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

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ABSTRACT

Background: An algorithm for managing inpatients with community-acquired pneumonia was implemented at Sunnybrook Health Sciences Centre in January 2002.

Objectives: To determine whether the evidence-based treatment algorithm adopted by the hospital was being followed, to identify the current therapeutic approach (or approaches) to managing patients with community-acquired pneumonia at this particular hospital, and to determine the need for revision of current institutional guidelines, according to clinical outcome and patterns of microbiological culture and sensitivity data, in the absence of updates to published guidelines at the time the study was undertaken.

Methods: The charts of all patients admitted to hospital with a diagnosis of community-acquired pneumonia between January 1, 2002, and December 31, 2005, were reviewed.

Results: Sixty-two (93%) of the 67 patients identified were eligible for inclusion. Their mean age was 67 years, 48 (77%) of them had presented from home, 52 (84%) were treated on the ward, and 37 (60%) had a pneumonia severity index of IV or V. Of the 59 patients whose initial antimicrobial regimen was selected empirically, 33 (56%) had received either empiric ß-lactam plus macrolide (18/59) or levofloxacin monotherapy (15/59), as recommended by the institution's guideline; there was no difference between these regimens in terms of frequency of use ($p > 0.05$). Empiric treatment with fluoroquinolone monotherapy was less expensive than appropriate non-guideline-based therapy ($p < 0.05$). Clinical cure was achieved for 51 (82%) of the patients. *Streptococcus pneumoniae* and *Hemophilus influenzae* were the organisms most commonly isolated from patients admitted to this hospital for treatment of community-acquired pneumonia.

Conclusions: The results reported here highlight the importance of conducting a quality assurance study to identify whether evidence-based guidelines for community-acquired pneumonia that have been implemented at an institution are actually being used. Furthermore, when considering the need to revise institution-specific recommendations for the treatment of patients with community-acquired pneumonia who must be admitted to hospital, and in the absence of recently published guidelines, it is important to evaluate institution-specific patient characteristics; patterns, duration, appropriateness, clinical outcome, and cost of antimicrobial therapy; and results of microbiological culture.

RÉSUMÉ

Historique : Un algorithme de prise en charge des patients atteints d'une pneumonie extra-hospitalière (PEX) a été mis en place au Sunnybrook Health Sciences Centre en janvier 2002.

Objectifs : Déterminer si l'algorithme de traitement de la PEX fondé sur les données probantes mis en place à l'hôpital était suivi, définir l'approche ou les approches thérapeutiques actuelles des patients atteints de PEX à cet établissement particulier, et évaluer le besoin de revoir les lignes directrices ayant cours à cet établissement, d'après les résultats cliniques et les particularités des cultures microbiologiques et des antibiogrammes, en l'absence de mises à jour des lignes directrices publiées au moment de l'étude.

Méthodes : Les dossiers médicaux de tous les patients hospitalisés par suite d'un diagnostic de PEX entre le 1er janvier 2002 et le 31 décembre 2005 ont été examinés.

Résultats : En tout, 93 % (62/67) des patients répertoriés étaient admissibles à l'étude. L'âge moyen des patients de l'étude était de 67 ans; 48 (77 %) de ces 62 patients arrivaient de leur domicile, 52 (84 %) ont été traités dans un service hospitalier et 37 (60 %) présentaient un indice de gravité de la pneumonie de IV ou V. Des 59 patients chez qui l'antibiothérapie initiale a été déterminée de façon empirique, 33 (56 %) avaient reçu une bêta-lactamine plus un macrolide (18/59) ou de la lévofloxacine en monothérapie (15/59), comme recommandé par les lignes directrices de l'établissement; on n'a observé aucune différence dans la fréquence d'utilisation de ces traitements ($p > 0,05$). La monothérapie empirique par la fluoroquinolone était moins dispendieuse que l'antibiothérapie appropriée déterminée sans égard aux lignes directrices ($p < 0,05$). La guérison clinique a été obtenue chez 51 (82 %) de ces patients. Streptococcus pneumoniae et Hemophilus influenzae étaient les principaux agents pathogènes qui ont été isolés chez les patients hospitalisés pour la traitement d'une PEX à cet hôpital.

Conclusions : Les résultats mettent en lumière l'importance de mener une étude d'assurance de la qualité afin de déterminer si les lignes directrices fondées sur les données probantes qui ont été mises en place dans un établissement pour le traitement de la PEX sont bel et bien utilisées. De plus, si l'on envisage de revoir les recommandations d'un établissement particulier relatives au traitement des patients présentant une PEX qui doivent être hospitalisés, et en l'absence de lignes directrices

Key words: community-acquired pneumonia, guidelines, empiric therapy

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publiées récemment, il est important d'évaluer les caractéristiques des patients spécifiques à cet établissement; les habitudes de prescription, la durée, la pertinence, les résultats cliniques et le coût de l'antibiothérapie; ainsi que les résultats des cultures microbiologiques.

