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Treatment of Bacterial Skin Infections in Emergency Department Observation Units: Factors Influencing Prescribing Practice

John P. Haran, MD¹, Gregory Wu, MD¹, Vanni Bucci, PhD², Andrew Fischer, MD¹, Edward W. Boyer, MD, PhD¹, and Patricia L. Hibberd, MD, PhD³

¹Department of Emergency Medicine, University of Massachusetts Medical School, Worcester, MA

²Department of Biology, University of Massachusetts Dartmouth, North Dartmouth, MA

³Department of Pediatrics and Division of Global Health, Massachusetts General Hospital, Boston, MA

Abstract

Objective—The Infectious Disease Society of America (IDSA) publishes evidence based guidelines for the treatment of skin and soft tissue infections. How closely physicians follow these guidelines is unknown, particularly in the Emergency Department Observation Unit (EDOU) where increasing numbers of patients are treatment for these infections. Our objectives were to describe: 1) the antibiotic treatment patterns EDOU patients, 2) physicians' adherence to the IDSA guidelines, and 3) factors that influence physician's prescribing practices.

Methods—This prospective cohort enrolled adult patients discharged from an EDOU at an academic medical center after treatment for a skin or soft tissue infection. Information was collected from chart review and patient interview pertaining to the patient's socio-demographic characteristics, presenting illness, and antibiotic treatment regimens. Treatment regimens were compared with national guidelines.

Results—The study included 193 patients of which only 43% were treated according to IDSA guidelines; 42% were over-treated and 15% were under-treated. Women were more likely to be under-treated (RR 1.58; 95% CI 1.21 to 2.06), while patients 50 years and older were at risk for over-treatment (RR 1.44; 95% CI 1.03, 2.02). Women also received shorter courses of antibiotic therapy with an average of 9.6 days of treatment compared with 10.6 days for men.

Corresponding Author: John P. Haran, MD, 55 Lake Avenue North, Worcester, MA 01655; Phone: 508-450-8688; john.haran@umassmed.edu; fax: 508-421-1490.

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Conclusions—Physician antibiotic prescribing practices demonstrated poor adherence to IDSA guidelines and were influenced by the patient's age and gender. Standardized antibiotic protocols for treatment of skin and soft tissue infections to IDSA guidelines in the EDOU would minimize physician bias.

1. Introduction

Failure of oral antibiotic treatment for skin and soft tissue infections (SSTIs) has led to the need for intravenous therapy that is often delivered in Emergency Department Observation Units (EDOU).¹⁻³ As treatment locations that focus on the brief treatment of medical problems of limited complexity, EDOU are increasingly the location in which intravenous antibiotic therapy for resistant SSTI is administered.⁴ Guidelines from the Infectious Disease Society of America (IDSA) recommend antibiotic coverage for abscesses and intravenous antibiotics for cellulitis, only in the presence of a systemic inflammatory response, if the patient is severely immunocompromised, or failing outpatient treatment.⁵ Adherence to IDSA guidelines is important given the increasing resistance to many commonly used antimicrobial agents caused by widespread antibiotic use. Unfortunately, physician discretion in selecting antibiotic regimens leads to a variability in ED treatment approaches to common bacterial infections.⁶ Given the risks of bacterial resistance due to inappropriate antibiotic use, physician practices in prescribing antibiotics in the EDOU is unknown and deserves attention.^{4,7} The objectives of this cohort study, therefore, were to: 1) describe the prevalence of various antibiotic prescribing practices for patients with SSTIs, 2) compare these management practices with national guidelines, and 3) identify factors that might influence physician's prescribing practices.

2. Methods

2.1. Study Design

We conducted a single-center, prospective cohort study. The hospital's institutional review board (IRB) approved the study (IRB docket #H00001871).

