Early Switch From Intravenous to Oral Antibiotics and Early Hospital Discharge

A Prospective Observational Study of 200 Consecutive Patients With Community-Acquired Pneumonia

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Objectives: To determine the proportion of patients who can be treated with early switch to oral antibiotics and early discharge, to evaluate clinical outcome and patient satisfaction for patients treated with early switch and early discharge, and to define the factors that interfere with early discharge for some of the patients who underwent early switch to oral antibiotic therapy.

Design: Prospective study.

Participants: Two hundred consecutive hospitalized patients with community-acquired pneumonia.

Main Outcome Measures: Number of days needed to switch to oral therapy and length of hospital stay. Clinical outcome and satisfaction with care were evaluated for those patients treated with early switch and early discharge.

Results: Early switch to oral antibiotics (within the first 3 days of hospitalization) was performed in 133 patients (67%). Clinical failure was documented in 1 patient. Early switch and early discharge was performed in 88 patients (44%). The mean length of hospital stay for this group was 3.4 days. The most common reason for prolonged hospitalization after the switch to oral antibiotics was the need for diagnostic workup. More than 95% of patients were satisfied with the care they had received.

Conclusions: Using simple clinical and laboratory criteria, a significant proportion of hospitalized patients with community-acquired pneumonia (44%) can be treated with early switch and early discharge. This model did not affect patient outcome, decreased the length of hospitalization, and was associated with a high level of patient satisfaction.

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IT IS ESTIMATED that half a million patients with community-acquired pneumonia (CAP) are hospitalized every year in the United States.[1] The initial treatment of these patients typically includes the use of empiric intravenous antibiotics for likely pulmonary pathogens.[2] Although some physicians believe the standard of care should consist of at least 7 days of intravenous antibiotic therapy,[3] recent clinical trials indicate that antibiotic therapy can be safely changed from intravenous to oral (switch therapy) once the hospitalized patient with CAP shows evidence of clinical improvement.[4-8]

Clinical improvement during the initial 3 days of intravenous antibiotic treatment is usually seen in hospitalized patients with CAP. It has been suggested that targeting these patients for early switch to oral antibiotic therapy followed by early hospital discharge will not affect patient outcome and will minimize the mean length of hospital stay and the treatment costs for the full population of hospitalized patients with CAP.[3] At least 3 factors that may be present in patients with CAP will prevent the early switch to oral antibiotic therapy followed by early hospital discharge. First, hospitalized patients whose conditions deteriorate while they are receiving empiric intravenous antibiotic therapy will not be candidates for oral antibiotic therapy. Second, among patients whose condition responds to intravenous antibiotic therapy, a subgroup of patients may have a late clinical response and therefore will not be candidates for the early use of oral antibiotics. Third, even if all patients who show evidence of early clinical improvement during the first 3 days of treatment are switched to oral antibiotic therapy, hospital discharge may be delayed in some of these patients because of conditions not related to pneumonia. If none of the above 3 factors are present, patients can be treated successfully with early switch from intravenous to oral antibiotic therapy and early discharge. This treatment approach can significantly reduce the average length of hos-

PATIENTS AND METHODS

PATIENTS

All patients admitted to the Veterans Affairs Medical Center of Louisville, Ky, from December 1, 1994, through June 22, 1997, who were treated with antibiotics were evaluated by 1 clinical pharmacist to determine if empiric antibiotic therapy was initiated for CAP.

Empiric therapy was defined as the initial use of antibiotics when the etiologic pathogen had not been identified. To ensure that all patients were treated initially with appropriate empiric therapy, a preprinted order form was used for all hospitalized patients with CAP. This form allowed the emergency department physician or internist to select antibiotics based on the initial guidelines for empiric therapy suggested by the American Thoracic Society.[2] All patients who received empiric therapy for CAP were evaluated by 1 physician investigator to determine whether they met clinical diagnosis of CAP according to the study protocol. The clinical diagnosis of CAP was based on the presence of a new pulmonary infiltrate plus at least 2 of the following 3 criteria: (1) cough or increase in cough and sputum production in patients with chronic lung disease, (2) fever or hypothermia, and (3) leukocytosis, increased proportion of immature cells, or leukopenia. All hospitalized patients who met the above diagnostic criteria for CAP were eligible to participate in this trial. There were no exclusion criteria. Informed consent was obtained from all patients or guardians. No patient refused to participate in the trial.