Mots clés : pneumonie extra-hospitalière, lignes directrices, traitement empirique

INTRODUCTION

Community-acquired pneumonia is defined as an acute infection of the pulmonary parenchyma occurring in patients residing outside of a hospital or in patients who have been living in a long-term care facility for longer than 2 weeks.[1] This disease is a leading cause of morbidity and mortality in Canada.[1] In 2001, pneumonia and influenza together represented the seventh leading cause of death in the United States.[2] In that country, the annual incidence of community-acquired pneumonia is 12 to 18 cases per 1000 population, resulting in 600 000 to 1 million admissions to hospital and an estimated 40 000 to 60 000 deaths per year.[1,2] Because of comorbidities, elderly people account for the majority of admissions and deaths.[1] Approximately 80% of infected patients are treated as outpatients, with the remaining 20% requiring admission to hospital.[3] Depending on the presence of comorbid conditions, mortality rates associated with community-acquired pneumonia range from 1% to 30%,[1] and in-hospital mortality has been reported to range from 5% to more than 30%.[4,5] The overall economic impact of community-acquired pneumonia in the United States is estimated at US$8 billion.[1] Canadian hospital admissions, deaths, and costs may be estimated by applying a factor of 0.1 (10%) to these US population-based data. Because of the substantial mortality and morbidity, as well as the high incidence, community-acquired pneumonia remains a serious health issue for patients and society as a whole.

The etiology of community-acquired pneumonia is often unknown, and a pathogen is recovered in only 40% to 60% of all cases.[2] The most common pathogen found among patients requiring hospital admission is *Streptococcus pneumoniae* (17.3%), followed by *Mycoplasma pneumoniae* (13.7%), *Chlamydia pneumoniae* (10.1%), *Hemophilus influenzae* (6.6%), aerobic gram-negative bacilli (4.0%), *Staphylococcus aureus* (2.9%), and *Legionella pneumophila* (1.3%).[6] Multiple pathogens have been identified in 2% to 11%[7] and even up to 30%[8] of cases. The spectrum of potential pathogens in a particular case may be predicted by factors such as age, severity of the pneumonia, comorbidities, clinical risk factors, and community location (residential home versus nursing home).[9-11]

The mortality rate is higher if the initial antimicrobial treatment is inappropriate.[4] However, as noted above, the disease can be caused by a number of organisms. The causative organism cannot be identified by clinical and radiologic findings, and conventional microbiological findings lack sensitivity and specificity,[4] yet it has been shown that shorter time to diagnosis and treatment initiation results in a better prognosis.[4] Therefore, therapy is selected empirically at the time of diagnosis. The development of evidence-based guidelines for community-acquired pneumonia has assisted physicians in the selection of antibiotics and has reduced variability in clinical care.[4] The implementation of guidelines has led to shorter duration of total antibiotic treatment, fewer days on IV antibiotics, lower costs, and assurance of better coverage for atypical bacteria.[12] Adherence to evidence-based guidelines has been shown to decrease the number of hospital admissions, shorten the length of stay in hospital, and reduce the mortality rate.[4,13,14]

Recommendations for the treatment of community-acquired pneumonia in patients requiring admission to Sunnybrook Health Sciences Centre (known at the time as the Sunnybrook campus of Sunnybrook and Women's College Health Sciences Centre) were approved by the Medical Advisory Committee and implemented in January 2002. These recommendations

were based on published guidelines that were available in 2002 and that were not updated or replaced by other guidelines up to and including 2006. Specifically, the approved guidelines at our hospital included IV use of either cefuroxime or ceftriaxone in conjunction with oral or IV azithromycin or monotherapy with oral or IV levofloxacin.[6,15] Data on the frequency of selection of each management strategy, the cost associated with the use of each strategy, the clinical outcome, and microbiological data about the patient population were lacking. A quality assurance study to collect this type of information was important to determine whether reassessment of current recommendations was necessary to optimize patient care, in the absence of any update to published, evidence-based treatment guidelines from 2002 through 2006.

Therefore, given that adherence to evidence-based guidelines for community-acquired pneumonia is beneficial, the objectives of this study were to determine whether the evidence-based treatment guideline adopted by Sunnybrook Health Sciences Centre was being followed, to identify the current therapeutic approach (or approaches) to managing patients with community-acquired pneumonia at this hospital, and to determine the need for revision of current institutional guidelines, according to clinical outcome and patterns of microbiological culture and sensitivity data, in the absence of updates to published guidelines at the time the study was undertaken.

METHODS

Study Design and Data Collection

This chart review was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre in December 2005. Sunnybrook is a 1275-bed university-affiliated tertiary care hospital in Toronto, Ontario, with approximately 26 605 patient discharges per year and an average length of stay of 7 days. All patients with a chart-documented diagnosis of community-acquired pneumonia who had been patients at the hospital between January 1, 2002 (when the guidelines for treatment of community-acquired pneumonia were implemented), and December 31, 2005, and who had been discharged or had died during this period were eligible for inclusion. Because International Classification of Diseases (ICD) codes were revised during the patient eligibility period, patients admitted between January 1 and March 31, 2002, were identified by ICD-9 (ninth revision) codes for pneumonia (481 to 483.8), and patients admitted between April 1, 2002, and December 31, 2005, were identified by ICD-10 codes for pneumonia (J13, J14, J15-16.0, A48.1, and J17.0) and type M diagnosis (i.e., community-acquired pneumonia as most responsible diagnosis influencing the length of stay).

