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Appropriateness of Antibiotic Prescribing for Veterans with Community-Acquired Pneumonia, Sinusitis, or Acute Exacerbations of Chronic Bronchitis

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Abstract

Background—Previous studies evaluating antibiotic appropriateness in bacterial respiratory tract infections have focused only antibiotic choice and ignored other important aspects of prescribing such as dosing, drug-drug interactions, and duration of therapy.

Objective—The objectives of this study were to determine the prevalence and factors associated with inappropriate antibiotic prescribing in outpatients with community-acquired pneumonia (CAP), sinusitis, or acute exacerbations of chronic bronchitis (AECB).

Methods—This is a retrospective case series of the appropriateness of antibiotic prescribing in 153 outpatients with CAP, sinusitis, or AECB who were evaluated in a Veterans Affairs Emergency Department over a one year period. Data on patient characteristics, diagnosis, comorbidities, concurrent medications, and antibiotic prescribed were collected. Using the reliable and valid Medication Appropriateness Index (MAI), a trained clinical pharmacist assessed antimicrobial appropriateness. The MAI rates the appropriateness of a medication along ten criteria: indication, effectiveness, dosage, directions, practicality, drug-drug interactions, drug-disease interactions, unnecessary duplication, duration, and expensiveness.

Results—Overall 65% of patients had one or more antibiotic prescribing problems as assessed by the MAI. The most frequently rated problems were with expensiveness (39%), impracticality (21%), and incorrect dosage (10%). Penicillins, quinolones, and macrolides were the most inappropriately prescribed antibiotic classes. A history of alcohol abuse was associated with a lower likelihood of inappropriate prescribing (Adjusted Odds Ratio [Adj. OR] 0.32; 95% Confidence Interval [CI] 0.10-0.98), while patients who were married were more likely to receive inappropriately prescribed antibiotics (Adj. OR 2.64; 95%CI 1.25-5.59).

Conclusions—Inappropriate antibiotic prescribing is common in patients with bacterial respiratory tract infections and often involves problems with impractical directions, incorrect dosage, and choosing an expensive antibiotic. Future interventions to improve antibiotic prescribing need to consider aspects beyond selection.

Keywords

antibiotic; Medication Appropriateness Index; respiratory tract infections

INTRODUCTION

Acute respiratory infections (ARIs) are common among adults. In 1998, there were approximately 76 million primary care visits for ARIs that resulted in 41 million antibiotic prescriptions.[1] Prescribing for ARIs where antibiotics are rarely indicated (e.g., acute bronchitis, non-specific upper respiratory infections) has declined recently, largely due to national educational efforts focused on antibiotic overuse because of antimicrobial resistance concerns.[2] Although antibiotics are indicated in ARIs with a likely bacterial etiology (e.g., pneumonia, acute sinusitis and acute exacerbations of chronic bronchitis), the prescribing process can be complicated by many additional factors that need to be considered.

Most previous studies evaluating antibiotic appropriateness in bacterial respiratory tract infections such as pneumonia have focused only on antibiotic choice.[3-5] While appropriate selection is essential, inappropriate prescribing in terms of dosage, duration of therapy, drug-drug interactions, and drug-disease interactions is also important because it can contribute to increased adverse drug reactions, health care costs, and bacterial resistance.[6;7] These aspects of prescribing are also important because under dosing patients can lead to therapeutic failures and increased bacterial resistance.[6] Only two studies of antibiotics have evaluated the appropriateness of multiple domains of antibiotic prescribing, but the populations were restricted to those patients who were institutionalized.[8;9] Moreover, neither study determined what factors were associated with inappropriate prescribing.[8;9]

Given this background, the objectives of this study were to determine the prevalence and factors associated with inappropriate antibiotic prescribing practices in outpatient veterans with community-acquired pneumonia (CAP), sinusitis, or acute exacerbations of chronic bronchitis (AECB).

PATIENTS AND METHODS

Study Design/Overview

Our study design was a retrospective cross-sectional study of veteran outpatients with community-acquired pneumonia, sinusitis, or acute exacerbations of chronic bronchitis. Patients were evaluated in the emergency department (ED) at the Veterans Affairs (VA) Pittsburgh Healthcare System (VAPHS) between June 15, 2003 and June 14, 2004. All veterans are eligible for ED care. ED physicians prescribe from a preferred formulary but can request approval for exceptions, and all veterans pay a nominal co-payment per prescription ($7.00/prescription at the time of the study). The patients were identified as part of a study of antibiotic prescribing for acute respiratory tract infections. Adults, who were diagnosed by the medical care provider in the ED with CAP, sinusitis, or AECB and prescribed oral antibiotics to be taken at home, were eligible for inclusion in the study. Patients who were immunosuppressed (e.g., systemic corticosteroid use, HIV positive, absolute neutrophil count <1000/mm3), had tuberculosis, were diagnosed with an acute respiratory infection (e.g., acute bronchitis, “flu”, sinusitis, otitis media, pneumonia) or discharged from the hospital within the preceding two weeks, were transferred to the ED from a nursing home or acute care hospital, or were evaluated in the ED by one of the study investigators were excluded. The VAPHS Institutional Review Board approved this study.

