

Effect of an emergency department sepsis protocol on the care of septic patients admitted to the intensive care unit

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ABSTRACT

Objective: We sought to determine whether the implementation of a sepsis protocol in a Canadian emergency department (ED) improves care for the subset of patients admitted to the intensive care unit (ICU).

Methods: After implementing a sepsis protocol in our ED we used an ICU database and chart review to compare various time-dependent end points and outcomes between a historical control year and the first year after implementation. We reviewed the charts of all patients admitted to the ICU within 24 hours of ED admission with a primary or other diagnosis of sepsis, severe sepsis or septic shock, who met criteria for early goal-directed therapy within the first 6 hours of their ED stay.

Results: We compared 29 patients from the control year with 30 patients from the year after implementation of our sepsis protocol. We found that patients treated during the postintervention year had improvements in time to antibiotics (4.2 v. 1.0 h, difference = -3.2 h, 95% CI -4.8 to -2.0), time to central line placement (above the diaphragm) (11.6 v. 3.2 h, difference = -8.4 h, 95% CI -12.1 to -4.7), time to arterial line placement (7.5 v. 2.3 h, difference = -5.2 h, 95% CI -7.4 to -3.0), and achievement of central venous pressure and central venous oxygen saturation goals (11.1 v. 5.1 h, difference = -6.0 h, 95% CI -11.03 to -1.71, and 13.1 v. 5.5 h, difference = -7.6 h, 95% CI -11.97 to -3.16, respectively). There were no statistically significant differences in ICU length of stay, hospital length of stay or mortality (31.0% v. 20.0%, difference = -11.0%, 95% CI -33.1% to 11.1%).

Conclusion: Implementation of an ED sepsis protocol improves care for patients with severe sepsis and septic shock.

Keywords: early goal-directed therapy, severe sepsis, septic shock, sepsis protocol, emergency department

RÉSUMÉ

Objectif : Nous avons voulu vérifier si la mise en œuvre d'un

protocole d'asepsie dans un service d'urgence canadien améliore les soins pour un sous-groupe de patients admis à l'unité des soins intensifs (USI).

Méthodes : Après la mise en œuvre du protocole d'asepsie dans notre service d'urgence, nous avons utilisé une base de données de l'USI et procédé à l'examen des dossiers pour comparer différents paramètres des résultats chronologiques entre une année historique témoin et la première année suivant la mise en œuvre du protocole. Nous avons examiné les dossiers de tous les patients admis à l'USI dans les 24 heures suivant leur admission à l'urgence avec un diagnostic principal ou secondaire de sepsis, sepsis grave ou choc septique, et répondant aux critères d'une prise en charge précoce fondée sur l'obtention d'objectifs thérapeutiques prédéterminés dès les six premières heures suivant l'arrivée à l'urgence.

Résultats : Nous avons comparé 29 patients de l'année témoin à 30 patients de l'année suivant l'application de notre protocole d'asepsie. Nous avons constaté que les patients traités durant l'année post-intervention présentaient de meilleurs résultats quant à l'intervalle avant l'antibiothérapie (4,2 c. 1,0 h, différence = -3,2 h, intervalle de confiance [IC] à 95 %, de -4,8 à -2,0), l'intervalle avant la pose d'un cathéter central (au-dessus du diaphragme) (11,6 c. 3,2 h, différence = -8,4 h, IC à 95 %, de -12,1 à -4,7), l'intervalle avant la pose d'un cathéter artériel (7,5 c. 2,3 h, différence = -5,2 h, IC à 95 %, de -7,4 à -3,0) et l'obtention des objectifs de tension veineuse centrale et de saturation veineuse centrale en oxygène (11,1 c. 5,1 h, différence = -6,0 h, IC à 95 %, de -11,03 à -1,71, et 13,1 c. 5,5 h, différence = -7,6 h, IC à 95 %, de -11,97 à -3,16, respectivement). On n'a noté aucune différence statistiquement significative dans la durée du séjour à l'USI, la durée de séjour à l'hôpital ou la mortalité (31,0 % c. 20,0 %, différence = -11,0 %, IC à 95 %, de -33,1 % à 11,1 %).