The following information was collected from each chart: patient demographic characteristics, past medical history (including comorbid conditions and past utilization of antimicrobials), patient factors that directed the requirement of hospital admission (i.e., patient factors necessary to determine pneumonia severity index; see Appendix 1), choice of empiric antibiotic therapy, results of culture and sensitivity testing, time to defervescence (defined as time to the first day that the patient remained afebrile for more than 24 h), duration of therapy, change in treatment regimen, length of hospital stay, total antimicrobial acquisition cost, and outcome. The medical ward or critical care setting to which the patient had been admitted was documented to note concordance or discordance with the patient triage location indicated by the pneumonia severity index. The empiric therapy selected for each patient was assessed to determine whether it was appropriate (i.e., concordant with the institution's guidelines). Empiric regimens that did not strictly fit the institution's guidelines were considered either appropriate or inappropriate non-guideline-based therapies on the basis of an evaluation of the patient's past medical history, initial pneumonia severity, and previous antibiotic utilization (within 6 months before admission). As examples, empiric antimicrobial therapy with levofloxacin and vancomycin for a patient admitted to hospital for community-acquired pneumonia and requiring *S. aureus* coverage secondary to transfer to the intensive care unit was identified as appropriate non-guideline-based therapy, whereas empiric treatment with ampicillin and ceftriaxone was considered inappropriate non-guideline-based therapy. The total antimicrobial acquisition cost for the treatment of community-acquired pneumonia was calculated for each patient. In addition, the cost of antimicrobials for guideline-based and non-guideline-based initial empiric management was determined. Costs for additional antimicrobial therapy for concurrent infections (e.g., urinary tract infection, *Clostridium difficile* infection) were not included. Resolution of community-acquired pneumonia was defined as any of the following clinical outcomes:

- Cure: Chart-documented resolution of infection or resolution of or improvement in signs and symptoms of community-acquired pneumonia, such as fever, crackles on auscultation, cough, sputum

purulence and volume, and leukocytosis, and discontinuation of antimicrobials.
- Death: Death due to infection or death due to any cause.
- Microbiological cure: Culture and sensitivity results indicating eradication of the causative organism(s).

Statistical Analysis

Descriptive statistics, including measures of central tendency (mean, median, mode) and measures of variation (standard deviation), were calculated with Microsoft Excel 2000. Nominal data were compared with either the χ^2 or Fisher exact tests. Interval data were compared with one-way analysis of variance (ANOVA) with a Tukey multiple-comparison post-test analysis or, when assumptions regarding Gaussian distribution or equal variance were not valid, the Kruskal–Wallis test (nonparametric one-way ANOVA) with a Dunn multiple-comparison post-test analysis) or, for comparisons of 2 groups of interval data in this setting, the Mann-Whitney test. A p value less than 0.05 was considered statistically significant for all comparisons. The appropriate multiple-comparison post-test was completed only when p was less than 0.05.

RESULTS

Sixty-seven eligible patients were identified by Health Data Resources staff. Upon review of the charts, a total of 5 patients were excluded; 2 of these had hospital-acquired pneumonia, 2 had pneumonia due to inhalation injury secondary to self-inflicted burns, and 1 was admitted solely for ventilation management of community-acquired pneumonia diagnosed and treated at another hospital. Therefore, a total of 62 charts documenting a diagnosis of community-acquired pneumonia were reviewed. The mean patient age was 67 years (median 71 years; range 20 to 95 years), and 18 (29%) of the patients were women (Table 1). Fifty-two (84%) of the patients had been treated on the ward, 3 (5%) had been treated on a high-intensity ward, and the remainder had been treated in the critical care unit. Thirty-seven (60%) of the patients had one or more risk factors for community acquired pneumonia. Immunocompromise (15 [41%] of these 37 patients) or residence in an institutional setting (13 [35%]) were the two most common risk factors. Forty-eight (77%) of the patients had presented from home. The majority of patients admitted for treatment had a pneumonia severity index of IV or V (37 [60%] of the patients). Of the 62 patients, 41 (66%) had concordance between the

Table 1. Characteristics of 62 Patients Admitted to Sunnybrook Health Sciences Centre with Community-Acquired Pneumonia between 2002 and 2005

Characteristic	No. (%) of Patients*
Age†	67 (18, 71, 20–95)
Women	18 (29)
Treatment location in hospital	
Ward	52 (84)
High-intensity ward	3 (5)
Critical care ward	7 (11)
Comorbidities or risk factors‡	37 (60)
Chronic obstructive pulmonary disease	2 (5)
Dementia§	4 (11)
Seizure disorder	5 (14)
Cigarette smoking	5 (14)
Congestive heart failure	3 (8)
Cardiovascular disease	8 (22)
Institutional setting	13 (35)
Alcoholism	4 (11)
Immunocompromise	15 (41)
Chronic infection due to gram-negative bacilli, secondary to respiratory condition (bronchiectasis and bronchitis)	1 (3)
Patient location before admission	
Home	48 (77)
Nursing home	7 (11)
Chronic care facility‖	3 (5)
Retirement home	3 (5)
Shelter for homeless people	1 (2)
Pneumonia severity index	
I	2 (3)
II	7 (11)
III	16 (26)
IV	22 (35)
V	15 (24)
Antibiotics used within 6 months before admission¶	22 (35)
ß-Lactams	17 (77)
Clindamycin	2 (9)
Fluoroquinolones	12 (55)
Macrolides	10 (45)
Metronidazole	1 (5)
Sulfonamides	3 (14)
Vancomycin	2 (9)

*Unless indicated otherwise.
†Mean (standard deviation, median, range).
‡Percentages for specific comorbidities or risk factors are based on a denominator of 37. Some patients had more than one comorbidity, so the sum of patients with specific comorbidities is greater than 37.
§One patient had a chart-documented history of Alzheimer disease.
‖Chronic care wing of a tertiary health care centre (Sunnybrook Health Sciences Centre).
¶Percentages for specific antibiotics are based on a denominator of 22. Some patients had taken more than one antibiotic in the 6 months before admission, so the sum of patients who took specific drugs is greater than 22.

treatment location indicated by the pneumonia severity index and the patient's actual hospital location on admission. Twenty-two (35%) of the patients had a history of using one or more antibiotics within 6 months before presentation with community-acquired pneumonia. The most commonly used antibiotics in the 6 months before hospital admission were ß-lactams (17/22 or 77%), fluoroquinolones (12/22 or 55%), and macrolides (10/22 or 45%).