2.2. Study Setting and Population

We identified adult ED patients retrospectively and prospectively enrolled and confirmed patient data into this cohort study after discharge from an EDOU at a large urban academic ED between January and December, 2013. Patients were eligible for participation if they were discharged home after an EDOU stay, and either received antibiotics for a SSTI in the EDOU or upon discharge. SSTI was defined as clinician diagnosis of a bacterially caused abscess or cellulitis upon discharge or a diagnosis of abscess or cellulitis that was treated with antibiotics. We identified potential subjects using EDOU census logs at the end of each month whom we contacted by phone 4 week after the discharge date. Eligible patients were English-speaking, 18 years of age or older, treated for a SSTI, and had a working cell or landline phone. We analyzed separately those patients who were admitted directly to the hospital after failing EDOU treatment. We excluded patients if they were unable to cooperate with the questionnaire or recall events surrounding their care. To minimize recall

bias, we also excluded patients whom we were unable to contact within 8 weeks of discharge from EDOU.

2.3. Data Collection

Research assistants trained in chart review and patient data extraction by the authors administered a standardized survey to consenting and enrolled patients with a SSTI over the telephone. We obtained data related to the patient's antibiotic compliance, healthcare visits/hospitalizations, and any other complications since initial EDOU discharge. We obtained medical histories, allergies, and antibiotic treatment regimens that we confirmed through chart review by reviewers blinded to the study objectives. We calculated the Charlson comorbidity index (CCI) to characterize patient's medical comorbidities.^{8,9} In addition, we obtained information pertaining to initial ED presentation, EDOU hospital course, and antibiotic treatments used from the medical records in a blinded manner. We reviewed the medical records of patients admitted to the hospital after failing EDOU therapy to obtain medical histories, EDOU visit details, and information about their subsequent hospital stay. We captured and extracted study data using REDCap electronic data capture tools.¹⁰

2.4. IDSA Classification

We determined two treatment categories of non-purulent and purulent SSTIs and then classified the disease as mild, moderate, or severe using the IDSA guidelines comparing observed antibiotic treatment regimens with recommended national guidelines (Table 1).⁵ Each patient received a score of 1 for mild, 2 for moderate, and 3 for severe. Independently, we ranked the observed antibiotic treatment regimen also as mild, moderate, or severe based off of IDSA recommendations. We compared the two scores with each other to determine if the observed antibiotic regimen matched the anticipated treatment class. We performed this in a blinded manner by two independent emergency department clinicians. Where there was disagreement, a third adjudicator served as a tie-breaker in the final determination. We categorized patients into expected treatment when the scores equaled each other, under-treated if the observed score was lower than the anticipated score, and over-treated when the observed score was higher than the anticipated score.

2.5. Outcomes

The primary study outcome was both under and over-treatment group classification after EDOU therapy for a SSTI. Secondary outcomes were failure of EDOU treatment defined as the patient being admitted to an inpatient ward from the EDOU, hospitalization up to 1 week after EDOU discharge for the same infection, completion of antibiotics as planned, and development of antibiotic-associated diarrhea defined as three or more loose stools per day for two or more consecutive days up to 30 days after EDOU discharge.^{11,12} Patients that were admitted to the hospital from the EDOU after failing therapy were analyzed for socio-demographic characteristics, presenting illness, and antibiotic treatment regimens. We defined failure of EDOU therapy as a continuation of SSTI symptoms in which additional antibiotic treatment was necessary to resolve the infection within two weeks of initial visit. This was identified as repeat emergency department visits, primary care or specialist visits, or hospitalizations. We counted only visits that resulted in a change in antibiotic therapy. For example, well visits or visits for rechecking abscess wounds were not considered as a

treatment failure. We also asked patients if they completed their antibiotic prescription, were hospitalized for the same infection, and if they had any diarrheal symptoms after discharge from the EDOU.

