Management of Hospital-Acquired Pneumonia at a Tertiary-Care Teaching Hospital

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ABSTRACT

Background: The rising resistance of pathogens commonly implicated in hospital-acquired pneumonia to currently recommended empiric therapy may necessitate a change in the management of this condition.

Objective: To determine the current therapeutic approach to the management of hospital-acquired pneumonia at an urban tertiary care hospital and to determine the need for a change to the institution's guidelines, according to patterns of bacterial culture and sensitivity.

Methods: A chart review was performed to identify patients in whom hospital-acquired pneumonia was diagnosed between January 1 and December 31, 2003.

Results: The charts of 50 patients (15% of the 325 patients with a diagnosis of hospital-aquired pneumonia) were reviewed. Most patients (43 or 86%) had stayed on a ward, and the overall mean age was 77 years. The initial choice of antimicrobial regimen was selected empirically for 41 (82%) of the patients; levofloxacin 500 mg daily was the most commonly chosen single agent (15/41 or 37%). Ceftriaxone was also chosen frequently (10/41 or 24%) for the empiric management of hospital-acquired pneumonia. For patients whose therapy was culture-directed, the most commonly chosen agent was ciprofloxacin (5/9 or 56%). Sputum samples were obtained from 19 of the patients, and 3 species of bacteria were each cultured in more than 15% of these 19 samples: methicillin-sensitive *Staphylococcus aureus* (MSSA) (3/19 or 16%), *Hemophilus influenzae* (4/19 or 21%), and *Serratia marcescens* (3/19 or 16%).

Conclusions: MSSA, *Hemophilus influenzae*, and *Serratia marcescens* were the most common causes of hospital-acquired pneumonia at this institution, but multidrug-resistant strains of these problematic organisms were not a concern. Therefore, broad-spectrum antibiotics, such as carbapenems, ceftazidime, and ciprofloxacin may be reserved for targeted use in appropriate patients. These agents should not be used in the routine empiric management of hospital-acquired pneumonia in the authors' institution at this time.

Key words: hospital-acquired pneumonia, pathogens, treatment

RÉSUMÉ

Historique : La résistance croissante des agents pathogènes généralement mis en cause dans la pneumonie nosocomiale au traitement empirique actuellement recommandé pourrait commander un changement dans la prise en charge de cette affection.

Objectif : Déterminer l'approche thérapeutique actuelle dans la prise en charge de la pneumonie nosocomiale au sein d'un hôpital urbain de soins tertiaires ainsi que la nécessité de modifier les lignes directrices de l'établissement selon les antibiogrammes.

Méthodes : Une analyse des dossiers médicaux de patients chez qui l'on a diagnostiqué une pneumonie nosocomiale entre le 1er janvier et le 31 décembre 2003 a été effectuée.

Résultats : Les dossiers de 50 patients ont été examinés (15 % des 325 patients avec un diagnostic de pneumonie nosocomiale). L'âge moyen des patients était de 77 ans et la plupart d'entre eux (43 ou 86 %) avaient séjourné dans un service hospitalier. L'antibiothérapie a été sélectionnée de façon empirique chez 41 (82 %) des patients; la lévofloxacine administrée à raison de 500 mg par jour était l'antibiotique le plus souvent choisi (15 patients sur 41 ou 37 %). La ceftriaxone était également choisie souvent (10 patients sur 41 ou 24 %) pour le traitement empirique de la pneumonie nosocomiale. Chez les patients dont le traitement était fondé sur les résultats de la culture, l'antibiotique le plus souvent retenu était la ciprofloxacine (5 patients sur 9 ou 56 %). Des échantillons de crachat ont été prélevés chez 19 des patients et trois souches de bactéries ont été chacune cultivées dans plus de 15 % des 19 échantillons : *Staphylococcus aureus* sensible à la méthicilline (3 échantillons sur 19 ou 16 %), *Haemophilus influenzae* (4 échantillons sur 19 ou 21 %) et *Serratia marcescens* (3 échantillons sur 19 ou 16 %).

