Implementation of sepsis management guideline in a community-based teaching hospital – can education be potentially beneficial for septic patients?

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SUMMARY

Objective: To assess clinical outcomes associated with the implementation of the sepsis guideline in a community-based hospital. In addition, evaluate the utility and effectiveness of a Sepsis Education Program. Research Design and Methods: This is an observational cohort study of patients presenting to the Emergency Department at a community-based teaching centre meeting severe sepsis or septic shock criteria. A quality improvement programme consisting of a comprehensive Sepsis Education Program based on recommendations from the Surviving Sepsis Campaign was implemented and evaluated. Patients were identified by the admission diagnosis and were evaluated over two time periods (7/2003–6/2004 and 7/2005–6/2006) and to show clinical outcomes before and after implementation of the sepsis guideline/quality improvement programme. Results: A total of 96 patients with severe sepsis (34 control group and 62 SSC group) were included. Both groups had similar intensive care unit (ICU)-length of stay (3 vs. 3 days, p = 0.647). Patients who required mechanical ventilation (MV) had similar MV time (4 vs. 3.5 days p = 0.349). A greater percentage of survival was found in the SSC group (45% vs. 73%, p = 0.006). Patient received similar care with regards to appropriate early antibiotics (85% vs. 90%, p = 0.459). The main difference between the two group was the early fluid resuscitation (2 l vs. 3 l, p = 0.006) over the first 3 h and a difference remained significant at 6 h (4.2 l vs. 6.3 l, p = 0.013). Conclusions: In a community-based teaching hospital, implementing the surviving sepsis campaign guideline through an education programme was feasible and resulted in early therapy with aggressive fluid administration and appropriate antibiotics. The Sepsis Education Program resulted in early therapeutic interventions and contributed to the survival benefits.

What’s known
Implementation of the Surviving Sepsis Campaign guideline can enhance outcomes and survival. Because certain guideline-recommended components of sepsis management can be costly (such as the use of drotrecogin alfa) potential barriers to guideline implementation may arise in hospitals with greater financial constraints.

What’s new
This study demonstrates that all recommended elements of the Surviving Sepsis Campaign guideline did not have to be incorporated to provide survival benefits in patients managed for sepsis and a formal education programme can improve outcomes. The Sepsis Education Program contributed to consistency in clinician practice patterns and enhanced agreement, acceptance, and communication amongst providers in a community-based teaching hospital.

Introduction

Sepsis-related mortality increases with age. Sepsis is also attributed to an approximate annual total cost of $17 billion (1,2). Of the 751,000 annual cases, 383,000 (51%) required admission to the intensive care unit (ICU) (1,2). Various interventions have independently shown to improve survival in severe sepsis such as appropriate early antibiotics (3,4), early goal-directed therapy (EGDT) (5), corticosteroids (6) and recombinant human activated protein C (rhAPC) (7). However, it is unclear whether all elements should be equally considered.

For early management of severe sepsis in particular, the Surviving Sepsis Campaign (SSC) Guidelines and the Institute for Healthcare Improvement recommend the implementation of the 6 hr resuscitation bundle, especially in patients presenting with sepsis in the emergency department (ED) (8,9). The resuscitation bundle incorporates early recognition, early administration of antibiotics, and EGDT. The initial SSC guideline was introduced in 2004 and provides a roadmap for clinicians; however, incorporating all the components in the guideline can be challenging in a community-based hospital because of financial constraints and a lack of consensus among providers. Therefore, a Sepsis Education Program was developed to overcome these constraints, to ensure awareness and enhance practitioner acceptance of the SSC Guidelines at our institution.

The purpose of this study is to evaluate the feasibility and incremental impact of implementing SSC...
Sepsis management guideline: education programme

Guidelines, as well as clinical outcomes and survival benefit associated with a comprehensive Sepsis Education Program in a community-based teaching hospital.

Methods

This is a prospective observational cohort study of all patients presenting to the ED between 2003 and 2006; meeting the diagnosis criteria for 2004 SSC guideline definition for severe sepsis or septic shock and admission to the medical-surgical intensive care unit (ICU) in a 350-bed community-based teaching hospital. All the patients were also entered into the hospital sepsis registry. The study and sepsis registry were approved by the Institutional Review Board.