2.6. Data Analysis

We used chi-square tests to compare study patient characteristics among the three classification groups in categories of single variables and ANOVA for continuous variables. To confirm these results we performed proportional logistic regression with ordered factor response as response variable.¹³ We considered as our ordered response variable the study outcome (*undertreated* > *expected* > *overtreated*), such that, depending on how we ordered the variables, this approach allows determining the risk of being undertreated with respect to being expected or over-treated (when combined) per unitary change in each covariate when all the others are kept constant. To do this we used the *polr* command from the R package.¹⁴ As logistic-regression with *polr* returns odd ratios, we used the function *orsk* to convert odd ratios into relative risk estimates.¹⁵

Based off of our previous work⁶ where we observed a 10% gender difference in the under-treated group and using a desired power of 0.8 with an alpha of 0.05 we arrived at a sample size of 188 patients. Given the EDOU volume from the preceding year we estimated that a twelve-month enrollment period would be sufficient to obtain this sample size.

3. Results

3.1 Characteristics of study subjects

During the one-year study period, 284 patients treated in the EDOU for a SSTI were discharged to their homes; 58 (17.0%) patients that were admitted to the hospital after failing EDOU therapy. Due to a lack of contact information, 53 patients were ineligible for enrollment. Among the remaining 231 patients, 24 (10.4%) declined to participate in the study, 7 (3.0%) could not communicate in English, 6 (2.6%) fell out of the 4 week window for contact, and 1 (0.4%) was unable to recall events surrounding their EDOU stay. The final study consisted of 193 patients.

Patients directly admitted to the hospital from the EDOU after failing antibiotic therapy had a mean age of 49.0 +/- 17.8 years old and 57% were women. From this cohort 29.6% of patients were treated in compliance with IDSA guidelines while 66.7% were over-treated and 3.7% were under-treated. This admitted cohort did not differ from the patients discharged home by either age, gender, ethnicity, CCI score, or infection type or location. The prevalence of intravenous drug abuse was greater in patients admitted to the hospital (17.2%) than those discharged home (3.1%). This resulted in patients with an intravenous drug abuse history being 3 times more likely to be admitted to the hospital from the EDOU than discharged home (RR 3.07; 95% CI 1.95 to 4.85). Additionally, there were a greater percentage of abscesses in the admitted group than in the group discharged home (22.4% versus 15.0%, respectively). Of the patients admitted, 33.3% underwent surgical drainage of infectious material after EDOU antibiotic treatment failure.

The final study population was primarily white non-Hispanic with a mean age of 47 $\pm$ 16.7 years and a similar distribution of men and women. The majority of patients had no medical comorbidities (CCI of 0) with 21.8% of patients taking antibiotics prior to the EDOU admission (i.e. failing outpatient therapy). The majority of patients were treated for cellulitis (85.0%). The most common EDOU antibiotics prescribed were vancomycin followed by 1st generation cephalosporins, clindamycin, and penicillin inhibitor combination antibiotics. Approximately two-thirds of patients were treated with a single antibiotic class within the EDOU.

3.2. Comparison to National Guidelines

To investigate how closely the observed EDOU patient treatment regimens correlated with published national guidelines, we compared their observed treatments with the IDSA 2014 published guidelines classifications. Accordingly, 43.3% of patients were treated in compliance with IDSA guidelines, 41.8% were over-treated (i.e. given antibiotic treatments consistent with a higher IDSA class than their own observed treatment), and 15.0% were under-treated.

