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Antibiotic prescribing at the transition from hospitalization to discharge: a target for antibiotic stewardship

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Abstract

Of 300 patients prescribed oral antibiotics at the time of hospital discharge, urinary tract infection, community-acquired pneumonia, and skin infections accounted for 181 (60%) of the treatment indications. Half of the prescriptions were antibiotics with broad gram-negative activity. Discharge prescriptions were inappropriate in 79 (53%) of 150 cases reviewed.

Keywords

oral antibiotics; antimicrobial stewardship; hospital discharge; transition of care

Introduction

The increasing public health burden of multi-drug resistant organisms and antibiotic-associated adverse events such as *Clostridium difficile* colitis has underscored the importance of curbing the misuse of antibiotics [1]. Although stewardship efforts have largely focused on antibiotic use in the hospital [2], for patients hospitalized with common infections, the majority of the antibiotic course is completed after hospital discharge [3,4]. This suggests that optimizing prescribing at the time of discharge may be important to overall antibiotic stewardship efforts. Despite this, data on prescribing practices at the transition from inpatient care to outpatient care are limited. The objectives of this study were to perform a comprehensive evaluation of prescribing practices at the transition from inpatient to outpatient care, to evaluate the appropriateness of antibiotic prescriptions at this transition, and to identify factors associated with inappropriate prescriptions. We

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hypothesized that a substantial proportion of antibiotics prescribed at the time of hospital discharge are inappropriate, thus representing an important opportunity for antimicrobial stewardship.

Methods

Study setting and population

Denver Health is a vertically integrated, urban, public safety net healthcare system with a 475-bed teaching hospital, emergency department, and federally qualified community health centers. Most patients are admitted to an inpatient teaching service with a minority managed by a non-teaching hospitalist service.

Study design

This was a retrospective cohort study of adult inpatients prescribed an oral antibiotic at the time of hospital discharge between 1 July 2012 and 30 June 2013. Using our data warehouse, we identified patients 18 years or older who filled an oral antibiotic prescription at a Denver Health pharmacy within 7 days of hospital discharge. By manual chart review, cases were excluded that involved antibiotic prescriptions unrelated to the hospital stay, intravenous antibiotics at discharge, long-term prophylactic or suppressive antibiotics, absence of documentation of the indication for antibiotics, transfer to or from an outside institution, leaving against medical advice, failure to fill prescribed antibiotics, infection with non-bacterial pathogens, and re-hospitalization for an ongoing infection. For patients with multiple hospitalizations, only the initial hospitalization resulting in an oral antibiotic prescription was included. Using a combination of electronic data extraction and manual chart review, we collected data on demographic and clinical characteristics, microbiology, inpatient antibiotic therapy, discharge antibiotics (indication, agent, dose, and treatment duration), and clinical encounters within the Denver Health system during the 30 days following hospital discharge. Treatment failure within the 30-day follow-up period was defined as change in antibiotic regimen or extension of planned treatment duration due to inadequate clinical response.

Appropriateness review

A random sample of the study cohort was selected for evaluation of the appropriateness of discharge antibiotic prescription(s) by two Infectious Disease (ID) subspecialists. Each independently reviewed the extracted data and hospital discharge summary and compared the prescription(s) with institutional or national prescribing guidelines, when applicable. Using a standardized reporting form, the reviewers assessed the appropriateness of the indication for antibiotics, antibiotic selection, dose, and duration of therapy. The duration of therapy was considered inappropriate only when more than two days longer or shorter than guideline recommendations [6]. When classifications of appropriateness by the ID physicians were discordant, the institutional Antimicrobial Stewardship Committee adjudicated the case.

Data Analysis

We selected a target sample size of 300 cases in order to obtain subgroups of 30 to 50 cases of the most common infections including pneumonia, skin and soft tissue infection, and urinary tract infection. Based on pilot data (unpublished), we estimated that 30–50% of discharge prescriptions would be classified as inappropriate. In order to develop a multivariate logistic regression model of factors associated with inappropriate prescriptions with 5 to 7 variables, we performed appropriateness reviews on a random sample of 150 cases. Variables with a univariate association p-value less than 0.2 were considered for inclusion in a multivariate logistic regression model. Multicollinearity and potential confounding were investigated. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

Results

The initial electronic search identified 1825 adults who filled an antibiotic prescription within 7 days of hospital discharge. 376 randomly selected cases were reviewed in order to achieve the target sample size of 300 included cases (76 were excluded). Of the cases meeting study entry criteria, 295 (98%) of the antibiotic prescriptions were filled within 24 hours after hospital discharge; all antibiotics were filled within 48 hours after discharge. Demographic and clinical characteristics were similar between the total cohort and the random sample of 150 cases reviewed for appropriateness (Table 1). Most antibiotics prescribed were for patients discharged from the general medical service (222 cases, 74%).

263 patients (88%) had a single indication for the antibiotic(s) prescribed at discharge. Urinary tract infections (UTI; 72, 24%), skin and soft tissue infections (SSTI; 62, 21%) and community acquired pneumonia (CAP; 52, 17%) accounted for 181 (60%) of all cases (Table 1).