Setting

The institution’s ED consists of 47 beds, with approximately 65,000 annual patient visits and 2490 ICU admissions from the ED. An additional 30,000 annual visits are seen in an on-campus urgent care department. Staffing in the adult section of the ED at any time includes two attending physicians, 2–4 resident physicians, and 8–10 nurses. The nurse-to-patient ratios range from 2:1 to 1:4, depending on the acuity of patient care. The ICU is a 24-bed open unit; patients are admitted by the primary care physicians and the majority of the care is delivered by the ICU medical residents and internists under the supervision of attending physicians, who are board certified in Pulmonary and Critical Care Medicine. The ICU team performs daily multidisciplinary rounds on all patients in the medical-surgical ICU.

Study design

We implemented a quality improvement programme/Sepsis Education Program to deliver a severe sepsis bundle that was largely based upon the 2004 SSC Guidelines, but modified to fit the institution’s resources. Quality indicators that were monitored were in accordance to the pre-existing hospital practice and policies. To facilitate continuity of care, the quality indicators were monitored and continued in the medical-surgical intensive care unit.

Implementation phase

To ensure adherence to the SCC guideline, we implemented a new protocol (severe sepsis bundle) and utilise a Sepsis Education Program to inform the hospital staff. Prior to the implementation of the bundle and education programme, acceptance was guaranteed from the ED and ICU physicians. The Sepsis Education Program included a lecture series to medical house-staff and attending physician(s), SSC guideline reinforcement during daily teaching rounds, laminates with SSC guideline/sepsis bundle recommendations were placed in the medical chart and reminders regarding the implementation of the SSC guideline/sepsis bundle were placed throughout the medical units.

Data collection

Data collection was completed through a review of medial charts of adult patients (at least 18 years of age) identified by admission diagnoses (ICD-9: 995.91 for Sepsis, 995.92 for Severe Sepsis and 785.52 for Septic Shock) of sepsis or septic shock admitted from the ED to the ICU. Diagnosis of severe sepsis was confirmed according to hospital protocol. Patients with an alternative diagnosis which could account for the shock state (e.g., myocardial infarction, haemorrhagic, pulmonary embolism), and those with a pre-existing do-not-resuscitate order were excluded from the study. Two time periods (7/2003–6/2004 and 7/2005–6/2006) were chosen to show clinical outcomes before and after implementation of the sepsis guideline/quality improvement programme. Medical records were reviewed with a standardised data collection form to collect patient demographics [such as age, sex, race, body weight, and severity of illness as assessed by the Acute Physiology and Chronic Health Evaluation (APACHE) II score] and clinical outcomes. The infectious diagnosis was verified when available in the medical record but not collected systematically for the purpose of this study. Obtaining cultures and lactate level on admission as part of the sepsis management best practice was collected as well as the status of mechanical ventilation. This data was collected for patient as a binary variable where the raw results were not included in the analysis for the purpose of this study. The determination of terminal illness was not possible from the chart review.

The primary outcomes evaluated were the total quantity of intravenous fluids administered and the
prescription of appropriate initial antimicrobial treatment in the emergency department. Secondary outcomes included hospital mortality and hospital length of stay. In accordance to the study protocol, vasopressors were targeted to maintain a mean arterial pressure of ≥65 mm Hg. Refractory septic shock was defined as the inability to maintain a mean arterial pressure of ≥65 mm Hg with the administration of vasopressors. Appropriate initial resuscitation and fluid therapy of patients was evaluated during their emergency department stay, before the transfer to an intensive care unit. The types of crystalloid fluids administered in the emergency department included 0.9% sodium chloride and lactated-ringer solution. For the purposes of this investigation, appropriate initial antimicrobial treatment was defined as the microbiological documentation of an infection (i.e. a positive culture result) that was being effectively treated based on in-vitro susceptibility results at the time of its identification. Corticosteroid therapy or stress dose steroid consisted of 200–300 mg/day of hydrocortisone or its equivalent dose. Patients were not required to have a diagnosis of adrenal insufficiency based on random cortisol levels. In addition, APACHE II scores were calculated on the basis of the worst clinical data available for patients while in the emergency department.

