Impact of 24-hour pharmacy call response on time to antibiotics in open fractures

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Purpose: Open fractures are associated with significant morbidity after trauma, which is driven, in part, by infection. Current literature and guidelines recommend that this patient population receive antimicrobial prophylaxis within 1 hour of emergency department (ED) arrival to minimize the risk of infection. The primary aim of this study was to investigate whether the addition of a trauma response to a pharmacy resident on-call program resulted in antibiotic administration within 1 hour of presentation to a higher proportion of patients with open fractures.

Methods: This was a retrospective, observational, quasi-experimental analysis that was conducted at an academic medical facility with a level 1 trauma center for patients presenting to the ED from January 2019 to December 2020 (preimplementation period) and from January 2021 to December 2022 (postimplementation period). Patients were included if they were 18 years of age or older and presented to the ED with an open fracture(s). Patients with independent fractures of fingers and those who died in route to or in the ED were excluded. The primary outcome was the proportion of patients with antibiotic administration within 1 hour of ED presentation for patients with open extremity fractures.

Results: A total of 292 patients met the eligibility criteria (49% in the preimplementation group and 51% in the postimplementation group). Patients were predominantly male (61% vs 58%), with an overall median age of 46 years. Following implementation of the on-call pharmacy resident trauma response, a significantly higher proportion of patients received antibiotics within 1 hour of presentation (70% vs 83%; $P = 0.019$). The median (interquartile range) time to antimicrobial administration was also significantly shorter in the postimplementation group (31 [16-68] minutes vs 19 [10-50] minutes; $P = 0.005$).

Conclusion: The addition of a 24-hour on-call pharmacy resident response in the ED was associated with improved antibiotic administration within 1 hour of presentation in patients with open fractures.

Keywords: antibiotic prophylaxis, clinical pharmacist, hospital emergency services, open fracture, pharmacy residency, wounds and Injuries

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Open extremity fractures occur in adults at an estimated annual incidence of 30.7 per 100,000 persons globally.[1] According to data from the US National Trauma Data Bank, over 65,000 patients were treated for an open extremity fracture in 2019 alone.[2] Open fractures place patients at an increased risk of infection, with reported infection rates of 25% to 50%.[3,4] Infection rates vary by Gustilo classification, with infections occurring at the highest rates in type III open fractures.[3,5] Subsequent development of infections has been shown to increase morbidity, including delayed wound healing and progression to osteomyelitis.[3] Early interventions, including wound cleaning, wound closure, and systemic antimicrobials, decrease the rate of infectious outcomes in these patients.[3-7]

Guidelines vary in their recommendations for antimicrobial selection based on Gustilo classification. Specifically, the Eastern Association for the Surgery of Trauma guidelines recommend gram-positive organism–directed antimicrobials for all open fracture types and additional gram-negative coverage for type III open fractures.[8] The more contemporary Surgical Infection Society guidelines for antibiotic use in open extremity fractures recommend only gram-positive organism–directed antimicrobial agents for all open fracture types.[3] However, the recommendation to withhold additional gram-negative coverage for type III fractures is based on low-quality observational data.[3]

Although choice of antimicrobial agent in open fractures has been debated, the literature has clearly demonstrated that shorter time to antimicrobial therapy leads to decreased incidence of wound infections.[6,7] The Trauma Quality Improvement Program of the American College of Surgeons benchmarks antibiotic administration within 1 hour of presentation as a best practice for the management of open fracture.[9] Various strategies, such as pay-for-performance initiatives, have been implemented to achieve this benchmark, but it continues to be operationally difficult to achieve in the emergency department (ED).[2,10]

Emergency medicine (EM) clinical pharmacists have been demonstrated to improve patient outcomes through reductions in time to medication therapy, guideline compliance, and antimicrobial selection and optimization, as well as providing cost savings to healthcare institutions.[11-15] Despite this, many institutions lack 24/7 EM pharmacist coverage, and utilizing a pharmacy resident in-house on-call program may provide alternative coverage and benefit in the ED.[16,17] The purpose of this study was to evaluate whether the addition of trauma response responsibilities to the institutional pharmacy residency on-call program improved institutional attainment of antibiotics within 1 hour of presentation for patients with open extremity fractures.