Conclusion : La mise en place d'un protocole d'asepsie à l'urgence améliore les soins aux patients souffrant de sepsis grave et de choc septique.

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INTRODUCTION

Severe sepsis and septic shock are conditions with a high rate of mortality that are commonly seen in emergency departments (EDs).¹ Despite extensive research, little progress has been made in improving the survival rates for patients with sepsis. In 2001, Rivers and colleagues² published an article describing early goal-directed therapy (EGDT), which used invasive hemodynamic monitoring and targeted physiologic goals to optimize resuscitation. The study found an absolute reduction in mortality of 16% when this technique was applied to severely septic patients in the ED. This is the most significant reduction of mortality reported to date in a randomized control trial examining severely septic patients.

The Society of Critical Care Medicine's "Surviving Sepsis Campaign" advocates EGDT in the ED treatment of severe sepsis and septic shock.³ In the years since the study by Rivers and colleagues, EGDT has been widely adopted in EDs and several groups have described improved outcomes.³⁻¹⁰ There have also been several abstracts published that compare patient outcomes before and after implementation of sepsis protocols.¹¹⁻¹³ Combined, these studies include 298 patients and describe a mean mortality before EGDT of 44.8% (standard deviation [SD] 7.8%), which was reduced to 24.5% (SD 5.5%) after implementation of a sepsis protocol.¹⁴

To date, there have been no full-paper publications on the effectiveness of a sepsis protocol in a Canadian centre. Through a collaboration of emergency medicine, critical care medicine, infectious disease, nursing and pharmacology, we created a sepsis protocol for our ED in 2005. Before the initiation of this protocol, there were no standardized protocols for the management of septic patients. The intensive care unit (ICU) and the ED shared responsibility for such patients, the use of EGDT was sparse and there was variable involvement of emergency physicians. The purpose of this study was to determine the effectiveness of our ED protocol in reducing the time to the achievement of process and physiologic goal-directed end points in septic patients admitted to the ICU.

METHODS

This was a retrospective cohort study that took place at Vancouver General Hospital, a tertiary level academic centre that has fellowship programs in both emergency

and critical care medicine. Vancouver General Hospital has approximately 69 000 visits to the ED and 1200 admissions to the ICU per year. The study was approved by our clinical research ethics board.

Protocol development

Members from the departments of emergency medicine, critical care medicine, infectious disease and pharmacology, as well as senior nursing staff, were invited to join a sepsis working group whose purpose was to develop a local sepsis protocol. A final protocol was developed in April 2005. Following an internal review, a preprinted order set was approved for use in the ED in May 2005, and equipment for the monitoring of central venous pressure (CVP) and invasive arterial monitoring was purchased.

The protocol was similar to that used by Rivers and colleagues,² and was implemented in multiple stages. The first stage involved a triage screening tool to alert physicians to patients who might fit the criteria for EGDT. If, at triage, patients met 2 out of 4 criteria for systemic inflammatory response syndrome (SIRS) and had a suspected infection, a sepsis protocol (Appendix 1, available at www.cjem-online.ca) was placed on the chart and the patient was assigned a Canadian Emergency Department Triage and Acuity Scale¹⁵ score of 2. It is important to note that we removed white blood cell count from the SIRS criteria used by Rivers and co-authors, as this would not be available to the triage nurse at the time of initial patient presentation. We also added decreased level of consciousness as a presumed marker of illness severity. Patients who met the above criteria underwent blood tests that included a complete blood count, electrolytes, renal and liver function, and a blood culture. Additionally, a chest radiograph and electrocardiogram were ordered. Finally, venous blood was obtained in an arterial blood gas syringe to facilitate assessment of venous lactate. If the patient was hypotensive, as defined by a systolic blood pressure of less than 90 mm Hg, an intravenous line was established and an initial 500-mL bolus of normal saline was given. After assessment by the emergency physician, it was determined whether the patient had severe sepsis or septic shock and met the criteria for EGDT, as reflected by a lactate level greater than 4 mmol/L or continued hypotension despite a 20–30 mL/kg bolus of intravenous fluids. If the patient met criteria for EGDT, the emergency physician or the ICU resident would place a central venous catheter (above the diaphragm) and an

