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ORIGINAL RESEARCH

Interdisciplinary Team Pilot to Reduce Time to Administration of Piperacillin/Tazobactam in the Emergency Department at a Veterans Affairs Medical Center

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Background: Sepsis is a condition of life-threatening organ dysfunction caused by a dysregulated host response to an infection. Adults with suspected sepsis or possible septic shock should receive antimicrobials within 1 hour. Early administration of antibiotics to patients with sepsis has been shown to decrease in-hospital mortality. Factors that affect antibiotic administration time include the antibiotic dispensary location, best practice alerts in electronic medical records, and staff "huddles" to continuously reinforce the importance of antibiotics.

Methods: At our Veterans Affairs Medical Center, we moved piperacillin/tazobactam from the central pharmacy to the emergency department automated dispensing cabinet. We implemented an interdisciplinary sepsis team comprised of emergency medicine (EM) nurses, pharmacists, and physicians. This was a retrospective chart review to assess whether our change in practice affected the time to administration of piperacillin/tazobactam in the emergency department. We assessed whether the change in practice had an effect on mortality in our population.

Results: Patients were reviewed 6 months pre- and post-implantation of the practice changes. There were 139 veterans in the pre-implementation group and 128 in the post-implementation group. The two groups were similar in age, sex, and African-American race. There was a statistically significant reduction in the average time from EM pharmacist verification to nurse administration when comparing the groups (46.5±49.8 vs 30.6±28.7 minutes, p=0.004). There were statistically significant reductions in the time from EM physician recognition to pharmacist order verification (54.37±50.22 vs 40.52±31.26 minutes, p=0.009). Eight patients died in the pre-pilot group compared to five in the post-pilot group. The relative risk of mortality was reduced between the two groups by 32%.

Conclusion: When piperacillin/tazobactam was stocked in the emergency department and we implemented an interdisciplinary sepsis team, there was a significant reduction in the time to administration in patients with sepsis.

Keywords: sepsis, veteran, interdisciplinary, emergency, antibiotic, piperacillin/tazobactam

Background

Sepsis is a condition of life-threatening organ dysfunction caused by a dysregulated host response to an infection.[1] Despite advances in medicine and advances in the understanding of pathophysiology of sepsis and septic shock, mortality remains as high as 33%.[2,3] A cornerstone of recent recommendations from the European Society of Intensive Care Medicine and the Society of Critical Care Medicine focuses on sepsis performance improvement programs. A recent meta-analysis found that sepsis performance improvement programs were associated with a reduction in mortality.[4]

Aside from fluid resuscitation goals, obtaining necessary laboratory tests, and any imaging that is needed, the diagnosis of infection and the prompt administration of necessary antibiotics are of utmost importance, as they have been shown to decrease mortality. Previous iterations of sepsis guidelines recommended that a full screen for infection should be obtained prior to starting antimicrobials whenever possible; however, because there is no "gold standard" and

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sepsis can present in many different forms, newer iterations of the guideline recommended continuously assessing patients to determine whether and when antimicrobials are needed.[5,6] According to the most recent update to the guideline, adults with suspected sepsis or possible septic shock should receive antimicrobials within 1 hour, against the most likely cause of the infection.[6]

Studies have shown that patients who develop septic shock, and do not receive antibiotics in a timely fashion, have a statistically significant increase in mortality for every hour without antimicrobials. The studies appear to show that patients with septic shock benefit most from early administration of antibiotics. However, those who are not experiencing septic shock may have an increase in mortality as early as 3 hours after identification.[7–10] As such, patients with sepsis who are not in septic shock should receive antibiotics no later than 3 hours, but ideally within 1 hour after sepsis is first suspected.[6] Patients who do not receive antibiotics within the first 1 hour of their sepsis diagnosis were associated with higher rates of in-hospital mortality. The choice of broad-spectrum antibiotic may differ from one institution to another, but a recent article reported that the four most common broad-spectrum agents are vancomycin, piperacillin–tazobactam, ceftriaxone, and levofloxacin.[11]