In 36 (58%) of the cases, the diagnosis of community-acquired pneumonia was based on clinical, radiologic, and laboratory evidence. Sputum cultures were obtained from 49 (79%) of the patients, and the results were positive for 31 (63%) of these (Table 2). Thirteen (21%) of the 62 patients did not have samples taken for sputum culture at the time of admission: 5 patients had insufficient sputum production; 3 patients had received a few days to a week of outpatient antimicrobial therapy before admission; 1 patient had received a dose of an antimicrobial upon admission; 1 patient had undergone drainage of pleural effusion with subsequent growth of coagulase-negative staphylococci, which was deemed insignificant by an infectious disease consultant; 1 patient had Hodgkin's lymphoma that was treated aggressively; 1 patient was unstable, received a course of antibiotic therapy, and died from asystolic arrest; and for 1 patient there was no indication of why a sputum culture had not been done. The most common organism isolated from sputum was *S. pneumoniae* (13/49 or 27%). The only gram-negative bacillus that was isolated from the sputum of more than 10% of patients was *H. influenzae* (6/49 or 12%). *Pseudomonas aeruginosa* (4/49 or 8%) and *Klebsiella pneumoniae* (2/49 or 4%) were isolated from a smaller number of patients.

Samples for blood culture were obtained from 57 (92%) of the patients, and the result was positive for 27 (47%) of these patients (Table 2). The only organism that was isolated from more than 10% of the patients with a sample for blood culture was *S. pneumoniae* (18/57 or 32%). Other bacteria isolated from blood samples are listed in Table 2. Samples for both sputum and blood culture were obtained from 44 (71%) of the patients (Table 2). The only organism isolated from both sputum and blood of individual patients was *S. pneumoniae* (3 or 7% of patients). Seven (16%) of the patients with both blood and sputum samples had no growth in either medium. Thirty-four (77%) of the patients had sputum and blood culture results that did not match. For example, for one patient, *H. influenzae* was grown from the sputum sample, but no organisms

Table 2. Microbiological Data for 62 Patients Treated for Community-Acquired Pneumonia at Sunnybrook Health Sciences Centre between 2002 and 2005

Culture Result	No. (%) of Patients
Sputum sample for culture (*n* = 62)	
Yes	49 (79)
No	13 (21)
Microbiological culture of sputum (*n* = 49)	
Monomicrobial	28 (57)
Candida sp.	1 (2)
Escherichia coli	1 (2)
Hemophilus influenzae, ß-lactamase negative	5 (10)
Hemophilus influenzae, ß-lactamase positive	1 (2)
Klebsiella pneumoniae	2 (4)
Pseudomonas aeruginosa	4 (8)
MSSA	1 (2)
Streptococcus pneumoniae	13 (27)
Polymicrobial	3 (6)
Candida sp. + MRSA	1 (2)
Pseudomonas aeruginosa + MRSA	1 (2)
MRSA + Group B ß-hemolytic *Streptococcus*	1 (2)
No growth*	18 (37)
Blood sample for culture (*n* = 62)	
Yes	57 (92)
No	5 (8)
Microbiological culture of blood (*n* = 57)	
Coagulase-negative *Staphylococcus epidermidis*	2 (4)
Escherichia coli	1 (2)
Group B ß-hemolytic *Streptococcus*	1 (2)
Group C ß-hemolytic *Streptococcus*	1 (2)
Hemophilus influenzae, ß-lactamase negative	1 (2)
Klebsiella pneumoniae	1 (2)
MRSA	1 (2)
MSSA	1 (2)
Streptococcus pneumoniae	18 (32)
No growth	30 (53)
Blood and sputum samples for culture (*n* = 62)	
Yes	44 (71)
No	18 (29)
Microbiological culture of both blood and sputum (*n* = 44)	
Streptococcus pneumoniae	3 (7)
No growth	7 (16)
Other†	34 (77)

MSSA = methicillin-sensitive *Staphylococcus aureus,*
MRSA = methicillin-resistant *Staphylococcus aureus.*
*For one patient the sputum sample had a negative result, but bronchoalveolar lavage yielded *Legionella*.
†For these patients, a combination of microbiological organisms was found in the sputum and blood cultures (e.g., *Hemophilus influenzae* [ß-lactamase positive] in sputum and no growth in blood).

were cultured from the blood sample. No sputum or blood samples grew penicillin-resistant *S. pneumoniae*, and no sputum samples grew macrolide-resistant *S. pneumoniae*. The occurrence of macrolide-resistant *S. pneumoniae* in blood and of fluoroquinolone-resistant *S. pneumoniae* in sputum and blood was unknown, since these types of testing are not routinely performed at this institution.

The average length of stay was 14 days (range 2 to 147 days). Patients were treated in hospital with antimicrobial agents for an average of 9 days (range 2 to 36 days). Fifty-nine (95%) of the patients had a change in antimicrobial regimen during the hospital admission (Table 3). The most common reason for a change in therapy was oral step-down of the antimicrobial agents (32/59 or 54%).

