.5 mL/kg/h for > 2 hrs	7 (3.9)	5 (6.4)	2 (1.9)	0.142
Bilirubin > 4.0	25 (13.8)	11 (14.1)	14 (13.6)	1.000
Platelet < 80,000 or >50% reduction	32 (17.7)	14 (17.9)	18 (17.5)	1.000
INR > 1.5 or aPTT > 60 sec	59 (32.6)	25 (32.1)	34 (33.0)	1.000
pH < 7.30 or lactate > 36	61 (33.7)	25 (32.1)	36 (35.0)	0.752
Acute alteration in mental status				
Septic shock	90 (49.7)	36 (46.2)	54 (52.4)	0.454

Note. Values are expressed as n (%) unless otherwise indicated. Percentage may not add up to 100% because of the missing data or rounding. Mann-Whitney test for continuous variables & chi-square test (Fisher's Exact Test) for categorical variables

Comparisons of pre- and postintervention groups

Comparisons of main outcome variables are shown in Table 4. There were no statistically significant differences between two groups in compliance with sepsis resuscitation bundle ($p > 0.05$). The percentages of measuring serum lactate and obtaining blood cultures prior to administration of an antibiotic for both groups were very high (> 95% in both groups). However, the compliance rate for administration of broad spectrum antibiotics within three hours of ED admission declined slightly in the postintervention group (76.7% postintervention vs 80.8% preintervention), even though the time to the first antibiotic administration improved numerically by 21 minutes in the postintervention group ($p > 0.05$). The compliance rate for fluid resuscitation within one hour for patients with hypotension and/or serum lactate > 4 mmol declined in the postintervention group (68.9% vs 83.3%), but rate of using vasopressors increased numerically in postintervention group (52.4% vs 39.8%). No statistically significant differences were found in the lengths of hospital stay or mortality rates.

Predictors of patient mortality

Bivariate correlations results suggested that several clinical variables have statistically significant associations with the mortality (Table 5). The increased oxygen requirement to keep oxygen saturation > 90%, elevated bilirubin level (> 4.0), prolonged INR (> 1.5) or aPTT > 60 sec, pH < 7.30 with elevated lactate level (> 36), altered mental status, and use of vasopressors and a metronidazole antibiotic had significant positive association with mortality. In contrast, body weight, urinary teach infection, measuring serum lactate, obtaining blood culture prior to antibiotic, and positive blood culture had significant negative association with the mortality.

Table 4: Comparisons of main outcomes between two groups

	Total (*N*= 181)	Pre-intervention (*n*= 78)	Post-intervention (*n*= 103)	*p* value
Compliance with sepsis resuscitation bundle				
Measuring serum lactate	177 (97.8)	75 (96.2)	102 (99.0)	0.316
Obtaining blood cultures prior to antibiotic	178 (98.3)	77 (98.7)	101 (98.1)	0.436
Antibiotic within 3 hours of ED admission	142 (78.5)	63 (80.8)	79 (76.7)	0.586
Fluid resuscitation within 1 hour	136 (75.2)	65 (83.3)	71 (68.9)	0.499
Administration of vasopressors	85 (47.0)	31 (39.8)	54 (52.4)	0.100
Time to 1st antibiotic administration median (range), min	117 (0-2880)	131 (0-699)	110 (20-2880)	0.357
Length of hospital stay, median (range), days	8.0 (1-69)	8.0 (2-57)	8.0 (1-69)	0.524
Mortality	34 (18.8)	12 (15.4)	22 (21.4)	0.342

Note. Values are expressed as n (%) unless otherwise indicated. Percentage may not add up to 100% because of the missing data or rounding.
Sepsis resuscitation bundle completed during the 6-hour window.
Mann-Whitney test for continuous variables & chi-square test (Fisher's Exact Test) for categorical variables

All these significant independent variables that correlated with the mortality were entered into a multivariate logistic regression model to identify the predictors of mortality (Table 5). Five variables emerged as significant predictors of mortality: elevated bilirubin level > 4.0 (OR=27.7; *p*=0.009), increased oxygen requirement to keep oxygen saturation > 90% (OR=6.32; *p*=0.007), prolonged INR (> 1.5) or aPTT > 60 sec (OR=4.08; *p*=0.016), use of vasopressors OR=3.05; *p*=0.050), and body weight (OR=0.96 per kilogram; *p*=0.007).

