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# Ofloxacin versus Standard Therapy in Treatment of Community-Acquired Pneumonia Requiring Hospitalization

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**Community-acquired pneumonia occurs 3 to 4 million times per year in the United States, accounting for about 500,000 hospitalizations annually. Empiric treatment is usually instituted because of a lack of early organism-specific diagnostic tests. This study compared empiric therapy with ofloxacin to standard antibiotic regimens (usually a beta-lactam with or without a macrolide) for patients hospitalized for community-acquired pneumonia. Therapy was administered to 298 patients (146 receiving ofloxacin and 152 receiving standard therapy); 227 patients (ofloxacin, 109; standard treatment, 118) were evaluable for treatment efficacy. The most common pyogenic respiratory pathogens were *Haemophilus influenzae* (30 isolates) and *Streptococcus pneumoniae* (24 isolates). There was evidence of infection with either *Mycoplasma pneumoniae* (38 patients), *Chlamydia pneumoniae* (40 patients), or a *Legionella* sp. (8 patients) in a total of 79 patients (35%). The clinical success rates were similar in both groups among evaluable patients (92%, ofloxacin; 87%, standard therapy) and among patients with atypical respiratory pathogens (88%, ofloxacin; 81%, standard therapy). The mean numbers (± the standard deviations) of intravenous doses of antibiotics were 7.5 ± 8.0 in the ofloxacin group and 18.4 ± 18.5 in the standard therapy group ($P < 0.001$); the mean number of oral doses of ofloxacin per patient was 19.7 ± 11.2, compared with 30.2 ± 16.0 oral antibiotic doses in the standard therapy group ($P < 0.001$). All treatments were well tolerated and associated with no significant clinical or laboratory abnormalities. The findings of this study indicate that ofloxacin is active against traditional bacterial pathogens as well as the major atypical respiratory pathogens. When given as monotherapy for the empiric treatment of community-acquired pneumonia, ofloxacin is as effective as standard antimicrobial therapy.**

There are approximately 3 to 4 million cases of community-acquired pneumonia annually in the United States, with about 500,000 of them resulting in hospitalization (1). While the most common pyogenic etiologies remain *Streptococcus pneumoniae* and *Haemophilus influenzae* (21–23), recent studies have demonstrated the importance of the atypical respiratory pathogens *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* (12–14, 18, 22, 26).

The initial therapy for community-acquired pneumonia is often empiric (11), and in 30 to 50% of cases the etiologic diagnosis is never established. Diagnosis of infections caused by atypical pathogens is often limited by the lack of routine diagnostic tests for these agents. Moreover, the growing incidence of beta-lactam and/or macrolide resistance in common bacterial pathogens such as *S. pneumoniae* and *H. influenzae* further complicates the selection of an appropriate antibiotic for initial empiric treatment (2, 3, 8, 16).

Ofloxacin is a broad-spectrum fluoroquinolone which demonstrated in vitro activity against standard respiratory pathogens, including *H. influenzae* and *S. pneumoniae*, as well as against *M. pneumoniae*, *L. pneumophila*, and *C. pneumoniae* (4). Ofloxacin has had clinical success against these atypical pathogens in anecdotal case reports (6, 9, 10, 17, 19).

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This clinical study was designed to assess the empiric use of ofloxacin in patients hospitalized for community-acquired pneumonia compared with standard therapeutic regimens selected by the attending physicians.

## MATERIALS AND METHODS

**Study design.** This randomized, open-label, multicenter study was conducted at three medical centers in Franklin County, Ohio (The Ohio State University Medical Center, Mount Carmel Medical Center, and Riverside Methodist Hospital) and one in Summit County, Ohio (Summa Health Systems) between June 1993 and May 1994.

Patients who fulfilled the entry criteria and gave written informed consent were randomized to receive either 400 mg of ofloxacin (parenterally or orally) every 12 h or standard antimicrobial therapy. Doses of ofloxacin were decreased for patients with reduced creatinine clearance levels according to recommendations in the package insert. The standard therapy used for a particular patient was determined by the attending physician and was not limited by the study design. The choice to change from parenteral to oral dosing in both regimens was at the discretion of the attending physician. A need to change the antimicrobial therapy to a broader-spectrum antibiotic in either treatment group was considered a failure of the initial regimen.

