## BRIEF REPORT







# Misuse of Discharge Antimicrobial Prescription in the Emergency Department: An Observational Study at a Tertiary Care Center

Yasuaki Tagashira, <sup>1,2</sup> Naofumi Yamane, <sup>1</sup> Satoshi Miyahara, <sup>1</sup> Azusa Orihara, <sup>1</sup> Yuki Uehara, <sup>2</sup> Keiichi Hiramatsu, <sup>2</sup> and Hitoshi Honda<sup>1,0</sup>

<sup>1</sup>Division of Infectious Diseases, Tokyo Metropolitan Tama Medical Center, Japan; <sup>2</sup>Department of Infection Control Science, Juntendo University Graduate School of Medicine, Tokyo, Japan

We conducted a restrospective cohort study of patients discharged from the emergency department at a tertiary care center with an antimicrobial prescription. More than half of the prescribed antimicrobials were misused and frequently inappropriate for various infectious diseases. In this study, we analyzed the physician-related and environment-related factors predicting misuse.

**Keywords.** antimicrobial misuse; discharge antimicrobial prescription; physician- and environment-related factors.

Antimicrobials are commonly prescribed in the emergency department (ED). In the United States, approximately 16% of patients discharged from the ED received an antimicrobial prescription [1]. Redundant antimicrobial use and the overuse of broad-spectrum antimicrobials are long-standing issues in the ED [2] and may contribute to the rise to resistant pathogens [3, 4].

Although studies have been done to estimate inappropriate antimicrobial use or test interventions to improve current antimicrobial prescription practices in the outpatient clinic [5, 6], few studies have described the current status of antimicrobial prescription in the ED using comprehensive clinical information. Moreover, the number of cases of discharge antimicrobial prescription misuse in the ED has not been clearly documented. The purpose of this study was to describe patterns in discharge

Received 16 November 2018; editorial decision 8 January 2019; accepted 9 January 2019; Published online January 11, 2019.

Correspondence: H. Honda, MD, PhD, Division of Infectious Diseases, Tokyo Metropolitan Tama Medical Center, 2-8-29, Musashidai, Fuchu, Tokyo, 183-8524, Japan (hondah@hotmail.com)

#### Open Forum Infectious Diseases®

© The Author(s) 2019. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com D0I: 10.1093/ofid/ofz016

antimicrobial prescriptions and assess the factors associated with their misuse in the ED.

### **MATERIAL AND METHODS**

This retrospective cohort study was conducted at Tokyo Metropolitan Tama Medical Center, a tertiary care center in Tokyo, from January 2016 through December 2016. The ED accepts adolescents and adults (age >15) but not children. Patients visiting the ED are initially seen by residents, with attending physicians assisting and supervising. Physicians, including the residents working in the ED, are able to refer patients to subspecialties for consultation if needed. Physicians in subspecialties are responsible for evaluating the patients and have the authority to discharge them. We enrolled all patients who were discharged to home or their living facilities with a discharge prescription of oral antimicrobials from the ED. If patients visited the ED multiple times within 30 days of their initial visit, we included only the first visit for analysis. Patients who had already received a diagnosis of an infectious disease before their ED visit and a discharge prescription of antimicrobial agents and those who were hospitalized later on the same day as their visit to the ED were also excluded. We extracted the clinical information, antimicrobial prescription, and the physician's diagnosis. Discharge antimicrobial prescription in the absence of a certain diagnosis by the treating physician was considered to be an instance of just-in-case antimicrobial use. We also tracked the prescribers' information, including primary service, sex, and postgraduate year (PGY) level. We described the physicians' status PGY level, which was categorized as PGY ≤3 years, PGY 4–7 years, or PGY ≥8 years, based on the duration of residency training common to the entire Japanese healthcare system. We classified the misuse of discharge antimicrobial prescription as unnecessary, inappropriate, or suboptimal based on previously proposed criteria [6-8], and all discharge antimicrobial prescriptions not meeting the classification of misuse were considered appropriate. A study flow assessing the necessity and appropriateness of discharge antimicrobial prescription in the ED is shown in Appendix 1. Two infectious disease physicians reviewed each case and assessed the indications for antimicrobial therapy and its appropriateness using a list of recommendations for common infectious diseases provided by international infectious disease treatment guidelines (Appendix 2 and 3) and a textbook. Disagreement between the 2 assessors was resolved through discussion. The primary outcome was the proportion of overall misuse of discharge antimicrobial prescription and misuse by each type of infectious disease in the ED. Predictors of the misuse of discharge antimicrobial prescriptions in the ED were also investigated. We performed multivariate logistic

regression to predict the misuse (ie, any of antimicrobial use categorized as unnecessary, inappropriate, or suboptimal) of discharge antimicrobial prescriptions in the ED. Variables were retained in the final model if P < .05.