The use of multidisciplinary teams has proven to be vital in the care of patients, especially those with sepsis. The results of one study found that after implementing an interdisciplinary team order set for patients with neutropenic fever in the emergency department (ED), the time to administration of antibiotics decreased from an average 128 minutes to 53 minutes.[12] Other studies have also shown that other ideas to decrease time to administration of antibiotics include best practice alerts in electronic medical records, staff "huddles" to continuously reinforce the importance of antibiotics, and stocking of antimicrobials in the automated dispensing cabinets.[13,14]

Methods

Study Site and Study Team

Jesse Brown Veterans Affairs Medical Center (JBVAMC) is 200-bed hospital in Chicago, Illinois, in the United States. The ED at JBVAMC has 17 beds, and services veterans of the US Armed Forces and veterans of foreign wars with non-trauma emergencies. To better address the needs of the sepsis patients seen at JBVAMC ED, an interdisciplinary sepsis team comprised of emergency medicine (EM) nurses, pharmacists, and physicians was developed and implemented on February 1, 2023. Each morning before the start of the workday, someone from the sepsis team would report on the sepsis cases seen in the previous 24 hours. As a part of this report, the team member would report the time the patient arrived at the ED, and the time the antibiotic order was placed by the physician, verified by the pharmacist, and administered by the nurse.

Eligibility

The study was a retrospective chart review of patients who presented to the JBVAMC ED in Chicago, Illinois, with sepsis and received piperacillin/tazobactam. The study population was generated from a list of all intravenous piperacillin/tazobactam orders verified from August 3, 2022 through July 31, 2023. Patients were included if they were at least 18 years of age, had a diagnosis of sepsis made by an ED physician, and received the first dose of piperacillin/tazobactam 4.5 g in the ED. Patients were excluded if they had received piperacillin/tazobactam doses other than 4.5 g or the antibiotic was administered outside the ED. We did not identify any ethical concerns in the implementation of this work. Following institutional protocol, the Jesse Brown Veterans Affairs Medical Center institutional review board (IRB) exempted this project (IRB number: 1728945–1) based on the project description, since it did not meet regulatory definition of research according to the US Code of Federal Regulations 38.16.102(I).

Endpoints

The primary endpoint was the mean difference in time from EM pharmacist verification to EM nurse administration prior to ("Pre" group) and following ("Post" group) the practice change of stocking piperacillin/tazobactam in the ED automated dispensing cabinet and the introduction of the interdisciplinary pilot. The secondary endpoints included the difference in mortality before and after the pilot introduction, difference in time from physician medication order entry to

nurse administration, difference in time from patient arrival at the ED to piperacillin/tazobactam administration, and difference in time from physician medication order entry to pharmacist verification. A subgroup analysis was performed, on the patients who died, comparing the mean difference in time to administration of piperacillin/tazobactam from order verification.

Statistical Analysis

Baseline characteristics and endpoints were analyzed using descriptive statistics. Categorical data were analyzed using chi-squared tests. Continuous data were compared using the *t*-test for means or *z*-test for proportions. The level of statistical significance (α) was set at 0.05.

Results

Enrollment

A list of all piperacillin/tazobactam orders was generated 6 months pre- and post-implementation of the interdisciplinary pilot. A total of 293 patients received piperacillin/tazobactam, of whom 26 patients were excluded as they had not received the antibiotic in the ED (Figure 1).

Baseline Characteristics

All baseline data are presented in Table 1. The average age of the Pre group was 67 years old compared to 66 years old in the Post group. The majority of patients in each cohort were male (94% vs 97%) and African-American (60% vs 70%), which is in concordance with the demographics of the population at our VA medical center. Overall, the demographics were similar between the two groups, except for the number of Caucasians and those who were identified as "other" or "unknown". Significantly more patients in the Pre group were diagnosed with pneumonia, while more patients in the Post group had sepsis of unknown origin.

