Reducing empirical use of fluoroquinolones for Pseudomonas aeruginosa infections improves outcome

Lee H. Nguyen1, Donald I. Hsu2, Vaidyanathan Ganapathy3, Kimberly Shriner4 and Annie Wong-Beringer3,4*

1Loma Linda University, School of Pharmacy, Loma Linda, CA, USA; 2Western University, Pomona, CA, USA; 3University of Southern California, Los Angeles, CA, USA; 4Huntington Hospital, Pasadena, CA, USA

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Background: We previously reported ciprofloxacin resistance (CR) and empirical use of fluoroquinolones as predictors of mortality in patients infected with Pseudomonas aeruginosa in a case–control study. Here, we assessed the clinical impact of reducing empirical fluoroquinolone use for P. aeruginosa infections in hospitalized patients by performing a follow-up study in 2005–06 [period 2 (P2)] and comparing this with prior data from 2001–02 [period 1 (P1)].

Methods: Medical charts of infected patients who received at least 72 h of antibiotic therapy were reviewed. Patients were subgrouped based on the susceptibility of infected strains into the CR or ciprofloxacin-susceptible group. Antibiograms, patient and treatment variables and outcome measures were compared between groups and between study periods.

Results: Study patients were elderly (median age, 76 years), had a median of three co-morbidities and a median APACHE II score of 13. Most (75%) had pneumonia or urosepsis. Empirical use of fluoroquinolones was reduced by 30% in P2 versus P1, with a corresponding 39% increase in piperacillin/tazobactam use. The resultant positive impact observed in the CR group during P2 includes shortened delay to receipt of effective therapy (1 versus 3.5 days, \( P < 0.0001 \)), reduced length of stay (13 versus 16 days, \( P = 0.03 \)) and 2-fold lower mortality (9% versus 22%, \( P = 0.05 \)). Susceptibility of P. aeruginosa improved by 10% to all antipseudomonal agents tested.

Conclusions: In settings where high rates of fluoroquinolone resistance exist, use of non-fluoroquinolone-based empirical regimens for P. aeruginosa infections improves patient outcomes and organism susceptibility over time.

Keywords: fluoroquinolone resistance, reduced mortality, prescribing changes

Introduction

Pseudomonas aeruginosa is a leading Gram-negative pathogen that causes nosocomial infections, accounting for 20% of pneumonia and 16% of urinary tract infections according to recent data from the National Nosocomial Infections Surveillance System.1 The rapid emergence of antibiotic-resistant strains of P. aeruginosa poses a significant challenge to clinicians. In particular, the rate of fluoroquinolone resistance has tripled over the last decade due to widespread prescribing of the fluoroquinolones.2 Many such strains also show cross-resistance to other structurally unrelated antipseudomonal agents (aminoglycosides, cephalosporins, carbapenems and \( \beta \)-lactamase inhibitor combinations)2–7 severely limiting potential treatment options.

We have performed a case–control study previously and reported that infections caused by fluoroquinolone-resistant P. aeruginosa are associated with prolonged illness and 3-fold higher mortality compared with susceptible strains.8 Specifically, fluoroquinolone resistance and empirical use of fluoroquinolones were independent predictors of mortality after controlling for underlying severity of illness using multivariate logistic regression analysis.8 We have subsequently implemented an institution-wide programme to reduce fluoroquinolone empirical prescribing through physician education and antibiotic use...
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guidelines emphasizing the use of β-lactam-based regimens as first-line therapy for a variety of infections. Therefore, we performed a follow-up study to assess the clinical impact of reducing empirical use of fluoroquinolones on outcomes of P. aeruginosa infections.

Methods

Study design

Both the prior and follow-up studies were conducted at a 525-bed community teaching hospital and were approved by the hospital's Institutional Review Board. The same retrospective case–control study design and definitions were used in both studies. Ciprofloxacin was used as a marker for fluoroquinolone susceptibility. Case patients were hospitalized adults infected with ciprofloxacin-resistant (CR) P. aeruginosa while those infected with ciprofloxacin-susceptible (CS) strains were used as controls. Study periods were May 2001 to July 2002 (period 1 (P1)) for the prior study and May 2005 to May 2006 (period 2 (P2)) for the current follow-up study. The microbiology laboratory computer records were screened for any hospitalized adult patients from whom P. aeruginosa was isolated. If P. aeruginosa had been isolated on multiple occasions within a 6 month period in the same patient, only the first episode of infection was reviewed.