**Patient population.** Patients eligible for the study included adults (age, >17 years) hospitalized with respiratory symptoms and the appearance of a new infiltrate on a chest radiograph. In order to replicate actual practice conditions, patients failing previous oral antibiotic therapy were eligible for enrollment. Patients were excluded for the following reasons: being treated for more than 24 h with any parenteral antimicrobial therapy; having a known hypersensitivity to or currently undergoing treatment with ofloxacin; having a neutrophil count of <1,000 cells per $mm^3$; having a systolic blood pressure of <90 mm Hg after fluid challenge; exhibiting acute tubular necrosis; having empyema; having a known infection with mycobacteria, fungi, or *Pneumocystis carinii*; being treated for a seizure disorder; pregnancy or nursing, or having childbearing potential and not using an acceptable means of birth control; being enrolled in this study previously; receiving any investigational agent within the prior month; or having an underlying condition that might limit survival during the study.

Data to determine the pneumonia prognostic index described by Fine et al. (7) were collected to assess the severity of illness at baseline in the two treatment groups.

The pharmacist at each hospital assigned patients to the treatment groups by using a series of computer-generated randomization envelopes which were blinded until patient enrollment. Institutional review board approval was obtained at each site.

Upon entering the study, each patient gave a history and was subjected to a physical examination and chest radiography. An acute-phase serum sample was drawn and saved for serological studies. Each patient provided a repeat history, underwent another physical examination and chest radiography (if clinically indicated), and supplied a sputum specimen for culture (if possible) prior to hospital discharge, at 2 to 3 weeks postenrollment, and at 4 to 6 weeks postenrollment. Convalescent-phase serum was obtained during the final visit.

Respiratory secretions were cultured for routine respiratory pathogens by standard methods. Blood cultures were performed by standard procedures. Susceptibility to ofloxacin and standard therapy antimicrobial agents was determined by broth microdilution by using National Committee for Clinical Laboratory Standards guidelines. Susceptibility testing was not performed on *Legionella*, *Mycoplasma*, or *Chlamydia* isolates. Standard respiratory pathogens (*S. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus*), when isolated from purulent respiratory secretions, were considered to be pathogens. Other gram-negative isolates from purulent respiratory secretions were considered to be pathogens if gram-negative bacilli were identified on Gram stain.

Respiratory specimens, with and without pretreatment with acid, were cultured for *Legionella* spp. on buffered charcoal-yeast extract agar with and without supplemental antibiotics. *Legionella* urinary-antigen assays were performed as previously described (26) with a commercial radioimmunoassay kit (Binax, S. Portland, Maine). A mean counts-per-minute result for $^{125}$I that was three times that of the negative control was considered a positive result. Throat swab specimens for *C. pneumoniae* cultures and PCR assays were frozen and shipped to the laboratory of J. T. Grayston (University of Washington, Seattle) and processed as previously described (12, 13).

Samples for serologic testing were frozen, and paired specimens were assayed simultaneously. *Mycoplasma* antibodies were measured by complement fixation. *Legionella* antibodies were measured by indirect immunofluorescence assay with *L. pneumophila* serogroup 1 antigens. Immunoglobulin M and immunoglobulin G antibodies to *C. pneumoniae* were measured by microimmunofluorescence assay.

A definitive diagnosis of Legionnaires' disease was made on the basis of a positive culture, a positive urinary-antigen assay result, or a fourfold increase in the antibody titer. A definitive diagnosis of *M. pneumoniae* infection was made on the basis of a fourfold increase in the titer of the convalescent-phase specimen compared with the acute-phase sample titer. A probable diagnosis of *M. pneumoniae* infection was made on the basis of a single reciprocal titer of ≥32. A definitive diagnosis of *C. pneumoniae* infection was made on the basis of a positive culture or a fourfold increase in the reciprocal titer, while a probable diagnosis was made on the basis of an immunoglobulin M reciprocal titer of ≥16 or an immunoglobulin G reciprocal titer of ≥512.