Fifteen (24%) of the patients were afebrile throughout the course of the infection (Table 3). For patients who were febrile on admission, the time to defervescence ranged from 1 to 16 days once antibiotics were initiated. Cure of the pneumonia was achieved in 51 (82%) patients. Nine patients (15%) died, 6 (10% of the total sample) as a result of the infection.

The initial antimicrobial regimen was selected empirically for 59 (95%) of the patients, and 3 (5%) patients received culture-directed antimicrobial therapy (Table 4). The patients whose therapy was directed by culture results received ceftriaxone (1 patient) or either ceftriaxone or ceftazidime combined with ciprofloxacin (2 patients). Thirty-three (56%) of 59 patients received appropriate empiric therapy according to the institution's guidelines. Adherence to these guidelines for patients admitted during the study period was 50% (11/22) in 2002, 55% (6/11) in 2003, 60% (9/15) in 2004, and 64% (7/11) in 2005 ($p = 0.60$). The most commonly selected single agent for initial empiric therapy was levofloxacin (15/59 or 25%). All of the patients who received levofloxacin empirically were admitted to the ward rather than to a critical care setting, but 4 (27%) of the 15 should have been admitted to the intensive care unit on the basis of their pneumonia severity index. A second- or third-generation cephalosporin plus a macrolide was the most commonly selected combination therapy used for initial empiric treatment (18/59 or 31%). Cefuroxime was frequently chosen as the empiric cephalosporinin in combination with azithromycin (10/18 or 56%). Appropriate non-guideline-based antibiotics were selected as empiric initial therapy in 25% (15/59) of patients. Therefore, 81% (48/59) of overall empiric antibiotic therapy was assessed as appropriate.

Table 3. Characteristics of Antibiotic Therapy for 62 Patients Treated for Community-Acquired Pneumonia at Sunnybrook Health Sciences Centre between 2002 and 2005

Characteristic of Therapy	No. (%) of Patients*
Changed during hospital stay (*n* = 62)	
Yes	59 (95)
No	3 (5)
Rationale for change in therapy† (*n* = 59)	
Oral step-down	32 (54)
Clinical improvement	27 (46)
Culture and sensitivity results	25 (42)
To broaden antibiotic coverage	9 (15)
Recommendation of infectious diseases consultant	8 (14)
Worsening of clinical condition	6 (10)
Antibiotic-associated diarrhea	5 (8)
Stool positive for *Clostridium difficile* toxin	3 (5)
Renal dose adjustment	3 (5)
Suggestion of pharmacist	3 (5)
Concurrent infection	2 (3)
Unknown	5 (8)
Duration of antibiotic therapy (days)‡	
In hospital	9 (6, 7, 2–36)
Total§	13 (5, 13, 2–36)
Length of hospital stay (days)‡	14 (21, 8, 2–147)
Time to defervescence (*n* = 62)	
Afebrile throughout	15 (24)
≤ 3 days	28 (45)
4–7 days	12 (19)
> 7 days	7 (11)

*Unless indicated otherwise.
†For some patients, there was more than one reason for a change in antibiotic therapy during the hospital stay.
‡Mean (standard deviation, median, range).
§Includes in-hospital treatment and outpatient treatment after discharge.

Eleven (19%) of the 59 patients received non-guideline-based initial empiric therapy that was inappropriate, given their past medical history, initial pneumonia severity, and antibiotic use in the 6 months before hospital admission (Table 4). Three (27%) of these 11 patients continued to receive inappropriate therapy for the entire duration of antimicrobial treatment, but the other 8 (73%) were changed to appropriate therapy (4 [36%] within 24 h, 3 [27%] within 48 h, and 1 [9%] within 96 h). The median duration of inappropriate empiric therapy was 24 h (Table 4). Two (18%) of the 11 patients who received inappropriate non-guideline-based therapy died. One of these patients was switched to appropriate antimicrobial therapy after 48 h and achieved clinical resolution, but a complicated and prolonged course in hospital led to the patient's death. The second patient was severely ill at the time of presentation, requiring intubation and admission to

Table 4. Initial Selection of Antimicrobials for the Management of Community-Acquired Pneumonia in 62 Patients Treated at Sunnybrook Health Sciences Centre between 2002 and 2005

Regimen	No. (%) of Patients
Initial selection (*n* = 62)	
Empiric	59/62 (95)
Culture-directed	3/62 (5)
Empiric selection of initial therapy (*n* = 59)	
Monotherapy	17/59 (29)
Fluoroquinolones*	15/59 (25)
Cephalosporin: cefuroxime	1/59 (2)
Aminoglycoside: tobramycin	1/59 (2)
Combination therapy	42/59 (71)
Second- or third-generation cephalosporin + macrolide	18/59 (31)
Cephalosporin used in combination	
Cefuroxime	10/18 (56)
Ceftriaxone	8/18 (44)
Macrolide used in combination	
Azithromycin	15/18 (83)
Clarithromycin	3/18 (17)
Fluoroquinolone + ß-lactam	4/59 (7)
Fluoroquinolone used in combination	
Ciprofloxacin	1/4 (25)
Levofloxacin	3/4 (75)
ß-Lactam used in combination	
Ceftriaxone	2/4 (50)
Ampicillin	2/4 (50)
Other	20/59 (34)
Empiric antimicrobial management (*n* = 59)	
Appropriate (either institutional-based guidelines or appropriate non-guideline-based therapy)	48/59 (81)
Monotherapy	17/48 (35)
Levofloxacin	15/17 (88)
Other	2/17 (12)
Combination therapy	31/48 (65)
Second- or third-generation cephalosporin + macrolide	18/31 (58)
Other	13/31 (42)
Inappropriate	11/59 (19)
Patient switched to appropriate therapy	8/11 (73)
Within 24 h	4/11 (36)
Within 48 h	3/11 (27)
Within 72 h	0/11 (0)
Within 96 h	1/11 (9)
Patient maintained on inappropriate therapy	3/11 (27)

*Fourteen patients received levofloxacin 500 mg, and 1 patient received 250 mg because of renal impairment.

critical care. The patient was not switched to appropriate antimicrobial therapy, and death, probably secondary to pneumonia, occurred within 2 days of presentation.