#### **RESULTS**

Of the 36 308 cumulative patients who visited the ED during the study period, 1674 (4.6% of visit) received a discharge oral antimicrobial prescription. Among these, 119 (0.3%) were excluded due to a pre-existing diagnosis of bacterial infection at the study institution (n = 101; 84.9%), history of antimicrobial prescription within 30 days (n = 4; 3.4%), or hospitalization on the same day as their ED visit (n = 14; 11.8%), leaving 1555 (4.3%) patients for analysis (Appendix 4). The baseline characteristics of the study patients are summarized in Appendix 5. Common diagnoses made by treating physicians that led to a higher frequency of antimicrobial prescriptions were as follows: pneumonia (17.8%, 7.6 per 1000 visits), skin and soft tissue infection (15.9%, 6.4 per 1000 visits), and urinary tract infection

(13.7%, 5.9 per 1000 visits) (Appendix 6). Overall, 813 (52.3%) antimicrobial prescriptions were considered to be cases of misuse. Unnecessary, inappropriate, and suboptimal discharge antimicrobial prescriptions accounted for 428 (27.5%), 337 (21.7%), and 48 (3.1%) cases, respectively (Appendix 7).

Table 1 shows the predictors of discharge antimicrobial prescription misuse in the ED. Factors related to the prescriber, including a higher PGY level (≥8 years) (adjusted odds ratio [aOR] = 1.77; 95% confidence interval [CI], 1.15–2.72), surgical subspecialty (aOR = 2.86; 95% CI, 1.94–4.22), and late-night visit (12:00 AM–7:59 AM) (aOR = 1.55; 95% CI, 1.04–2.30), were significantly associated with the misuse of discharge antimicrobial prescriptions.

#### **DISCUSSION**

This study comprehensively evaluated the appropriateness of discharge antimicrobial prescriptions in the ED at a Japanese tertiary care center by retrospectively reviewing the prescription patterns. The use of antimicrobials in the ED has not been

Table 1. Predictors of the Misuse of Discharge Antimicrobial Prescriptions in the Emergency Department (N = 1555; Misuse of Discharge Antimicrobial Prescription [n = 813] and Appropriate Discharge Antimicrobial Prescription [n = 742])

Variables	Adjusted Odds Ratio—Reference	<i>P</i> Value
Physician-Related Factors		
Prescriber's PGY level ≤3 years		
Prescriber's PGY level 4–7 years	1.17 (0.86–1.61)	.32
Prescriber's PGY level ≥8 years	1.77 (1.15–2.72)	.01
Physicians in the emergency department		
Physicians in medical subspecialties	1.66 (0.99–2.77)	.05
Physicians in surgical subspecialties	2.86 (1.94–4.22)	<.001
Environment-Related Factors		
Daytime visit (8:00 AM-4:59 PM)		
Nighttime visit (5:00 PM-11:59 PM)	1.13 (0.83–1.53)	.43
Late-night visit (12:00 AM-7:59 AM)	1.55 (1.04–2.30)	.03
Physician's Diagnosis		
Pneumonia		
Animal bite	1.23 (0.52–2.93)	.64
Intra-abdominal infections	4.58 (2.41–8.69)	<.001
Urinary tract infection	6.12 (3.45–10.86)	<.001
Pharyngitis	6.59 (3.41–12.77)	<.001
Skin and soft tissue infection	10.64 (6.13–18.48)	<.001
Gastroenteritis	48.56 (16.75–140.80)	<.001
Composite upper respiratory tract infections <sup>a</sup>	50.03 (24.17–103.54)	<.001
Prophylaxis for traumatic injury	59.51 (28.21–125.53)	<.001
Others <sup>b</sup>	12.32 (6.13–24.78)	<.001

 $Abbreviations: ED, \ emergency \ department; \ PGY, \ postgraduate \ year; \ SIRS, \ systemic \ inflammatory \ response \ syndrome.$ 

The outcome variable was the misuse of antimicrobial prescriptions in the emergency department.