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Methods

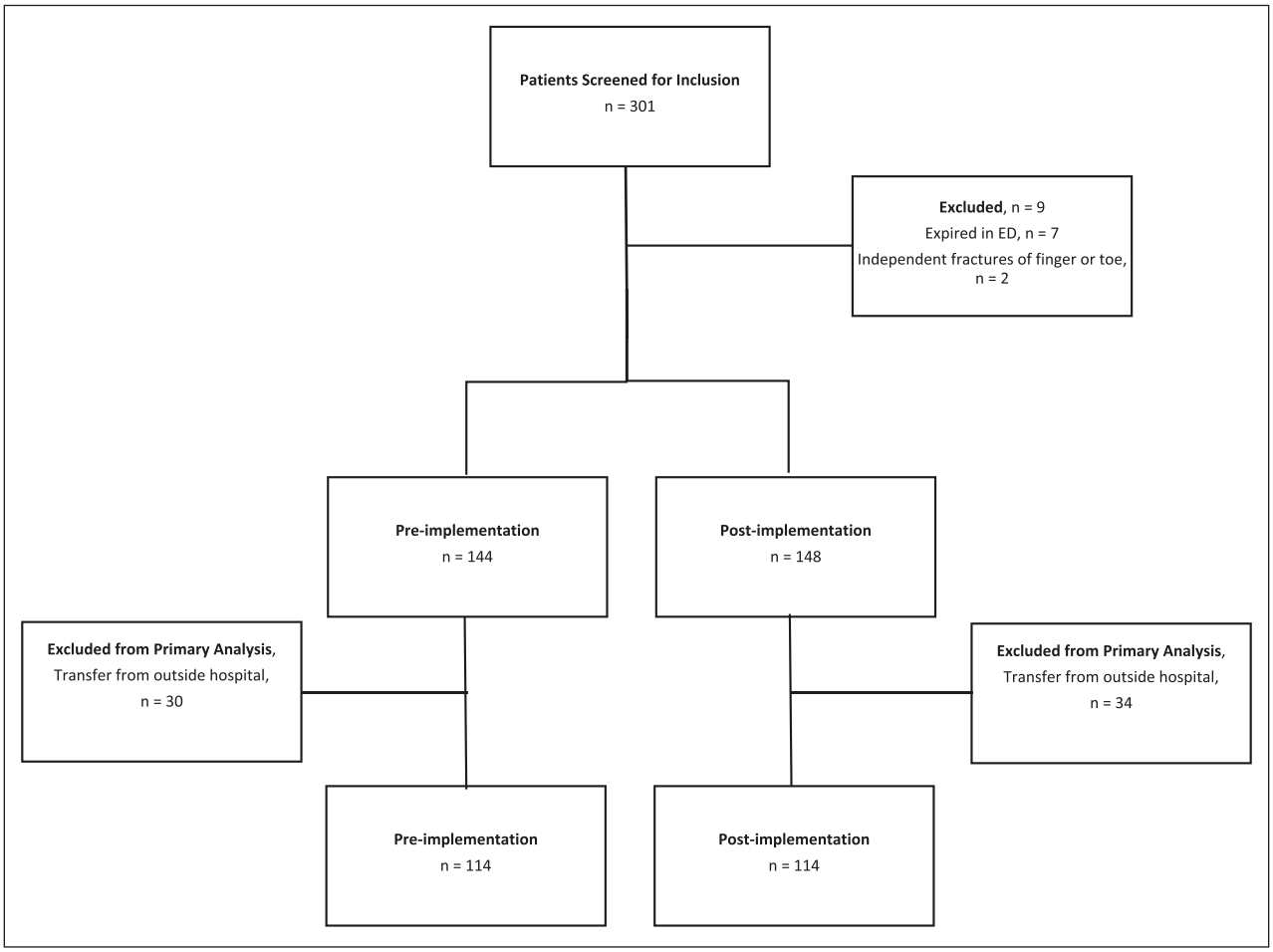
This was a retrospective, observational, quasi-experimental analysis that was conducted at an academic medical facility with a level 1 trauma center for patients presenting to the ED from January 2019 to December 2020 (preimplementation period) and from January 2021 to December 2022 (postimplementation period). All patients 18 years of age or older who presented to the ED with an open extremity fracture were included. Patients were excluded if they died in route to the hospital or in the ED or if they had independent open fractures of the fingers.[18] Patient lists were obtained via institutional trauma bank.