arterial catheter to facilitate resuscitation of the patient according to our EGDT protocol.

An extensive education program on the utility and implementation of the sepsis protocol was provided to all emergency physicians, residents and nursing staff. This included a group lecture conducted in June 2005. Independent sessions were also held for nursing staff exclusively, and this was repeated in November 2006 to incorporate new staff. In addition, every month a lecture was given to incoming residents in the ICU so that they would be aware of the protocol and how to correctly provide EGDT. Finally, a poster with a flow chart of EGDT was placed in the ED as a reference tool.

Our sepsis protocol was introduced into the ED in July 2005. There was no formal data collection during the first 5 months after implementation, as this was considered a grace period during which the staff could become familiar with the use of the protocol. Formal data collection was carried out between Dec. 1, 2005, and Dec. 1, 2006.

Data collection

To identify study patients we electronically searched a pre-existing ICU patient database that included demographic and clinical parameters on all patients admitted to our ICU. Data entry to the database is performed by ICU nurses, and data are collected concurrently on a daily basis with the review of all notes written about patients by physicians. This includes admission notes, daily progress notes and discharge summaries. The database is maintained, and queries are performed, by a local regional analyst. Using this database, we conducted 2 independent searches. The first search focused on patients admitted approximately 1 year before the implementation of the sepsis protocol (between Jun. 1, 2004, and Jun. 1, 2005) and these patients served as a historical control group. The second search included all patients admitted the year after formal implementation of the sepsis protocol and the previously mentioned grace period, and these patients served as the treatment group. The decision to collect data 1 year before and 1 year after implementation was made for ease of data collection. Inclusion criteria were patients admitted to the ICU within 24 hours of arrival to the ED, who did not require surgery, and who had a primary or secondary diagnosis of sepsis, severe sepsis or septic shock. The database classifies patients as having sepsis, severe sepsis or septic shock if, anywhere in ICU admission notes, daily progress notes or discharge summary, a

physician documented the words “sepsis,” “severe sepsis” or “septic shock” associated with the patient. Additionally, inferences are made; for example, if a patient was documented as having pneumonia and was on vasopressors, a diagnosis of septic shock would be coded. We excluded patients who went immediately to the operating room from the ED, as we believed resuscitation in the operating room may differ from that in the ED or ICU.

For our primary analysis, we determined which patients in the control and treatment groups qualified for EGDT during the first 6 hours of ED admission, as defined previously, and reviewed all progress notes and nursing notes in their charts to obtain the required data elements. The 3 data abstractors who carried out the chart review were trained by the principle investigator using sample charts. There were no data collection forms, as the data were entered directly into an electronic database. The principle investigator then reviewed all charts and confirmed the information in the electronic database. Regular meetings were then held with the second author, and any discrepancies or ambiguous data were discussed and a final decision made; there were no missing data. There was no blinding of data abstractors and no determination of inter-rater agreement.

Statistical analyses

We compared patient characteristics and explanatory variables for differences using SPSS version 16.0. We used 95% confidence limits around the differences between the groups. Tests of inference were conducted on all outcome variables, using χ^2 tests for categorical variables, such as mortality, and t tests for continuous data, such as length of stay. The small number of participants precluded further adjusted analyses.

