

Respiratory Infection

Community-Acquired Pneumonia: Recent Insights Into an Old Disease

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Abstract and Introduction

Abstract

Rapid diagnostic tests, analysis of outcomes in large databases, and application of technology to assist clinicians in decision making have all helped improve the diagnosis and management of community-acquired pneumonia. Managed care has provided pressure to consider cost-effectiveness of therapy. Outpatient parenteral antibiotic therapy is an increasingly available and routine option. Practice guidelines have been published but often are not followed; they are most useful in settings in which pneumonia is a frequent event, such as emergency departments.

Introduction

Despite the achievements of modern antimicrobial therapy, community-acquired pneumonia (CAP) remains a formidable foe, and its incidence and associated mortality have changed relatively little in recent years. Yet there have been advances in our knowledge regarding CAP and how to treat it most effectively. These changes have been based principally on our growing use and understanding of computerized data gathering, improved diagnostic technologies, and an expanded armamentarium of antimicrobials. They also reflect recognition of outside forces and constraints, from increasing antibiotic resistance to managed care cost-containment requirements.

Changes in our understanding of how to treat CAP fall into 2 principal categories: increased information -- new *facts* -- about the pathogens, patients, and payers involved in CAP; and the development of guidelines -- new *interpretations* -- for treatment, including standardized decision-support systems and guidelines for the expanded use of outpatient

parenteral antibiotic therapy (OPAT). I will briefly examine here the major changes in perception about CAP treatment and the resulting changes in practice.

Changes in Perception

Information Sharing and Diagnostic Technologies

Computers have made collection and analysis of large amounts of patient care information and other data possible, and the Internet has allowed those data and analyses to be disseminated rapidly. Information technology is being used to track and project patterns of antibiotic resistance and to alert physicians to new or mutated infectious pathogens. As a result, we know that although the primary pneumonia-causing pathogens have remained the same over the years, we must now also take into consideration new pathogens, such as hantavirus, metapneumovirus, and the severe acute respiratory syndrome virus.

Multicenter studies now being conducted will contribute substantially to our patient care database -- and, of course, vast amounts of Medicare data are already available. One such database, that of the Pneumonia Patient Outcomes Research Team (PORT), already contains information on more than 38,000 patients with CAP.^[1]

Improvements in rapid diagnostic testing include kits that can be used to detect a specific antigen or piece of genetic material to identify a specific infectious cause, such as influenza type A virus, before the patient leaves the office.^[2] Also, a variety of handheld computers have become available to provide quick guidance on antimicrobial information and selection.

Even with the latest diagnostic technology, however, a specific pathogen is not identified in the majority of CAP cases, and we do not yet have practical antigen-detection systems for the primary bacterial pathogens in CAP: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella (Branhamella) catarrhalis*, and *Staphylococcus aureus*. In addition, recent studies suggest that many episodes of pneumonia involve coinfections, with a bacterial infection superimposed on a viral one.

Antimicrobial Resistance and Antibiotic Use

Antimicrobial resistance is, of course, a major factor in decisions related to CAP therapy, and patterns of resistance are continually changing. Penicillins were once the standard of therapy but are no longer active

against a large and growing number of strains of *Spneumoniae*, *Haemophilus*, and staphylococci. The number of antibiotics available for CAP has increased with the addition of new cephalosporins, macrolides, and fluoroquinolones. However, there are few comparative trials in the literature. The cephalosporins have been the standard of therapy, but even they may not be universally active against pneumococci. Laboratory measures of resistance have been revised to more clearly reflect clinical efficacy.^[3]

Azithromycin has become a mainstay of therapy for respiratory infections, although its activity against *S pneumoniae* and *Hinfluenzae* may be a problem. The fluoroquinolones have been demonstrated to be effective in CAP and offer an oral formulation, but growing resistance and adverse effects are concerns.^[4] Resistance appears to occur with increasing use in the community and may even occur during the course of treatment.^[5] The situation will continue to change as microbes respond with new resistance mechanisms and as new pathogens emerge.

Another important question about antibiotic use is whether, because of the difficulty in identifying a causative pathogen and the possibility of multiple pathogens, more than 1 antibiotic should be used (eg, whether findings suggestive of meningitis with CAP should still lead to consideration of adding vancomycin and/or rifampin to the treatment regimen).

Current data give clearer direction with respect to the speed of antibiotic delivery after a diagnosis of CAP is made. Studies of patients admitted with CAP indicate that there is a statistically significant increase in 30-day mortality if the antibiotic infusion is not given until 8 hours or more after admission.^[6] A more recent study also shows a correlation between the speed of delivery and the duration of hospitalization.^[7] More investigations on how to best use antibiotics are clearly needed.

A more fundamental debate addresses the suggestion that oral antibiotic therapy could be as effective as parenteral therapy; however, since it has not been studied as empiric therapy in hospitalized, high-risk patients, no definite conclusions have been reached. "Switch" therapy from parenteral to oral route of administration is of considerable interest and holds promise for patient convenience as well as for reduced costs.^[8,9] However, appropriate parameters for its application and limits to its usefulness have not been established. Moreover, optimal dosing and duration of therapy remain as much an unresolved issue in CAP as in many other infections.