The institutional pharmacy residency program offers an in-house on-call program allowing for 24/7 clinical pharmacist coverage in the hospital. The on-call shift rotates among 18 to 21 pharmacy residents, with the primary responsibilities including code blue response throughout the hospital, management of direct thrombin inhibitor initiation, management of complex anticoagulation and kinetics, and response to drug information questions. In January 2021, bedside ED trauma response was added as a responsibility of the on-call pharmacy residents between the hours of 11:00 PM and 8:00 AM, when there was not an EM clinical pharmacist onsite. If the trauma involved an open fracture, on-call residents were trained, via lecture and simulation laboratory scenarios, to provide appropriate antimicrobial selection following the institutional open fracture antibiotic prophylaxis protocol (eFigure 1). To facilitate timely administration of antimicrobial prophylaxis, on-call pharmacy residents would obtain the antibiotic from the automated dispensing cabinet, prepare the appropriate agent and dose, and facilitate nursing administration of the agent.

The primary outcome was the proportion of patients with antibiotic administration within 1 hour of ED presentation in patients with open extremity fractures. Secondary outcomes included the time to antibiotic therapy, the appropriateness of the antibiotic therapy based on the open fracture type and patient-specific factors, and the 90-day infection rate. Open fracture type was defined by diagnosis in the operating room after initial management in the ED. Time to antibiotic administration was defined as the time from ED arrival to first administration of an antibiotic, while the appropriateness of antibiotic therapy was based on the institutional protocol.

In the primary analysis, if patients were administered appropriate antimicrobials by emergency medical services (EMS), the time of the first antibiotic administration was considered to be the patient's arrival time at the ED. Patients transferred from an outside hospital were excluded from analysis of the primary endpoint, as

Figure 1. Identification of eligible patients: flowchart of patients included for analysis. ED indicates emergency department.



well as the secondary endpoint of time to antimicrobial therapy, as antimicrobial therapy was likely initiated before transfer. Subgroup analyses were performed for patients who presented during overnight hours (11:00 PM to 8:00 AM) when there was no EM pharmacist onsite, patients who presented during all hours of the day excluding those who received antimicrobial therapy via EMS and those transferred from an outside hospital, and patients presenting during overnight hours excluding those who received antimicrobial therapy via EMS and those transferred from an outside hospital. Demographic and outcomes variables were collected through electronic health record (EHR) data reports as well as manual chart review.

A c^2 or Fisher's exact test was utilized for nominal variables, while Student's t test or a Mann-Whitney U test was utilized for continuous variables, based on the normality of the data. All statistical tests were evaluated for significance using an a level of 0.05. Statistical analyses were performed using SPSS, Version 28.0 (IBM Corporation, Armonk, NY). This project was submitted as a quality improvement project to the institutional review board and was considered to be nonregulated research.

Results

A total of 301 patients were eligible for the study, and 292 patients were included in the final analysis (Figure 1). Baseline characteristics were generally well balanced between the groups, with the exceptions that more patients in the postimplementation group received antimicrobials from EMS and Gustilo classification varied between the groups (Table 1). All patients who were given antimicrobials by EMS were given the appropriate dose and agent aside from one patient in the preimplementation group.

