Antibiotic Choice And Patient Outcomes In Community-Acquired Pneumonia

William J. Hueston, MD, and Maria A. Schiaffino, MD

Background: **We investigated whether any clinical or nonclinical variables were associated with physician choice of antibiotic therapy and whether outcome differences existed among patients given agents to treat infections caused by atypical gram-negative organisms.**

Methods: **A retrospective review of 157 immunocompetent patients admitted to a hospital between 1 February 1992 and 31 January 1993 with a diagnosis of community-acquired pneumonia was performed. Patient groups were defined by whether their initial antibiotic therapy was a broader spectrum antibiotic, such as a second- or third-generation cephalosporin, which would treat atypical gram-negative infection (n = 85), or narrower spectrum agents, such as ampicillin or erythromycin (n = 72).**

Results: **Patients who were given broader spectrum antibiotics were slightly older than those receiving narrower agents (73 versus 66 years, $P = 0.06$). Otherwise, no clinical factors or comorbid states were associated with antibiotic selection. When examining physician-related factors, internists were more likely to prescribe broad-spectrum agents than were family physicians. No differences existed in overall mortality, length of stay, readmission rate, or change in antibiotic.**

Conclusions: **Although physicians appear to prescribe broader agents for pneumonia in older patients, there were no other clinical predictors of antibiotic selection. Physician-related factors, such as training and specialty, might influence prescribing habits. (J Am Board Fam Pract 1994; 7:95-9.)**

The selection of an antibiotic for patients who are hospitalized with community-acquired pneumonia is controversial. Because routine microbiologic evaluation of community-acquired pneumonia is often not helpful or results of tests can be delayed,[1] in many situations the initial selection of an antibiotic for pneumonia therapy is empiric.[2] Because of an increase in the frequency of pneumonia caused by resistant organisms, such as *Haemophilus influenzae*,[3-5] some experts recommend prescribing second- or third-generation cephalosporins, which provide coverage against atypical gram-negative organisms when treating community-acquired pneumonia.[4,6] Previous epidemiologic studies, however, suggest that the primary causes of community-acquired pneumonia continue to be viral agents and *Streptococcus pneumoniae*,[7,8] which are organisms that do not require broad-spectrum antibiotic coverage.

Admission of a patient to the hospital for the treatment of pneumonia is expensive. The typical cost of inpatient treatment for pneumonia is about $5000 for an average stay of more than 7 days.[9] The cost of antibiotics for the treatment of pneumonia can vary considerably.[10,11] For example, 10 days of therapy with a first-generation cephalosporin, such as cefazolin, is estimated to cost $309, whereas a similar duration of therapy with cefotaxime, a third-generation cephalosporin, is three and one-half times higher at $1133.[11] Thus, the selection of an antibiotic for the treatment of pneumonia can have a major impact on the total cost of inpatient care.

This study was undertaken to determine (1) which antibiotics are most commonly used to treat community-acquired pneumonia in a community hospital, (2) what factors influence the selection of initial antibiotic therapy, and (3) whether there are any differences in patient outcomes between those who receive broader spectrum antibiotics and those whose therapy is begun with narrower spectrum antibiotics.

Submitted, revised, 16 November 1993.

From St. Claire Medical Center, Morehead, Kentucky, and the Department of Family Medicine, Case Western Reserve University, Cleveland, Ohio. Address reprint requests to William J. Hueston, MD, Eau Claire Family Practice Residency, 807 South Farwell Street, Eau Claire, WI 54701.

Methods

A retrospective review was performed on the charts of all patients older than 18 years of age admitted to a 125-bed rural community hospital from 1 February 1992 to 31 January 1993 with a diagnosis of pneumonia. The hospital medical staff at the time of the study included 16 physicians who admitted adults to the general medical services. Six of these physicians were family physicians and 10 were internists, including 2 nephrologists, 1 cardiologist, and 1 hematologist-oncologist. The family physicians were associated with a single group practice, and the internists were associated with another group practice. In addition to the medical staff, residents from a state university performed 1st-year rotations at the hospital with the internal medicine group.

The diagnosis of pneumonia was determined from a review of discharge abstracts. Patients who were transferred to the hospital from another institution (either another hospital or nursing home) and all patients with nosocomial pneumonia were excluded. In addition, patients who were being treated with immunosuppressive medications, such as chemotherapeutic agents, patients who were neutropenic, and patients who were infected with the human immunodeficiency virus (HIV) were also excluded from study.