Data Collection

Trained research assistants created a study chart that included information on date and time of presentation to the ED, provider-assigned diagnosis (i.e., Community Acquired Pneumonia, sinusitis, Acute Exacerbation of Chronic Bronchitis), patient demographics, allergies, comorbidities, smoking status, alcohol abuse, temperature, serum creatinine, white blood cell count (WBC), antibiotic therapy in the previous three months, and provider characteristics as part of the study on antibiotic prescribing in outpatient veterans with acute respiratory infections. For all antibiotics, the name of the antibiotic, dosage, schedule, days supply, and quantity were collected. In addition, information was collected by a clinical pharmacist about concurrent medications using the pharmacy section of the reports tab in the electronic medical record and the cost per course of antibiotic therapy using the local VA drug file. The drug file contains information such as dosage strength and formulation, formulary status, and cost of the medication to the VA.

Assessment Using the Medication Appropriateness Index

This study used the Medication Appropriateness Index (MAI) to assess the quality of antibiotic prescribing (**see Appendix I**). The MAI is an instrument that has demonstrated good intra- and inter-rater reliability, face validity, and feasibility when applied to medications taken by patients.[8-15] The MAI measures ten domains of prescribing (i.e., indication, effectiveness, dosage, directions, practicality, drug-drug interactions, drug-disease interactions, unnecessary duplication, duration, and expensiveness) as illustrated in **Appendix I**.[10;11] For each criterion, the index has specific instructions, operational definitions, and examples. Prior to evaluating antibiotic prescribing practices, the MAI instructions were modified to be more specific to antibiotic therapy guidelines for the

management of patients with community-acquired pneumonia (CAP), acute exacerbations of chronic bronchitis (AECB), and sinusitis in CAP, sinusitis, and AECB. [16-19]

In addition, MAI instructions for appropriate antibiotic doses for patients with renal impairment and clinically important antibiotic drug interactions were specified using a standard pharmacotherapy information source. [20] The developer of the instrument (JTH) trained the two clinical pharmacists (CCT and SLA) in the use of the modified MAI. A clinical pharmacist (CCT) reviewed each patient's study chart that included clinical information and each antibiotic prescription and applied the modified MAI by rating each of the 10 items as “A” appropriate, “B” marginal”, or “C” inappropriate. To assure that the MAI was being applied consistently, a senior investigator (SLA) verified the accuracy of MAI application for every tenth patient evaluated.

Outcome Measure

For descriptive purposes, the percent of patients with an inappropriate or “C” rating for any of the 10 MAI items was calculated. Also the percent of patients with one or more “C” rating for any of the 10 MAI was calculated by antibiotic classes. For purposes of analyses, a dichotomous measure was created for the percentage of patients with one or more inappropriate MAI ratings. For those few patients who received more than one antibiotic, therapy was classified as inappropriate if one or more criteria for any antibiotic were rated as inappropriate (“C”).

Independent Variables

A modified health care service use model was used to ascertain factors that may be associated with inappropriate drug use.[21] Andersen’s Behavioral Model of Health Services Use has been used extensively internationally as a framework for studies of health services utilization including inappropriate prescribing. [21] Independent variables were grouped into three domains: 1) sociodemographic characteristics, 2) need or health status characteristics, and 3) enabling or access to health care characteristics. Enabling factors often include information about available health personnel and services that may vary with the time of day a patient is seen.[21]

Sociodemographic characteristics included categorical measures for gender, race/ethnicity (Caucasian, African American or Other), and marital status (married versus all others). A continuous measure was created for age.

Health status was represented by a dichotomous variable for the number of comorbidities (i.e., none and ≥ 1) and dichotomous variables for the presence of chronic pulmonary disease, heart disease (coronary artery disease and/or congestive heart failure), diabetes, or renal disease. Continuous measures were created for temperature, WBC, and number of chronic medications (excluding antibiotics). Health behaviors were represented by dichotomous measures for smoking status and history of alcohol abuse. Alcohol abuse was operationally defined as the presence of alcohol abuse, tolerance, or dependence in the social or past medical history sections of the physician note for the ED visit or the most recent visit to a primary care provider.