Managed Care Constraints

Managed care cost constraints have also had an impact on the evaluation and treatment of pneumonia. The initial emphasis on the acquisition cost of antibiotics has gradually broadened to include investigations into areas that hold even greater potential for limiting expenditures, such as reducing the number of days of hospitalization. Cost savings from more effective antimicrobial therapy is an area of great interest, but there have been few studies documenting advantages of one antimicrobial regimen over another. Under managed care economic pressures, concerns about quality of care have also arisen relative to reductions in patient care services and physician consultations.

Responding to the new constraints is a growing interest, if not a mandate, in order to ensure the quality of patient care and the appropriate use of medical resources. In this environment, outcome measures and quality-of-care indicators now being formulated and evaluated will become increasingly important, and the extent to which costs can be reduced before patient outcomes are seriously affected will be tested.

Changes in Practice

OPAT Management in CAP

The PORT study drew on data from more than 38,000 patients to assess its selected outcome indicator -- mortality at 30 days following hospital admission -- against initial patient physical and laboratory findings.^[1] Variables found to correlate with the study end point included age, renal function, comorbidities (eg, cancer and liver disease), altered mental state, respiration rate greater than 30 breaths per minute, arterial pH less than 7.35, and blood urea nitrogen level greater than 30 mg/dL. The data analysis was used to gain insight into the risk factors for 30-day mortality and to construct a system for grouping CAP patients into 5 risk categories. These categories have been validated and are now being widely used to decide whether a patient should be hospitalized and how aggressive antimicrobial therapy should be. [Table 1](#) displays the risk categories and the resultant recommendations for inpatient or outpatient therapy.^[2]

Hospitalization is generally recommended for patients in risk classes IV and V. Mortality rates associated with classes IV and V are 8.2% and 29.2%, respectively.^[1] Patients in risk class III, with only a 2.8% rate of mortality at 30 days, were felt to be reasonable candidates for outpatient therapy. More detailed analysis of the data indicated that patients treated

as outpatients fared as well as hospitalized patients, although the numbers are small. Patients in risk groups III and IV should be further studied to determine on an individual basis whether they need to be hospitalized or not.

Patients in class I, II, or III -- those with a 30-day mortality risk of 2.8% or less in the PORT study -- were further studied to determine the reasons for their hospitalization. Physicians in 472 cases were surveyed concerning their decisions to admit patients with CAP.^[10] The primary reasons given for admission were hypoxemia, inability to maintain oral intake, and a lack of home care services. It was estimated that hospitalization could have been avoided for more than 50% of patients in this study if outpatient services had been a viable option at the time. Duration of hospitalization was also investigated.^[11] It was estimated that patients could have been discharged a mean of 2.5 days earlier. The primary reasons offered for delay were ongoing evaluation and treatment of comorbid illnesses and the lack of viable outpatient services or support. Accordingly, 26% of patients could have been discharged earlier if OPAT had been feasible.^[11]

The patient perspective on OPAT has also been studied, and patients treated with OPAT have indicated a strong preference for outpatient therapy.^[12] Patients with pneumonia also indicated a preference for OPAT - - even to the point of being willing to pay up to 24% of a month's income for such care.^[13]

Decision Support for Antibiotic Therapy

Decisions about site of treatment (outpatient or inpatient) and antimicrobial therapy for CAP should incorporate multiple factors, including the severity of disease, expected and actual microbiologic findings, recent antibiotic therapy, comorbid conditions, and the home environment when outpatient therapy may be an option. The physician needs to consider all of these factors in the design of a treatment regimen. Once therapy has been instituted and the patient responds, it is essential to have a plan for follow-up that is tailored to the patient's needs.

With the new tools, information, and antibiotics now available, guidelines for evaluation and management of CAP have been developed by various organizations.^[2,14-16] A recent and comprehensive set of guidelines was developed by the Infectious Diseases Society of America (IDSA).^[2] These guidelines recommend a careful and thorough patient evaluation with rapid diagnostic tests; they also endorse and reflect the PORT risk classification system. The IDSA guidelines for empiric antibiotic therapy, along with

specific antibiotic regimens recommended for each site of service, are shown in [Table 2](#).

Although the site of treatment relates to severity of illness, decisions about admission are often based on social and payer factors. The IDSA guidelines, however, overlook the potential value of using outpatient parenteral therapy for patients in risk class III or IV who might otherwise be hospitalized. They may also encourage parenteral therapy for patients who are hospitalized for social or home care reasons when oral therapy may otherwise be sufficient.