**Clinical response.** The patients were monitored for chills, fever, pleuritic chest pain, cough, sputum production, dyspnea, and chest radiograph abnormalities. A patient's clinical response was categorized as cured (i.e., a return to preinfection baseline clinical status), improved (i.e., decreases in some of the parameters were evident, but the patient was not back to preinfection baseline), or failed (i.e., the patient required additional antimicrobial therapy because of the persistence of clinical symptoms or died because of the illness). Patients were considered nonevaluable for clinical efficacy if they were improving but had received less than 48 h of antibiotic treatment, if they had received concomitant antibiotics for treatment of different infections, if they had failed to demonstrate evidence of community-acquired pneumonia, or if they did not return for follow-up visits. Responses categorized as cured or improved were combined and classified as clinical successes, while those categorized as failed or nonevaluable were combined and classified as clinical failures in subsequent intent-to-treat analyses. The secondary end points included the length of hospitalization, the duration of therapy, and adverse events.

**Statistical analysis.** A sample size of 300 was chosen to determine if ofloxacin was as effective as standard therapy. There was an 82% power of detecting at least a 12% difference in the clinical cure rate between the two treatment groups. The calculations assumed a 90% cure rate in the standard therapy group and a two-sided significance level of 5%.

The primary clinical-efficacy analyses were based on clinically evaluable patients ($n$ = 227). Intention-to-treat analyses based on all 298 patients were also conducted. The distributions of clinical responses in the two treatment groups were compared by using Wilcoxon's rank sum test. The Breslow-Day test was applied to assess treatment-by-center interactions. A two-sided 95% confidence interval for the difference in clinical success rates was determined to evaluate the equivalence of the two therapies. For the secondary end points, the differences in duration of hospitalization, number of doses, and therapy duration were compared by using the Student's $t$ test. Separate subgroup analyses of patients with evidence of infection due to various types of atypical (*Legionella*, *Mycoplasma*, or *Chlamydia*) and typical pathogens were also performed. However, analyses of infections caused by specific pathogens were only descriptive, as the numbers of cases were too small for statistical comparison. Since there were no differences in the outcomes for the probable and definitive diagnostic categories, the data for the two were combined.

TABLE 1. Study demographics (all patients)

| Characteristic | Results for group treated with: | | Treatment group comparisons ($P$) |
|---|---|---|---|
| | Ofloxacin | Standard therapy | |
| Total subjects | 146 | 152 | NS[a] |
| No. (%) of: | | | |
| Males | 77 (53) | 74 (49) | 0.490 |
| Females | 69 (47) | 78 (51) | NS |
| White | 120 (83) | 128 (84) | 0.757 |
| African-American | 24 (17) | 21 (14) | NS |
| Other | 1 (1) | 3 (2) | NS |
| Age (mean ± SD) | 58.3 ± 18.2 | 57.3 ± 19.9 | 0.656 |
| No. (%) over age 65 | 60 (41) | 62 (41) | NS |
| Pneumonia prognostic index (mean + SD) | 1.7 ± 1.6 | 2.0 ± 1.8 | 0.194 |
| No. (%) in prognostic index class: | | | |
| I | 5 (3) | 0 (0) | NS |
| II | 38 (26) | 48 (32) | NS |
| III | 96 (66) | 89 (59) | NS |
| IV | 7 (5) | 13 (9) | NS |
| V | 0 (0) | 2 (1)[b] | NS |

[a] NS, not significant.
[b] One patient had staphylococcal pneumonia and was cured; the second was lost to follow-up.

## RESULTS

**Demographics.** There were 302 patients enrolled in the study between June 1993 and May 1994. Four patients were removed or dropped out before receiving any therapy (two had positive pregnancy tests, and two declined to participate for personal reasons), leaving 298 considered evaluable for treatment safety. There was an equal distribution of patients ($P$ = 0.97; $n$ = 298) among the participating centers ($n$ = 76, 68, 83, and 71 patients). Since the clinical response rates of the centers were not different ($P$ = 0.899; $n$ = 298), the pooled data are presented in this analysis.