CRITERIA FOR SWITCH THERAPY

A patient was determined to be a candidate for a switch from intravenous to oral antibiotic therapy when the following criteria were met: cough and shortness of breath improved, temperature fell below 37.8°C for at least 8 hours, white blood cell count was normalizing, and oral intake and gastrointestinal absorption were adequate.[9] Patients were given antipyretics if their temperature was 38.9°C or higher. When no organism was identified as the cause of the pneumonia, the oral antimicrobial agent selected for switch therapy was equivalent to the agent used for intravenous empiric therapy in its spectrum of antimicrobial activity. When a microbial cause was identified, the choice of the oral antimicrobial agent for switch therapy was determined by the susceptibility pattern of the identified microorganism. Second-generation macrolides, cephalosporins, and new-generation quinolones were the most common oral antibiotics used during the study period.

NUMBER OF DAYS TO CLINICAL IMPROVEMENT

Patients were considered to have clinical improvement on the day they met all 4 criteria for switch therapy. Patients who met the criteria for switch therapy during the first 3 days of hospital treatment were considered to have early clinical improvement. Patients who met the criteria for switch therapy from day 4 to 7 of hospital treatment were considered to have late clinical improvement.

CRITERIA FOR HOSPITAL DISCHARGE

A patient was determined to be a candidate for hospital discharge on the day the following criteria were met: the patient was a candidate for oral therapy, there was no need to treat comorbid conditions (eg, congestive heart failure), there was no need for diagnostic workup (eg, bronchoscopy for lung mass), and there were no social needs (eg, unstable home situation).

pital stay and treatment costs, but only if applied to a significant proportion of hospitalized patients with CAP.

We conducted a prospective observational study of 200 consecutive hospitalized patients with CAP using objective criteria to define the number of days required to switch to oral therapy and the length of hospital stay. The objectives of our study were to determine the proportion of patients who can be treated with early switch and early discharge, to evaluate clinical outcome and patient satisfaction for patients treated with early switch and early discharge, and to define the factors that interfere with early discharge for some of the patients who underwent early switch to oral antibiotic therapy. Finally, the population that reached clinical stability during the first 7 days of hospitalization was analyzed retrospectively to evaluate whether there was any correlation between the severity of disease and the number of days to clinical improvement.

RESULTS

CANDIDATES FOR SWITCH THERAPY

From the total population of 200 patients, 173 (86%) showed evidence of clinical improvement during the first 7 days of intravenous antibiotic therapy. The number of patients who were determined to be candidates for switch therapy on the first through the seventh day of hospitalization is depicted in **Figure 1**. Clinical improvement during the first 3 days of intravenous antibiotic therapy (early improvement) was documented in 133 patients (67%). Clinical improvement from day 4 to 7 of intravenous antibiotic therapy (late improvement) was documented in 40 patients (20%).

LENGTH OF HOSPITAL STAY

The length of hospital stay for the 133 patients with early clinical improvement is depicted in **Figure 2**. The mean length of stay was 4.8 days. The pneumonia-related length of stay was identified in 88 patients (44% of the total population). The mean length of stay for the 88 patients treated with early switch and early discharge was 3.4 days. The length of stay for those who remained hospitalized for treatment of comorbid conditions, the need for diagnostic workup, or social needs was identified for 45 patients. The mean length of stay for this group was 7.6 days. The length of hospital stay for these 2 groups is depicted in **Figure 3**.