221 patients (74%) had at least one microbiologic specimen collected. A specific pathogen was identified in 94 (31%) cases, leaving 213 (69%) cases without microbiologic data to guide the discharge prescriptions. When a pathogen was identified, the most common organisms were *Staphylococcus aureus* (26, 14%), *Escherichia coli* (31, 10%), and streptococcal species (24, 8%).

The median total antibiotic duration was 10 days (interquartile range [IQR] 7–13), with a median inpatient duration of 3 days (IQR 3–5) and outpatient duration of 6 days (IQR 4–10). The most commonly prescribed antibiotics were levofloxacin (115, 38%), amoxicillin/clavulanate (37, 12%), and azithromycin (37, 12%) (Table 1). In total, antibiotics with broad gram-negative activity – a fluoroquinolone or amoxicillin/clavulanate – were prescribed in 154 (51%) of cases.

A follow-up encounter within 30 days of hospital discharge was documented in 209 (70%) cases. In total, treatment failure occurred in 32 cases (11%), re-admission for the same condition occurred in 17 cases (6%), and an antibiotic-related adverse event occurred in 16 cases (5%). Of the antibiotic-related adverse events, gastrointestinal side effects were the most common (11 cases, 4%); *Clostridium difficile* colitis occurred in 4 cases (1%).

Of the 150 cases for which the discharge prescription(s) were reviewed for appropriateness, there was independent agreement between the two ID specialists in 115 (77%; kappa coefficient = 0.53, $p = 0.028$). After adjudication of the 35 cases with discordant classifications, a total of 79 (53%) cases were classified as having inappropriate discharge prescriptions. UTI, CAP, and SSTI accounted for 53 (67%) of the conditions associated with inappropriate prescriptions. The most common reasons prescriptions were classified as inappropriate were excessive treatment duration (49 cases, 33%), suboptimal antibiotic selection (27 cases, 17%), incorrect dose (14 cases, 9%), and conditions not warranting antibiotic therapy (7 cases, 5%).

In the logistic regression model, gender was associated with inappropriate prescribing while use of azithromycin at discharge and ID consultation were significantly associated with appropriate prescribing by univariate analysis (Table 2). In the final multivariate logistic regression model, CAP was independently associated with inappropriate prescriptions while azithromycin and ID consultation were independently associated with appropriate prescriptions.

Discussion

To our knowledge, this is the first comprehensive description of oral antibiotics prescribed at hospital discharge for all treatment indications. It is notable that three common infections – UTI, CAP, and SSTI – accounted for 60% of antibiotic prescriptions at the time of discharge. This mirrors a recent review of inpatient prescribing for antimicrobials in which genitourinary infections, lower respiratory tract infections, and SSTI accounted for 61% of all infection-related indications for therapy [6]. Of particular interest was that UTI, CAP, and SSTI accounted for two-thirds of the inappropriate prescriptions despite the presence of well-established institutional treatment guidelines for oral step-down therapy and duration of therapy for these conditions. Our findings suggest that these three conditions may be particularly high-yield for future interventions. Of note, we previously implemented institutional treatment algorithms for the management for inpatient SSTIs [3] and CAP (unpublished data); these interventions reduced the use of broad-spectrum antibiotics and shortened treatment durations. We were therefore surprised to find that CAP remained an independent predictor of inappropriate discharge prescriptions. This suggests that although institutional treatment guidelines can impact prescribing practices at the time of hospital discharge, novel interventions to improve prescribing at this transition in care are clearly needed.

It is notable that half of patients were discharged with antibiotics with broad gram-negative activity, most commonly a fluoroquinolone which comprised nearly 40% of prescriptions. This was also somewhat unexpected since neither fluoroquinolones nor amoxicillin/clavulanate are promoted as oral step-down therapy for common infections in our local treatment guidelines. In fact, use of levofloxacin for UTI and CAP has specifically been discouraged due to the problem of progressive fluoroquinolone resistance among *E. coli* in our institution [7] and its association with *Clostridium difficile* infection [8]. Although use of levofloxacin was not an independent predictor of inappropriate prescriptions in our logistic regression model, the volume of prescribing of this antibiotic indicates that it may be

an important target for stewardship efforts. Since microbiological data are available to guide discharge antibiotic selection in only a minority of cases, specific recommendations for fluoroquinolone-sparing regimens in the absence of microbiological data are likely needed to reduce use of this broad-spectrum antibiotic.

Similar to prior studies of SSTIs [3] and CAP [4], approximately two thirds of total treatment durations were completed after hospital discharge. This highlights that antimicrobial stewardship interventions focusing solely on inpatient antibiotic use may only impact a minority of the total antibiotic exposure for common infections and that interventions to shorten the total duration of therapy are necessary.

Our study has several important limitations. First, it involved a single academic safety-net hospital. Because local antimicrobial susceptibilities and treatment guidelines may impact prescribing, our findings may not be generalizable. Second, the retrospective study design and reliance on the discharge summary to document the indication for the antibiotics prescribed may have led to the misclassification of the appropriateness of therapy in some cases. Third, the retrospective design did not allow us to evaluate the underlying causes of inappropriate prescriptions. Fourth, only patients filling their prescriptions within the Denver Health system were identified. It is unknown whether prescribing patterns were different for patients who filled their prescriptions at a pharmacy outside our system.