After excluding the above, there remained 159 patients admitted for community-acquired pneumonia. Charts could be located for 157 (99 percent) of them. Their charts were reviewed by one of the authors (MAS) or a chart abstractor from the hospital quality-assurance office.

A variety of clinical and demographic variables were recorded for each patient. Variables related to the severity of the patient's illness included admission to an intensive care unit, initial temperature, initial white cell count, and percentage of neutrophil forms. Variables related to the type of pneumonia included results of sputum and blood cultures. Variables associated with other clinical conditions that might have influenced antibiotic choice included the presence of any cardiac, pulmonary, renal, or oncologic comorbidities. Finally, variables reflecting patient outcome included mortality, length of stay, readmission within 30 days, and change in the antibiotic from the initial drug to an alternate intravenous medication during the hospital stay. The physician-related factors thought to influence antibiotic choice included specialty and level of training of the admitting physician and the physician who wrote the initial antibiotic orders.

To compare outcomes between patients treated with different types of antibiotics, two classes of antibiotics were defined. Antibiotics that are more active against atypical gram-negative infections were called broad-spectrum agents and included second- and third-generation cephalosporins, ampicillin-sulbactam, quinolones, aminoglycosides, and synthetic penicillins, such as pipericillin. Antibiotics that do not include coverage for these atypical gram-negative infections but are useful for more common respiratory tract pathogens were called narrow-spectrum agents and included penicillin, ampicillin, doxycycline, erythromycin, and cefazolin. Using these criteria, 72 patients were included in the narrow-spectrum group and 85 patients were in the broad-spectrum group. For a comparison of lengths of hospital stay, this sample size yielded a power of 95 percent with an alpha of 0.05 for a variation in 1 day between groups assuming a variance of 5 days in the length of stay for each group.

Data were entered into EpiInfo Version 5[12] and analyzed using the chi-square test for categorical variables and the Student t-test for continuous variables. Where noted, regression analyses were performed using True Epistat software.[13]

Results

Table 1 displays the wide range of antibiotics that were prescribed for the treatment of pneumonia in these patients. The most commonly prescribed antibiotic was cefotaxime (47 patients, 30 percent of total) followed by cefazolin (39 patients, 25 percent of total).

Patients initially given broad-spectrum antibiotics tended to be older than those initially given narrow-spectrum medications, although this difference did not reach statistical significance ($P = 0.06$). Other clinical variables, such as admission to an intensive care unit, mean white cell count, percentage of neutrophils on smear, or average initial temperature, were not associated with selection of a class of antibiotic (Table 2). Furthermore, we found no association between antibiotic selection and the documentation of other pulmonary, cardiac, renal, or oncologic diseases.

The results of microbiologic testing of patients were also not helpful in predicting antibiotic

Table 1. Number of Times Specific Antibiotics Were Used (and Percentage of Total) for Community-acquired Pneumonia.

Antibiotic Class	No. (%)
Narrow spectrum	
Cefazolin	39 (25)
Erythromycin	17 (11)
Ampicillin	9 (6)
Penicillin	4 (3)
All others	3 (2)
Total	72 (47)
Broad spectrum	
Cefotaxime	47 (30)
Ampicillin/sulbactam	16 (10)
Gentamicin	7 (4)
Cefuroxime	5 (3)
Ceftazidime	4 (3)
All others	6 (3)
Total	85 (53)

selection. We found no difference between patients who initially received narrow- or broad-spectrum antibiotics and the percentage of patients having blood cultures performed (67 percent versus 76 percent, respectively, $P = 0.30$) or sputum cultures performed (61 percent versus 59 percent, respectively, $P = 0.92$). We also found no significant difference between the narrow- and broad-spectrum groups and the percentage of patients who had a positive blood culture (4 percent versus 8 percent, $P = 0.34$) or a positive sputum culture (11 percent versus 13 percent, $P = 0.69$). The most common organism identified on sputum cultures for both groups was *Streptococcus pneumoniae*, which was positive in 5 patients (7 percent) in the narrow-spectrum group and 7 patients (8 percent) in the broad-spectrum group.

When we examined the effects of physician-related factors on prescribing patterns, we found that patients who were admitted by internists were given broad-spectrum antibiotics more frequently than those admitted by family physicians ($P = 0.005$) (Table 3). The level of training of the physician writing the admitting orders, however, did not appear to influence the selection of antibiotics. Because of the possibility that the prescribing patterns of internists were influenced by caring for an older patient population, logistic regression was performed using age and specialty as dependent variables and antibiotic class as the dependent variable. Regression analysis confirmed an effect of physician specialty independent of patient age with an adjusted odds ratio for using broad-spectrum antibiotics of 3.53 (95 percent confidence interval 1.51, 8.24, $P = 0.003$) for internists when compared with family physicians.