Endpoints

The average time (mean ± SD) from pharmacist verification to nurse administration before the interdisciplinary pilot was launched was 46.5±49.8 minutes, compared to 30.6±28.7 minutes after the pilot (p=0.004). Of the secondary endpoints, the time from physician order entry to nurse administration, and the time from arrival at the ED to nurse administration were both significantly reduced after the launch of the interdisciplinary pilot. The difference in mortality between the two

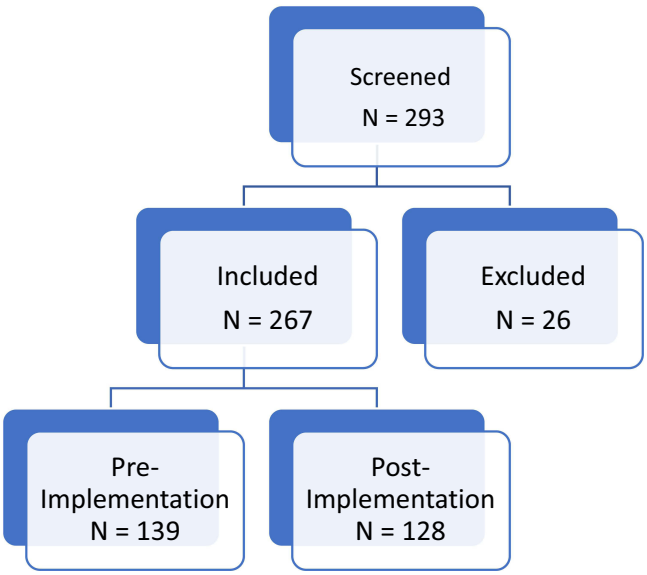

Figure 1 Enrollment of patients in each treatment arm of the study.

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Table 1 Baseline Characteristics

Characteristic	Pre (N=139)	Post (N=128)	*p*-Value
Age (years)	67.1±14.6	66.4±12.9	0.69
Sex, male, n (%)	131 (94.2)	125 (97.7)	0.16
Race, n (%)			
African-American	83 (59.7)	90 (70.3)	0.7
Caucasian	50 (36)	22 (17.2)	0.001
Unknown	6 (4.3)	16 (12.5)	0.015
Septic source, n (%)			
Abscess	6 (4.3)	10 (7.8)	0.23
Appendicitis	6 (4.3)	3 (2.3)	0.37
Cellulitis	19 (13.7)	15 (11.7)	0.63
Diabetic foot infection	6 (4.3)	10 (7.8)	0.23
Diverticulitis	5 (3.6)	2 (1.6)	0.3
Osteomyelitis	11 (7.9)	11 (8.6)	0.84
Pneumonia	17 (12.2)	6 (4.7)	0.029
Unknown	36 (28)	51 (39.8)	0.015
Urinary tract infection	13 (9.4)	5 (3.9)	0.7

Note: Data are expressed as mean ± standard deviation where appropriate.

Table 2 Endpoints

	Group 1 (N=139)	Group 2 (N=128)	*p*-Value
Time (minutes) from pharmacist verification to nurse administration	46.5±49.8	30.6±28.7	0.004
Time (minutes) from physician order entry to pharmacist verification	7.8±10.6	9.9±11	0.12
Time (minutes) from physician order entry to nurse administration	54.4±50.2	40.5±31.3	0.009
Time (minutes) from arrival at emergency department to physician order entry	162.6±146.9	128±76.1	0.001

Note: Data are expressed as mean ± standard deviation where appropriate.

group was not statistically significant (8 vs 5, p=0.23). All results are listed in Table 2. In a subgroup analysis of the patients who died, there was no statistically significant difference in the average time to administration from verification (68.8 vs 33 minutes, p=0.26). A subgroup analysis was also performed between Pre (N=28) and Post (N=22) patients who received antibiotics after 60 minutes. While the differences were not statistically significant, there was a trend toward statistical significance in the difference in time from verification to antibiotic administration (103±68.4 vs 75 ±25.8 minutes, p=0.075).