Conclusions : *S. aureus* sensible à la méthicilline, *Haemophilus influenzae* et *S. marcescens* étaient les principaux agents pathogènes responsables de la pneumonie nosocomiale dans cet établissement, et les souches de ces microorganismes résistantes à de multiples antibiotiques ne posaient pas problème. Par conséquent, les antibiotiques à large spectre, comme les carbapénèmes, la ceftazidime et la ciprofloxacine peuvent être réservés pour un usage ciblé chez des patients choisis. Ces agents ne devraient pas être utilisés comme traitement empirique systématique de la pneumonie nosocomiale dans cet établissement pour le moment.

Mots clés : pneumonie nosocomiale, agents pathogènes, traitement

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INTRODUCTION

Hospital-acquired pneumonia (HAP) is defined as the clinical development of pneumonia occurring at least 48 hours after admission to hospital and not incubating at the time of admission.[1] The lungs are the third most common site of nosocomial infections (after the urinary tract and the bloodstream).[2] HAP accounts for 31% of all nosocomial infections and affects 0.5% to 2.0% of all hospital inpatients.[3] HAP is a major cause of morbidity and mortality among hospital patients. All-cause mortality among patients with HAP has been reported at up to 70%.[4] However, most patients who are critically ill with HAP and subsequently die have an underlying severe illness that is ultimately the cause of death. Therefore, a more accurate estimate of the mortality directly attributable to HAP ranges from 33% to 50%.[4] Development of HAP prolongs the hospital stay by an estimated 7 to 9 days.[5] Because of its frequency and considerable morbidity and mortality, HAP is a major health problem.

Organisms colonizing the oropharynx of hospital patients represent the most common cause of HAP. Such organisms may include E*nterobacter* spp., *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Serratia marcescens*, *Hemophilus influenzae*, *Pseudomonas aeruginosa*, *Acinetobacter* spp., methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), and *Streptococcus pneumoniae*.[6] The spectrum of potential pathogens in a particular case may be predicted by evaluating factors such as severity of the pneumonia, presence of comorbid conditions, previous use of antibiotics, and length of hospital stay.[7]

At the authors' institution, an 1100-bed university-affiliated tertiary care hospital in Toronto, Ontario, with approximately 16 800 admissions each year and an average length of stay of 8.5 days, the currently recommended empiric therapy for HAP in a ward patient is ceftriaxone. According to long-term antimicrobial resistance data collected by the Department of Microbiology, Sunnybrook and Women's College Health Sciences Centre, resistance to ceftriaxone in *Klebsiella pneumoniae* at this institution climbed from 4% in 1998 to 15% in 2003. A similar trend was seen for both *Enterobacter* spp., with a rise in resistance from 10% in 1998 to 55% in 2002, and *Serratia marcescens*, with a rise in resistance from 0% in 2001 to 55% in 2002. The changing resistance patterns of these organisms may necessitate a change in the empiric management of HAP. As a result of evidence indicating a higher risk of death among patients with HAP for whom appropriate empiric antibiotic therapy is delayed, the initial use of broad-spectrum antibiotics followed by de-escalation therapy when culture and sensitivity results become available has been recommended.[8] The appropriate choice of empiric antimicrobial therapy requires an awareness of potential causative pathogens, antibiotic susceptibility data, and host factors that may contribute to infections or development of resistance in a given institution.

The objectives of this study were to determine the current approach to management of patients with HAP at the authors' hospital and to determine if there was a need to change the institution's guidelines for the empiric management of HAP.

METHODS

Study Design and Data Collection

This chart review was approved by the Research Ethics Board, Sunnybrook and Women's College Health Sciences Centre. All patients with a chart-documented diagnosis of HAP who had been patients at the hospital between January and December 2003 and who had been discharged or had died during this period were eligible for inclusion. Patients with a diagnosis of HAP were identified on the basis of code 486 for pneumonia and type 2 diagnosis (i.e., conditions acquired after admission to hospital) of the International Classification of Diseases revision 10 (ICD-10). For each month of 2003, the charts of 4 or 5 patients who had been discharged in that month were arbitrarily selected by Health Data Resource staff for review, to ensure an even distribution of patients throughout the 2003 calendar year. A total of 50 charts were reviewed.