There was no statistically significant difference between the number of patients who received Sunnybrook guideline-based therapy (33/59 or 56%) and the number who received non-guideline-based therapy (26/59 or 44%) (p = 0.43) (Table 5). There was also no statistically significant difference among the number of patients who received fluoroquinolone monotherapy (15/59 or 25%), the number who received a second- or third-generation cephalosporin plus macrolide (18/59 or 31%), and the number who received non-guideline-based therapy (26/59 or 44%) (p = 0.26). Finally, there was no statistically significant difference among the number of patients who received fluoroquinolone

Table 5. Comparison of Initial Empiric Management for 59 Patients with Community-Acquired Pneumonia Admitted to Sunnybrook Health Sciences Centre

	Fluoroquinolone Monotherapy	2nd- or 3rd-Generation Cephalosporin + Macrolide	Non-guideline-based Therapy		Statistical Analysis*
			Appropriate	Inappropriate	
No. of patients (%)	15 (25)	18 (31)	15 (25)	11 (19)	$p > 0.05$†
PSI mortality risk classification (no. of patients)					$p = 0.99$‡
Low (I to III)	6	8	6	5	
Moderate (IV)	5	7	5	3	
High (V)	4	3	4	3	
Duration of empiric therapy (no. of days)					Kruskal–Wallis: $p = 0.004$
Median	5	3	4	1	Dunn multiple-comparison: $p < 0.05$§
Mean	5	4	5	2	
SD	3	2	3	1	
Range	1–9	1–7	1–13	1–4	
Cost of empiric therapy (Can$)					Kruskal–Wallis: $p = 0.014$‖
Median	25	85	159	46	
Mean	68	115	184	60	
SD	85	87	180	48	
Range	5–320	25–324	5–746	5–170	
Duration of total antibiotic course (no. of days)					Kruskal–Wallis: $p = 0.67$
Median	7	8	8	6	
Mean	10	9	8	6	
SD	9	6	4	4	
Range	3–36	3–22	3–16	2–15	
Cost of antibiotic therapy (Can$)¶					Kruskal–Wallis: $p = 0.12$
Median	81	91	270	128	
Mean	197	273	300	140	
SD	284	382	224	107	
Range	10–917	25–1536	28–776	12–385	
Clinical outcome					$p = 0.74$**
Cure	13 (87)	15 (83)	12 (80)	9 (82)	
Death	2 (13)	3 (17)	1 (7)	2 (18)	
Unknown			2 (13)††		
Clostridium difficile–associated diarrhea (no. of patients)	0	2	1‡‡	0	No statistical analysis

PSI = pneumonia severity index, SD = standard deviation.
*Nominal data were compared with the χ^2 test; interval data were compared with analysis of variance (using Tukey multiple-comparison post-test analysis) or Kruskal–Wallis test (using Dunn multiple-comparison post-test analysis), with $p < 0.05$ considered statistically significant. The appropriate multiple-comparison post-test was completed only when $p < 0.05$.
†The following comparisons were performed, with the χ^2 test used to determine goodness of fit for each comparison: guideline-based therapy versus non-guideline-based therapy; fluoroquinolone monotherapy versus second- or third-generation cephalosporin + macrolide versus non-guideline-based therapy; and fluoroquinolone monotherapy versus second- or third-generation cephalosporin + macrolide versus appropriate non-guideline-based therapy versus inappropriate non-guideline-based therapy.
‡Comparison of the number of patients in the "moderate" (PSI category IV) + "high" (PSI category V) mortality risk classes for each type of therapy, with the χ^2 test used to test goodness of fit.
§The duration of inappropriate non-guideline-based therapy was significantly less than fluoroquinolone monotherapy ($p < 0.01$), ß-lactam + macrolide therapy ($p < 0.05$), and appropriate non-guideline-based therapy ($p < 0.05$), according to the Dunn multiple-comparison post-test analysis.
‖The cost of fluoroquinolone monotherapy was significantly less than the cost of appropriate non-guideline-based therapy ($p < 0.05$); all other cost comparisons were not statistically significant, according to the Dunn multiple-comparison post-test analysis.
¶Refers to cost of all antibiotics related to treatment of community-acquired pneumonia, including but not limited to empiric management.
**Based on frequencies of cured versus not cured; Fisher's exact test comparing outcomes for guideline-based and non-guideline-based empiric therapy.
††Patients were transferred to other health care facilities, with no indication of improvement.
‡‡Patient received an 8-day course of ß-lactam therapy, and metronidazole 500 mg PO bid was initiated 2 days later for *C. difficile*–associated diarrhea.

monotherapy (15/59 or 25%), the number who received a second- or third-generation cephalosporin plus macrolide (18/59 or 31%), the number who received appropriate non-guideline-based therapy (15/59 or 25%), and the number who received inappropriate non-guideline-based therapy (11/59 or 19%) ($p = 0.74$).