LENGTH OF HOSPITAL STAY

Length of hospital stay was calculated for the patients who met the criteria for switch therapy during the first 3 days of hospitalization. A further analysis of length of hospital stay was performed by dividing this population into 2 groups, patients with a pneumonia-related hospital stay and patients whose hospital stay was not pneumonia-related.

PATIENTS WITH PNEUMONIA-RELATED HOSPITAL STAY

This group of patients was treated with early switch and early discharge. They were discharged home within 48 hours after they became candidates for switch therapy. There was no need to treat comorbid conditions, no need for diagnostic workup, and no social needs for any of these patients at the time they were switched to oral antibiotic therapy.

PATIENTS WHOSE HOSPITAL STAY WAS NOT PNEUMONIA-RELATED

This group of patients included those who were switched to oral antibiotic therapy but remained hospitalized for treatment of comorbid conditions, the need for diagnostic workup, or social needs.

CLINICAL OUTCOME

Patients with an early switch to oral antibiotic therapy and early hospital discharge had 1 telephone contact 3 days after discharge and 2 follow-up clinic visits. The first visit was during the first week after completion of oral antibiotic therapy and the second visit was 4 to 5 weeks after completion of oral antibiotic therapy. The outcome was classified as clinically cured if the signs and symptoms related to CAP had resolved by the last clinic visit. A patient's treatment was considered a clinical failure if a deterioration of signs and symptoms during oral antibiotic therapy or a relapse of signs and symptoms during the follow-up period was documented.

SATISFACTION WITH CARE

Data for patient satisfaction were collected for patients who were treated with early switch and early discharge. The following questions were used to evaluate patient satisfaction: Were you sent home too soon? Were you satisfied with the care that you received? Did you receive adequate follow-up? The same study nurse who was in charge of patient education prior to hospital discharge was in charge of obtaining data for patient satisfaction after oral antibiotic therapy was completed.

CORRELATION OF SEVERITY OF DISEASE WITH TIME TO IMPROVEMENT

The severity of CAP for each patient was evaluated according to the number of risk factors for complicated course,[2] the Acute Physiology and Chronic Health Evaluation II (APACHE II) score,[10] and the patient's risk class.[11] Regarding risk factors for complicated course, patients were stratified as group 1 if no risk factor for complicated course was present, group 2 if 1 to 3 risk factors were present, group 3 if 4 to 6 risk factors were present, group 4 if 7 to 9 risk factors were present, and group 5 if 10 or more risk factors were present. Regarding APACHE II scores, patients were stratified as group 1 if their APACHE II scores were 1 to 5, group 2 if scores were 6 to 10, group 3 if scores were 11 to 15, group 4 if scores were 16 to 20, and group 5 if scores were greater than 20. Regarding risk class, patients were stratified into risk classes 1, 2, 3, 4, or 5 as previously described.[11] A Cox proportional hazard analysis of the data was performed to determine which of the models used to evaluate CAP severity was most predictive of when the patient reached the stage of clinical improvement.

The conditions other than CAP that prolonged the length of hospital stay for the 45 patients in the latter group were diagnostic workup in 21 patients, treatment of comorbid conditions in 18 patients, and social reasons in 2 patients. In 4 patients, the prolonged length of hospital stay was caused by violations of study protocol. In 1 case, oral antibiotic therapy was not implemented after the patient met the criteria for switch therapy. In 3 cases, patients remained hospitalized for observation while receiving oral antibiotic therapy. The practice of hospital observation for patients receiving oral antibiotic therapy was not part of the study protocol. If there is no other reason for hospitalization, the observation of patients receiving oral antibiotic therapy will not improve outcome and will increase the length of stay.

CLINICAL OUTCOME

Of the 133 patients who had an early switch to oral antibiotic therapy, 118 patients were evaluable for clinical outcome analysis. Fifteen patients were unevaluable (8 were lost to follow-up, 3 required antibiotic therapy during follow-up because of infections unrelated to pneumonia, and 1 died of respiratory failure caused by end-stage chronic obstructive pulmonary disease).

