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ORIGINAL RESEARCH

Sepsis Early Alert Tool: Early recognition and timely management in the emergency department

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Abstract

***Introduction*:** The Surviving Sepsis Campaign guidelines recommend administration of appropriate antibiotics within 1 h in patients with severe sepsis, with two sets of blood cultures taken prior to administration.
***Objective*:** We evaluated the effect of introducing a Sepsis Early Alert Tool (SEAT) in the ED. Outcomes were antibiotic timing, antibiotic choice and obtaining adequate blood cultures.
***Methods*:** A retrospective chart review compared consecutive severe sepsis presentations admitted to ICU via the ED during two equivalent 6 month periods before and after SEAT introduction.
***Results*:** The analyses included 55 patients before and 45 following SEAT introduction. The groups were similar in age, sex, triage category, sepsis source, Acute Physiology and Chronic Health Evaluation III scores and hospital mortality. The percentage receiving antibiotics within 60 min of triage increased from 24% (95% CI 13–37%) to 44% (95% CI 30–60%), $P = 0.03$. Median time from triage to first antibiotic was 105 (IQR 65–170) min and 85 (IQR 50–140) min before and after SEAT introduction, respectively, $P = 0.15$. Percentages receiving antibiotics within 60 min of first recognition of severe sepsis were 67% (95% CI 53–79%) and 71% (95% CI 56–84%) before and after SEAT introduction, $P = 0.83$. The percentage having two sets of blood cultures drawn prior to antibiotic administration increased from 18% (95% CI 9–34%) to 44% (95% CI 27–60%), $P = 0.008$. Appropriateness of antibiotics was 58% (95% CI 44–71%) and 75% (95% CI 60–87%) before and after SEAT implementation, $P = 0.09$.
***Conclusion*:** The introduction of a SEAT in the ED is associated with earlier recognition of severe sepsis and improvements in quality of care.

Key words: *diagnosis, emergency service, hospital, quality of healthcare, sepsis.*

Key findings

- Recognition of sepsis in the ED can be challenging.
- Introducing a screening tool and clinical pathway improves timely recognition and treatment.

Introduction

Sepsis is a generalised inflammatory response to infection and remains a significant global health problem. The incidence of sepsis appears to be increasing.[1] Recent data from the Australian and New Zealand Intensive Care Society (ANZICS) adult database show that sepsis accounts for 11% of admissions to ICU and although mortality has fallen significantly in recent years, this remains high at around 20% within 30 days.[2]

The ED is a key entry point for patients with community-acquired sepsis into the healthcare system. It is recognised that early identification and treatment of patients with sepsis-associated organ dysfunction (severe sepsis) or septic shock (hypotension despite fluid resuscitation) is important in optimising outcomes.[3–5] International consensus guidelines from the Surviving Sepsis Campaign (SSC) make a number of recommendations for interventions within specific time frames in patients with severe sepsis.[6] This presents a number of challenges given the significant clinical heterogeneity and lack of straightforward diagnostic criteria for sepsis. Previous studies have found significant delays can occur in the timely treatment of patients admitted with sepsis to ICU from the ED.[7] For this reason, a number of screening tools have been developed for use in the ED to identify those at risk in a timely manner.[8–10]

We adapted the New South Wales Clinical Excellence Commission Sepsis Pathway[10] and introduced this Sepsis Early Alert Tool (SEAT) into our urban general hospital ED in March 2014 (Appendix S1). Significant resources accompanied the implementation of the sepsis pathway to the EDs throughout NSW, and recently published data have shown an associated reduction mortality from sepsis in that state.[11] Whether these improvements can be replicated at an individual hospital

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level in the absence of a government-sponsored education and awareness campaign is unknown. The present study evaluated the effect of the introduction of the pathway on two SSC guideline recommendations – time to antibiotic administration and obtaining a minimum of two sets of blood cultures prior to antibiotics. We also investigated the appropriateness of antibiotic choice for the suspected source of infection.

Methods

Design and setting

This was a retrospective chart review. The study was conducted in a mixed adult–paediatric urban general hospital with 65 000 annual ED presentations and a level II ICU.[12] The local hospital Quality and Safety committee approved the study as a quality improvement activity, and the requirement for written informed consent was waived.

Participants

Consecutive adult patients fulfilling severe sepsis or septic shock criteria admitted to the ICU from the ED (either directly or from the ward within 48 h of ED presentation) during two 6 month periods (March–September) in consecutive years (2013 and 2014) before and after the introduction of the SEAT. Sepsis was defined according to the Surviving Sepsis Campaign guidelines.[6] Details are listed in Appendix S2. Patients were excluded if they had a limitation of care order or were not expected to survive >90 days or if their transfer to ICU was >48 h following ED presentation. We also excluded patients whose primary reason for admission to ICU was related to an underlying condition rather than the acute infective episode, for example, exacerbation of chronic airways disease requiring respiratory support.