3.3. Factors Influencing Prescribing

We observed differences in various patient characteristics among the over-treated, under-treated, or expected groups (Table 2). Patients in the over-treated group were older with the majority of them being men. Older patients (≥ 50 years old) were 48% more likely to be over-treated than their younger counterparts (RR 1.44; 95% CI 1.03 to 2.02, RR regression 1.39; 95% CI 1.00 to 1.90, Figure 1-A). Additionally patients with abscesses were more likely to be over-treated (RR regression 3.33; 95% CI 2.20 to 5.96, Figure 1-B.). Conversely, patients in the under-treated group were younger with more than 2 out of 3 patients being female. Thus women were 58% more likely to be under-treated in comparison to men (RR 1.58; 95% CI 1.21 to 2.06, RR regression 1.47; 95% CI 1.07 to 2.05, Figure 1-C). Moreover, women comprised 80% of patients in the group that was under-treated by two class categories (i.e. they should have been treated in the severe category and instead received antibiotic treatment consistent with the mild category). Women also received a lower number of antibiotic classes with 1.6 classes prescribed (95% CI 1.5 to 1.7), as compared to 1.9 classes prescribed (95% CI 1.7 to 2.1) for men. Additionally, women received shorter courses of antibiotic therapy with an average of 9.6 days of treatment (95% CI 9.0 to 10.3) compared to 10.6 days of treatment for men (95% CI 9.7 to 11.4). Also, patients with previous history of antibiotics are more likely to be undertreated (RR regression 3.64; 95% CI 2.36 to 5.66, Figure 1-D). Among the infection types, abscesses were over-treated the majority of the time (Table 3). Table 4 lists the antibiotics used in each group. Vancomycin followed by Clindamycin and 1st generation cephalosporins were the classes of antibiotics utilized the most with the majority of patients receiving more than one class of antibiotic during the course of their treatment.

3.4. Patient Outcomes

Upon follow-up, the majority of patients (87.1%) completed the antibiotics prescribed from the EDOU. Major reasons for stopping the home antibiotic prescription were gastrointestinal upset followed by resolving infection and stoppage based on another clinician's advice.

Diarrhea was reported in 26.4% of all patients. Patients reported a failure of antibiotic therapy after EDOU discharge only 6.7% of the time with 38.5% of these patients subsequently requiring hospital admission to the cure the infection. We observed no differences in these secondary outcomes among patients in the over-treated, under-treated or expected groups.

4. Study Strengths and Limitations

This study is the first, to our knowledge, to combine SSTI treatment outcomes reported from EDOU antibiotic therapy while assessing physician compliance with IDSA guidelines. It is, however, limited by reporting outcomes from a single site. We did not investigate other factors that may influence physician prescribing practice, such as proximal streaking with cellulitis, however these factors are not included in the guidelines decision making algorithms. We did however have completeness of data concerning systemic symptoms such as fever and the other factors necessary to make a decision using the guidelines obtained from both the patient and through the medical record. Finally the failure rate of EDOU treatment was lower than expected and did not permit analyzing associations of failure rates to treatment categories. There is a lack in patient-centered outcomes of treatment failures between IDSA-compliant and noncompliant treatment groups which needs to be better explored in future studies to link IDSA guidelines compliance to outcomes.

5. Discussion

EDOU treatment of bacterial infections poorly follow IDSA guidelines and conformed with these guidelines less than half the time. Furthermore, we observed striking disparities in treatment regimen based on gender: women were 58% more likely to be under-treated while adults older than 50 years of age were 48% more likely to be over-treated. Additionally, women received antibiotic regimens that utilized a lower total number of antibiotic classes used and they were treated for a shorter period of time despite having the same infection types and severity as men.

The misuse and overuse of antibiotics continues to be a widespread public health and quality concern in the United States. Bacterial skin infections are one infection type with clear treatment guidelines⁵ that has risen to become one of the most common reasons for seeking emergent care with a tripling of ED visits between 1993 and 2005.² Antibiotic treatment of community-associated methicillin-resistant *Staphylococcus aureus* continues to rise despite national guidelines advising against their use.¹⁶ Given the increasing rates of antibiotic resistance in common bacterial community-acquired infections,¹⁷ the overuse of antibiotics and the increasing incidence and severity of *Clostridium difficile* infections (CDI)¹⁸ are important public health issues. We found that intravenous use of vancomycin and clindamycin in the EDOU were the most common reasons for patients being over-treated when an oral or narrow spectrum antibiotic would have been a more appropriate choice. The need not only for standardized evidence-based appropriate antibiotic treatment protocols, but evaluation of how well physicians adhere to these protocols, is critical.