The clinical outcomes and mean cost of therapy were compared for patients receiving levofloxacin monotherapy, second- or third generation cephalosporin plus macrolide combination therapy, appropriate non-guideline-based therapy, and inappropriate non-guideline-based therapy (Table 5). There was no statistically significant difference in the numbers of patients with pneumonia severity index IV or V among these 4 treatment regimens (range 6 to 10 patients) ($p = 0.99$). The duration of inappropriate empiric non-guideline-based therapy was significantly shorter than that of appropriate empiric regimens ($p < 0.05$). However, the median duration of total antimicrobial therapy was not significantly different among the treatment regimens (range 6 to 8 days, $p = 0.67$). The cost of fluoroquinolone monotherapy as an initially selected empiric antibiotic regimen was significantly less than the cost of appropriate non-guideline-based therapy ($p < 0.05$). The costs of all other empiric antibiotic regimens were not significantly different from each other ($p > 0.05$). The median cost for the total course of antimicrobial treatment for community-acquired pneumonia ranged from $81 to $270 for the 4 types of regimens ($p = 0.12$). There was a trend for lower cost for the guideline-based regimens relative to appropriate non-guideline-based regimens ($p = 0.0504$, Mann–Whitney test), although this did not achieve statistical significance. The median acquisition cost for the total duration of guideline-based therapy was $88.20 (range $10.42 to $1536.40) per patient.

Clinical cure rates were at least 80% with all 4 initial empiric management strategies (range 80% to 87%, $p = 0.74$). Three patients, all of whom had received a course of ß-lactam antimicrobial therapy, experienced *Clostridium difficile*–associated diarrhea, but because of the low frequency, no statistical analysis was performed (Table 5). None of the patients in this study had community-associated methicillin-resistant *S. aureus*, according to the Centers for Disease Control and Prevention definition of this condition.[16]

DISCUSSION

During the study period, the recommended empiric regimen for patients admitted to our institution for treatment of community-acquired pneumonia was either combination therapy with IV cefuroxime or ceftriaxone in conjunction with oral or IV azithromycin or monotherapy with oral or IV levofloxacin. The institution's recommendations for management of community-acquired pneumonia were based on published North American practice guidelines[6,9,15] that were current at the time this study was conducted; therefore, the principles of conducting a quality assurance investigation and the observations we obtained may be useful to other Canadian hospitals. The benefits of implementing evidence-based treatment guidelines for patients with community-acquired pneumonia who require hospital admission are well documented.[4,13,14]

Mean reported adherence to empiric treatment guidelines for patients admitted to hospital with community-acquired pneumonia ranges from 47% to 97%.[4] At our institution, 56% (33/59) of patients received guideline-recommended empiric therapy, and there was a nonsignificant trend toward increased adherence over the 4-year period of the study. There was no significant difference in the frequency of selection of the 2 guideline-recommended regimens (i.e., fluoroquinolone monotherapy versus second- or third-generation ß-lactam plus macrolide combination therapy), and there was no indication that severity of illness dictated the choice of empiric antimicrobial treatment. Halm and others[17] found that the use of guideline-recommended antimicrobial therapy increased from 78.1% to 83.4% ($p = 0.003$) after implementation of a multidisciplinary quality initiative, in which opinion leaders developed evidence-based treatment guidelines and critical pathways, conducted a series of educational lectures with house staff, distributed pocket reminder cards, and promoted standardized orders. After the implementation of institutional guidelines at Sunnybrook in 2002, adherence rates increased steadily, from 50% in 2002 to 64% in 2005; however, the difference over time was not statistically significant. Ongoing education of house staff by pharmacists may be an initial effective means to further increase compliance with the treatment guidelines. Twenty-five percent of the patients in this study received appropriate non-guideline-based empiric therapy and 56% received appropriate guideline-based therapy, for a total of 81% (48/59) of patients receiving empiric antibiotic therapy that was assessed as appropriate. The median duration of inappropriate, non-guideline-based therapy was only 24 h, which indicates efficient therapeutic intervention to modify inappropriate therapy. Of the 11 patients who were initially prescribed inappropriate, non-guideline-based antimicrobials, 8 (73%) were switched to an appropriate

antimicrobial regimen. The clinical cure rate was greater than 80% for all patients; among those with an initially inappropriate treatment regimen, the cure rate was 82% (9/11), but 8 of these 9 patients were promptly switched to appropriate guideline-based therapy. The objectives of this study did not include evaluating the effectiveness of guideline-based therapy, and the study was therefore not powered to determine any difference in cure rate. For both of these reasons, the absence of a statistically significant difference in cure rate between appropriate and inappropriate therapy is not surprising. However, initial empiric monotherapy with levofloxacin was significantly less expensive than appropriate non-guideline-based therapy, which supports the use of guideline-based therapy rather than appropriate non-guideline-based therapy, provided there is no clinical rationale to deviate from the treatment algorithm.

The all-cause in-hospital mortality rate among these patients was 15% (9/62), and the mortality rate attributable to infection was 10% (6/62). The mortality rate attributable to community-acquired pneumonia in this study is in keeping with the reported attributable mortality rate of 5% to more than 30%.[4,5]

High incidence rates of *C. difficile*–associated diarrhea in Canadian hospitals have been reported recently.[18-21] Three of the patients in the current study who had received a course of ß-lactam antimicrobial therapy experienced *C. difficile*–associated diarrhea, but no statistical analysis was performed.