### Table 1 Patients characteristics

| Patient demographics               | Control group | SCC group | p value |
|-----------------------------------|---------------|-----------|---------|
| Age (yrs) *                        | 66 (53, 73)   | 74 (60, 82) | 0.017   |
| Gender (% male)                    | 58            | 46        | 0.259   |
| Time to admission                 | 5 h 20 min    | 4 h 48 min | 0.281   |
| Apache II *                        | 28 (21, 34)   | 29 (22, 36) | 0.631   |
| Comorbid conditions (n)           |               |           |         |
| Cardiac diseases                  | 5             | 11        | NS      |
| Chronic renal disease             | 6             | 6         | NS      |
| COPD                              | 7             | 12        | NS      |
| Diabetes mellitus                 | 11            | 16        | NS      |
| Hypertension                      | 4             | 7         | NS      |
| Liver disease                     | 3             | 4         | NS      |
| Underlying malignancy             | 5             | 8         | NS      |
| Diagnosis/Identifiable infectious source % (n)‡| | | |
| Undetermined source               | 5.9% (2)      | 4.8% (2)  |         |
| Abdominal                         | 14.7% (5)     | 12.9% (8) |         |
| CNS                               | 5.9% (2)      | 3.2% (2)  |         |
| Blood stream or catheter related  | 2.9% (1)      | 1.6% (1)  |         |
| Skin and soft tissue              | 8.8% (3)      | 9.7% (6)  |         |
| Pulmonary                         | 32.4% (11)    | 38.7% (24) |         |
| Urinary tract                     | 29.4% (10)    | 29.0% (18) |         |

*Median (IQR). ‡There no statistical difference in the diagnosis/ identifiable sources between the two groups, p = 0.98. SSC, Surviving Sepsis Campaign; COPD, Chronic obstructive pulmonary disease; CNS, infection related to the center nervous system. Time from presentation to the ED to transfer to the ICU.

### Statistical analysis

Two-sided statistical testing was used with a type I error rate of 0.05. χ² tests and/or ANOVA were used to compare patient characteristics. The χ² test with Yates’ continuity correction or Fisher’s exact test was used to test for associations between categorical variables and outcomes. Continuous variables are presented as the mean ± standard deviation and were compared using the independent two-sample t-test. Highly skewed data were analysed with the non-parametric Mann–Whitney rank-sum test and presented as median values with the 25th and 75th percentiles. Logistic regression analysis was used to control for confounders and the adjusted odds ratio was used to identify variables with effect modification. The logistic regression model was used to assess the impact of a priori identified covariates on mortality. Candidate variables for logistic regression included age, gender, type of physician service, time to admission, ventilation indicators, APACHE II, comorbid conditions, in addition to the variables of the sepsis management bundle (Table 1 and 2). A dummy variable was included in the model to allow entry of each variable individually. Variables with p < 0.2 in the univariate analyses were included in a stepwise selection, and the final model included age, gender, fluid resuscitation volume, fluid resuscitation timing, appropriate antibi-
otics, vasopressor type, drotrecogen alpha, deep venous thrombosis (DVT) and stress gastric ulcer prophylaxis. Age was included in the multivariate analysis because of the potential influence on survival, and gender because of the physiologic importance. Results of the logistic regression model were analysed as estimates of the odds ratio associated with each co-
varying and the 95% confidence interval.

Analyses were conducted on an intention-to-treat basis and performed with SPSS (version 11.5: SPSS Inc., Chicago, IL, USA). We calculated post hoc that we would need a sample size of 128 patients to identify an absolute difference in the amount of fluid administration to patients before starting vasopressors of 5 ml/kg (estimated SD, 10 ml/kg) with a power of 0.8 (two-tailed) at a significance level of 0.05. We did not conduct a post hoc analysis to assess the effect of comorbidities on mechanical ventilation (MV) outcomes.

Results

A total of 96 patients with severe sepsis [34 control group (pre-education) and 62 SSC group (post education)] were included in the analysis. Both groups (control group vs. SSC group) had similar APACHE II scores [28 (21–34) vs. 29 (21–36), p = 0.631], gender (58 vs. 46% male p = 0.259), and ER to ICU time (5 h 20 min vs. 4 h 48 min, p = 0.281). However, the control group was found to be younger [66 (53, 73) vs. 74 yrs (60, 82) p = 0.017]. (Table 1)