There is growing recognition of the public health importance of gender disparities in the treatment of common medical conditions including acute myocardial infarction,¹⁹ stroke,²⁰ and sepsis.^{21,22} These disparities not only exist for women but for minorities and the elderly as well.^{23,24} Differences between men and women in terms of antibiotic prescribing practices in patients with SSTIs has not been previously explored. Despite the fact that SSTIs are common in the elderly, the medically accepted treatment regimens for this group of patients should not differ from their younger counterparts.^{25,26} Per IDSA guidelines, these treatments should also remain consistent across age and gender. Older age is not a risk factor for EDOU treatment failure for SSTI²⁷; however, advanced age and antibiotic exposure are the strongest known risk factors for *Clostridium difficile* infection.^{28,29} Therefore, more aggressive antibiotic treatment of older patients may impart more harm without providing any additional benefit. The older adults in our study received more aggressive antibiotic therapy with intravenous antibiotics where an oral antibiotic was indicated. Intravenous antibiotic use is associated with higher rates of antibiotic-associated diarrhea.⁶ We identified one case of *Clostridium difficile* infection following EDOU treatment in a 54 year old woman that was, according to national guidelines, over-treated for leg cellulitis.

This study contributes to the growing body of literature that demonstrates gender disparities in medicine.^{22,30} Our study showed that women were less aggressively treated for a SSTI than men. Women were under-treated not only by the IDSA guidelines antibiotic choice but in the duration of therapy as well. This poor adherence to SSTI guidelines with physicians prescribing patterns being influenced by factors not tied to clinical outcomes speaks to the need for strict protocol-driven ED and EDOU treatment algorithms. This study was not powered to detect differences among the groups with respect to treatment failure after EDOU discharge, however it is not surprising that patient that did fail were older adults with higher medical comorbidity scores. Addition research will further define how undertreating patients contributes to worse outcomes.

We also identified patient characteristics that herald the likely failure EDOU therapy. For example, intravenous drug abusers were 3 times more likely to fail EDOU therapy and require subsequent hospital admission for further management. The other major factor associated with treatment failure was infection type; 1 in 3 abscesses managed in the EDOU required subsequent admission and surgical intervention. We therefore recommend that hospital admission be considered in any patient with a history of intravenous drug abuse; furthermore, abscesses may deserve incision and drainage in conjunction with antibiotic therapy. Importantly, we observed that older adults fared just as well as younger during the course of therapy within the EDOU making this an important alternative treatment location compared to hospital admission.

5. Conclusions

Based on our findings, we recommend that EDOUs and EDs standardize antibiotic therapy to better align with national guidelines. Physician-driven treatment decisions led to under-treatment of women and over-treatment of older adults. The EDOU is a good alternative to hospitalization for the treatment of SSTIs, especially among older adults; however,

antibiotic treatments should follow IDSA guidelines which would hopefully lead to a reduction in bacterial resistance.

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Figure 1.

Practice Guidelines for Skin and Soft Tissue Infections Adapted from the 2014 Infectious Disease Society of America Update

Table 1

Type	Non-Purulent			Purulent		
	Severe	Moderate	Mild	Severe	Moderate	Mild
Signs and Symptoms	<ul style="list-style-type: none"> • Malignancy on chemotherapy • Neutropenia • Severe cell-mediated immunodeficiency • Immersion injuries • Animal bites • Penetrating trauma • Evidence of MRSA infection/colonization elsewhere • Injection drug use • SIRS 	<ul style="list-style-type: none"> • Systemic signs of infection 	<ul style="list-style-type: none"> • No SIRS • No AMS • Hemodynamic Stable 	<ul style="list-style-type: none"> • Failed initial antibiotic treatment • Impaired host defenses • SIRS with hypotension 	<ul style="list-style-type: none"> • SIRS 	<ul style="list-style-type: none"> • No SIRS
Treatments	Intravenous Rx <ul style="list-style-type: none"> • Combination Rx * 	Intravenous Rx <ul style="list-style-type: none"> • Single Class * 	Oral Rx <ul style="list-style-type: none"> • Penicillin VK or Cephalosporin or • Dicloxacillin or • Clindamycin 	I&D Empiric Rx <ul style="list-style-type: none"> • Vancomycin • Clindamycin • Other * 	I&D Empiric Rx <ul style="list-style-type: none"> • TMP/SMX or Doxycycline or • Dicloxacillin or • Cephalixin 	I&D alone