The demographic characteristics of the 146 patients randomized to the ofloxacin treatment group were similar to those of the 152 patients receiving standard therapy (Table 1). The mean ages (± the standard deviations [SDs]) were 58.3 ± 18.2 and 57.3 ± 19.9 years in the ofloxacin and standard therapy groups, respectively. There were equal proportions of elderly patients in both groups, and there were no differences in the sex or race distributions of the two groups. The pneumonia prognostic indices were similar, with means (± SDs) of 1.7 ± 1.6 and 2.0 ± 1.8 in the ofloxacin and standard therapy groups, respectively. Most patients (92%, ofloxacin; 91%, standard therapy) were rated class II (0 points) or III (1 to 4 points) according to the prognostic index.

**Etiologic characteristics.** The most common typical bacterial pathogens were *S. pneumoniae* (isolated from 24 sputum specimens), *S. pneumoniae* (isolated from 8 blood specimens), and *H. influenzae* (isolated from 35 sputum specimens). Legionnaires' disease was identified in 12 patients, *M. pneumoniae* was found in 49 (27 definitive and 22 probable), and *C. pneumoniae* was identified in 52 (19 definitive and 33 probable).

Of the 298 patients receiving study antibiotics, there were 37

TABLE 2. Reasons for discontinuing therapy

| Reason | No. (%) of cases in group treated with: | | *P* value |
|---|---|---|---|
| | Ofloxacin | Standard therapy | |
| Adverse event | 14 (10) | 11 (7) | 0.327 |
| Resistant pathogen | 1 (1)[a] | 3 (2) | NS[b] |
| Clinical failure | 9 (6) | 15 (10) | 0.334 |
| Pneumonia not confirmed | 4 (3) | 2 (1) | NS |
| Personal | 2 (1) | 1 (1) | NS |
| Other | 7 (4) | 9 (6) | NS |
| Total | 37 (25) | 41 (27) | 0.445 |

[a] Culture negative; patient's therapy was discontinued because the investigator suspected a resistant pathogen.
[b] NS, not significant.

(25%) ofloxacin group cases and 43 (22%) standard therapy group cases considered nonevaluable for clinical efficacy; therefore, 227 (76.2%) patients could be evaluated. The reasons for nonevaluability included a lack of follow-up evaluation (22 and 21 patients in the ofloxacin and standard therapy groups, respectively), an insufficient course of therapy (5 and 7 cases, respectively), the administration of additional antibiotics for unrelated reasons (6 and 4 cases, respectively), and failure to confirm the initial chest radiograph interpretation (4 and 2 cases, respectively). Seventy-eight patients discontinued treatment during the study (Table 2). The most common reasons were adverse events and clinical failures.

**Clinical results.** Of the 227 evaluable patients, etiologic diagnoses were determined in 147 (64%) (Table 3). The most common pyogenic respiratory pathogens were *H. influenzae* (30 isolates) and *S. pneumoniae* (24 isolates). Among these patients were six cases of bacteremia due to *S. pneumoniae*. There was evidence of infection with either a *Legionella* sp. (8 patients), *M. pneumoniae* (38 patients, 24 definitive and 14 probable), or *C. pneumoniae* (40 patients, 16 definitive and 24 probable) in a total of 79 evaluable patients (35%). There were no differences in outcome between definitive and probable infections with *Mycoplasma* or *Chlamydia* organisms. There were 28 patients for whom two respiratory pathogens were identified. The most common combinations of pathogens were *C. pneumoniae* with *S. pneumoniae* (six cases) and *C. pneumoniae* with *M. pneumoniae* (five cases).

The initial parenteral regimens used in the standard therapy group were a beta-lactam agent alone (47 patients), a beta-lactam agent plus erythromycin (42 patients), erythromycin alone (14 patients), or other regimens (13 patients). Overall, 56 of 116 patients (48%) in the standard therapy group received a macrolide. The beta-lactam agents used most commonly were ampicillin-sulbactam, ceftizoxime, and ticarcillin-clavulanate. The choice of beta-lactam agents reflected the formulary of each study site.