Table 5: Bivariate correlations for mortality (*N*= 181)

Variables	Mortality
Age, ≥ 65 yr	0.124
Body weight	-0.127*
Infection	
Urinary Trach Infection	-0.261**
Pneumonia	0.172*
Septic shock	0.257**
Positive blood culture	-0.185*
Severe sepsis criteria	
Systolic blood pressure <90, or MAP < 65	0.041
Increased O2 requirement to keep Sat > 90%	0.218**
Urine output < 0.5 mL/kg/h for > 2 hrs	0.029
Bilirubin > 4.0	0.270**
Platelet < 80,000 or >50% reduction	0.053
INR > 1.5 or aPTT > 60 sec	0.259**
pH < 7.30 or lactate > 36	0.239**
Acute alteration in mental status	0.226**
Compliance with sepsis resuscitation bundle	
Measuring serum lactate	-0.024
Obtaining blood culture prior to antibiotic	-0.158*
Antibiotic within 3 hours of ED admission	-0.143*
Fluid resuscitation within 1 hour	-0.112
Vasopressors	0.228**
Time to 1st antibiotic administration	-0.054

Note. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ by Kendall's Tau test.

Chapter Five: Discussion

The aims of this study were to evaluate the impacts of an online education program and a nurse-initiated sepsis protocol on compliance with sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign and to identify predictors of mortality among patients admitted with severe sepsis or septic shock to the emergency departments. The study results indicate that the implementation of a nurse-initiated sepsis protocol and online educational program had no statistically significant impacts on compliance rates with sepsis resuscitation bundle guidelines.

The nurse-initiated sepsis protocol was developed to improve the patient outcomes by early and aggressive treatments according to the evidence-based guidelines. However, the compliance rates of obtaining serum lactate and blood culture before administration of antibiotic among ED patients were approximately 100% even before implementation of the protocol. No statistically significant differences were found in the compliance rate of administering antibiotics within 3 hours of ED admission even though the actual time to administrating of the first antibiotic was decreased numerically by 21 minutes after implementation of nurse-initiated sepsis protocol. The compliance was already very high before preintervention. Furthermore, the patient outcomes of mortality and length of hospital stay were similar between the two groups.

Despite the apparently significant negative correlation between early administration of antibiotics and mortality in bivariate Kendall's Tau test, it was surprising that early administration of antibiotics was not a significant predictor of mortality in the multivariate logistic regression analysis. This current study result is consistent with results from another large prospective study of emergency department patients with septic shock that no increase in mortality was shown with each hour delay to antibiotics after triage (Puskarich, et al., 2011). Sweet (2010) showed that although time to antibiotics was improved by 3.1 hours no reductions

in mortality or length of stay resulted. However, the result from the current study contradicted the results from other studies which found that delayed times from triage to administration of antimicrobials are primary predictors of mortality in patients with severe sepsis and septic shock (Gaieski et al., 2010; Kumar, et al., 2006; Sharpio et al., 2006). It seems likely that reason for decrease in mortality lies in other variables, rather than early antibiotic administration. Higher numbers of septic shock as well as mortality occurred in the study group, so it is possible that distinct interventions used to treat those patients contributed to the increased incidence of mortality. More research is indicated to determine which, if any treatment elements are unintentionally contributing to increases of mortality.

As expected, the criteria for severe sepsis were found to be significant predictors of mortality, i.e. the elevated bilirubin, increased oxygen requirement, prolonged bleeding time, acute mental status change and low body weight. Several studies have shown poor oxygenation has a strong correlation with mortality in septic patients (Colin, et al., 2012; Pope., et al., 2010; Vorwek & Coats, 2012). It is interesting that low systolic blood pressure at triage did not correlate with mortality. Additionally, many patients presented to the ED with blood pressure within normal limits, but quickly deteriorated to low blood pressures within the first few hours after admission. These results may indicate that single blood pressure measurement at triage may not be helpful in identifying those at high risk for mortality. Perhaps assessing blood pressure over time may be more useful for identifying them.

Fluid resuscitation also decreased numerically in the postintervention group but rate of vasopressor administration numerically increased. It is unclear why fluid resuscitation decreased but it is possible that since more patients in study group were identified as septic shock, more focus was on initiation of vasopressors than fluid resuscitation.