The guidelines from the American Thoracic Society (ATS) use a less complex system in evaluating risk factors relative to antibiotic selection.^[15] These consist of modifying factors, such as age greater than 65 years, recent antibiotic therapy, alcoholism, immunosuppressive illnesses, corticosteroid therapy, multiple comorbidities, malnutrition, and nursing home or day-care exposure. They, too, recommend empiric therapy based in part on hospitalization, but they add consideration of underlying cardiopulmonary disease or modifying factors. [Table 3](#) summarizes the ATS recommendations for empiric antibiotic therapy. They are similar to those of the IDSA but do not restrict parenteral therapy to the inpatient setting.

Numerous other organizations have written guidelines for the evaluation and management of CAP.^[16,17] They vary considerably, depending on geographic location and antibiotics used over time. In addition to these variations in guidelines, there are problems with the application of the guidelines. Despite all the work put into developing them, it turns out they are often not used.^[18] This may be a result of their complexity for the primary care physician, who may not see pneumonia frequently. It may also reflect an uncertainty as to which guidelines are the best ones to follow.

There are also seasonal and local factors, such as antimicrobial resistance and differing pathogens, that make it difficult to apply general rules to an individual situation. Knowledge of local antibiotic susceptibility patterns may be helpful. Application of guidelines is most practical in areas where pneumonia is a frequent finding, such as in emergency departments and when used by admitting hospitalists. Making guidelines readily available on office desktop and handheld computers may also be helpful, especially if they are incorporated as part of an electronic medical record or ordering system.

Changing physician prescribing practices is not easy; publications and education are not enough. Difficulties encountered when attempting to change physician prescribing patterns with regard to guidelines often lead to more restrictive approaches, such as limiting formularies, substitutions by the pharmacy department, and antibiotic credentialing. Another approach is to gather outcomes data on an ongoing basis and provide continuous feedback to physicians with results from a registry.^[19] Hospital or managed care campaigns with chart reviews and interventions may also be helpful.

Summary

Diagnosis and management of CAP can be improved by the use of rapid diagnostic tests, analyses of outcomes with large databases, practice guidelines, and application of technology to help clinicians in decision making. Information technology is providing real outcomes data to analyze and apply, and managed care is pressuring the medical community to understand what is cost-effective. Outpatient services are increasingly available, and OPAT is an increasingly routine option. Practice guidelines have been created and are available on the Internet.

The complexity of decisions seems to be increasing as we gather more and more information, learn from our experience, and work to incorporate new tools and treatment options for CAP diagnosis and management. Further studies are needed to explore the value of OPAT for patients who would otherwise be hospitalized, to establish when it is safe to use oral antibiotics, and to determine how best to use antimicrobial agents within the context of developing patterns of resistance.

Tables

Table 1. Risk classes, mortality rates, and site-of-service recommendations for patients with CAP*

Risk class	Number of points[†]	Number of patients	Mortality (%)	Recommended site of service
I	No predictors	3034	0.1	Outpatient
II	<= 70	5778	0.6	Outpatient
III	71 - 90	6790	2.8	Outpatient or brief inpatient
IV	91 - 130	13,104	8.2	Inpatient
V	> 130	9333	29.2	Inpatient

CAP, community-acquired pneumonia.

*Based on 38,039 inpatients with CAP prospectively enrolled in the Pneumonia Patient Outcomes Research Team (PORT) cohort study to independently validate the Pneumonia PORT prediction rule.

[†]As allocated to all patients not assigned to class I, and based on demographic variables, comorbid conditions, findings on physical examinations, and laboratory/radiographic findings.

Adapted from Bartlett JG et al. Clin Infect Dis. 2000.^[2] Original copyright © 2000, University of Chicago.

Table 2. Infectious Diseases Society of America recommendations for generally preferred empiric antibiotic therapy in patients with CAP

Outpatients

Doxycycline

Macrolide

Fluoroquinolone

Hospitalized -- general medicine

Extended-spectrum cephalosporin with a macrolide

β -Lactam/ β -lactamase inhibitor with a macrolide

Fluoroquinolone

Hospitalized -- ICU

Extended-spectrum cephalosporin

β -Lactam/ β -lactamase inhibitor plus a fluoroquinolone or a macrolide

CAP, community-acquired pneumonia. Adapted from Bartlett JG et al. Clin Infect Dis. 2000.^[2] Original copyright © 2000, University of Chicago.

Table 3. American Thoracic Society recommendations for preferred empiric antibiotic selection in patients with CAP

Outpatients without cardiopulmonary disease or modifying factors*

Azithromycin
Clarithromycin
Doxycycline

Outpatients with cardiopulmonary disease or modifying factors*

β -Lactam (oral or parenteral ceftriaxone) plus a macrolide/doxycycline
Fluoroquinolone alone

Hospitalized patients with cardiopulmonary disease or modifying factors*

Intravenous β -lactam plus a macrolide/doxycycline or a fluoroquinolone alone.

CAP, community-acquired pneumonia.

*Modifying factors: age > 65 years, recent antibiotic therapy, alcoholism, immunosuppressive illness, corticosteroid therapy, multiple comorbidities, nursing home or day-care exposure, malnutrition.

Adapted from Niederman MS et al. *Am J Respir Crit Care Med*.^[15]

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