RESULTS

In the control year, 40 patients were identified who were transferred to the ICU within 24 hours of their admission to the ED with the diagnosis of sepsis, severe sepsis or septic shock. Of these, 29 were determined to have qualified for EGDT by a lactate level of greater than 4 mmol/L or by persistent hypotension despite a 20–30 mL/kg bolus of normal saline within the first 6 hours of admission. In the treatment year, 60 patients met inclusion criteria, 30 of whom qualified for EGDT. All 30 patients during the treatment year were treated

using the sepsis protocol and preprinted orders. Table 1 shows the demographics, comorbidities, physiologic variables and sources of infection for the 2 study groups.

Table 2 compares treatments and resuscitation end points between the control and treatment groups. Patients in the treatment year had statistically significant improvements in time to antibiotic administration, time to placement of invasive monitors and time to achievement of hemodynamic end points, with the exception of mean arterial blood pressure. In addition, the treatment group was less likely to require vasopressor support or transfusion of blood products. All patients in both groups received central venous catheters and arterial catheters. Surprisingly, the time to blood culture acquisition, and the amount of volume

resuscitation in hours 1, 6 and 24 after admission were similar between the 2 groups. There was a statistically significant reduction in transfusion and steroid use in the treatment group.

Outcome data for the treatment and control groups are displayed in Table 3. There was no statistically significant difference in mortality rates in the ICU (16.7% v. 20.7%, difference = -4.0%, 95% CI -23.9% to 15.9%) and in hospital (20.0% v. 31.0%, difference = -11.0%, 95% CI -33.1% to 11.1%). In addition, there was no statistical difference in ICU length of stay, hospital length of stay or days on mechanical ventilation.

DISCUSSION

We found that the implementation of an ED sepsis protocol reduced the time to key interventions and hastened the achievement of physiologic goals in patients with sepsis, severe sepsis or septic shock who required ICU admission. Patients treated with our sepsis protocol received antibiotics, central venous catheters and arterial catheters sooner than patients in the control group. Additionally, they reached physiologic end points of CVP and central venous oxygen saturation (ScvO₂) sooner. There was a trend toward more crystalloid volume administered within the first 6 hours during the treatment year, with a median volume given of 6.0 L compared with 4.9 L in the control year. These findings parallel those of Rivers and colleagues.² Increased volume delivery may have led to slight improvements in the achievement of hemodynamic variables, but we feel it is more likely that the earlier commencement of hemodynamic monitoring led to earlier documentation of achievement of CVP and ScvO₂ goals.

We found a significant improvement in the time to delivery of antibiotics in our treatment group. As demonstrated by Kumar and colleagues,¹⁶ earlier delivery of antibiotics to patients with septic shock dramatically improves outcomes. As such, we hypothesize that this, along with early attentive care and trends toward greater volumes of crystalloid administered within the first 6 hours, may explain the trends we found toward better clinical outcomes.

Our study demonstrated improved clinical outcomes with decreased vasopressor and steroid use, and trends toward a reduction in ICU and hospital mortality in the treatment group. Additionally, we found decreased APACHE II scores, lactate levels and positive blood cultures in the treatment group. We considered all of these

Table 1. Characteristics of patients in the control and treatment groups

Characteristic	No. (%) of patients*	
	Control, <i>n</i> = 29	Treatment, <i>n</i> = 30
Mean age (SD), yr	62.5 (17.4)	53.4 (17.7)
Sex		
Male	19	19
Female	10	11
Comorbidities		
Alcohol use	5 (17)	5 (16)
Cardiovascular	8 (28)	4 (13)
Respiratory	6 (21)	5 (16)
Diabetes	6 (21)	2 (7)
Hypertension	6 (21)	3 (10)
Liver disease	14 (48)	9 (29)
Neurologic disease	6 (21)	4 (13)
History of cancer	3 (10)	3 (10)
Renal insufficiency	3 (10)	4 (13)
HIV	1 (3)	3 (10)
MAP at triage, mm Hg	73.4	69.4
Criteria met for EGDT because of		
Hypotension	20 (69)	21 (70)
Elevated lactate levels	14 (48)	13 (43)
Hypotension and elevated lactate levels	9 (31)	7 (23)
Diagnosis		
Pneumonia	14 (48)	18 (58)
Urosepsis	7 (24)	4 (13)
Gastrointestinal infection	4 (13)	2 (6)
Skin and soft tissue infection	0 (0)	3 (10)
Other	4 (13)	3 (10)