The post intervention group had numerically greater septic shock and mortality. This could be due to the newly established inclusion criteria for septic shock, where more patients were diagnosed with septic shock than in the preinternvention group. It is possible that the postintervention group was sicker or that greater improvement in sepsis criteria could have observed with more accurately identification of sepsis in the postintervention group.

There are several limitations to the current study. First, the educational intervention was ongoing at the time of preintervention. Therefore, the effects of educational intervention may have already impacted the preintervention group, which may have resulted in high rate of compliance with sepsis resuscitation bundle guidelines. This may have contributed to lack of differences between two groups. Second, the effects of an educational program on nurses' posttest knowledge were not analyzed in this study. Therefore, the effects of education on nurses were not documented. Third, this study was performed through retrospective chart review by relying on ICD-9 coding of severe sepsis and septic shock, which may have introduced bias in the sample selection through erroneous coding. Fourth, the study findings on predictors of mortality should be not taken as cause-and-effect relationship in this retrospective chart review. Finally, the study results from a single study site may limit the generalizability of the findings to other ED settings.

Additional studies are needed to improve the compliance with the sepsis resuscitation bundle and its impacts on patient outcome and quality of care. Further studies are needed to identify the importance of sepsis bundle elements in decreasing mortality for septic shock. Although it seems that treatment elements and time to interventions may vary between severe sepsis and septic shock, future research is indicated to identify best treatment for each to maximize outcomes.

Conclusion

A nurse-initiated sepsis protocol in the ED was implemented to reduce time to antibiotics and increase prompt use of vasopressors in compliance with sepsis resuscitation bundle guidelines from the Surviving Sepsis Campaign. Even though there were no statistically significant improvements after implementation of a nurse-initiated sepsis protocol, this study demonstrated that severe sepsis criteria were the significant predictors of patient mortality. Other strategies to improve the compliance need to be explored.

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Appendix A

Data Collection Tool

ASN:_____
□Pre-intervention □Post-intervention

1. Age:_____Gender: □Male □ Female
2. Ethnicity: □White □Asian □African American □ Hispanic □Other
3. ED Admission Date:_____/_____/_____Time:_____.
   □ from other healthcare setting; □ from home
4. ED discharge Date:_____/_____/_____Time:_____.
   □to ICU □ to Non-ICU □ to Surgery □to Home
5. ICU admission date: _____/_____/_____
6. ICU discharge date: _____/_____/_____
7. Discharge Date from hospital: _____/_____/_____
8. Death: □ Yes □ No
9. Cause of death: _____
10. Death date: :_____/_____/_____
11. Sepsis Protocol Order Set Used: □Yes □No

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12. Code Sepsis Stage 1 Criteria at admission: (select "Yes-No" option for Code Sepsis Stage 1 criteria)
    - Temperature:
    - Hypoperfusion SBP< 90, MAP <65, or SBP drops >40 from baseline: □Yes □No
    - Heart rate > 90: □Yes □No
    - Respiratory rate (XXXXXX): □Yes □No
    - XXXX □Yes □No
    - XXXX
    - XXX

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13. Initial Lactate Level: _____
14. Blood Cultures completed: □Yes □No
15. Broad-spectrum antibiotics: □Yes □No

16. Broad-spectrum antibiotics administration time: _____
17. Blood culture results: □Positive □Negative
18. Initial fluids at 60 min: _____
19. Initial fluids at 180 min: _____
20. Code Sepsis Stage 2:
    - Vasopressors: □Yes □No
    - Vasopressor initiation: □ED □ICU
    - Vasopressors administration time: _____
    - Central venous catheter: □Yes □No
    - CVP parameters > ??: □Yes □No
    - ScvO2 or SvO2 > ?? □Yes □No
    - Vasopressors administration: □Yes □No
21. Sepsis Resuscitation Bundle during the 6-hour time window:
    A. Initial Lactate ordered: □Yes □No.
    B. Blood Cultures completed before antibiotics administration: □Yes □No
    C. Broad-spectrum antibiotics within 3 hours of ED admission: □Yes □No
    D. Fluid resusication/vassopressor: □Yes □No
    E. CVP parameters > ??: □Yes □No
    F. ScvO2 or SvO2 > ?? □Yes □No