Clinical failure was documented in 1 patient; 117 patients from the population of 118 evaluable patients were clinically cured. The patient who experienced clinical failure while receiving switch therapy was a 74-year-old white man with a history of adenocarcinoma of the colon with metastasis to the liver, diabetes, chronic lung disease, and congestive heart failure; he was admitted to the hospital with pneumonia in the middle lobe of the right lung. He was treated empirically with an intravenous β-lactam–β-lactamase inhibitor. No microbial cause for his pneumonia was identified. This patient met the criteria for switch therapy on day 3 of his hospitalization and was switched to oral antibiotic therapy with a β-lactam–β-lactamase inhibitor. After 2 days of oral antibiotic therapy, he experienced clinical deterioration, with an elevated temperature and white blood cell count. He responded clinically after reinitiation of intravenous antibiotic therapy.

SATISFACTION WITH CARE

Of the 88 patients treated with early switch and early discharge, 84 (95%) responded that they were not sent home too soon, and 86 (98%) responded that they had re-

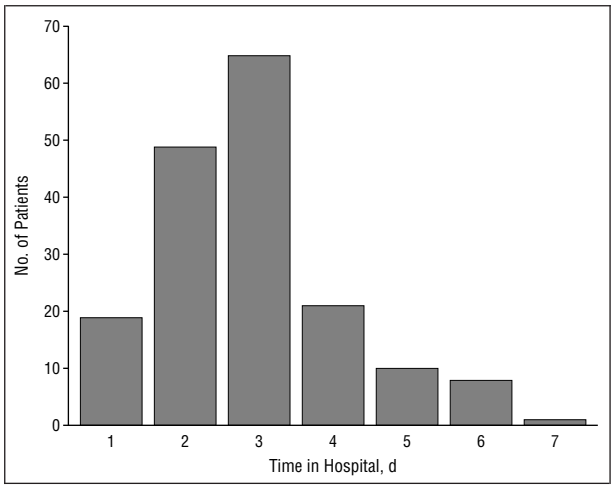

Figure 1. *Number of patients who met the criteria for switch therapy according to days of hospitalization.*

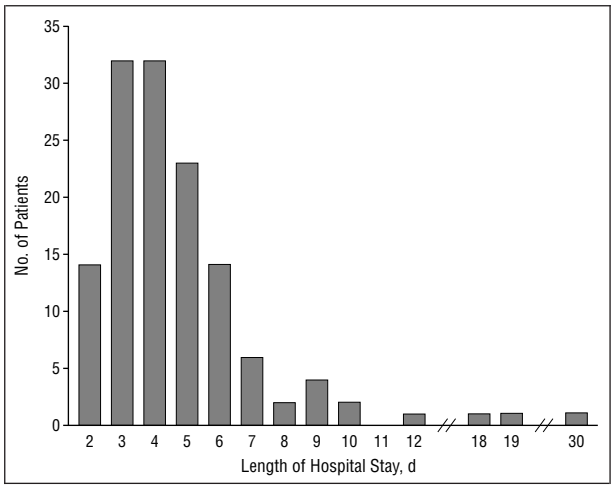

Figure 2. *Length of hospital stay for the patients who met the criteria for switch therapy during the first 3 days of hospitalization.*