COPD = chronic obstructive pulmonary disease; EGDT = early goal-directed therapy; MAP = mean arterial pressure; SD = standard deviation.
*Unless otherwise indicated.

variables to be outcomes rather than baseline characteristics, as they are dependent on early resuscitation. It is possible that the differences we found arose from an unexpected difference in the severity of illness; however, the differences can also be explained by the way our data were obtained. For example, the APACHE II score is calculated based on the worst physiologic values recorded during the first 24 hours of admission, and, therefore, patients with superior early management would logically have improved scores. Furthermore, improved early management may have also reduced the requirement for vasopressors and/or steroid supplement-

ation and reduced the number of patients with positive cultures because of early antibiotic delivery.

The implementation of our sepsis protocol may have also resulted in a lower recorded initial lactate level when compared with the control group. As mentioned previously, part of our protocol was to obtain a venous lactate level in an arterial blood gas syringe when the patient was at triage. This would comprise the first lactate level recorded for the patient. In the control year the first lactate level may not have been sent until several hours into the ED visit and potentially after deterioration. Of note, to be included in our study, the sample

Table 2. Time to treatment and therapies for patients in the control and treatment groups

Variable	Median*		Difference* (95% CI)
	Control, n = 29	Treatment, n = 30	
Time from arrival to blood culture taken, h	1.64	1.28	-0.35 (-1.06 to 0.36)
Time from arrival to first antibiotic given, h	4.22	1.01	-3.2 (-4.77 to -1.96)
Lactate level, mmol/L	4.7	3.2	(0.9 to 15.4)‡ (0.8 to 13.8)
Culture confirmed positive, no. (%)	22 (76%)	16 (53%)	23% (-1% to 46%)
APACHE II score†	26.86	22.00	4.89 (1.30 to 8.49)
Time from arrival to ATD CVC placed, h	11.60	3.20	-8.40 (-12.08 to -4.71)
Time from arrival to arterial line placed, h	7.52	2.32	-5.20 (-7.39 to -3.03)
Time from arrival to CVP goal obtained, h	11.08	5.13	-5.95 (-11.03 to -1.71)
Time from arrival to MAP goal obtained, h	2.79	2.17	-0.61 (-2.08 to -0.86)
Time from arrival to ScvO ₂ goal obtained, h	13.10	5.53	-7.56 (-11.97 to -3.16)
Resuscitation volume in 1 h, mL	1 098.4	1 307.9	209.5 (-326.0 to 745.0)
Resuscitation volume in 6 h, mL	4 931.7	5 975	1043.2 (-707.2 to 2794.0)
Resuscitation volume in 24 h, mL	10 410.9	10 037.3	-373.6 (-3489.3 to 2742.1)
Received transfusion, %	52	31	19% (6.4% to 43.2%)
Received steroids, %	52	23	28% (4.7% to 52.0%)
Received APC, %	7	7	0% (-13.1% to 12.6%)
Required vasopressors, %	96	74	22% (6% to 44%)
Received dobutamine, %	17	19	-2% (-22.6% to 17.1%)
Received mechanical ventilation, %	93	87	6% (-8.7% to 22.5%)
Time from arrival to ICU consult, h	4.61	2.68	-1.93 (-4.10 to 0.24)

APC = activated protein C; ATD CVC = above-the-diaphragm central venous catheter; CI = confidence interval; CVP = central venous pressure; ICU = intensive care unit; MAP = mean arterial pressure; ScvO₂ = central venous oxygen saturation.
 *Unless otherwise indicated.
 †Based on worst values for the first 24 hours of care in the ICU.
 ‡Group range.