Following implementation of the on-call pharmacy resident trauma response, a significantly higher proportion of patients received antibiotics within 1 hour (70% for the preimplementation group vs 83% for the postimplementation group; P = 0.019) (Table 2). Findings for secondary outcomes can be found in Table 2. In 85 patients, inappropriate antimicrobial agents were given based on the institutional protocol (n = 36 in the preimplementation group and n = 49 in the postimplementation

Table 1. Patient Demographics

Characteristic[a]	Preimplementation group (n = 144)	Postimplementation group (n = 148)	*P* value
Male gender[b]	87 (60)	86 (58)	0.635
Age, median (IQR), years	43 (29-60)	44 (29-63)	0.624
BMI,[b] median (IQR), kg/m^2	28 (24-32)	27 (23-31)	0.119
ISS,[b] median (IQR)	10 (9-22)	10 (9-19)	0.389
Transfer from OSH	30 (20.8)	34 (23)	0.659
Antimicrobials given by EMS	6 (4)	18 (12)	0.013
PWID	5 (4)	6 (4)	0.794
Diabetes	15 (10)	21 (14)	0.327
Gustilo open fracture classification			
Type I	71 (49)	54 (37)	0.027
Type II	27 (19)	64 (43)	<0.001
Type III	46 (32)	30 (20)	0.023

Abbreviations: BMI, body mass index; EMS, emergency medical services; IQR, interquartile range; ISS, Injury Severity Score; OSH, outside hospital; PWID, person who injects drugs.
[a]Data presented as No. (%) unless indicated otherwise.
[b]Not all patients had documented values.

Table 2. Selected Outcomes

Outcome[a]	Preimplementation group (n = 114)	Postimplementation group (n = 114)	*P* value
Primary outcome			
Antimicrobials administered within 1 hour	80 (70)	95 (83)	0.019
Secondary outcomes			
Time to antimicrobial therapy, median (IQR), minutes	31 (16-68)	19 (10-50)	0.005
Appropriateness of antimicrobial therapy[b]	108 (75)	99 (67)	0.127
90-day infection rate[b]	19 (13)	18 (12)	0.791
90-day osteomyelitis rate[b]	4 (3)	3 (2)	0.720

Abbreviation: IQR, interquartile range.
[a]Data presented as No. (%) unless indicated otherwise.
[b]Preimplementation n = 144 and postimplementation n = 148.

group). Of note, one patient was given clindamycin due to a penicillin allergy, which was not included as an inappropriate agent. In all cases of inappropriate therapy, cefazolin or ceftriaxone was given when the other was indicated. Among these patients, 10 patients in the preimplementation group received overly broad gram-negative coverage compared to 39 patients in the postimplementation group. Alternatively, 26 patients in the preimplementation group and 10 patients in the postimplementation group received overly narrow gram-negative coverage when broader coverage was indicated (Table 3).

When excluding transfers, 67 patients presented to the ED during the overnight hours. Within this subgroup, a significantly higher proportion of patients in the postimplementation group received antibiotic therapy within 1 hour of presentation and the median time to antibiotic therapy was significantly shorter in the postimplementation group (Table 4). In a subgroup analysis of patients who presented during overnight hours that excluded those who were transferred from outside hospitals or given antibiotics via EMS, a significantly higher proportion of patients were administered antibiotics within 1 hour (46% vs 82%; $P = 0.003$) and the median (interquartile range) time, in minutes, to antibiotic administration

Table 3. Inappropriate Antimicrobial Use

Outcome[a]	Preimplementation group (n = 36)	Postimplementation group (n = 49)	*P* value
Patients with a type III open fracture who received cefazolin	26 (72)	10 (20)	<0.001
Patients with a type I or II open fracture who received ceftriaxone	10 (28)	39 (80)	<0.001

[a]Data presented as No. (%) unless indicated otherwise.