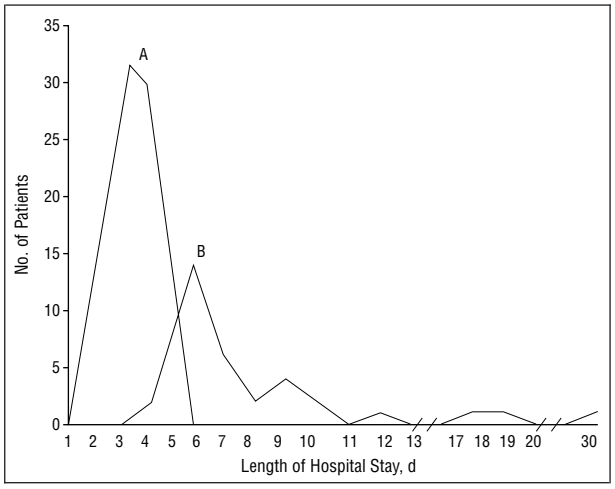

Figure 3. *Length of hospital stay for subgroups of patients who met the criteria for switch therapy during the first 3 days of hospitalization. A indicates patients with pneumonia-related length of hospital stay; B, patients whose length of hospital stay was affected by treatment for comorbid conditions, the need for diagnostic workup, or social needs.*

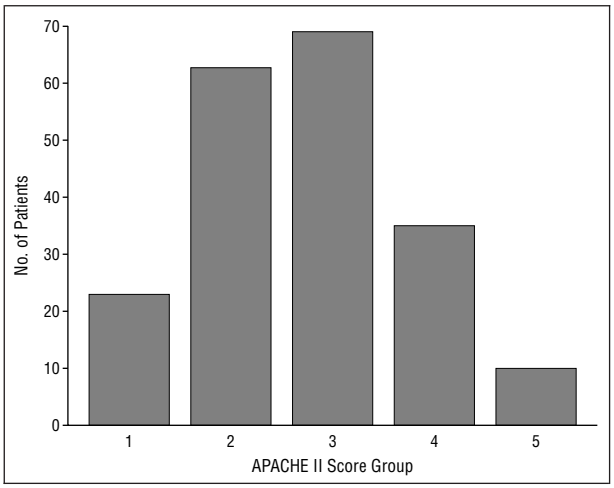

Figure 4. *Classification of patients in 5 groups according to Acute Physiology and Chronic Health Evaluation II (APACHE II) scores (group 1, 1-5; group 2, 6-10; group 3, 11-15; group 4, 16-20; and group 5, >20).*[10]

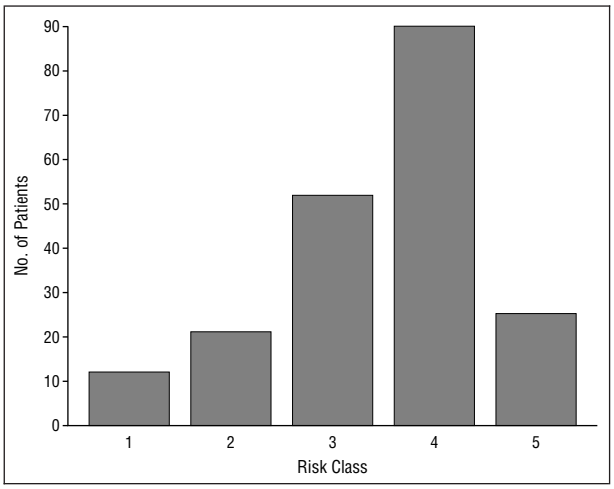

Figure 5. *Classification of patients in 5 risk classes according to risk of death and adverse outcomes.*[11]

ceived adequate follow-up and were satisfied with the care they had received.

CORRELATION OF SEVERITY OF DISEASE WITH NUMBER OF DAYS TO CLINICAL IMPROVEMENT

The classification of patients at the time of admission with the APACHE II score, risk class, and number of risk factors is depicted in **Figure 4**, **Figure 5**, and **Figure 6**. The Cox proportional hazard analysis showed that only the APACHE II score was significantly correlated with the number of days to clinical improvement ($P = .001$). When comparisons were made among the 5 APACHE II score subgroups, the scores for patients in groups 4 and 5 were significantly different from those in group 1 ($P = .002$ for both). Patients in groups 4 and 5 were at a 2.3- and 3.2-fold higher risk, respectively, of not having early clinical improvement during their hospital course.