In summary, interventions to improve antibiotic prescribing at the time of hospital discharge for common infections such as UTI, CAP, and SSTI are needed. We found that half of discharge prescriptions were for agents with broad gram-negative activity, and over half of all discharge prescriptions were inappropriate. Our findings, along with the paucity of previous studies addressing this topic, suggest that oral antibiotic prescribing at the transition from inpatient to outpatient care is an important and under-recognized opportunity to improve antimicrobial use.

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Table 1

Patient characteristics, treatment indications, and antibiotics prescribed at discharge

	Total cohort n=300	Cases reviewed for appropriateness n=150 ^a
Demographic and Clinical Characteristics ^a		
Age, mean (standard deviation)	52.8 (15.8)	53.6 (17.2)
Male	171 (57)	85 (57)
Diabetes mellitus	87 (29)	48 (32)
Antibiotic use within 6 months	67 (22)	40 (27)
COPD	48 (16)	27 (18)
Hospitalization within 90 days	45 (15)	21 (14)
HIV infection	17 (6)	6 (4)
Pregnancy	13 (4)	5 (3)
Cirrhosis	13 (4)	5 (3)
History of multi-drug resistant organism ^b	12 (4)	7 (5)
End-stage renal disease	9 (3)	4 (3)
Hospital length of stay, median days (IQR)	4 (3–5)	4 (3–6)
ICU admission	53 (18)	27 (18)
Infectious Diseases consultation	42 (14)	16 (11)
Failed outpatient antibiotics ^c	17 (6)	9 (6)
Indications for antibiotic therapy ^a		
Urinary tract infection	72 (24)	35 (23)
Community-acquired pneumonia	52 (17)	26 (17)
Skin and soft tissue infection	62 (21)	33 (22)
Gastrointestinal infection	46 (15)	22 (15)
Osteoarticular infection	22 (7)	12 (8)
COPD exacerbation	23 (8)	11 (7)
Head and neck infection	15 (5)	7 (5)
Bacteremia	15 (5)	9 (6)
Other	40 (13)	19 (13)
Two or more indications for therapy	37 (12)	14 (9)
Antibiotic prescribed at discharge ^a		
Fluoroquinolone ^d	117 (39)	55 (37)
Amoxicillin/clavulanate	37 (12)	19 (13)
Azithromycin	37 (12)	17 (11)
Metronidazole	29 (10)	11 (7)
Clindamycin	26 (9)	16 (11)
Trimethoprim/sulfamethoxazole	20 (7)	11 (7)

	Total cohort n=300	Cases reviewed for appropriateness n=150 ^a
Doxycycline	19 (6)	12 (8)
Penicillin or amoxicillin	15 (5)	7 (5)
Clarithromycin	11 (4)	5 (3)
Nitrofurantoin	8 (3)	6 (4)
Other	14 (5)	4 (3)
Received ≥ 2 antibiotics	50 (17)	21 (14)

Data presented as n (%) unless otherwise specified.

^aNo significant differences between the total cohort and the subset of cases reviewed for appropriateness ($p>0.05$ for all subgroups)

^bDefined as prior infection with methicillin-resistant *Staphylococcus aureus*, vancomycin resistant *Enterococci*, or extended spectrum beta-lactamase producing *Enterobacteriaceae*.

^cDefined as lack of clinical response to outpatient therapy requiring hospital admission.

^dlevofloxacin 115 (38%) and ciprofloxacin 2 (1%) of total cohort

IQR, interquartile range; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus

Table 2

Logistic regression model of factors associated with inappropriate antibiotic prescriptions

	Appropriate discharge prescription n=71 (%)	Inappropriate discharge prescription n=79 (%)	Univariate analysis odds ratio (95% CI)	Multivariate analysis odds ratio (95% CI)	Multivariate P-value
Female	25 (35)	40 (51)	1.9 (1.0–3.6)	2.0 (0.9–4.4)	0.07
ICU admission	9 (13)	18 (23)	2.0 (0.9–4.9)	2.4 (0.8–6.8)	0.10
Infectious Diseases consultation	13 (18)	3 (4)	0.2 (0.1–0.7)	0.2 (0.06–0.8)	0.03
Community-acquired pneumonia	9 (13)	17 (22)	2.2 (0.9–5.4)	3.7 (1.1–12.9)	0.04
Azithromycin at discharge	16 (23)	1 (1)	0.04 (0.01–0.3)	0.02 (0.002–0.2)	<0.001
Levofloxacin at discharge	21 (30)	33 (42)	1.7 (0.9–3.4)	0.8 (0.4–1.9)	0.67
Bacteremia ^a	4 (6)	5 (6)	1.1 (0.3–4.4)		
Treatment Failure ^a	13 (18)	16 (20)	1.1 (0.5–2.6)		

CI, confidence interval

^aExcluded from multivariate model due to non-significance in best-fit model