Appendix B

120042

UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM

TO: Rose Bruce

RE: Project #120042
Evaluation of a Nurse-Initiated Sepsis Protocol in the Emergency Department

Dear Dr. Bruce:

The above-referenced project was reviewed and approved by one of this institution's Institutional Review Boards in accordance with the requirements of the Code of Federal Regulations on the Protection of Human Subjects (45 CFR 46 and 21 CFR 50 and 56), including its relevant Subparts. This approval, based on the degree of risk, is for 365 days from the date of **IRB review and approval** unless otherwise stated in this letter. The regulations require that continuing review be conducted on or before the 1-year anniversary date of the IRB approval, even though the research activity may not begin until some time after the IRB has given approval.

The IRB determined that waiver of informed consent may be granted for this project as it meets the requirements outlined in 45 CFR 46.116(d). The research is minimal risk; the waiver or alteration will not adversely affect the rights and welfare of the subjects; the research could not practicably carried out without the waiver or alteration.

In addition, a waiver of individual authorization for use of Protected Health Information (PHI) was granted by the Institutional Review Board as stipulated by the HIPAA Privacy Rule, 45 CFR 164 Section 512(I). The Institutional Review Board determined that the proposed research satisfies following criteria:

1. The use or disclosure of PHI involves no more than minimal risk.
2. Granting of waiver will not adversely affect privacy rights and welfare of the individuals whose records will be used.
3. The project could not practicably be conducted without a waiver.
4. The project could not practicably be conducted without use of PHI.
5. The privacy risks are reasonable relative to the anticipated benefits of research.
6. An adequate plan to protect identifiers from improper use and disclosure is included in the research proposal.
7. An adequate plan to destroy the identifiers at the earliest opportunity, or justification for retaining identifiers, is included in the research proposal.
8. The project plan includes written assurances that PHI will not be re-used or disclosed for other purposes.

The PHI for which use has been determined to be necessary by the IRB includes:

1. Age, gender, interventions used, rate of mortality, and length of stay.

The IRB determined that this project presents more than minimal risk to human subjects in that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of

themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Date of IRB review and approval: **1/26/2012**

On behalf of the Institutional Review Board,

/jd

Michael Caligiuri, Ph.D.
Director, Human Research Protections Program
(858) 657-5100

Note: All Human Subject research conducted at the VA facility and/or utilizing VA/VMRF funds MUST BE APPROVED by the VA Research and Development Committee prior to commencing any research. In addition, please ensure that the clinical trial agreement or other funding is appropriately in place prior to conducting any research activities.

IRB approval does not constitute funding **or other institutional required approvals.** Should your studies involve other review committees such as Conflict of Interest (COI), Protocol Review Monitoring Committee (PRMC), and committees under Environmental Health & Safety (EH&S) such as Institutional Biosafety Committee (IBC), Human Exposure Committee (HERC), and RSSC (Radiation Safety and Surveillance Committee), it is the researchers responsibility to ensure that all approvals are in place prior to conducting research involving human subjects or their related specimens.

Approval release date: 4/9/2012

Appendix C

PLNU IRB
Exempt From Further Review
1087

PI: Bruce, Rose
Additional Investigators: NA
Faculty Advisor: Maiden, PhD
Title: Evaluation of Nurse Initiated Sepsis Protocol in Emergency Department

The research proposal was reviewed and verified as an exempt from further review under category 4 and has been approved in accordance with PLNU's IRB and federal requirements pertaining to human subjects protections within the **Federal Law 45 CFR 46.101 (b)**. Your project will be subject to approval for one year from the date of approval.

After completion of your study or no later than the same month and date in 2013, you must submit a summary of your project or a request for continuation to the IRB. If any changes to your study are planned or you require additional time to complete your project, please notify the IRB chair.

For questions related to this correspondence, please contact the IRB Chair, Patricia Leslie, M.A., S.S.A. at the contact information below. To access the IRB to request a review for a modification or renewal of your protocol, or to access relevant policies and guidelines related to the involvement of human subjects in research, please visit the PLNU IRB web site.

Best wishes on your study,

Patricia Leslie, M.A. – S.S.A.
Associate Professor
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