Factors that enable or hinder access to health care were represented by categorical variables for provider type (i.e., attending physician, house staff, or nurse practitioner). The type of health care provider was a considered because house staff rotating through the ED are less likely to be familiar with the VA formulary, which could be a factor when addressing the cost of the medication prescribed. In addition, a dichotomous variable was created for time of day of presentation to the ED (i.e., 0801 to 1800 Monday through Friday versus all other times).

Analyses

Baseline patient characteristics for all continuous variables are presented as means and standard deviations. Dichotomous and categorical variables are presented as frequencies and percents of the respective totals. For descriptive purposes, MAI data is provided at the patient level for each of the ten MAI criteria. We also calculated the percent of persons with one or more inappropriate MAI ratings by class of antibiotics. We tested the univariable relationship between the independent variables and the dichotomous dependent variable for inappropriate prescribing of an antibiotic using logistic regression. Those that were significant at an alpha of 0.1 or less were included in a multivariable logistic regression model. Those that remained significant at an alpha of 0.05 or less were retained in the final model.[22] SAS® software (Cary, NC) was used for all analyses.

Results

We evaluated 153 patients, who received 154 antibiotics prescribed as outpatient therapy. Only one patient received prescriptions for two different antibiotics at the same ED visit. **Table 1** describes the characteristics of the patients. The majority of patients were male, Caucasian and had at least 1 or more chronic conditions. Slightly more than one third were married and only one in ten had a history of alcohol abuse.

Of the 153 patients, 99 or 65% had a problem with antibiotic prescribing according to the MAI criteria **(Table 2).** The types of inappropriate prescribing were similar across the three types of bacterial upper respiratory infections. The most common problems were seen with expensiveness, practicality, or the dosage of the antibiotic. In the majority of cases the daily dosage was lower than recommended.

Table 3 represents the percent of patients with inappropriate prescribing by antibiotic class. Patients who were prescribed macrolides, quinolones, or penicillins had inappropriate ratings more commonly than other antibiotic classes according to the MAI criteria. Inappropriate ratings for quinolones and penicillins were frequently due to incorrect dosing. Impractical directions were also commonly seen with penicillins. Quinolones and macrolides were often rated as more expensive than other alternatives.

In our univariable analyses, only a history of alcohol abuse and being married were associated with inappropriate prescribing (**Table 4**).These findings held in our multivariable analyses (history of alcohol abuse: Adjusted Odds Ratio [Adj. OR] 0.32; 95% Confidence Interval [CI] 0.10-0.98 and being married: Adj. OR 2.64; 95% CI 1.25-5.59).

DISCUSSION

Our study is among the first to evaluate multiple dimensions of antibiotic prescribing practices for acute respiratory infections. We found that nearly two thirds of patients had one or more prescribing problems with antibiotics. This rate is higher than the rates ranging from 15 – 55% found in previous studies that only evaluated inappropriate antibiotic prescribing practices for upper respiratory infections unlikely to have a bacterial etiology in the ambulatory care setting. [1-3] This form of inappropriate prescribing was not only ineffective but also costly.

This rate of inappropriate prescribing of antibiotics is also higher than that seen by the only other studies that used the MAI to specifically evaluate antibiotic use. In the first study, Miller et al. evaluated the quality of prescribing for urinary tract infections in long-term care facilities.[8] They found that approximately 40% of antibiotic orders were rated as inappropriate. The antibiotics that were most often prescribed inappropriately were ciprofloxacin, cotrimoxazole, and nitrofurantoin due to expensiveness, incorrect duration, and incorrect dosage, respectively. Similarly, Taylor et al. evaluated antimicrobial appropriateness in hospitalized patients and found that 34% of antibiotic orders were rated as inappropriate.[9] The study involved only fifty-three patients, which may have contributed to the lower incidence of inappropriate prescribing practices. The difference in the rates of inappropriateness could also be due to the types of infections and antibiotics studied. For instance, our study looked specifically at the diagnoses of CAP, sinusitis, and AECB, which is a more diverse group of infections than urinary tract infections. Regardless, our study confirms problems with prescribing, even for infections like CAP, sinusitis, and AECB where antibiotics are generally indicated.