Predictors of antimicrobial misuse in the outpatient setting identified in previous studies, including patients' age, gender, underlying diseases, the presence of an allergy to any antimicrobial, and prescribers' training status (as PGY level), were included in our multivariate logistic regression model.

The Hosmer Lemeshow test was used for goodness-of-fit for the logistic regression model with a P value of .10.

Variables considered but not retained in the final model were patient age, patient gender, allergy for antimicrobial agents, history of asthma, chronic lung disease, chronic liver diseases, active solid organ malignancies, hypertension, chemotherapeutic agent use in the last 28 days, symptoms meeting SIRS criteria, duration of symptom, days of visiting ED, spring-summer, and patient's request for antimicrobial agents.

<sup>&</sup>lt;sup>a</sup>Composite upper respiratory tract infections included acute tonsillitis, acute otitis media, otitis externa, sinusitis, bronchitis, asthma attack, and other upper respiratory tract infections.

<sup>&</sup>lt;sup>b</sup>Others include sexually transmitted disease, other genitourinary infections, odontogenic infection, miscellaneous bacterial infections, sialadenitis, febrile neutropenia, lymphangitis, bursitis, septic arthritis, and tonsillar abscess.

studied well in Asia; previous Asian studies only examined antimicrobial misuse for certain infectious diseases in the ED or reported a point prevalence survey of antimicrobial prescriptions in the ED [9, 10]. In contrast, this study included all patients who received a discharge antimicrobial prescription for any of a variety of infectious diseases in the ED throughout a 1-year period, enabling us to estimate the proportion of antimicrobial misuse in the ED and to explore the factors related to the misuse of discharge antimicrobial prescriptions.

Similar to other Asian studies of ED antimicrobial prescriptions [9, 10], the present study found that more than half of the discharge antimicrobial prescriptions in the ED were instances of misuse while one third were unnecessary. These findings strongly support the need for an effective antimicrobial stewardship program in the ED.

In the multivariate model for predictors of discharge antimicrobial prescription misuse, physicians with a higher PGY status (≥8 years) and those in a surgical subspecialty were more frequently responsible. As in other clinical settings [11, 12], the difficulty of updating clinical knowledge, weaker adherence to the current guidelines, and reliance on experience might have accounted for the higher risk of antimicrobial misuse among physicians with a higher PGY level. In general, most surgical training programs do not offer adequate training in infectious disease treatment and antimicrobial use. Moreover, awareness about antimicrobial agents among surgeons appeared to be lower [13]. However, it is worth noting that awareness about appropriate antimicrobial use among the surgical subspecialties in the era of antimicrobial stewardship is on the rise [14].

Late-night visit was significantly associated with the misuse of discharge antimicrobial prescription in the ED. We hypothesize that decision fatigue, hesitation in asking for a late-night subspecialty consultation, and the fear of possible complications due to not prescribing antimicrobials may have led to a higher prescription rate involving the misuse of discharge antimicrobial prescriptions during the midnight shift.

Besides the factors noted above, antimicrobial misuse more frequently occurred for certain infectious diseases. Not only inadequate knowledge of the treatment choices for certain infectious diseases and a misunderstanding of the antimicrobial indications, but also underlying behavioral drivers including time constraints and uncertain diagnoses might also lead to the misuse of discharge antimicrobial prescriptions.

This study has several limitations. Because it was a single-center, retrospective study of the Japanese healthcare system, the findings may not be generalizable to other institutions with different healthcare systems. Although the appropriateness of discharge antimicrobial prescriptions was evaluated using prespecified criteria generated by reliable references, these criteria have not been validated. The determination of appropriateness through a review of the medical records might be biased due to the limited information in the medical charts.