The improvement in clinical parameters between the initial and final visits was similar in each treatment group. The clinical outcomes of therapy with ofloxacin or standard therapy are shown in Table 3 by etiologic agent. The clinical success rates (number cured plus number showing improvement) were similar in both groups. For the evaluable ofloxacin-treated patients, the clinical success rate was 92% (100 of 109), compared with a rate of 87% (103 of 118) for those receiving standard therapy. Although the number of cases due to any specific pathogen was small, there were no apparent differences in outcomes between the regimens. For example, the clinical success rate for patients with *S. pneumoniae* pneumonia was 92% for ofloxacin therapy and 91% for standard therapy; for patients with *H. influenzae* pneumoniae, the success rate was 93%

TABLE 3. Outcome by etiology for common pathogens at enrollment among evaluable patients

| Etiologic agent[a] | No. (%) per outcome category in group treated with: | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Ofloxacin | | | | Standard therapy | | | |
| | *n* | Cured | Improved | Failed | *n* | Cured | Improved | Failed |
| Typical pathogen | | | | | | | | |
| *S. pneumoniae* | 13 | 10 (77) | 2 (15) | 1 (8) | 11 | 10 (91) | 0 | 1 (9) |
| *H. influenzae* | 13 | 11 (85) | 1 (8) | 1 (8) | 17 | 10 (59) | 4 (24) | 3 (18) |
| *S. aureus* | 4 | 4 (100) | 0 | 0 | 3 | 2 (67) | 1 (33) | 0 |
| *M. catarrhalis* | 1 | 1 (100) | 0 | 0 | 2 | 2 (100) | 0 | 0 |
| *Pseudomonas aeruginosa* | 1 | 1 (100) | 0 | 0 | 1 | 1 (100) | 0 | 0 |
| *Neisseria meningitidis* | 1 | 1 (100) | 0 | 0 | 1 | 1 (100) | 0 | 0 |
| Other[b] | 8 | 2 (25) | 5 (62) | 1 (13) | 10 | 7 (70) | 1 (10) | 2 (20) |
| Total | 41 | 30 (73) | 8 (20) | 3 (7) | 45 | 33 (73) | 6 (13) | 6 (13) |
| Atypical pathogen | | | | | | | | |
| *L. pneumophila* | 6 | 5 (83) | 1 (17) | 0 | 2 | 0 | 0 | 2 (100) |
| *C. pneumoniae* | 24 | 18 (75) | 2 (8) | 4 (17) | 16 | 11 (69) | 1 (6) | 4 (25) |
| *M. pneumoniae* | 16 | 13 (81) | 1 (6) | 2 (13) | 22 | 16 (73) | 4 (18) | 2 (9) |
| Total | 42 | 34 (81) | 3 (7) | 5 (12) | 37 | 25 (68) | 5 (13) | 7 (19) |
| Total patients with pathogen | 71 | 54 (76) | 11 (16) | 6 (8) | 76 | 55 (72) | 10 (13) | 11 (15) |
| Total patients without pathogen | 38 | 29 (76) | 6 (16) | 3 (8) | 42 | 35 (83) | 3 (7) | 4 (10) |
| Total patients in study | 109 | 83 (76) | 17 (16) | 9 (8) | 118 | 90 (76) | 13 (11) | 15 (13) |

[a] Two patients had organisms that were resistant to initial therapy. One patient with a β-lactamase-producing *H. influenzae* was initially treated with parenteral ampicillin. Therapy was changed to ampicillin-sulbactam on day 3, and the patient improved and was discharged on amoxicillin-clavulanate. The other patient had *S. pneumoniae* (isolated from sputum) and was treated with parenteral sulfamethoxazole-trimethoprim, to which the isolate was resistant. The patient had improved and was discharged before the susceptibility tests were performed. He was found to be clinically cured at his follow-up visit.
[b] Includes *Klebsiella* spp., *E. coli*, and *Enterobacter* spp.