Information collected from each chart included patient demographic characteristics, past medical history (comorbid conditions and antimicrobial use within 3 months before the diagnosis of HAP), choice of empiric antimicrobial regimen, culture and sensitivity results, changes in treatment regimen, duration of therapy, clinical outcome, and length of hospital stay. The medical or surgical service to which the patient had been admitted was documented to facilitate comparison of microbiological data between the critical care setting and the ward setting. Resolution of HAP was assessed by the following criteria:

- clinical outcome (cure assessed by chart documentation of resolution of fever, cough, sputum purulence and volume, and leukocytosis and discontinuation of antimicrobials versus death due to infection versus death due to any cause)
- culture and sensitivity results (eradication of causative pathogens or need to change antimicrobial therapy)
- resolution (improvement in pulmonary infiltrate on chest radiography)

Statistical Analysis

A convenience sample of 50 patients (15%) was selected from the 325 patients in whom HAP was diagnosed during the period January 1 to December 31, 2003. Descriptive statistics, including measures of central tendency (mean, median, mode) and measures of variation (standard deviation), were calculated (using Microsoft Excel 2000).

RESULTS

A total of 50 patient charts were reviewed. The mean patient age was 77 years (median 78 years; range 36 to 95 years), and 46% of the patients were women (Table 1). Forty-three (86%) of the patients had been treated on a ward and the remainder of the patients, in critical care units. The majority of patients had more than one comorbid condition, with cardiac disease predominating (37 [74%] of the patients). Twenty-four (48%) of the patients had a history of antibiotic use within 3 months before the diagnosis of HAP. The antimicrobial agents most commonly administered within 3 months preceding diagnosis of HAP were ß-lactams (20/24 or 83%), fluoroquinolones (14/24 or 58%), and agents active against oral and gut anaerobic organisms (13/24 or 54%).

On average, HAP was diagnosed on the eighth day of admission (median 6 days, range 1 to 29 days). Late-onset HAP, defined as occurring 5 or more days after hospital admission, was observed in 34 (68%) of the patients.

The diagnosis of HAP was based on clinical, laboratory, and radiologic evidence in 19 (38%) cases. Sputum was obtained for culture from 19 patients, and the result was positive for 14 patients (74%) (for some of whom more than one organism was isolated). For most patients, the organisms isolated were gram-negative bacilli, including *Hemophilus influenzae* (4 patients), *Serratia marcescens* (3), *Klebsiella* spp. (2), *Pseudomonas* spp. (2), *Acinetobacter* spp. (1), *Escherichia coli* (1), *Moraxella catarrhalis* (1), and *Morganella morganii* (1). MSSA (a gram-positive organism) was isolated from 3 samples.

Blood was taken for culture from 41 patients, and the result was positive for 7 (17%) of these patients. The following organisms were isolated from blood: MSSA (3 patients), *Klebsiella* spp. (2), *Bacteroides fragilis* (1), *Enterococcus faecalis* (1), *Proteus mirabilis* (1), and *Serratia marcescens* (1). There was no concordance between sputum cultures and blood cultures, which indicates that the positive blood culture results might have reflected concurrent infections.

The initial choice of antimicrobial regimen was selected empirically for 41 patients (82%) (Table 2). Levofloxacin was the most commonly chosen single agent (15/41 or 37%) for initial empiric therapy. All patients who received levofloxacin empirically were situated in a ward setting rather than a critical care setting. Ceftriaxone was also chosen frequently as empiric therapy (10/41 or 24%). Other empiric choices included first- and second-generation cephalosporins, macrolides, fluoroquinolones, vancomycin, and combination therapy with agents that are active against anaerobic organisms (i.e., clindamycin or metronida-