Moreover, interrater variation between the 2 infectious disease physicians may have affected the assessment of the appropriateness of discharge antimicrobial prescriptions. The duration of an antimicrobial prescription was unable to be tracked and evaluated because physicians in the ED encouraged patients to have follow-ups with the primary care providers, and usually prescribed antimicrobials until the next follow-up outpatient appointment. Because the purpose of the study was to assess the appropriateness of antimicrobial prescriptions based on the physicians' diagnosis, the accuracy of the diagnoses was not evaluated. Because the physicians' diagnoses may have been incorrect and thus have led to antimicrobial misuse, exploring the association between the diagnostic accuracy and antimicrobial use in the ED warrants further study. Patient-related factors, especially patients' request for discharge antimicrobial prescription, may have been underestimated due to the absence of this information in the electronic medical records. Finally, other factors potentially influencing antimicrobial prescription, such as physicians' previous training status and the patient volume for each treating physician in the ED, were unavailable for evaluation in this study.

#### **CONCLUSIONS**

Our study found that more than half of oral antimicrobial prescriptions upon discharge from the ED were misused. Misuse frequently occurred during late-night visits, and older physicians and physicians in a surgical subspecialty were most often responsible. Given the significant proportion of misused discharge antimicrobial prescriptions in the ED, the implementation of effective antimicrobial stewardship focusing on physician- and environment-related factors is urgently needed.

### **Supplementary Data**

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

#### **Acknowledgments**

We are indebted to James R. Valera for his assistance in editing the manuscript.

*Author contributions.* Y. T. was the principle researcher in this study. Y. T. and H. H. designed the study protocol. N. Y., S. M., A. O., and Y. T. collected the patient data. Y. T. performed the data analysis and drafted the first version of the manuscript. Y. U. and K. H. performed the critical review. H. H. and Y. T. revised the manuscript. All the authors contributed to the final version of manuscript.

*Financial support.* This work was funded by the Japan Society for the Promotion of Science (KAKENHI) (Grant no. JP18K17347).

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

#### References

 Niska R, Bhuiya F, Xu J. National hospital ambulatory medical care survey: 2007 emergency department summary. Natl Health Stat Report 2010; 1–31.

- Timbrook TT, Caffrey AR, Ovalle A, et al. Assessments of opportunities to improve antibiotic prescribing in an emergency department: a period prevalence survey. Infect Dis Ther 2017; 6:497–505.
- Vanderweil SG, Tsai CL, Pelletier AJ, et al. Inappropriate use of antibiotics for acute asthma in United States emergency departments. Acad Emerg Med 2008; 15:736–43.
- Mistry RD, Dayan PS, Kuppermann N. The battle against antimicrobial resistance: time for the emergency department to join the fight. JAMA Pediatr 2015; 169:421–2.
- Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. JAMA 2016; 315:562–70.
- Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. JAMA 2016; 315:1864–73.
- 7. Spivak ES, Cosgrove SE, Srinivasan A. Measuring appropriate antimicrobial use: attempts at opening the black box. Clin Infect Dis **2016**; 63:1639–44.

- Gyssens IC, van den Broek PJ, Kullberg BJ, et al. Optimizing antimicrobial therapy.
  A method for antimicrobial drug use evaluation. J Antimicrob Chemother 1992; 30:724-7.
- 9. Bishara J, Hershkovitz D, Paul M, et al. Appropriateness of antibiotic therapy on weekends versus weekdays. J Antimicrob Chemother **2007**; 60:625–8.
- Ojeniran M, Shouval R, Miskin IN, et al. Costs of appropriate and inappropriate use of antibiotics in the emergency department. Isr Med Assoc J 2010; 12:742–6.
- Schmidt ML, Spencer MD, Davidson LE. Patient, provider, and practice characteristics associated with inappropriate antimicrobial prescribing in ambulatory practices. Infect Control Hosp Epidemiol 2018; 39:307–15.
- Charani E, Castro-Sanchez E, Sevdalis N, et al. Understanding the determinants of antimicrobial prescribing within hospitals: the role of "prescribing etiquette". Clin Infect Dis 2013; 57:188–96.
- Lucet JC, Nicolas-Chanoine MH, Roy C, et al. Antibiotic use: knowledge and perceptions in two university hospitals. J Antimicrob Chemother 2011; 66:936–40.
- Leeds IL, Fabrizio A, Cosgrove SE, Wick EC. Treating wisely: the surgeon's role in antibiotic stewardship. Ann Surg 2017; 265:871–3.