The major limitations of this study were the small sample size and the retrospective design. Inclusion of patients with a type 1 diagnosis (i.e., comorbid condition, rather than community-acquired pneumonia, as the most responsible diagnosis influencing the length of stay) would have ensured a larger sample size, but for reasons of feasibility as a residency project and the desire to obtain a sample of patients admitted specifically for community-acquired pneumonia, only patients for whom this diagnosis was the most responsible diagnosis influencing the length of stay were reviewed (i.e., type M diagnosis). The treatment guideline for community-acquired pneumonia used at Sunnybrook is a general guideline for medical staff and residents. Although the guideline is directed toward patients admitted to the ward, and not nursing home residents, patients with specific comorbidities, or patients in the intensive care unit, the objective of this study was still achievable with our methodology.

There was no significant difference in frequency between levofloxacin monotherapy and second- or third-generation cephalosporin plus macrolide combination therapy at this institution, and 56% of the patients in the study received one of these guideline-based options. To improve compliance with the guidelines for treatment of community-acquired pneumonia in use at Sunnybrook Health Sciences Centre, ongoing education of house staff by pharmacists is recommended. Among the patients treated at this institution during this study, the most commonly identified organisms causing community-acquired pneumonia were *S. pneumoniae* and *H. influenzae*, and the cure rate was 82%. Fluoroquinolone monotherapy selected as initial empiric therapy was significantly less expensive than appropriate non-guideline-based therapy. Therefore, on the basis of efficacy, cost, clinical outcome, and patterns of microbiological culture and sensitivity data and in the absence of any new published guidelines during the period this study was conducted, we concluded that there was no need for revision of institutional guidelines for the management of patients admitted for treatment of community-acquired pneumonia at this tertiary care teaching hospital. However, since this study was conducted, new North American guidelines for the management of community-acquired pneumonia have been published,[22] and the Sunnybrook treatment algorithm for patients admitted to hospital was modified in March 2007 to reflect these new guidelines. The treatment pathways now offered include IV ceftriaxone plus IV or oral azithromycin or IV or oral levofloxacin at a dose of 750 mg (previously 500 mg) administered at an interval determined by renal function. The results of the study reported here highlight the importance of conducting a quality assurance study to identify whether evidence-based guidelines for community-acquired pneumonia that have been implemented at an institution are actually being used. Furthermore, when considering the need to revise institution-specific recommendations for the treatment of patients with community-acquired pneumonia who must be admitted to hospital, and in the absence of recently published guidelines, it is important to evaluate institution-specific patient characteristics; patterns, duration, appropriateness, clinical outcome, and cost of antimicrobial therapy; and results of microbiological culture.

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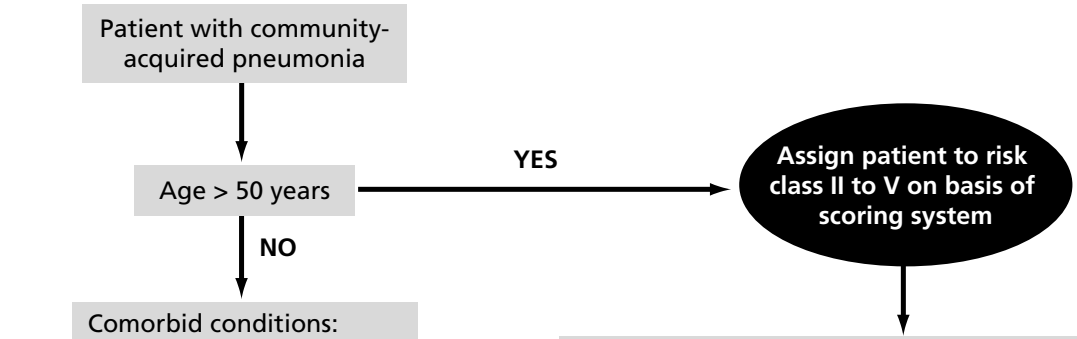
Appendix 1. Prediction Rules for Assessment of Mortality Risk and Recommendations for Site of Care. BUN = blood urea nitrogen, PO_2 = partial pressure of oxygen. Reproduced, with permission, from Gin AS, Tailor SAN. Community-acquired pneumonia. *Can J Hosp Pharm* 2001;54(Suppl 1):1-16.



Scoring System

Characteristic	Points
Demographic characteristics	
Age: male	age (in years)
Age: female	age (in years) – 10
Nursing home resident	+10
Comorbid conditions	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥ 30 breaths/min	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature < 35°C or ≥ 40°C	+15
Pulse ≥ 125 beats/min	+10
Laboratory findings	
pH < 7.35	+30
BUN ≥ 11 mmol/L	+20
Sodium < 130 mmol/L	+20
Glucose ≥ 14 mmol/L	+10
Hematocrit < 30%	+10
PO_2 < 60 mm Hg or O_2 saturation < 90%	+10
Pleural effusion	+10
Sum of points applicable to patient (use to determine risk class)	_____

Risk Class	Basis for Assignment	Mortality Risk	Recommendations for Site of Care
I	Algorithm	Low (0.1%)	Outpatient
II	≤ 70 total points	Low (0.6%)	Outpatient
III	71–90 total points	Low (2.8%)	Outpatient or brief inpatient
IV	91–130 total points	Moderate (8.2%)	Inpatient
V	> 130 total points	High (29.2%)	Inpatient