TABLE 4. Total number of reports of adverse events[a]

| Adverse event | No. reporting adverse event in group treated with: | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Ofloxacin | | | | Standard therapy | | | |
| | Mild | Moderate | Severe | Total | Mild | Moderate | Severe | Total |
| Nausea | 0 | 0 | 0 | 0 | 1 | 6 | 0 | 7 |
| Vomiting | 1 | 1 | 0 | 2 | 2 | 5 | 0 | 7 |
| Abdominal pain | 1 | 0 | 1 | 2 | 0 | 2 | 0 | 2 |
| Diarrhea | 1 | 2 | 0 | 3 | 2 | 2 | 0 | 4 |
| *Clostridium difficile* colitis | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 |
| Dehydration | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| Rash | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 2 |
| Phlebitis | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 |
| Insomnia | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |
| Glossitis | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| Genital candidiasis | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 2 |
| Empyema | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| Total events | 4 | 5 | 3 | 12 | 9 | 19 | 0 | 28 |

[a] Adverse events considered definitely or probably related to the drugs used in the study; patients may have more than one adverse event.

for ofloxacin therapy and 83% for standard therapy. For patients with infections caused by the atypical pathogens, the clinical success rate was 88% (37 of 42) for the ofloxacin group and 81% (30 of 37) for those receiving standard therapy; these differences were not statistically different. Similar results were obtained for the intent-to-treat analysis of all patients ($n$ = 298). The clinical success rates were 72.6% (60.3% cured plus 12.3% improved) for the ofloxacin treatment group and 69.1% (60.5% cured plus 8.6% improved) for the standard therapy group.

**Microbiological assessments.** The standard respiratory pathogens in both groups were susceptible to ofloxacin. All but two patients in the standard therapy group were treated empirically with at least one antimicrobial agent to which the typical pathogens were susceptible (Table 3). No penicillin-resistant isolates of *S. pneumoniae* were identified.

**Effect of drug use and hospitalization.** Among the 227 patients evaluable for clinical efficacy, the mean durations (± SDs) of total antibiotic therapy were 14.5 ± 5.3 days with ofloxacin and 15.7 ± 108 days with standard therapy ($P$ = 0.768). The mean durations of hospitalization were 6.1 ± 4.9 days in the ofloxacin group and 6.4 ± 5.4 days in the standard therapy group ($P$ = 0.746). The mean numbers of intravenous doses of antibiotics were 7.5 ± 8.0 in the ofloxacin group and 18.4 ± 18.5 in the standard therapy group ($P < 0.001$). The mean number of oral antibiotic doses in the ofloxacin group was 19.7 ± 11.2 per patient, compared with 30.2 ± 16.0 oral antibiotic doses in the standard therapy group ($P < 0.001$).

**Safety.** The antibiotics in both treatment groups were well tolerated (Table 4). Of the 298 patients who were considered evaluable for treatment safety, 27 (9%) experienced adverse events that were thought to be attributable to antimicrobial therapy. Of the 12 adverse events reported in the ofloxacin group, 9 were mild or moderate and 3 were severe in intensity (one each for abdominal pain, dehydration, and empyema). All of the 28 events reported in the standard therapy group were mild or moderate in nature; the most common adverse events were gastrointestinal.

## DISCUSSION

Community-acquired pneumonia is a common problem, and its treatment poses new challenges because of the growing incidence of antibiotic resistance among traditional respiratory pathogens and the increasing recognition of pneumonia caused by atypical respiratory pathogens (23).

Because rapid diagnosis of the etiologic agents causing respiratory infections is difficult, the treatment of patients with respiratory infection is usually empiric.