Table 1. Characteristics of 50 Patients with Hospital-Acquired Pneumonia

Characteristic	No. (and %)*
Age†	77 (13, 78, 36–95)
Sex (no. and % of women)	23 (46)
Floor	
Ward	43 (86)
Critical care units	7 (14)
Past medical history	
Cardiac	37 (74)
Malignancy	16 (32)
Musculoskeletal	14 (28)
Respiratory	13 (26)
Endocrine	12 (24)
Gastrointestinal	11 (22)
Psychiatric	11 (22)
Neurologic	9 (18)
Renal	4 (8)
Dermatologic	2 (4)
Other	9 (18)
Reason for admission	
Cardiac	10 (20)
Surgery‡	10 (20)
Malignancy	8 (16)
Stroke	7 (14)
Fracture	3 (6)
Gastrointestinal	2 (4)
Infection	2 (4)
Chronic lung disease	1 (2)
Trauma	1 (2)
Other	6 (12)
Antibiotics used recently§	24 (48)
ß-Lactams	20 (83)
Fluoroquinolones	14 (58)
Agents with anaerobic coverageǁ	13 (54)
Aminoglycosides	4 (17)
Vancomycin	1 (4)
Sulfonamides	1 (4)
Other	1 (4)

*Unless indicated otherwise.
†Mean (standard deviation, median, range).
‡Cardiac surgery for 6 patients, neoplastic surgery for 4 patients.
§Recent antibiotic use is defined as use of any antibiotics within 3 months preceding diagnosis of hospital-acquired pneumonia.
ǁAnaerobic coverage refers to coverage for both oral and gut anaerobes.

Table 2. Initial Selection of Antimicrobials for the Management of Hospital-Acquired Pneumonia

Regimen	No. (%) of patients
Initial antimicrobial selection (*n* = 50)	
Empiric	41 (82)
Culture-directed	9 (18)
Empiric regimen selected (*n* = 41)	
Monotherapy	
Fluoroquinolones	17 (41)
Levofloxacin	15 (37)
Ciprofloxacin	2 (5)
Cephalosporins	13 (32)
Ceftriaxone	10 (24)
Cefuroxime	2 (5)
Ceftazidime	1 (2)
Macrolides	2 (5)
Other	2 (5)
Combination therapy	1 (2)
Fluoroquinolone + ß-lactam or anti-anaerobic agent	2 (5)
Second- or third-generation cephalosporin + macrolide or anti-anaerobic agent	5 (12)
Culture-directed regimen selected (*n* = 9)	
Ciprofloxacin	5 (56)
Cefazolin + fluoroquinolone or aminoglycoside	4 (44)

Table 3. Characteristics of Antibiotic Therapy

Characteristic of Therapy	No. (%) of patients*
Changed during hospital stay (*n* = 50)	
Yes	37 (74)
No	13 (26)
Rationale for changes in therapy (*n* = 37)	
PO step-down	10 (27)
Culture and sensitivity results	6 (16)
Suspected aspiration	6 (16)
Clinical improvement	3 (8)
Concurrent infection	2 (5)
Renal dose adjustment	2 (5)
Clinical worsening	1 (3)
Hypersensitivity	1 (3)
Unknown	6 (16)
Length of treatment (days)†	
In hospital	8 (5.7, 7, 1–27)
Total	10 (6.2, 8, 1–27)
Length of hospital stay†	24 (23.9, 17, 4–129)

PO = by mouth.
*Unless indicated otherwise.
†Mean (standard deviation, median, range).

Table 4. Outcomes for 50 Patients Treated for Hospital-Acquired Pneumonia

Outcome	No. (%) of patients
Time to defervescence	
Afebrile throughout	27 (54)
<3 days	16 (32)
4–7 days	5 (10)
>7 days	2 (4)
Clinical outcome	
Cure	34 (68)
Death	16 (32)

zole). In patients whose therapy was directed by the culture results, the most commonly chosen agent was ciprofloxacin (5/9 or 56%).