Table 4. Subgroup Analysis of Patients Presenting During Overnight Hours

Outcomes	Preimplementation group (n = 27)	Postimplementation group (n = 40)	*P* value
Primary outcome			
Antimicrobials administered within 1 hour, No. (%)	13 (48)	34 (85)	0.001
Secondary outcome			
Time to antimicrobial therapy, median (IQR), minutes	67 (34-94)	25 (12-54)	0.002

Abbreviation: IQR, interquartile range.

was significantly shorter (69 [39-95] vs 30 [17-58]; $P = 0.009$). In a subgroup analysis of this patient population that included patients who presented at any time of day, a numerically higher proportion of patients were administered antibiotics within 1 hour in the postimplementation group (70% vs 80%; $P = 0.085$) and the median (interquartile range) time, in minutes, to antibiotic administration was shorter (32 [17-71] vs 25 [14-57]; $P = 0.125$).

Discussion

This was the first study to demonstrate the benefit of an on-call pharmacy residency trauma response in the ED on time to antibiotics in patients with open extremity fractures. Two key findings were the significant improvements in the proportion of patients who received antimicrobial therapy within 1 hour of presentation and the decrease in overall time to antimicrobial administration following implementation of trauma response for on-call pharmacy residents. These findings support existing literature that show the benefits of having 24-hour clinical pharmacist coverage in the ED.[11-15]

Lack et al[7] previously demonstrated that antimicrobial administration within 1 hour of open extremity fractures was associated with a decreased rate of infection development. The addition of pharmacy resident trauma response led to overall better rates of antimicrobial administration within 1 hour. However, both groups had EM clinical pharmacist coverage throughout the day, which makes it difficult to ascertain the full benefit of the pharmacy on-call program. The subgroup analysis focused on patients presenting during the overnight hours, when an EM pharmacist was not present, demonstrated a more pronounced effect of the intervention. The subgroup continued to show a significantly higher proportion of patients receiving antibiotics within 1 hour and a shorter time to therapy after implementation. Specifically, the median time of 30 minutes to antimicrobial therapy in the postimplementation group was well below 1 hour and significantly shorter than the median time of 67 minutes in the preimplementation group. This decrease in time may be explained by timely antibiotic preparation by the pharmacist. Furthermore, a study conducted by Barnard et al[2] reported that less than 50% of patients with open fractures received antibiotics within 1 hour, based on data from the National Trauma Data Bank. A similar 40% of patients received antibiotics within 1 hour in the overnight hours subgroup in this study before intervention, which was improved to 70% after implementation of the pharmacy resident trauma response. This highlights that implementation of overnight pharmacy resident coverage in the ED is a key intervention in meeting the 1-hour antibiotic administration benchmark for open fractures.

Other studies have demonstrated the benefits of EM clinical pharmacists in the ED on patient outcomes and cost. Roman et al[13] conducted a study to determine the effects of implementing a sepsis alert response via EM pharmacists and found that a significantly higher proportion of patients were administered antimicrobials within 60 minutes of presentation with an EM pharmacist responding. Other studies have reported similar benefits on time to administration of other medication

classes when EM pharmacists are involved.[19] The PHARM-EM study aimed to quantify cost avoidance generated by EM clinical pharmacists. This study estimated that initiation and streamlining of antimicrobials accounted for an overall annual cost avoidance of $846,244 from the 88 EM pharmacists during the 6-month study period.[12] Most recently, Nguyen et al[20] conducted a single-center study evaluating the cost avoidance generated by EM clinical pharmacists during night hours and found an overall cost avoidance of $60,101 during their 4-month study period. Cost avoidance through continued streamlining of antimicrobial initiation may be an unrecognized benefit of pharmacy resident trauma response in the ED.

While the proportion of antimicrobial therapy that was appropriate did not significantly differ between the pre- and postimplementation groups, it is noteworthy that most patients received appropriate antimicrobials in both cohorts. However, inappropriate antimicrobial selection did occur in 29% of patients. One explanation for the inappropriate choice of antimicrobial agents could be mis-categorization of the open fracture in the trauma bay, as official categorization was determined during surgical repair. Another reason for this could be that open fractures are not paged out as a trauma at our institution if patients self-present to the ED, which may also lead to delays in antimicrobial administration. Despite this, a post hoc analysis performed on patients who received inappropriate antimicrobial therapy revealed that the pharmacy residents may have had a beneficial impact, with a significantly higher number of patients in the postimplementation group receiving broader antimicrobial coverage when it was not indicated, whereas undercoverage was more common in the preimplementation group.