Discussion

This retrospective chart review of patients who presented to the JBVAMC ED in Chicago, Illinois, with sepsis was used to evaluate the efficacy of the interdisciplinary sepsis team that was implemented and the time to administration of piperacillin/tazobactam before and after the antibiotic was added to the ED's automated dispensing cabinet. This study found that the average time from pharmacist verification to nurse administration before the interdisciplinary pilot was launched was 46.5 minutes, compared to 30.6 minutes after the pilot (p=0.004). The time from physician order entry to nurse antibiotic administration was 54.4 minutes before the pilot was launched and 40.5 minutes after the pilot (p=0.009). The time from patient arrival at the ED to nurse antibiotic administration before and after the pilot was launched also showed a statistically significant difference (217 vs 168.5 minutes, p=0.015). The difference in mortality between the two groups was not statistically significant (8 vs 5, p=0.23). The difference in the number of patients who received

piperacillin/tazobactam within 60 minutes was also not statistically significant (111 vs 106, p=0.08). There were more patients who had septic shock in the post-implementation group; however, this difference was not statistically significant. Because there were more sick patients in the post-implementation group, this may explain why mortality overall was not significantly reduced in the post-implementation group.

We report on the utility of an interdisciplinary sepsis team and stocking of antibiotics in the ED. The results of our study are in line with others; however, there are a few caveats. Emerson et al found that local stocking of antibiotics in the ED rather than the central pharmacy led to a decrease in time from patient arrival to antibiotic administration by 30 minutes, from 154 minutes to 114 minutes.[13] This occurred after several other project implementation ideas, such as a sepsis-specific order set and staff education, had been put in place. Our project used the simultaneous implementation of a sepsis team with the relocation of antibiotics to the ED. In a study by Wayne et al, trends in time to antibiotics among veterans hospitalized with sepsiswere investigated. Among the more than 111,000 patients in the cohort, time from patient presentation to antibiotic administration decreased about 22% from 4.5 hours to 3.5 hours over a 6-year period.[15,] Our study found also found a decrease in the time from patient arrival to antibiotic administration of about 22.5%; however, the decrease from 217 minutes to 168.5 minutes occurred over a 6-month period. While patients in the study by Wayne et al were not as severely ill as those in previous studies, the mortality rate in their study mirrored ours.[7,8,16,17]

As with any study, our study is not without limitations. Our single-site study may not be applicable to every VA medical center, as our patient population and institutional protocols may not mirror those of other centers. This study was a quality-improvement initiative, and the small number of patients receiving piperacillin/tazobactam during the study period at our VA medical center means that the study may not have been sufficiently powered to detect a difference in the primary outcome. Lastly, when evaluating mortality, we did not assess compliance with other sepsis measures, such as fluid resuscitation or lactate clearance. To that end, future directions to enhance this study are being undertaken and will include using a sepsis scoring tool to identify patients who should be triaged with higher priority to further decrease the time to administration of antibiotics. Also, compliance with other measures of the sepsis bundle will be investigated to determine the individual and collective impact that they have on veterans at our institution.

Conclusion

In conclusion, when piperacillin/tazobactam was stocked in the automated dispensing cabinet in the emergency department and we implemented an interdisciplinary sepsis team, there was a significant reduction in the time to administration of antibiotics in patients with sepsis, leading to a reduction in mortality. This study highlights the important role that all providers play as part of interdisciplinary teams and how a systemic approach to sepsis care can improve veterans' access to timely, high-quality care. This study further highlights the significantly improved outcome in patient care when life-saving medications are placed closer to their ultimate destination.

Disclosure

The authors report no conflicts of interest in this work.

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