Bacterial isolation and testing

P. aeruginosa was identified by its characteristic positive oxidase reaction and blue-green pigmentation and with the use of the Gram-Negative Identification Panel (Vitek, bioMérieux, Hazelwood, MO, USA). In vitro susceptibility testing was carried out by broth microdilution testing (Vitek, bioMérieux) and results interpreted according to CLSI guidelines.7 The agents tested included: ciprofloxacin, levofloxacin, piperacillin/tazobactam, cefazidime, ceftazidime, imipenem, gentamicin, tobramycin and amikacin. Strain ATCC 27853 was used as a reference strain. Specifically, fluoroquinolone resistance included strains with intermediate susceptibility as defined by ciprofloxacin MIC ≥2 mg/L and levofloxacin MIC ≥4 mg/L.

Definitions and data collection

Medical charts were reviewed for pertinent demographic, laboratory and clinical data. A structured data collection form was used to record the abstracted data which were later compiled into a single data set using a relational database management program (Microsoft Access). Demographic data included age, gender, co-morbid conditions, residence prior to hospitalization (home, transferred from outside hospital or facility), source of infection, time to infection, intensive care unit (ICU) and length of stay (LOS). Co-morbid conditions included diabetes mellitus, coronary artery disease, cerebrovascular disease, pulmonary disease (asthma, chronic obstructive pulmonary disease), hepatic dysfunction (total bilirubin >2.5 mg/dL or 42.75 mmol/L, alanine aminotransferase/aspartate aminotransferase >2 × normal limits, or known liver disease), renal insufficiency (serum creatinine >2.0 mg/dL or 34.2 mmol/L), malignancy, neutropenia (<500 cells/mm³), corticosteroid use (prednisolone ≥20 mg/day or equivalent) and use of an immunosuppressive agent within 30 days. An Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated for each patient at the time of admission to assess the severity of the underlying illness.10 Details of antimicrobial therapy prescribed (agent, dose and duration) were recorded. A regimen was considered effective if it contained at least one agent active against the isolated P. aeruginosa strain.

Patients eligible for inclusion were those who had a documented infection defined by criteria established by the CDC11 and who received at least 48 h of effective therapy. Patients were excluded if they received any investigational agents within 14 days or had had previousantipseudomonal agents were arbitrarily grouped as follows: piperacillin/tazobactam, cefazidime or cefepime, imipenem or meropenem, ciprofloxacin or levofloxacin, and gentamicin or tobramycin or amikacin. Multidrug resistance (MDR) was defined as resistance to two or more antipseudomonal agents from at least two different groups.

Data analysis

Eligible patients were evaluated on the following outcome measures: (i) delay to receipt of effective treatment; (ii) clinical response; (iii) LOS after isolation; (iv) total length of stay (TLOS); and (v) in-hospital mortality (infection-related and overall). The above outcome variables were compared between patients from P1 versus P2 among those infected with CS-P. aeruginosa (controls) and CR-P. aeruginosa (cases), respectively. In addition, antibiograms for P. aeruginosa between study periods (P1 versus P2) were compared.

Responders included complete and partial response while failure and relapse were considered non-response. Complete response was defined as resolution of fever, leucocytosis and signs of infection, whereas an improvement of the above was considered as partial response. Treatment failure was defined as the absence of resolution or worsening of signs and symptoms of infection. Relapse was considered when an infection with P. aeruginosa occurred at any body site within a month after discontinuation of therapy. Outcomes defined as indeterminate due to incomplete information were excluded from the final analysis.

Statistical analysis

Statistical analyses were carried out with SPSS version 15.0 (Chicago, IL, USA) and GraphPad Prism version 4.0 (San Diego, CA, USA). Case and control variables were compared using Student’s t-test, Mann–Whitney U-test, χ² or Fisher’s exact test where applicable. Linear and logistic regression analysis was performed to adjust for confounders that contribute to differences in outcome measures between study periods. All statistical tests were two-tailed; P ≤ 0.05 was considered significant.