We found that the most common prescribing problems involved expensiveness, practicality, or the dosage of the antibiotic. Similarly, the study by Miller et al. reported the greatest problems with dosage, drug-disease interactions, and expensiveness.[8] Taylor et al. also found the biggest problems involved dosage and expensiveness.[9] One reason Miller et al. discovered inappropriate antibiotic prescribing practices due to drug-disease interactions is likely related to the presence of multiple comorbidities in the older population of long-term care facilities. Problems with expensiveness generally meant that a broad spectrum antibiotic was prescribed when a narrow spectrum agent was also indicated (e.g., levofloxacin instead of amoxicillin or cotrimoxazole for sinusitis). While this does not increase the cost for patients within the VA, it typically increases pharmacy costs. More importantly, in the era of multi-drug resistance among *Streptococcus pneumoniae*, guidelines emphasize the need to restrict first line use of broad spectrum agents such as the respiratory fluoroquinolones to indications in which therapeutic superiority has been demonstrated.[23;24]

Our study is among the first to evaluate patient factors that contribute to inappropriate prescribing of antibiotics. Of all the factors we evaluated, only a history of alcohol abuse and being married were independently associated with inappropriate prescribing**.** One possible explanation is that practitioners taking extra time to think about medication interactions or proper dosing in patients with alcohol abuse since they are relatively immunosuppressed.[25] One possible explanation is that married patients may have been accompanied by spouses

who requested the use of newer, albeit more expensive, antibiotics.[26] It is interesting to note that other patient demographics and health status were not associated with inappropriate prescribing practices.

Improving the appropriate use of antibiotics is a difficult task, but necessary in order to decrease the development of antibiotic-resistant bacteria. The authors of a recent review of the literature on the effectiveness of interventions designed to improve antibiotic selection, dosing, and/or duration of therapy for any type of infection in the ambulatory care setting concluded that only multi-faceted interventions (e.g., combination of physician education, audit and feedback, physician reminders, patient education, pharmacist intervention) that address local barriers to change were sufficiently potent to potentially reduce the incidence of antibiotic resistance.[27] However, additional studies are needed in this area in order to determine which components of the intervention are most effective for specific infections and antibiotic prescribing problems.

There are a number of potential limitations to note. First, due to the invasiveness of the procedure, no respiratory culture information was available to assess the appropriateness of the "choice" of antibiotic. [16-19] However, the choice of antibiotic was rated as appropriate for effectiveness if the antibiotic choice was consistent with those recommended by national guidelines. Secondly, fewer drug-drug interactions may have been seen because the VA has computerized physician order entry with a database that automatically checks and flags clinically important drug interactions. Thirdly, our finding about the use of expensive antibiotics may be conservative because VA physicians prescribing may have been influenced by the preferred formulary and their knowledge that all veteran patients pay only a nominal co-payment for medicines dispensed by a VA pharmacy. A fourth limitation is that we were not able to evaluate other factors associated with inappropriate prescribing (e.g., patient preferences), as the study did not collect this information. A fifth limitation is that due to the cross-sectional nature of the study we were not able to follow patients to determine their clinical outcomes. Finally, this is a small select sample, and our findings may not generalize to other non-VA emergency departments.

CONCLUSIONS

Our study demonstrated that there is a high rate of inappropriate antibiotic prescribing that extends beyond antibiotic selection for patients diagnosed with CAP, sinusitis, and AECB in an emergency department. Impractical directions, incorrect dosing, and choosing a more expensive medication were all common reasons for inappropriate prescribing. Being married was the only factor independently associated with inappropriate prescribing practices, while a history of alcohol abuse was the only factor associated with more appropriate prescribing. Future interventions to improve antibiotic prescribing need to consider aspects beyond selection.

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Table 1

Characteristics of Outpatient Veterans with Community-Acquired Pneumonia, Sinusitis, or Acute Exacerbations of Chronic Bronchitis (n=153) (continued)

Characteristic	N (%)	Mean (SD)
Sociodemographics		
Gender		
Male	140 (92)	
Female	13 (8)	
Race/Ethnicity		
Caucasian	99 (65)	
African American	51 (33)	
Other (1 Asian, 2 Hispanics)	3 (2)	
Marital status		
Married	58 (38)	
Not married	95 (62)	
Age (years)	58 ± 15	
Health Status		
One or more comorbidities	87 (57)	
Chronic pulmonary disease	62 (41)	
Heart disease	33 (22)	
Diabetes	36 (24)	
Renal disease	5 (3)	
Temperature (° Fahrenheit)		95.8 ± 15.8
WBC (K/cmm)		9.8 ± 3.5
Number of chronic medications		7.7 ± 7.0
Health Behaviors		
Smoker	53 (35)	
History of alcohol abuse	15 (10)	
Access to Health Care		
Provider type		
Attending physician	77 (50)	
House staff	51 (33)	
Nurse practitioner	21 (14)	
Other	4 (3)	
Time of presentation		
Monday-Friday (0801-1800)	91 (60)	
All other times	62 (40)	