On average, the duration of hospital stay was 24 days (range 4 to 129 days). Patients were treated with antimicrobial agents for HAP for an average of 8 days in hospital. Thirty-seven (74%) patients had a change in their antimicrobial regimen during their hospital admission (Table 3). The most common reason for an alteration in therapy was oral step-down of the antimicrobial agents (10/37 or 27%).

Twenty-seven patients (54%) were afebrile throughout the course of the infection (Table 4). In the remaining patients, time to defervescence ranged from 1 to 18 days once antibiotic therapy was initiated. A cure of the pneumonia was achieved in 34 patients (68%).

DISCUSSION

At the authors' institution, the currently recommended choice of empiric therapy for HAP in patients outside the intensive care unit is ceftriaxone. However, this recommendation is not being followed. Levofloxacin 500 mg daily was in fact the most commonly prescribed empiric therapy for HAP. At the time of this study, levofloxacin did not appear in the institution's HAP management guidelines. However, in a recently published evaluation, West and others[9] concluded that levofloxacin 750 mg daily was at least as effective and well tolerated as imipenem–cilastatin followed by oral ciprofloxacin for the treatment of nosocomial pneumonia in adults. Although the small retrospective analysis reported here indicates that levofloxacin 500 mg daily may be effective in the treatment of nosocomial pneumonia, confirmation of these results with a prospective, randomized design (comparing levofloxacin 500 mg daily and levofloxacin 750 mg daily) to assess microbiological outcome, clinical outcome, safety, and risk of organisms developing resistance would be necessary before any recommendations could be made concerning the use of levofloxacin 500 mg for HAP.

Antimicrobial susceptibility surveillance data for this institution showed rising resistance in *Klebsiella pneumonia*, *Enterobacter* spp., and *Serratia marcescens*. In contrast, the results reported here indicate that of

these potentially problematic organisms, only *Serratia marcescens* caused HAP with an incidence of greater than 5%. At this time, it does not appear that either *Klebsiella pneumoniae* or *Enterobacter spp.* are commonly implicated as causes of HAP at this institution. The only bacteria seen in more than 15% of sputum culture samples were MSSA (3/19 or 16% of samples), *Hemophilus influenzae* (4/19 or 21% of samples), and *Serratia marcescens* (3/19 or 16% of samples). Sensitivity testing of *Serratia marcescens* to ceftriaxone is no longer reported at this institution because ceftriaxone would not routinely be selected for use against this pathogen. There were no outbreaks of problematic bacteria (e.g., MRSA or extended-spectrum ß-lactamase-producing gram-negative bacilli [ESBL]) during this study.

Although either ceftriaxone or levofloxacin appears to be a reasonable initial empiric agent for the management of HAP at this institution, the findings of MSSA and *Serratia marcescens* in 16% of positive cultures indicate that culture and sensitivity information may be important in guiding antimicrobial management. Given the sensitivity profiles of the 3 organisms seen most often in patients with HAP at this institution, multidrug-resistant strains are not yet a concern. Therefore, it is not yet necessary to broaden the current spectrum of empiric coverage to include agents active against multidrug-resistant bacteria (e.g., carbapenems).

All-cause mortality in the patients reviewed was approximately 32%, which is in keeping with HAP-attributed mortality figures of 33% to 50% reported elsewhere.[4] The mortality attributable to HAP could not be determined because information regarding the cause of death was not consistently documented in the charts.

The major limitations of this study were the retrospective design and the small sample size.

In conclusion, the most commonly identified causes of HAP at this institution were *Staphylococcus aureus*, *Hemophilus influenzae*, and *Serratia marcescens*. Multidrug-resistant strains of these organisms are not yet a concern. Therefore, broad-spectrum antibiotics, such as carbapenems, ceftazidime, and ciprofloxacin, should not be used in the routine empiric management of ward patients with HAP at the authors' institution at this time. This study highlights the importance of incorporating antimicrobial use patterns, patient demographic characteristics, and occurrence of pathogenic organisms and their antimicrobial susceptibility in the development of institution-specific recommendations for the treatment of HAP. A larger interventional study is needed to assess the clinical efficacy of levofloxacin 500 mg daily for HAP.

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