Data collection

Patients were identified using the ICU admission register, and those whose principal clinical diagnosis was consistent with sepsis were included. Two investigators (MI and KK) undertook chart reviews using a structured data collection tool. In addition to demographic variables, abstracted data included Australian Triage Score category, time of triage, time of antibiotic administration, number and timing of blood cultures, appropriateness of antibiotic choice according to Therapeutic Guidelines (eTG),[13] infective source (suspected or confirmed), blood results in ED (including lactate), Sequential Organ Failure Assessment score[14] on admission, peak Acute Physiology and Chronic Health Evaluation III score,[15] duration of hospital stay and in-hospital mortality. Time of recognition of severe sepsis was estimated from the documented time of abnormal vital signs in the ED chart, or blood gas analysis demonstrating abnormal lactate or creatinine, or by adding 45 min to the time of sampling for abnormal blood results processed in the laboratory (e.g. platelets or bilirubin) in cases not meeting vital sign or blood gas criteria.

Outcome variables and sample size calculation

The SSC recommends the administration of appropriate broad-spectrum antibiotics within 60 min of the recognition of severe sepsis/septic shock. Because of the difficulty and potential bias in estimating this retrospectively, we chose the proportion of patients receiving antibiotics within 60 min of triage as our primary outcome. Preliminary data suggested that this was being achieved in approximately 30% of patients prior to introduction of the SEAT. To demonstrate an increase to 60% would require 42 patients in each group ($\alpha = 0.05$, power 80%). Secondary outcomes were the median time from triage to antibiotics, proportion receiving antibiotics within 1 h of recognition of severe sepsis, proportion of patients in whom two sets of blood cultures were taken prior to antibiotic administration and the appropriateness of the antibiotic choice. This was determined by comparing the prescribed antibiotic(s) with those recommended by eTG[13] for the documented source (presumed or proven) in the ED chart.

Group comparisons were by Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical data. Statistical analysis was performed using STATA version 13 (College Station, TX, USA).

Results

The study included 90 patients, 55 in the period prior to introduction of the SEAT and 45 in the period post-SEAT implementation. These are summarised in Table 1. There was no significant difference between the groups in age, sex, Australian Triage Score category, sepsis source, Acute Physiology and Chronic Health Evaluation III scores and hospital mortality. In the post-SEAT group, there were a higher proportion with urinary sepsis, and the median Sequential Organ Failure Assessment score in ED was lower.

Those receiving antibiotics within 60 min of triage increased from 24% (95% CI 13–37%) to 44% (95% CI 30–60%), $P = 0.03$ (Fig. 1). The overall median time from triage to antibiotics was 105 (IQR 65–170) min before and 85 (IQR 50–140) min following introduction of the SEAT ($P = 0.15$). Those receiving antibiotics within 60 min of first recognition of severe sepsis were 67% (95% CI 53–79%) and 71% (95% CI 56–84%) before and after SEAT introduction, $P = 0.83$. The percentage having two sets of blood cultures drawn prior to antibiotic administration increased from 18% (95% CI 9–34%) to 44% (95% CI 27–60%), $P = 0.008$. Appropriateness of antibiotic choice was 58% (95% CI 44–71%) and 75% (95% CI 60–87%) before and after SEAT implementation, $P = 0.09$.

While there was no significant difference in the proportion admitted to ICU directly from ED between the two time periods, there was a significant difference in the median time from triage to antibiotics among those who were admitted directly to ICU from ED compared to those admitted initially to the ward: 100 (IQR 45–160) min *versus* 180 (IQR 105–285) min, $P = 0.03$ in the pre-

TABLE 1. *Participant characteristics*

	Pre-SEAT	Post-SEAT	*P* value
n	55	45	
Age (years)	58 (39, 71)	59 (43, 72)	0.47
% Male	56	51	0.6
ATS	2 (2, 3)	3 (2, 3)	0.47
Admission source			
Direct from ED	48	35	0.28
From ward	7	10	
Sepsis source, *n* (%)			
Respiratory, *n* (%)	37 (67)	24 (54)	0.21
Urinary (%)	2 (4)	10 (22)	**0.005**
Skin/soft tissue, *n* (%)	5 (9)	1 (2)	0.21
Other/unknown, *n* (%)	11 (20)	10 (22)	0.81
Lactate (mmol/L)	2.3 (1.5, 3.1)	2.0 (1.3, 2.8)	0.27
Creatinine (υmol/L)	95 (73, 173)	92 (71, 120)	0.25
SOFA score	3 (2,5)	2 (1,4)	**0.005**
APACHE III score	49 (30, 87)	41 (30, 58)	0.36
LOS (days)	8 (5,17)	7 (5,11)	0.31
Died, *n* (%)	7 (12)	5 (11)	0.54