Results

Patient characteristics

Over a 5 year span from 2001 to 2006, a total of 578 patients were screened positive for P. aeruginosa isolation from any body site during study periods P1 and P2. A total of 230 episodes of infection were deemed evaluable for the study, 119 from P1 and 111 from P2. The remaining 348 patients were excluded for the following reasons: incomplete medical records, treatment duration ≤48 h or duplicate patients with repeat episode of infection within 6 month period of initial infection.
Results for patients from P1 have been published previously and were used as the basis for comparing data from patients evaluated during P2. CR- \textit{P. aeruginosa} accounted for 130 cases of infectious episodes (65 each; P1 and P2) while CS strains accounted for 100 controls (54, P1; 46, P2).

A comparison of clinical characteristics between cases and controls and between study periods is shown in Table 1. The overall study population represented primarily elderly hospitalized patients (median age 76 years, IQR 60–84) with multiple co-morbidities (median 3, IQR 2–5) and moderately severe underlying illness (median APACHE II score 13, IQR 9–20). When compared with controls, cases were more likely to have: (i) advanced age (median 78 versus 74 years, \( P = 0.0075 \)); (ii) a higher APACHE II score (median 16.5 versus 11.5, \( P < 0.0001 \)); (iii) a greater number of co-morbidities (median 3 versus 2, \( P = 0.0001 \)); and (iv) resided in an acute or long-term care facility prior to hospitalization (\( 63\% \) (82/130) versus 29\% (29/100), \( P < 0.0001 \)). Cases and controls between study periods were similar in characteristics with a few exceptions. When compared with cases from P1, P2 cases: (i) had a slightly higher APACHE II score (17 versus 15, \( P = 0.2 \)); (ii) were less likely to have underlying cerebrovascular or pulmonary disease; and (iii) were equally likely to have resided in the community versus acute/long-term care setting prior to hospitalization (Table 1).

### Microbiological characteristics

Overall, infected isolates were obtained most frequently from sputum (40\%, 92/230) followed by urine (36\%, 83/230), wound (14\%, 33/230), blood (5\%, 12/230) and other sites (4\%, 10/230) during both periods. Notably, CR strains were more frequently isolated from sputum (44\% versus 35\%, \( P = 0.17 \)) but less frequently from blood (2.3\% versus 9\%, \( P = 0.03 \)) compared with CS strains. The rate of fluoroquinolone susceptibility among \textit{P. aeruginosa} strains at our institution has declined markedly from 80\% in 1997 to a nadir of 43\% in 2004, with a return to 56\% based on the 2006 antibiogram (Figure 1). Fluoroquinolone resistance was significantly associated with cross-resistance to other antipseudomonal agents for strains recovered from both study periods (Figure 2). Only 12\% (15/130) of the CR strains from both study periods were resistant to ciprofloxacin alone; nearly 68\% (88/130) were resistant to ≥3 drug classes, with 2.3\% (3/130) resistant to all antipseudomonal agents tested (Figure 2). In contrast, cross-resistance with other antipseudomonal compounds occurred rarely among all CS-\textit{P. aeruginosa}.