This study was an attempt to replicate the conditions observed in actual community practices and to determine the effectiveness of ofloxacin therapy compared with that of the standard regimens prescribed by attending physicians. Our study suggests that ofloxacin is effective against both atypical and traditional respiratory pathogens. The majority of patients in both treatment groups were clinically cured or showed improvement at the end of therapy (100 of 109 [92%], ofloxacin; 103 of 118 (87%), standard therapy). Clinical success rates were similarly high for patients infected with the atypical pathogens (88%, ofloxacin; 81%, standard therapy). Several patients with atypical pneumonia who received only beta-lactam therapy were categorized as failures because a macrolide was added to the treatment regimen several days later. We included both definitive and probable cases of *M. pneumoniae* and *C. pneumoniae* infections, as the clinical success rates were not different. The presence of dual infections with respiratory pathogens has been reported previously (15, 22, 24). Recent studies indicate that an initial infection with another pathogen may improve the adherence of pneumococci to respiratory endothelial cells by increasing the number of available receptor sites (5). An antecedent infection with *Mycoplasma* or *Chlamydia* organisms may predispose the patient to a secondary pyogenic infection. Alternatively, some patients may have a specific antibody response to the offending pathogen and a nonspecific increase in (cross-reacting) antibodies to an additional respiratory pathogen.

All bacterial pathogens identified were susceptible to ofloxacin. There were two patients in the standard therapy group from whom bacterial pathogens were isolated that were resistant to the antibiotics selected. Ofloxacin and standard antibiotic regimens were well tolerated and not associated with any unexpected clinical or laboratory test abnormalities.

Traditional antibiotics are now losing microbiologic and clinical effectiveness against common respiratory pathogens because of the emergence of several types of antibiotic resistance. In a recent study of respiratory isolates obtained from patients in the United States, 84% of *M. catarrhalis* isolates and

17% of *H. influenzae* isolates were resistant to penicillin, ampicillin, and amoxicillin (16). In a recent survey of 499 *S. pneumoniae* isolates from bacteremic patients, penicillin resistance was noted in 8.0% of the isolates, while 2.8% were resistant to ofloxacin (25).

Cross-resistance to antibiotics is also emerging in these pathogens. A recent survey of 13 hospitals in 12 states was conducted by the Centers for Disease Control and Prevention to determine the susceptibilities of *S. pneumoniae* isolates to common antibiotics. Preliminary findings indicated that 36 of 544 (6.6%) pneumococcal isolates were penicillin resistant. Of the 36 isolates, 19 were also resistant to trimethoprim-sulfamethoxazole, 15 were resistant to cefaclor, and 8 were resistant to erythromycin (2).

In another recent study of *S. pneumoniae* isolates from bacteremic patients, 4 of 81 (5%) isolates were resistant to erythromycin and clarithromycin (20).

Our findings were similar to those of other clinical studies of lower respiratory tract infection comparing oral ofloxacin with the usual treatment regimens in a multicenter trial of hospitalized patients with bacterial pneumonia (27). Patients in both groups had favorable responses to therapy. *S. pneumoniae* was isolated from the sputa of 37 patients, 9 of whom were bacteremic.

Similar successful results of ofloxacin therapy were observed for community-acquired lower respiratory infection by Gentry et al. (10) and also for nosocomial pneumonia (8).

In our study, physicians could choose the antibiotics they preferred for patients randomized to standard therapy group. We commonly observed the use of two antimicrobial agents in the standard therapy group; while this provided broad antibacterial coverage, it resulted in the administration of a greater number of antibiotic doses than was given in the ofloxacin group. The mean numbers of intravenous doses were 7.5 in the ofloxacin group and 18.4 in the standard therapy group. Attending physicians could change from parenteral to oral therapy in either arm of the study when they felt that the patient was improved and could tolerate oral therapy.

The mean numbers of oral doses were 19.7 in the ofloxacin group and 30.2 in the standard therapy group. For the ofloxacin group, this represents the use of fewer than half the number of intravenous doses and a 35% reduction in oral doses compared with the standard therapy group doses.

The findings of this study indicate that ofloxacin, when given as monotherapy for the empiric treatment of bacterial community-acquired pneumonia, was as effective as standard antibiotic therapy (frequently combination antimicrobial therapy) with a variety of antibiotics. Ofloxacin was active both in vitro and in vivo against traditional bacterial pathogens and was clinically active against the three most common atypical respiratory pathogens (*C. pneumoniae*, *M. pneumoniae*, and *L. pneumophila*). Ofloxacin may result in better patient acceptance and compliance because fewer doses are required.

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