P values calculated by Wilcoxon rank sum test or Fisher's exact test. Values are medians (IQR) unless otherwise specified. Bold values indicate significant results ($P < 0.05$). APACHE, Acute Physiology and Chronic Health Evaluation; ATS, Australian Triage Score; LOS, length of stay; SEAT, Sepsis Early Alert Tool; SOFA, Sequential Organ Failure Assessment (on admission).

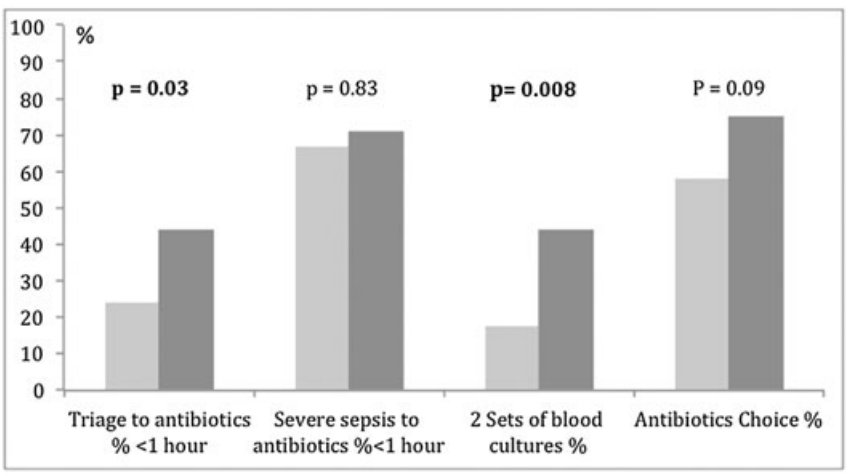

Figure 1. *Outcome measures percentages before and after Sepsis Early Alert Tool introduction. P values calculated by Fisher's exact test. (□), Pre-SEAT; (■), post-SEAT.*

SEAT group, and 55 (IQR 40–135) min *versus* 110 (IQR 90–300) min, $P = 0.03$ in the post-SEAT group (Fig. 2). The presumed source of infection at ED departure matched that at hospital discharge in around three quarters of cases of those admitted both directly to ICU and to the ward from ED (data not shown).

Discussion

In this single centre before and after study, we found that the introduction of a SEAT in the ED led to a significant improvement in the proportion of patients with severe sepsis with antibiotics administered within 1 h of presentation. Around two thirds of patients received antibiotics within 1 h of recognition of severe sepsis at baseline, and this did not significantly change. This suggests that the introduction of the SEAT resulted in earlier recognition of patients with severe sepsis. It is worth noting that these time-based targets for antibiotic administration are an 'ideal' and acknowledged not to be a 'standard of care' by the SSC.[6] Our results are consistent with published practice data.[11,16]

We also found improvement in the proportion of patients who had at least two sets of blood cultures taken prior to antibiotics, although this remained sub-optimal. Overall, there was no significant change in the appropriateness of antibiotic choice for the presumed source of sepsis, as recommended by eTG. This metric includes use of a broad-spectrum agent where a narrower spectrum drug or combination for a known source is recommended. This is important from the perspective of good antimicrobial stewardship.

Strengths of the study include the recruitment of consecutive cases admitted to the ICU, standardised data definitions and objective outcome measures. Limitations include retrospective recruitment, and the before and after design introduces a risk of bias as well as potential unmeasured confounding. Of note, despite this, the patients in the two study periods were reasonably matched in terms of age and severity of illness. There was a greater preponderance of urinary sepsis compared to respiratory infection in the post-intervention period; however, whether this would account for more rapid recognition of sepsis is uncertain.