COMMENT

Sixty-five percent of the hospitalized patients with CAP at the Veterans Affairs Medical Center of Louisville were switched to oral therapy during the first 3 days of hospital therapy. The early switch from intravenous to oral antibiotic therapy followed by early discharge was safely performed in 44% of all of our hospitalized patients. The early switch and early discharge approach was safely and effectively applied to almost half of our patients. To evaluate whether our findings could be generalized to other populations, we compared our patients with other populations of hospitalized patients with CAP described in the literature. When the study population was stratified into 5 risk classes according to the risk of death within 30 days,[11] patients in risk class 4 and 5 constituted 58% of the population, with only 6% of patients in risk class 1. The distribution of our patients according to risk class was very similar to the distribution reported for the Pneumonia Patient Outcomes Research Team cohort study.[11] Stratification of patients from this database indicated that among 38 039 patients who were hospitalized with CAP, patients in risk classes 4 and 5 constituted 58% of the population, with only 8% of patients in risk class 1. Data on 14 199 adult patients who were hospitalized with CAP from 78 hospitals in 23 states obtained from the MedisGroups Comparative Hospital Database also indicated a similar stratification.[11] Patients in risk classes 4 and 5 constituted 55% of the population, with 10% of patients in risk class 1. Using a well-established prediction rule for the risk of death and other adverse outcomes, these data indicate that the population of patients with pneumonia admitted to our hospital is similar to the population of patients admitted to other hospitals around the country. Therefore, our finding that a high proportion of patients who are hospitalized with pneumonia may be considered candidates for an early switch to oral antibiotic therapy may be generalized to other populations. Some physicians have been reluctant to treat patients with early switch and early discharge because of the lack of clinical data from trials other than those that used selected populations. Our results indicate that this approach may be safely applied as long as appropriate criteria for switch therapy and hospital discharge are followed.

In theory, the time required for a patient with CAP to show evidence of clinical improvement and to become a candidate for switch therapy depends on these primary factors: the selection of the initial empiric antimicrobial regimen, the immunocompetence of the patient, and the virulence of the etiologic agent. For all patients in our trial, the administration of antimicrobial therapy was in accordance with the guidelines published by the American Thoracic Society.[2] This minimized the selection of appropriate antimicrobial therapy as a factor to account for the differences in the length of time to clinical improvement observed in our study population. The immunocompetence of the patient and the virulence of the etiologic agent will manifest clinically as severity of disease. In our limited study population, the best predictor for the length of time to clinical improvement and to become a candidate for switch therapy was related to the initial APACHE II score. Our data suggest that the APACHE II score can be used prognostically to stratify hospitalized patients with CAP and assess the length of time to clinical improvement. This scoring index may be useful in designing future clinical studies that evaluate which antimicrobial therapy is most effective in decreasing the length of time to clinical improvement.

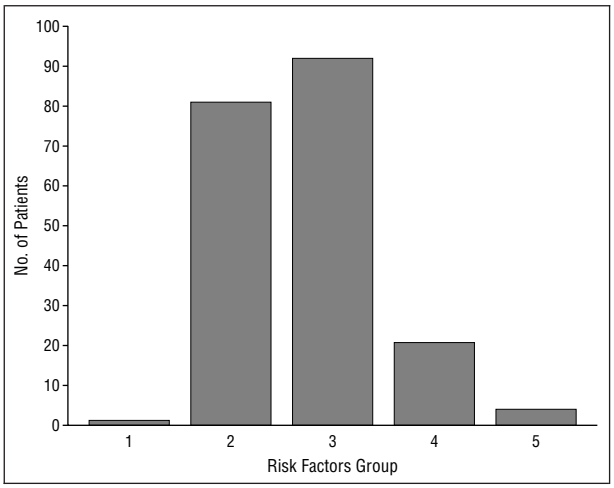

Figure 6. *Classification of patients in 5 groups according to number of risk factors for a complicated course (group 1, no risk factors; group 2, 1-3 risk factors; group 3, 4-6 risk factors; group 4, 7-9 risk factors; and group 5, ≥10 risk factors).*[2]

Once a patient with CAP is hospitalized and empiric antibiotic therapy started, clinicians should closely evaluate the patient's clinical response to therapy. In this regard, it is important to know when clinical improvement will be expected and when reevaluation of therapy is warranted. Our finding that two thirds of patients who are hospitalized with CAP will show evidence of clinical improvement by day 3 supports the concept that reevaluation should be performed by day 3 of the hospital stay for these patients when there is failure to improve.