SIRS, systemic inflammatory response syndrome; Rx, antibiotic; AMS, altered mental status; I&D, incision and drainage; MRSA, methicillin-resistant staphylococcus aureus; TMP/SMX, Trimethoprim/Sulfamethoxazole;

* Please refer to Stevens DL, Et. Al. for complete list of antibiotic choices³

Table 2

Characteristics of study patients.*

Demographics	Under-treated n=41	Matched n=72	Over-treated n=80
Age (SD)	44.7 (18.1)	45.1 (14.2)	50.1 (17.8)
Female	29 (70.7)	36 (50.0)	32 (40.0)
White	34 (82.9)	59 (81.9)	62 (77.5)
Hispanic	5 (12.2)	6 (8.3)	11 (13.8)
African American	0 (0.0)	3 (4.2)	3 (3.8)
Asian	0 (0.0)	2 (2.8)	1 (1.3)
Medical History			
CCI 0 (SD)	70.7 (0.46)	61.1 (0.49)	58.8 (0.50)
CCI 1 (SD)	12.2 (0.33)	19.4 (0.40)	23.8 (0.43)
CCI 2 or more (SD)	17.1 (0.38)	19.4 (0.40)	17.5 (0.38)
Current Abx.	18 (43.9)	23 (31.9)	1 (1.3)

* Data are presented as percentage unless otherwise indicated.

Hx, history; Abx, antibiotics; CCI, Charlson comorbidity index;

Table 3

Infection Characteristics

Type	Under-treated n=41	Matched n=72	Over-treated n=80
Cellulitis	37 (90.2)	68 (94.4)	59 (73.8)
Abscess	4 (9.8)	4 (5.6)	21 (26.3)
Location			
Face	11 (26.8)	8 (11.1)	8 (10.0)
Hand	11 (26.8)	7 (9.7)	14 (17.5)
Foot	2 (4.9)	9 (12.5)	11 (13.8)
Trunk	4 (9.8)	7 (9.7)	6 (7.5)
Extremity	11 (26.8)	34 (47.2)	33 (41.3)
Buttocks	2 (4.9)	6 (8.3)	7 (8.8)

Data are presented as percentage unless otherwise indicated.

Table 4

Antibiotics *

	Under-treated n=41	Matched n=72	Over-treated n=80
1 st Cephalosporin	4 (9.8)	16 (22.2)	17 (21.3)
3 rd Cephalosporin	5 (12.2)	4 (5.6)	5 (6.3)
Vancomycin	0 (0.0)	30 (41.7)	46 (57.5)
Clindamycin	9 (22.0)	9 (12.5)	18 (22.5)
Macrolide	0 (0.0)	1 (1.4)	0 (0.0)
Penicillin	0 (0.0)	1 (1.4)	0 (0.0)
Penicillin/I	11 (26.8)	3 (4.2)	4 (5.0)
Quinolone	1 (2.4)	0 (0.0)	2 (2.5)
Sulfonamide	0 (0.0)	6 (8.3)	3 (3.8)
Doxycycline	1 (2.4)	1 (1.4)	1 (1.3)
Nitrofurantoin	0 (0.0)	0 (0.0)	0 (0.0)
Metronidazole	0 (0.0)	1 (1.4)	0 (0.0)
Number of Classes (SD)	1.4 (0.59)	2.1 (1.1)	2.1 (0.90)

* Data are presented as percentage unless otherwise indicated.

Penicillin/I, penicillin inhibitor combination; Totals for frequency prescribed columns sum to >100% as patients received multiple antibiotics.