When patient outcome variables were examined, we found no significant difference between classes of antibiotics and the length of stay, mortality, and readmission within 30 days (Table 4). In addition, we found that patients who started their therapy with narrow-spectrum drugs had their medication changed to other parenteral agents less often than did those who began with

Table 2. Comparison of Demographic Variables, Medical Comorbidities, and Measures of Illness Severity.

Variable	Narrow-Spectrum Antibiotics (n = 72)	Broad-Spectrum Antibiotics (n = 85)	*P* Value
Demographic variables			
Mean age (years ± SD)	66.4 ± 21.3	73.1 ± 15.8	0.06
> age 65 years (%)	55	69	0.07
> age 80 years (%)	36	40	0.53
Initial disease characteristics			
Admitted to intensive care unit (%)	8	7	0.54
Initial white-cell count ($\times 10^3/mm^3$ ± SD)	14.4 ± 6.3	15.6 ± 7.3	0.29
Initial neutrophil count (% ± SD)	70.4 ± 14.6	71.8 ± 13.9	0.57
Initial temperature (°F ± SD)	99.7 ± 1.5	98.7 ± 8.6	0.43
Frequency of comorbidities*			
Cardiac (%)	32	38	0.39
Pulmonary (%)	43	53	0.22
Renal (%)	13	16	0.57
Oncologic (%)	13	13	0.89

*Patients could have more than 1 comorbid condition.
SD = standard deviation.

Table 3. Effects of Specialty and Training on Selection of Antibiotics in 157 Patients with Community-acquired Pneumonia.

Physician Training Characteristics	Narrow-Spectrum Antibiotics (n = 72) No. (%)	Broad-Spectrum Antibiotics (n = 85) No. (%)	*P* Value
Specialty			
Internal medicine	45 (39)	70 (61)	
Family practice	22 (67)	11 (33)	
Emergency medicine	5 (55)	4 (44)	0.005
Level of training*			
Attending physician	49 (47)	55 (53)	
Resident physician	18 (41)	26 (59)	0.49

*Excluding emergency medicine physicians.

broad-spectrum drugs (20 percent versus 33 percent, $P = 0.04$). Of patients whose physicians changed their parenteral antibiotics during the hospitalization, 71 percent were switched from narrow-spectrum agents to broad-spectrum agents, while 67 percent were switched from broad-spectrum agents to narrow-spectrum agents ($P = 0.48$). When the subgroup of patients with positive sputum cultures was examined, again we found no difference in any outcome variable based on the class of antibiotic chosen for initial therapy.

Because we found that broad-spectrum antibiotic therapy was more likely to be used in older patients, we were uncertain whether age-related bias in antibiotic selection could obscure outcome differences between the two classes of antibiotics. Therefore, we performed linear regression using length of stay as the dependent variable and age and antibiotic class as independent variables to discover if antibiotic class was significantly associated with length of stay when adjusted for age. Regression analysis showed that neither antibiotic class ($P = 0.58$) nor age ($P = 0.98$) was associated with length of stay.

Discussion

Our results show that selection of an antibiotic for the treatment of community-acquired pneumonia was influenced by the patient's age but not by other clinical variables or comorbid conditions. The only other factor related to antibiotic choice was the specialty of the physician admitting the patient to the hospital. Internists and emergency physicians were more likely than family physicians to select broad-spectrum antibiotics. This difference could be related to subtle clinical variations in the patient populations served by internists and family physicians that were not measured in this study. Reports that generalists tend to use other types of medical technology in a more cost-efficient manner[14] have suggested that a true difference in prescribing habits might exist based on specialty training.

In addition, contrary to the recommendations of others,[6,9] findings from this retrospective study of community-acquired pneumonia suggest that antibiotics which do not provide coverage for atypical gram-negative organisms are as clinically effective as the broader spectrum, more expensive alternatives. Patients initially given narrower spectrum antibiotics had similar lengths of hospital stay, readmission rates, changes in intravenous antibiotics during treatment, and mortality as those initially prescribed broad-spectrum drugs. These data suggest that most patients benefit from narrow-spectrum antibiotics, and only a small population requires more aggressive therapy. Initial use of narrower spectrum antibiotics for the treatment of community-acquired pneumonia is equally effective and less expensive than broad-spectrum alternatives.[10,11] For example, the average cost of 7 days of intravenous therapy with cefazolin is $216 compared with $793 for 7 days of cefotaxime.[11] Thus, for every patient treated with cefotaxime, an additional $577 is spent on antibiotic drug costs, an amount equal to 11 percent of the total hospital expenses for treatment of pneumonia.[9]

While our findings from this study suggest that narrower spectrum antibiotics achieved the same outcomes as broad-spectrum drugs for patients hospitalized with community-acquired pneumonia, these results must be considered in light of

Table 4. Outcomes for Patients Treated with Narrow- and Broad-Spectrum Antibiotics.