### Table 1. Comparison of patient characteristics (cases versus controls; period 1 versus period 2)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (%)</th>
<th>Control (%)</th>
<th>( P ) value</th>
<th>Case (%)</th>
<th>Control (%)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>79 (62.5–84.5)</td>
<td>78 (62.5–83.5)</td>
<td>NS</td>
<td>70.5 (56.5–82)</td>
<td>76 (52.5–85.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Age P1 + P2 combined</td>
<td>78 (62.5–84)</td>
<td>55/45</td>
<td>NS</td>
<td>74 (56.5–82)</td>
<td>37/63</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (%M/F)</td>
<td>46/54</td>
<td>55/45</td>
<td>NS</td>
<td>52/48</td>
<td>11.5 (8–16)</td>
<td>NS</td>
</tr>
<tr>
<td>APACHE II score, median (IQR)</td>
<td>15 (10–21.5)</td>
<td>17 (11–25.5)</td>
<td>NS</td>
<td>0.20</td>
<td>11.5 (8–16)</td>
<td>NS</td>
</tr>
<tr>
<td>APACHE II score—P1 + P2 combined</td>
<td>16.5 (11–23)</td>
<td>11.5 (8–16)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>nosocomial</td>
<td>49 (75)</td>
<td>33 (51)</td>
<td>0.0036</td>
<td>15 (28)</td>
<td>17 (37)</td>
<td>NS</td>
</tr>
<tr>
<td>community</td>
<td>16 (25)</td>
<td>32 (9)</td>
<td>0.0036</td>
<td>39 (72)</td>
<td>29 (63)</td>
<td>0.34</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>21 (32)</td>
<td>23 (35)</td>
<td>0.71</td>
<td>7 (13)</td>
<td>16 (35)</td>
<td>0.0098</td>
</tr>
<tr>
<td>CAD</td>
<td>16 (25)</td>
<td>14 (22)</td>
<td>0.68</td>
<td>15 (28)</td>
<td>9 (20)</td>
<td>0.34</td>
</tr>
<tr>
<td>CVA</td>
<td>30 (46)</td>
<td>16 (25)</td>
<td>0.0102</td>
<td>20 (37)</td>
<td>11 (24)</td>
<td>0.16</td>
</tr>
<tr>
<td>renal dysfunction</td>
<td>12 (19)</td>
<td>14 (22)</td>
<td>0.66</td>
<td>13 (24)</td>
<td>5 (11)</td>
<td>0.087</td>
</tr>
<tr>
<td>hepatic dysfunction</td>
<td>3 (5)</td>
<td>1 (2)</td>
<td>0.31</td>
<td>2 (1)</td>
<td>1 (2)</td>
<td>0.91</td>
</tr>
<tr>
<td>pulmonary disease</td>
<td>26 (40)</td>
<td>14 (22)</td>
<td>0.0226</td>
<td>16 (30)</td>
<td>10 (22)</td>
<td>0.37</td>
</tr>
<tr>
<td>No. co-morbidities, median (IQR)</td>
<td>3 (2–4)</td>
<td>3 (2–4)</td>
<td>NS</td>
<td>0.8</td>
<td>2 (1–3)</td>
<td>0.0145</td>
</tr>
<tr>
<td>No. co-morbidities—P1 + P2 combined</td>
<td>3 (2–4)</td>
<td>2 (1–3)</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
strains, with only 10% of the isolates demonstrating a multidrug-resistant pattern.

**Outcome analysis**

A total of 130 cases and 100 controls were evaluated for outcomes. The majority of the infections involved the respiratory ($n = 92/230, 40\%$) and urinary tract ($n = 83/230, 36\%$). Data related to antimicrobial therapy administered are shown in Table 2. Following implementation of an institution-wide programme to reduce fluoroquinolone prescribing, the overall prescribing of ciprofloxacin or levofloxacin as empirical antipseudomonal agents was significantly reduced by 30\% [59\% (44/74) in P1 versus 29\% (27/92) in P2; $P < 0.0001$] with a corresponding increase of 39\% in piperacillin/tazobactam use in P2 [8\% (6/74) in P1 to 47\% (43/92) in P2; $P < 0.0001$]. This reduction in empirical prescribing of the fluoroquinolones resulted in nearly twice the number of CR-P. aeruginosa-infected patients receiving an effective empirical regimen [43\% (28/65) versus 25\% (16/65), $P = 0.02$] during the follow-up period. In addition, delay in receipt of effective therapy was shortened by 2.5 days (P1 median of 3.5 days versus P2 median of 1 day; $P < 0.0001$) in the CR group and 1 day (P1 median of 1 day versus P2 median of 0 days; $P = 0.009$) in the CS group when compared with the initial study.

A comparison of outcome measures between cases and controls and between study periods is shown in Table 3. More favourable outcomes were consistently observed for patients infected with CS- compared with CR-P. aeruginosa strains. Specifically, a significantly higher proportion of patients achieved clinical stability [72\% (72/100) versus 58\% (75/130); $P = 0.025$] and infection-related mortality was 2-fold lower [6\% (6/100) versus 15\% (20/130); $P = 0.026$] for patients infected with CS strains. For patients infected with CR-P. aeruginosa strains,