WBC=white blood cell count

Table 2

Patients with Inappropriate Prescribing According to MAI Criteria (n=153)

MAI Criteria	N (%)
Indication	0 (0)
Effectiveness	4 (3)
Dosage	15 (10)
Directions	1 (1)
Practicality	32 (21)
Drug-Drug Interactions	0 (0)
Drug-Disease Interactions	0 (0)
Duplication	2 (1)
Duration	2 (1)
Expensiveness	60 (39)
Patients with Any of the Above Criteria	99 (65)

Table 3

Inappropriate Prescribing by Antibiotic Class According to MAI Criteria (n=153)

Antibiotic Class	N (%)
Penicillin	33 (22)
Cephalosporin	2 (1)
Quinolone	19 (12)
Macrolide	42 (27)
Sulfonamide	3 (2)
Tetracycline	0 (0)

Table 4

Factors Univariably Associated with Inappropriate Antibiotic Prescribing (n=153)

Factor	Crude Odds Ratio	95% CI	P-value
Male	1.64	0.52-5.16	0.40
Caucasian	1.44	0.72-2.86	0.30
Married	2.63	1.26-5.50	0.01
Age	1.01	0.99-1.03	0.46
Comorbidities			
None	0.97	0.49-1.89	0.92
1 or more	Referent category		
Chronic pulmonary disease	0.99	0.50-1.94	0.97
Heart disease	1.33	0.58-3.05	0.50
Diabetes	1.57	0.69-3.56	0.28
Renal disease	2.23	0.24-20.48	0.48
Temperature	0.99	0.97-1.02	0.61
WBC	1.01	0.93-1.09	0.90
Number of chronic meds	0.99	0.94-1.03	0.53
Smoker	0.59	0.29-1.17	0.13
History of alcohol abuse	0.32	0.11-0.96	0.04
Provider type			
House staff	1.25	0.59-2.65	0.56
Nurse practitioner	0.76	0.29-2.03	0.59
Attending physician/other	Referent category		
Time of presentation			
Monday-Friday 0801-1800	1.14	0.58-2.24	0.70
All other times	Referent category		

CI=confidence interval; OR=odds ratio; WBC=white blood cell count

APPENDIX I

Medication Appropriateness Index *

1. Is there an indication for the drug?	A_____ Indicated	B_____	C_____ Not Indicated

Indication is defined as the sign, symptom, disease, or condition for which the medication is prescribed.

2. Is the medication effective for the drug?	A_____ Effective	B_____	C_____ Not Effective

Effective is defined as producing a beneficial result. The question assesses whether the drug prescribed is capable of being effective for the indication in a population of patients.

3. Is the dosage correct?	A_____ Correct	B_____	C_____ Not Correct

Dosage is defined as the total amount of medication taken per 24-hour period for regularly scheduled medications.

4. Are the directions correct?	A_____ Correct	B_____	C_____ Not Correct

Directions are defined as the instructions in the use of a medication by a patient. The question assesses the route of administration, relationship to food and liquid, the schedule, and time of the day.

5. Are the directions practical?	A_____ Practical	B_____	C_____ Impractical

Practical is defined as capable of being used or being put into practice. This question assesses whether the directions for use are practical for the patient to take and takes into consideration the potential for patient adherence without sacrificing efficacy, as well as formulary status.

6. Are there clinically significant drug-drug interactions?	A_____ Insignificant	B_____	C_____ Significant

A drug-drug interaction is defined as the effect that the administration of one medication has on another drug. Clinical significance connotes a harmful interaction.

7. Are there clinically significant drug-disease/condition interactions?	A_____ Insignificant	B_____	C_____ Significant

Drug-disease interaction is defined as the effect that the drug has on a pre-existing disease or condition. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question may be worsening the patient's disease or condition.

8. Is there unnecessary duplication with other drugs (s)?	A_____ Necessary	B_____	C_____ Unnecessary

Unnecessary duplication is defined as nonbeneficial or risky copying of drug(s). Unnecessary duplication exists when two drugs from the same chemical or pharmacological class are prescribed simultaneously.

9. Is the duration of therapy acceptable?	A_____ Acceptable	B_____	C_____ Not Acceptable

Duration is defined as the length of therapy. This question assesses whether the length of time that the patient has received the drug is acceptable.

10. Is this drug the least expensive alternative compared to others of equal utility?	A_____ Least Expensive	B_____	C_____ Most Expensive

This question assesses how the cost of the drug compares to other agents of equal efficacy and safety.

* Complete instructions are available upon request from Dr. Hanlon