Table 3. Outcomes for patients in the control and treatment groups

Variable	Control, n = 29	Treatment, n = 30	Difference* (95% CI)
Median ICU LOS, d	5.0	4.1	0.14 to 30.00† (0.03 to 33.1)
Median hospital LOS, d	19.0	19.5	0.0 to 59.0† (0.0 to 72.0)
Median time on mechanical ventilation, d	3.7	3.0	0.0 to 22.2† (0.0 to 22.6)
Mortality in the ICU, %	20.7	16.7	-4.0 (-23.9 to 15.9)
Mortality in hospital, %	31.0	20.0	-11.0 (-33.1 to 11.1)

CI = confidence interval; ED = emergency department; ICU = intensive care unit; LOS = length of stay.
 *Unless otherwise indicated.
 †Group range.

had to be drawn during the first 6 hours of the patient's ED admission.

It is useful to compare our results with those of other locations where sepsis protocols have been implemented in the ED. Jones and colleagues⁴ implemented a sepsis protocol and prospectively recorded data on 79 patients before implementation and 77 patients after implementation. These patients had similar demographic characteristics and lactate levels to the patients in our study, and these investigators found similar results with respect to improvement in time to antibiotics and increased early delivery of fluid. With the implementation of their sepsis protocol, they found an absolute and relative reduction in mortality of 9% and 33%, respectively. Trzeciak and colleagues³ performed a similar study with fewer patients ($n = 38$). They found similar results regarding early fluid delivery, rapidity of antibiotic initiation and a trend toward reduced mortality (43.8% v. 18.2%, $p = 0.09$). Nguyen and coauthors¹⁰ found similar results in a study examining the completion of 6-hour and 24-hour sepsis bundles. Patients who completed a 6-hour sepsis bundle, which included early invasive monitoring, EGDT and antibiotics, were found to have decreased rates of mortality (20.8% v. 39.5%, $p < 0.01$).

This study has several limitations that should be considered. The greatest limitation of our study is its single-centre design, as it is possible our results may not be generalizable to other centres with a different case mix or organizational structure. Also, in this study we specifically examined patients with sepsis, severe sepsis and septic shock who were admitted to the ICU. As such, if patients were successfully resuscitated in the ED and never required ICU admission, or died in the ED before ICU admission, they would not be captured in our study.

Another limitation is that we had to rely heavily on documentation in medical records to obtain our primary data. We are therefore prone to all the errors and biases that are known to be associated with a retrospective medical record review. These potential problems would have been reduced with a prospective design.

Finally, our design involves the risk of selection bias when comparing an intervention group against a historical control. The characteristics of our 2 groups may differ, as they were treated differently in the ED. Additionally, as the 2 groups were from different periods, there may be other differences in treatment and management beside the sepsis protocol that influenced outcomes. Although we acknowledge these risks, we believe that the patients in the treatment group who

came to the ICU may in fact have been a sicker group of patients compared with the control group, as the less sick individuals would have been resuscitated early in the ED and would not have required ICU admission.

CONCLUSION

Our findings demonstrate that the implementation of an ED sepsis protocol in a Canadian centre can reduce time to delivery of antibiotics and placement of central venous and arterial catheters and can hasten achievement of physiologic variables. Given the ongoing controversies regarding the utility of EGDT, and the call by many for a repeat of the original trial by Rivers and colleagues, we believe that the jury remains out on the effectiveness of ED-driven sepsis protocols and on whether changes in the process of care and early attentive management improve outcomes. Whether value lies in the measurement of ScvO₂ and the augmentation of oxygen delivery, or benefits arise simply from attentive care by a specialized team still needs to be determined. Hopefully, the ongoing ProCESS trial by Angus and colleagues¹⁷ will shed further light on this question.

Competing interests: None declared.

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