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**Table 2. Antimicrobial regimens**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (%)</th>
<th>Control (%)</th>
<th>$P$ value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical antipseudomonal (overall)</td>
<td>CR-P1 $n = 65$</td>
<td>CR-P2 $n = 65$</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ciprofloxacin or levofloxacin</td>
<td>35 (54)</td>
<td>57 (88)</td>
<td></td>
</tr>
<tr>
<td>ceftazidime or cefepime</td>
<td>19 (54)</td>
<td>16 (28)</td>
<td>0.0119</td>
</tr>
<tr>
<td>piperacillin/tazobactam</td>
<td>8 (23)</td>
<td>6 (11)</td>
<td>NS 0.11</td>
</tr>
<tr>
<td>imipenem or meropenem</td>
<td>5 (14)</td>
<td>29 (51)</td>
<td>0.0004</td>
</tr>
<tr>
<td>combination therapy</td>
<td>3 (9)</td>
<td>4 (7)</td>
<td>NS 0.78</td>
</tr>
<tr>
<td></td>
<td>7 (20)</td>
<td>5 (9)</td>
<td>NS 0.39</td>
</tr>
<tr>
<td>Non-antipseudomonal regimen</td>
<td>30 (46)</td>
<td>8 (12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Receipt of effective empirical therapy</td>
<td>16 (25)</td>
<td>28 (43)</td>
<td>0.02</td>
</tr>
<tr>
<td>Time to effective therapy, median days (IQR)</td>
<td>3.5 (3–4)</td>
<td>1 (0–3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total duration of treatment, median days (IQR)</td>
<td>10 (5–17)</td>
<td>12 (8–17)</td>
<td>NS 0.43</td>
</tr>
</tbody>
</table>

<sup>a</sup>$x^2$. 

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*Figure 2. MDR phenotype of P. aeruginosa by number of drug classes. CR, ciprofloxacin-resistant; CS, ciprofloxacin-susceptible; P1, period 1; P2, period 2. *Susceptibility of colistin was unknown.*
P2 patients had a shorter LOS (total, 15 versus 25 days; $P = 0.006$ and after isolation, 13 versus 16 days; $P = 0.03$) and lower infection-related mortality [9% (6/65) versus 22% (14/65); $P = 0.05$] when compared with patients in P1. While the time to achieve clinical stability was prolonged by 2 days for CR-$P. \text{aeruginosa}$-infected patients compared with CS-$P. \text{aeruginosa}$-infected patients, the overall duration of illness was similar between study periods within the respective groups.

To control for potential confounders (e.g. co-morbid conditions, APACHE II score and invasive versus non-invasive infection) that may affect the observed differences in outcome measures between study periods for CR-$P. \text{aeruginosa}$-infected patients, a multivariate logistic regression analysis was performed. Invasive infection ($P < 0.001$), underlying severity of infection as measured by APACHE II score ($P < 0.001$) and fluoroquinolone resistance ($P = 0.007$) significantly predicted LOS. After adjusting for co-morbid conditions and significant predictors of LOS above, reduced use of fluoroquinolone for empirical therapy remains a significant variable accounting for a 5 day reduction in LOS in the P2 cohort compared with P1 ($P < 0.002$). In addition, the odds ratio favouring mortality was 0.5 for the P2 cohort after adjustment. The above analysis demonstrated that the favourable outcomes observed in the P2 cohort (with respect to reduced LOS and mortality) were not attributable to differences in patient variables that impact outcome.

Discussion

We have implemented an institution-wide programme to reduce empirical fluoroquinolone prescribing and measured its impact on outcomes of patients infected with $P. \text{aeruginosa}$. A significant reduction in fluoroquinolones prescribed for empirical anti-pseudomonal therapy was observed post-intervention from 59% to 29%, with a corresponding increase in the use of piperacillin/tazobactam from 8% to 47%. During the span of 5 years between study periods, $P. \text{aeruginosa}$ susceptibility improved for ciprofloxacin from 45% to 56% while piperacillin/tazobactam remains stable at 81%. Notably, susceptibility to other antipseudomonal agents also improved in the last 2 years of the study (2005 and 2006). Positive clinical impact resulted from the change in prescribing pattern and included a shortened delay to receipt of effective therapy by 2.5 days, reduced TLOS by 10 days and a 2-fold reduction in infection-related mortality from 22% to 9% for patients infected with fluoroquinolone-resistant $P. \text{aeruginosa}$. Similar trends but less dramatic improvements in outcomes were observed for those infected with susceptible strains post-intervention.

