American Journal of Emergency Medicine 37 (2019) 762–793

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

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Pharmacist impact on sepsis bundle compliance through participation on an ED sepsis alert team☆

The 2012 Surviving Sepsis Campaign's guidelines for the management of severe sepsis and septic shock introduced 3-hour and 6-hour sepsis management bundles to facilitate appropriate and timely treatment [1]. These bundles emphasize the importance of early identification through collection of blood cultures, lactate measurements, fluid resuscitation, and prompt administration of broad-spectrum antibiotics [1-2]. Multiple studies have shown a reduction in mortality with bundled sepsis management [3,4]. The impact of sepsis management bundle compliance on clinical and financial outcomes has also been recognized by the Centers for Medicare and Medicaid Services (CMS), which may eventually include Early Management Bundle, Severe Sepsis/Septic Shock (SEP-1) compliance as a composite core measure for hospital reimbursement [5]. Appropriate selection and timing of antibiotics are vital for optimal patient outcomes [6,7].

We conducted a prospective, two-arm, parallel design study that evaluated the impact of the presence of a pharmacist on completion of sepsis management bundles in ED patients. This study was reviewed by the institutional review board and conducted in the adult ED of a quaternary community hospital with approximately 110,000 adult visits per year.

A sepsis alert is generated in our ED when a patient meets ≥2 systemic inflammatory response syndrome (SIRS) criteria with a suspected infection which prompts an overhead page. Patients were included if they were ≥18 years old, generated an initial sepsis alert, and met severe sepsis or septic shock criteria in the ED between January and October 2017. Patients were excluded if they were not committed to life-sustaining therapy, bone marrow transplant patients, pregnant, or prisoners. Data was compared in patients which a pharmacist attended the sepsis alert versus those when a pharmacist was absent.

At the time of sepsis alert generation, the pharmacist responded to the patient's room for code sepsis with the multidisciplinary sepsis alert team and reviewed the patient's electronic medical record (EMR) for pertinent medical history. The pharmacist used a standardized checklist and empiric antibiotic guide for bundle completion and made recommendations to ensure bundle components were completed [2]. Data collected included patient demographics, bundle times, suspected source of infection, SIRS criteria, organ dysfunction, septic shock criteria, and quick Sepsis Related Organ Failure Assessment criteria. Comparator group data was collected from the EMR and an internal sepsis screening tool. The primary endpoint was completion rates of SEP-1 3-hour and 6-hour bundles. Secondary endpoints were time to completion of sepsis management bundles and of their individual components.

Eighty patients were analyzed, 22 patients in the intervention group and 58 patients in the comparator group. Patient demographics were similar in both groups (Table 1) with the exception of the intervention group having a significantly higher body weight (83.3 kg vs. 72.6 kg, $p = 0.02$), more immunosuppressed patients (45.4% vs. 17.2%, $p = 0.02$), and average number of SIRS criteria (3.1 vs. 2.6, $p = 0.01$), respectively.

Three-hour bundle compliance occurred in 90.9% of patients in the intervention and 84.5% of patients in the comparator group ($p = 0.72$). Six-hour bundle compliance and time to completion of individual bundle components are shown in Table 2. Time to 3-hour bundle completion was significantly shorter in the intervention group than the comparator (median 59 min vs 71 min; $p = 0.013$). This was accompanied by significantly shorter times to fluid and antibiotic administration. 73% of patients in the intervention group received antibiotics within an hour of the sepsis alert vs 33% in the comparator, $p = 0.002$. There were no differences shown in other endpoints assessed.

Table 1
Patient demographics.