Outcomes	Narrow-Spectrum Antibiotics (n = 72)	Broad-Spectrum Antibiotics (n = 85)	P Value
Mortality (%)	4	8	0.34
Antibiotic changed (%)	20	33	0.04
Average length of stay (days ± SD)	7.1 ± 5.2	7.5 ± 4.6	0.63
Readmission rate* (%)	10	8	0.54

*Readmitted within 30 days.
SD = standard deviation.

some limitations of the data. First, this study focused on 157 patients admitted to one community hospital. The sample size limited the power to detect differences in such rare outcomes as mortality. Second, because the prescribing habits of only relatively few physicians were included in this study, the results could have been biased by unusual prescribing behaviors of 1 or 2 physicians. Follow-up examination of this issue with a larger population at other facilities would be useful to confirm these findings.

Finally, no measure of pneumonia severity was used to determine the influence of severity of illness on antibiotic selection. Several proxy measures, such as fever, elevated white cell count, and admission to an intensive care unit were used to estimate the severity of illness, but some other factor could have contributed to physicians' assessments of disease severity.

As health care costs rise, providers must examine technology use and prescribing habits. Evidence suggests physicians are not aware of the costs of their prescribing habits.[15] Physicians need to become more aware of the economic implications of their prescribing behavior and examine the outcomes resulting from these choices. Examining antibiotic selection for common clinical problems, such as community-acquired pneumonia, is one example of how close evaluation might result in more appropriate and cost-effective use of medical technology.

References

1. Woodhead MA, Arrowsmith J, Chamberlain-Webber R, Wooding S, Williams I. The value of routine microbial investigation in community-acquired pneumonia. Respir Med 1991; 85:313-7.
2. Kemper CA, Deresinski SC. Diagnosis and management of pneumonia. Pharmacotherapy 1991; 11: 84S-9S.
3. Fang GD, Fine M, Orlaff J, Arisumi D, Yu VL, Kapoor W, et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy. A prospective multicenter study of 359 cases. Medicine 1990; 69:307-16.
4. Cunha BA. Atypical pneumonia. Clinical diagnosis and empirical treatment. Postgrad Med 1991; 90(5):89-90, 95-8, 101.
5. Winter JH. The scope of lower respiratory tract infection. Infection 1991; 19(Suppl 7):359S-64S.
6. Regamey C. Therapeutics of community-acquired pneumonia. Infection 1990; 18:1-2.
7. British Thoracic Society Research Committee and the Public Health Laboratory Service. The aetiology, management, and outcome of severe community-acquired pneumonia on the intensive care unit. Respir Med 1992; 86:7-13.
8. Sanders WE, Morris JF, Alessi P, Makris AT, McCloskey RV, Trenholme GM, et al. Oral ofloxacin for the treatment of acute bacterial pneumonia: use of a nontraditional protocol to compare experimental therapy with "usual care" in a multicenter clinical trial. Am J Medicine 1991; 91:261-6.
9. Rodnick JE, Gude JK. Diagnostic and antibiotic treatment of community-acquired pneumonia. West J Med 1991; 154:405-9.
10. Thompson RL. Cephalosporin, carbapenen, and monobactam antibiotics. Mayo Clin Proc 1987; 62: 821-34.
11. Choice of cephalosporins. Med Lett Drugs Ther 1990; 32:107-10.
12. Dean AG, Dean JA, Burton AH, Dicker RC. EpiInfo, Version 5: a word processing, database and statistics program for epidemiology on microcomputers. Stone Mountain, GA: USD, Incorporated, 1990.
13. True Epistat [computer program]. Version 4.2. Richardson, TX: Epistat Services, 1992.
14. Greenfield S, Nelson EC, Zubkoff M, Manning M, Rogers WL, Kravitz RL, et al. Variations in resource utilization among medical specialties and systems of care. Results from the medical outcomes study. JAMA 1992; 267:1624-30.
15. Miller LG, Blum A. Physician awareness of prescription drug cost: a missing element of drug advertising and promotion. J Fam Pract 1993; 36:33-6.