Patients evaluated during both study periods represented an elderly population with multiple co-morbidities who had a $P. \text{aeruginosa}$ infection, primarily of the respiratory or urinary tract. Linear regression and logistic regression models were used to adjust for differences between study cohorts in clinical variables that could impact outcome such as co-morbid conditions, APACHE II score and the presence of invasive infection. Nonetheless, improvement in outcome measures following fluoroquinolone educational intervention remains significant even after adjustment of potential confounders, affirming that antimicrobial prescribing practice is a modifiable practice pattern that plays a key role in affecting patient outcomes.
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Consistent with our findings, others have shown that inadequate empirical therapy is a significant predictor of mortality in critically ill infected patients. As shown by Kollef et al.13 infected patients who received inadequate antimicrobial regimens had a 4-fold increased risk of hospital mortality. Infections caused by P. aeruginosa were most frequently associated with receipt of inadequate therapy due to the multidrug-resistant phenotype of this pathogen. Prior use of a fluoroquinolone has been identified as a significant risk factor for the acquisition of fluoroquinolone-resistant and multidrug-resistant P. aeruginosa by our group and others. In a large cohort of patients infected with fluoroquinolone-resistant P. aeruginosa (n = 332), Gasink et al. observed significantly greater median hospital charges ($62 325 versus $48 732, P = 0.007) and higher mortality (47% versus 35%, P = 0.004) compared with those infected with susceptible strains (n = 540). However, this study did not specify whether those with positive cultures for P. aeruginosa were colonized or infected. More importantly, appropriateness of initial or definitive therapy was not assessed in this study, precluding analysis of the role of initial therapy on outcome of infections. In another study, by Nseir et al., more than half of the 236 patients (56%) in the ICU received either ciprofloxacin or ofloxacin during the study period. Again, prior fluoroquinolone use was significantly associated with subsequent infection or colonization of ICU-acquired multidrug-resistant bacteria which included ceftazidime- or imipenem-resistant P. aeruginosa. Separately, in a large retrospective cohort study of 305 patients with P. aeruginosa bloodstream infection, 25% (n = 75) of patients were treated with inappropriate initial therapy; most of whom (88%) received an antipseudomonal agent for which the isolated bacteria demonstrated resistance by in vitro susceptibility testing. Notably, use of ciprofloxacin was associated with statistically greater likelihood of inappropriate therapy than cefepime or ceftazidime. Those who received inappropriate initial therapy had significantly higher mortality (31% versus 18%, P = 0.018) and longer LOS (41 versus 24 days, P = 0.006) compared with those who received appropriate therapy. The above studies suggest a significant relationship between prior fluoroquinolone use and subsequent infection or colonization with fluoroquinolone-resistant or multidrug-resistant P. aeruginosa and that inappropriate initial therapy significantly affects outcomes of infections. Specifically, in this study which was conducted in a setting where the rate of fluoroquinolone resistance exceeds 50% for P. aeruginosa, we confirmed that initial treatment with fluoroquinolones for P. aeruginosa infections is associated with poor outcomes as measured by in-hospital mortality and length of hospital stay.

Thus, in a setting where a high rate of fluoroquinolone resistance and cross-resistance to antipseudomonal agents exists among P. aeruginosa strains, avoiding the use of fluoroquinolones for empirical treatment is prudent. We have demonstrated that by changing our prescribing practice from fluoroquinolone- to β-lactam-based empirical therapy, a delay in receipt of effective therapy was significantly reduced from 3.5 days to 1 day for patients infected with CR-P. aeruginosa. In addition, when empirical use of fluoroquinolone was minimized at large, we observed a positive impact not only on the individual patient but also on the overall susceptibility of P. aeruginosa to all antipseudomonal agents. This latter observation may be related to a reduced selection pressure for strains overexpressing the broad substrate multidrug efflux pumps that confer resistance to fluoroquinolones and other structurally unrelated antipseudomonal agents.3,19

Our study has several potential limitations: the retrospective chart review may miss confounding variables on patient outcomes and our population of elderly patients may not be generalized to other settings. However, the relationship between inappropriate initial therapy and poor infection outcomes appears to be universally applicable, particularly among those with serious infections such as pneumonia and bloodstream infection and those with co-morbidities and severe underlying illness. Additionally, it is possible that infection or colonization rates with fluoroquinolone-resistant P. aeruginosa be further reduced with a more stringent infection control practice in place as part of our intervention programme. Nonetheless, the lack of infection control practice change between study periods further demonstrates how changes in prescribing practice alone, in this case, reduction in fluoroquinolone prescribing, can positively impact patient outcome. By limiting the use of fluoroquinolone agents for empirical therapy, we have significantly reduced LOS and mortality among patients infected with fluoroquinolone-resistant P. aeruginosa and improved the overall antibiogram for this pathogen thereby restoring utility of all existing antipseudomonal agents.

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Transparency declarations
None to declare.

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