Variable	Intervention n = 22	Comparator n = 58	p-Value
	Median [IQR] or n (%)		
Age (years)	57.5 [51.5–64.8]	61.5 [44.3–71.5]	0.82
Gender (male)	15 (68)	35 (60)	0.61
Height (inches)	68 [66–71]	67 [65–70]	0.1
Total body weight (kg)	83.3 [68–101]	72.6 [59–85.7]	0.02
Serum creatinine (mg/dL)	0.97 [0.7–1.79]	1.08 [0.8–7.74]	0.2
Creatinine clearance (mL/min)	88.4 [45–106]	69.8 [33–94]	0.92
Immunosuppressed	10 (45.4)	10 (17.2)	0.02
qSOFA score ≥ 2	6 (27)	12 (21)	0.53
SIRS criteria			
# of SIRS criteria met	3.1	2.6	0.01
Temperature > 38.3 °C or <36 °C	9 (69)	27 (69)	1
Heart rate > 90 beats per min	13 (100)	36 (92)	0.564
Respiratory rate > 20 breaths per min	9 (69)	23 (59)	0.743
WBC count > 12,000 or <4000 cells/mm^3 or >10% bandemia	8 (62)	25 (64)	1
Organ dysfunction			
SBP < 90 mm Hg, MAP < 65 mm Hg, or SBP decrease > 40 mm Hg from known baseline	5 (23)	14 (24)	0.89
SCr > 2 mg/dL or UOP < 0.5 mL/kg/h for ≥2 h	6 (27)	12 (21)	0.52
Bilirubin > 2 mg/dL	0 (0)	8 (14)	0.28
Platelet count < 100,000/mm^3, INR > 1.5, or aPTT > 60 s	5 (23)	11 (19)	0.70
Altered mental status	8 (36)	13 (22)	0.21
Lactate > 2 mmol/L	15 (68)	43 (74)	0.59
Septic shock			
Persistent hypotension (SBP < 90 mm Hg or MAP < 65 mm Hg) after initial fluid resuscitation (30 mL/kg)	2 (9)	4 (7)	0.74
Persistent hypotension + follow-up lactate > 4 mmol/L	0 (0)	2 (3)	0.63

☆ This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 2
Primary and secondary endpoints.

Sepsis management bundle	Intervention	Comparator	p-Value
	Median [IQR] or n (%)		
	$n = 22$	$n = 58$	
3-hour bundle completion	20 (91)	49 (85)	0.72
Time to completion (minutes)	59 [34.5–64.3]	70.5 [49–121.5]	0.013
	$n = 13$	$n = 37$	
6-hour bundle completion	11 (84.6)	29 (78.4)	1.0
Time to completion (minutes)	181 [91–208]	183 [126–211]	0.58
Time to completion of individual bundle components (minutes)	$n = 22$	$n = 58$	
Fluids	13 [12–24.3]	35 [20.8–61.8]	0.002
Blood cultures	22 [12–29]	25.5 [17–53]	0.09
Antibiotics	46 [31–61.5]	68 [49–96]	0.009
Antibiotics within 60 min	16 (72.7)	19 (32.8)	0.002

We found no difference between groups for the primary endpoint of 3-hour or 6-hour bundle compliance, but the time to completion of the 3-hour bundle and several individual components were significantly shorter when a pharmacist was present, which is consistent with a previous study [8]. Rapid antibiotic administration and completion of the 3-h bundle has been associated with lower risk-adjusted in-hospital mortality [9]. In 2018, the Surviving Sepsis Campaign published a special article advocating the combination of the 3- and 6-hour bundles into a single "hour-1 bundle." This is intended to promote more rapid initiation of treatment and prevent the extension of resuscitation measures over a long period of time [10].

There are multiple limitations of this study. First, a single center study may have less external validity and generalizability to other institutions. There may have been missed opportunities as daily activities do not always allow for prompt pharmacist response to sepsis alerts. Finally, the definitions used for sepsis, severe sepsis, and septic shock are based on current CMS definitions and criteria that differ from those used by guidelines updated after the initiation of this study [11].

Early identification and appropriate management of sepsis and septic shock is critical for improving patient outcomes. The results of this study suggest that the incorporation of pharmacists as a standard part of the multidisciplinary sepsis response team may significantly decrease time to treatment in patients presenting to the ED with sepsis.

Conflicts of interest

None.

Acknowledgements

At the time of the study, the authors were employed by Florida Hospital Orlando, Orlando, FL.

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15 May 2018

https://doi.org/10.1016/j.ajem.2018.08.009

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Platelet indices may not be associated with diagnosis and prognosis of gastrointestinal bleeding

Dear Editor,

I read with a great interest the article of Senel et al. about the diagnostic and prognostic value of platelet indices in the gastrointestinal system bleeding [1]. The authors reported that platelet indices might be used in diagnosis and prognosis of gastrointestinal bleeding. I would like to comment about this paper.

Firstly, the data of this study were obtained retrospectively. Pre-analytical and analytic factors are important sources of variations or errors in clinical laboratory measurements. Several factors like as partially clotting of specimen with activation and aggregation of platelets during venipuncture, ethylenediaminetetraacetic acid (EDTA)-induced platelet aggregation, severe microcytosis, fragmentation of red cells or presence of cryoglobulinemia may affect the correct measurement platelet count and indices. If there is any suspicion about occurrence of the measurement error, the complete blood count should be repeated with a second sample. Reliability of tests cannot provide completely in retrospective

Abbreviations: EDTA, ethylenediaminetetraacetic acid, MPV, mean platelet volume, PCT, plateletcrit.