During our investigation, we collected information on patient satisfaction. Since patients are discharged home when they are still symptomatic with the early switch and early discharge approach, patients may dislike this approach, even though clinical improvement is achieved. Our follow-up survey addressed patient satisfaction with the early switch and early discharge approach. Patients were asked if they felt they were sent home too soon after hospitalization. Our data indicate that 95% of the patients for whom the early switch and early discharge approach was used felt the length of hospitalization was appropriate. This suggests that patients may prefer early discharge once they reach the stage of clinical improvement. This finding is in agreement with a recent report indicating preferences for home therapy vs hospital therapy for patients with low-risk CAP.[12]

In the past, many patients with pneumonia were treated in the hospital with intravenous antibiotic therapy for approximately 7 days. The length of their hospital stay was justified by the perceived "need" for intravenous antibiotic therapy to obtain a good clinical outcome. During this lengthy term of hospitalization, physicians had enough time to treat comorbid conditions, perform a diagnostic workup, or address a patient's social needs. Be-

cause the majority of patients with pneumonia stayed in the hospital for more than 7 days, factors that were not related to pneumonia probably did not play an important role in the length of stay. With the advent of shorter courses of intravenous antibiotic therapy and early switch to oral antibiotic therapy, there are now hospitalized patients who are already receiving oral therapy but who cannot be discharged because of factors not directly related to pneumonia. In our study, one third of the patients who had early clinical improvement and were switched to oral antibiotic therapy had to remain hospitalized because of factors other than pneumonia. Hospitals will have to determine which other factors interfere with early discharge. Changes in the process of care may become necessary to avoid delayed discharge once patients reach clinical stability.

In an ideal situation, the day that the patient with CAP reaches clinical stability should be the day that the patient is switched to oral antibiotic therapy and discharged from the hospital. There should be no delay in starting oral antibiotic therapy once a patient reaches clinical stability, and there should be no delay in hospital discharge based on factors that are not related to pneumonia. We found that the early switch and early discharge approach could be safely and effectively applied to 44% of the patients with CAP we studied. The mean length of hospital stay for this population was 3.8 days. A recent observational multicenter study of 686 adult hospitalized patients with CAP indicated that the majority of patients stayed in the hospital a median of 4 additional days after reaching clinical stability; the mean length of hospital stay was 8.9 days.[12] The length of hospital stay is the single most important factor affecting the treatment costs for the hospitalized patient with pneumonia. In our study, the mean duration of hospitalization was safely reduced by more than 2 days for 44% of the patients we studied who were hospitalized with CAP. Extrapolating our results to include the 500 000 patients hospitalized every year with CAP in the United States, the early switch and early discharge approach could theoretically be used effectively for 220 000 patients. If all 500 000 patients hospitalized every year with CAP in the United States stayed in the hospital for a median of 4 additional days after reaching clinical stability, then with a conservative decrease of 2 days of hospitalization per patient, our results suggest that the total reduction for 1 year could amount to 440 000 hospital days. Considering that the average cost of 1 hospital day in the United States is $903,[13] we estimate annual savings of $397 320 000 if the early switch and early discharge approach becomes standard practice.

In summary, using simple clinical and laboratory criteria, 44% of our patients who were hospitalized with CAP were candidates for an early switch to oral antibiotic therapy followed by early hospital discharge. The treatment of this population with the early switch and early discharge approach did not have a negative impact on clinical outcome, was associated with a high level of patient satisfaction, and significantly decreased the total cost of treatment.

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