Despite the overall improvements in antibiotic administration, this study did not find a significant difference in 90-day infection rates between the pre- and postimplementation groups. This may be attributed to various factors, including not being able to detect a difference with the relatively small cohort of patients. Other studies have reported similar rates of infection with antimicrobial use. Lack et al[7] found that patients who received antibiotics within 1 hour had an infection rate of 6.8%, and the Surgical Infection Society has reported infection rates of 5% to 20% in patients who receive antibiotics.[2,7] Future prospective studies with an established follow-up protocol, as well as studies with larger sample sizes, may provide further insight into the impact of timely antibiotic administration on long-term infectious outcomes.

Limitations of our study included its retrospective, single-center design, which increases the risk of bias and may limit the generalizability of the findings to other healthcare settings. Because of variability in trauma documentation, there was no way to accurately determine whether a pharmacist or pharmacy resident was directly responsible for antimicrobial therapy. This limitation continues to apply overnight as the on-call pharmacy resident may not be able to respond to the trauma if they are occupied with other emergent on-call responsibilities (eg, code blue response). Additionally, the data analyzed were limited to what was available in the EHR. This limitation most likely impacts the secondary outcome of 90-day infection rate, as patients may not have presented to the same institution for infection management. Previous studies that demonstrated the benefit of prompt antimicrobial therapy in this patient population focused on time to administration from time of injury.[5,6] As time of injury is not something that is documented in our EHR, this study reported times from ED arrival. This may affect our results as patients given appropriate antibiotics before arrival via EMS had documented times of zero and more patients received antibiotics via EMS in the postimplementation group. Furthermore, around the same time the intervention analyzed in this study occurred, there was a change in protocol allowing more patients to receive antibiotics via EMS. However, we conducted a subgroup analysis excluding patients who were transferred from outside hospitals and patients who received antibiotics via EMS at all hours and during overnight hours. Continued significance was found for the proportion of patients with antibiotics administered within 1 hour as well as the median time to antibiotic administration during overnight hours while no significant difference was found when including patients who presented at all hours of the day. However, the median time to antibiotic administration for patients admitted at all hours was under 1 hour in both groups, indicating the effect of the EM clinical pharmacist.

Despite the limitations, this study has many strengths worth noting. The definitions of both primary and secondary outcomes mirror those in other studies examining this patient population.[6,9] Another strength was the pragmatic design of the study and generalizability to real-world practice with an outcome that is known to improve quality metrics for trauma center verification as well as patient-centered morbidity outcomes. This research joins the small pool of literature that emphasizes the benefits that a 24-hour, in-house on-call pharmacy resident program has on the institution.[16,17] The intervention described in this study makes up only one of the numerous responsibilities that give pharmacy residents a unique and robust learning experience. These responsibilities allow institutions to further recognize the professional contributions of pharmacists and, in turn, continue the growth in pharmacy practice.

Conclusion

In conclusion, this study highlights the potential impact that integration of trauma response to a pharmacy residency on-call program may have on timely antimicrobial administration to patients with open extremity fractures. This intervention has the potential to

improve patient-centered outcomes by reducing the risk of infection complications. These findings also align with existing literature, reinforcing the benefits of 24-hour clinical pharmacist coverage in the ED. Continued research should focus on confirming these findings that suggest that clinical pharmacist involvement in trauma response correlates with timely administration of antimicrobial therapy.

Data availability

The data underlying this article cannot be shared publicly for the privacy of individuals who participated in the study.

Disclosures

Dr. Morrisette currently receives grant funding through Stellus Rx and AbbVie, has participated in scientific advisory boards for AbbVie and Basilea Pharmaceutica, has provided expert witness testimony to Copeland, Stair, Valz & Lovell, and has received honoraria from Infectious Diseases Special Edition. The remaining authors have declared no potential conflicts of interest.

Previous affiliations

At the time of the study, Dr. Kadi was affiliated with Medical University of South Carolina.

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