Appropriate initial resuscitation and fluid therapy was achieved in 64.7% of the control vs. 86% of SCC group (p = 0.030) and the SCC group received more fluid therapy in the first 3 h of resuscitation, 2 l (1–2.7) vs. 3 l (1–4) (p = 0.006). The difference remained significant at 6 h (4.2 l vs. 6.3 l, p = 0.013). Blood transfusion was similar in both groups 2 units (2–2) vs. 2 (1–2) units of packed red blood cells, p = 0.65. Compared with control group, the SSC group had more use of norepinephrine as the preferred initial vasopressor (27% vs. 9%, p = 0.003), higher rates of assessment for relative adrenal insufficiency (61.3 vs. 23.5%, p = 0.001), and higher rates of DVT (85 vs. 62%, p = 0.014) and stress ulcer prophylaxis implementation (97 vs. 76%, p = 0.002). SSC patients also had shorter time-in-shock [22 (14–33) vs. 10 (1–25) h, p = 0.002]. Utilization of other therapeutic recommendations from the sepsis guideline was similar [e.g. appropriate early antibiotics (85% vs. 90%, p = 0.459), corticosteroid use (29.4% vs. 36%, p = 0.194) and drotrecogin alfa (3% vs. 3%, p = 0.939)]

| Clinical outcomes % (n) | Control group n = 34 | SCC group n = 62 | p value |
|-------------------------|----------------------|------------------|---------|
| Appropriate initial fluid resuscitation | 64.7% (22) | 85.5% (53) | 0.03 |
| Fluid resuscitation in the first 3 h of resuscitation (litres) | 2 (1, 3) ± 2.00 | 3 (1, 4) ± 2.60 | 0.006 |
| Serial lactate measurements | 50% (17) | 48% (30) | 0.76 |
| Blood cultures drawn before antibiotics | 73.5% (25) | 83.9% (52) | 0.22 |
| Appropriate early antibiotics (within 1 h) | 85% (29) | 90% (56) | 0.45 |
| Norepinephrine as initial vasopressor | 9% (3) | 27% (17) | 0.003 |
| Inotropic agent (dobutamine) | 6% (2) | 3% (2) | 0.53 |
| Cortisol stimulation test | 23.5% (8) | 61.3% (38) | 0.001 |
| Corticosteroid use | 29.4% (10) | 36% (22) | 0.19 |
| Drotrecogin alfa (Xigris) use | 3% (1) | 3% (2) | 0.93 |
| Glucose control <150 mg/dl | 53% (18) | 37% (23) | 0.13 |
| DVT chemoprophylaxis | 62% (21) | 85% (53) | 0.014 |
| Stress ulcer prophylaxis | 76% (26) | 97% (60) | 0.002 |
| Limitation of support | 6% (2) | 6% (4) | 0.95 |

*Median (IQR). †Mean ± standard deviation. Patient’s next of kin or surrogate decision makers requested a ‘do not resuscitate’ status.
SSC, Surviving Sepsis Campaign.
predictor for survival; however, none of the interventions individually were statistically significant in predicting survival.

**Discussion**

Our study demonstrated that initiating SCC guideline in the ED, with the intent to be followed in the medical-surgical intensive care unit (ICU), at a community-based teaching hospital is achievable and enhanced survival in patients with severe sepsis when paired with a Sepsis Education Program.

Implementation of various components within the SCC guideline has demonstrated survival benefits in University-based hospitals, where management is directed under formal departmental supervision and where medical/house-staffs follow the protocol in a closed-setting ICU (10,11). Unlike university-based hospitals that receive supplemental funding from grants and external contributors, community-based hospitals face a constant challenge to minimise variability of care in the ICU because of limited resources and funding. Similar to other institutions, the resistance to the implementation and acceptance of clinical practice guidelines are attributed to a lack of awareness, insufficient staff, and concerns of increased practice cost (12). In our study, we overcame these potentials barriers through the use of an education programme. The Sepsis Education Program enhances awareness and continuity of care from the ED to ICU without significant financial burden to the institution. The Sepsis Education Program consisted of formal lectures to ICU nurses, house staff, ED and private providers, as well as educational/guideline reminders that were made available to medical providers in the intensive care unit and in patient charts. Additionally, we identified key physicians and nurses to advocate and communicate vital information with their respective peers. A multidisciplinary approach included collaboration amongst physicians, nursing, pharmacists, dieticians, social workers, and respiratory therapists during daily teaching rounds.