Various SEAT have been investigated. Sawyer *et al*. developed an

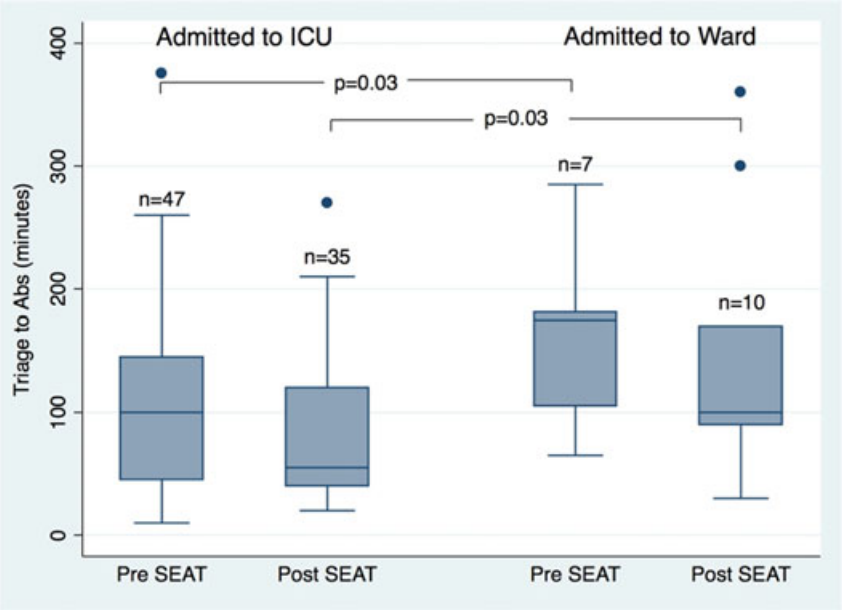

Figure 2. *Median time to from triage to antibiotics before and after introduction of Sepsis Early Alert Tool, by disposition from ED.*

automated sepsis alert system for use among inpatients that increased timely interventions (e.g. IV fluids and antibiotics).[17] Systematic screening of surgical ICU patients was found to be accurate and associated with reduced mortality.[18] Kent and Fields developed and evaluated a severe sepsis screening tool for nursing staff in ED; however, only 2% of patients screened had severe sepsis.[19] LaRosa *et al.* studied 58 patients with sepsis admitted to ICU, predominantly from the ED, and found that among those for whom a protocolised sepsis identification and alert system was activated, there was superior compliance with early sepsis care bundle interventions.[20] Nachimuthu and Huang adopted a dynamic Bayesian network approach that identified sepsis within 2 h of ED presentation.[21] Finally, Bruce *et al.* implemented a screening protocol for sepsis in the ED that resulted in improved compliance with lactate testing and reduced time to antibiotics.[22] A key feature of the present study was the screening was performed by triage nurses who were empowered to initiate investigation protocols and facilitate early medical review.

A common feature of all these systems is they are based on the presence of systemic inflammatory response syndrome (SIRS) criteria. However, recent evidence has demonstrated the limitations of SIRS for sepsis identification.[23] Of note, the screening tool developed by the NSW Clinical Excellence Commission, which we adapted for our study, is based on risk factors and 'red flags' for sepsis, rather than reliance of the presence of SIRS criteria.[10,11]

Accurate and timely recognition of sepsis in the ED is challenging because of marked clinical heterogeneity, dynamic clinical presentation and the lack of straightforward diagnostic criteria. In addition, a clinical presumption of sepsis on admission often correlates poorly with the presence of infection on post-hoc assessment.[24] Our results show that the employment of a screening tool, emphasising risk factors rather than SIRS criteria, embedded within a clinical pathway leads to earlier recognition of severe sepsis and compliance with guideline recommendations regarding blood culture collection.

An inherent assumption underlying this research is that processes to increase timely recognition of severe sepsis leads to better patient outcomes. This is based on observational studies that have found associations between delayed treatment, for example in the administration of antibiotics[3] or commencement of vasopressors,[25] and increased mortality. However, the relationship between timing of antibiotics, at least within the first 6 h, and outcome in sepsis has been challenged by a recent meta-analysis[26] and by a prospective observational ED-based study.[27] The effect of failure to make the diagnosis of sepsis is a different question. In our study, a proportion of patients were admitted to ICU from via the ward within 48 h of ED presentation. There was a significantly higher time to antibiotic administration among those admitted via the ward, but we are unable to determine from the data if any of these represented a failure to make the diagnosis of sepsis or simply clinical deterioration. Our results show that improvements in process-related outcomes are associated with introducing a SEAT. A positive effect on patient-centred clinical outcomes demonstrated in the NSW sepsis registry[11] may be due to a combination of both process improvements and increased focus on the condition arising from the implementation campaign.

Conclusion

The introduction of a SEAT in the ED is associated with earlier recognition of severe sepsis and improvements in quality of care.

Acknowledgements

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Author contributions

MI, KK and SPJM had the original study idea. MI undertook a literature review and designed the data