Implementing the Sepsis initiative at the institution resulted in a robust survival benefit that is exceeded recent published studies (10,11). The survival benefit was particularly evident in older patients, despite being older than the control group. In addition, there was an observed trend toward a shorter time for transfer from the ED to the ICU and improvement in resuscitative pattern in the earlier stages of care. The intervention group received more IV fluid in the first 3 h of care and that persisted throughout the later stages of care in the intensive care unit. Appropriate early antibiotic therapy was greater than 80% and was comparable among the two groups. Norepinephrine, in comparison to dopamine, was utilised more often as the initial vasopressor of choice. The sample size may have been too small to detect independent predictors of survival, but previous studies have shown that this intervention improves outcome. There was a lower incidence of adverse effects (e.g. arrhythmia) with norepinephrine compared with dopamine in patients with septic shock (13,14). In addition, cortical stimulation to evaluate for relative adrenal insufficiency was used more in the SCC group; however, there was not a significant increase in the usage of corticosteroids.

Interestingly, the use of drotrecogin alfa was unchanged between the two groups, even though previous reports showed a survival benefits with drotrecogin alfa administration (7). There was a noted robust survival benefit without a corresponding increase in drotrecogin alfa use when the median APACHE for the cohort (pre and post) was 29; indicating ample opportunity for drotrecogin alfa use. The noted underutilization of drotrecogin alfa may reflect the practice preferences of the clinicians and we did not conduct a retrospective review of whether drotrecogin alfa was considered and/or not given because a contraindication was present. Therefore, we cannot clearly identify the reason for the lack of attention for drotrecogin alfa administration. This might be related to the institutional experience, need for additional evidence supporting its use, side effect concerns, or simply the extra costs for the institution. It is unclear whether the survival benefit would have been more pronounced if the drotrecogin alfa administration was increased.

The study results show that an education programme can enhance survival. The Sepsis Education Program resulted in early intervention with aggressive and appropriate IV resuscitation as well as early appropriate antibiotics therapy. These quality indica-

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| Clinical outcomes | Control group (n=34) | SSC group (n=62) | p value |
|------------------|---------------------|-----------------|---------|
| Days on MV†      | 2.8 ± 4.0           | 2.3 ± 3.7       | 0.3     |
| ICU LOS*         | (3, 2)              | (2, 5)          | 0.6     |
| Died % (n)       | 55.9% (19)          | 27.4% (17)      | 0.006   |

*Median (IQR). †Mean ± Standard deviation. ICU, intensive care unit; MV, mechanical ventilation; SSC, Surviving Sepsis Campaign.
tors have been associated with survival benefits (8,9). The Sepsis Education Program resulted in early intervention and was brought upon by the increased awareness of the SCC guideline. As a result of the enhanced emphasis and awareness, the Sepsis Education Program addressed previous barriers to the implementation of protocol-based management/guideline. A barrier that has been reported is a lack of agreement between providers because of poor communication. (15) The Sepsis Education Program was supported by the providers prior to implementation and lead to better communication between providers, especially the providers in the ED and ICU. Implementing the SCC guideline improved adherence to the other quality indicators such as deep vein thrombosis and stress ulcer prophylaxis. Therefore, appropriate implementation of sepsis management is an achievable goal in a community-based teaching hospital through a coordination of efforts and an on-going Sepsis Education Program.

Weakness of the study included a small sample size and retrospective retrieval of control group data. Further, the diagnosis of severe sepsis was dependent on a review of the medical charts and a low utilization of drotrecogin alfa limited further inference on drotrecogin alfa’s administration value. Assessment for effective communication and treatment consensus were also not performed. The time period was comparable and there were no other projects, research or quality improvement initiatives being conducted in the ICU within the time periods of the study, but potential source biases included a general interest in sepsis with the surviving sepsis campaign which may of influence the ED physicians to be more vigilant about sepsis management. In addition, the retrospective nature of study may have introduced unknown biases and being limited by cases ICD-9 coding there is a possibility that severe sepsis cases may not have been coded. Even though all the cases classified within the ICD-9 codes were requested, severe sepsis cases that may not have been coded could be missed.

Conclusion
Implementing Surviving Sepsis Campaign guideline with an intensive and comprehensive Sepsis Education Program is a feasible method to enhance survival in a community-based teaching hospital. Early therapeutic interventions with intravenous fluid resuscitation and appropriate antibiotics therapy were essential elements from the sepsis guideline.

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