Letter

Do fluoroquinolones actually increase mortality in community-acquired pneumonia?

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See related research by Mortensen *et al*. in this issue [http://ccforum.com/content/10/1/R8]

I read with interest the report by Mortensen and coworkers [1], who found the use of initial empiric antimicrobial therapy with a β-lactam and a fluoroquinolone to be associated with increased short-term mortality in patients with severe community-acquired pneumonia (CAP) compared with other guideline-concordant antimicrobial regimens. However, the study has a number of limitations other than those stated by the authors.

First and foremost, almost 51% of the patients had a PORT (Pneumonia Patient Outcomes Research Team) score of 1–4 and did not meet the inclusion criteria as specified by the authors. Second, almost 9% of the patients received antibiotics after 8 hours, which alone is known to influence outcomes in patients with pneumonia. Two large studies showed that antibiotic administration within 4 hours [2] and 8 hours [3] of arrival in the hospital was associated with decreased mortality and length of stay. It is possible that this group of patients who received treatment after 8 hours was composed entirely of those who received fluoroquinolones, thus accounting for the adverse outcomes with this treatment. Another important point pertains to the choice of antibiotic; almost 25% of the patients in the study received piperacillin–tazobactam for CAP. This treatment should be reserved for serious hospital-acquired infections, and routinely is not necessary for management of CAP except in situations where *Pseudomonas aeruginosa* infection is suspected [4]. Using inappropriate antibiotics in such situations has increased the incidence of expanded-spectrum β-lactamases, which are resistant to multiple classes of antibiotics [5].

Finally, the results of this retrospective study are discordant with the recently published MOXIRAPID study [6]. This multicenter trial, conducted among adult patients hospitalized with CAP, compared fluoroquinolone monotherapy (moxifloxacin) with standard therapy (cephalosporin with or without a macrolide). Although the clinical outcomes were similar in the groups, patients randomly assigned to receive moxifloxacin had rapid resolution of fever and relief of symptoms such as chest pain, as recorded in patient diary entries.

Authors' response

EM Mortensen, MI Restrepo, A Anzueto and J Pugh

We appreciate Dr Agarwal's interest in our article. However, we should like to respond to the comments made.

First, the statement that 51% of patients had pneumonia severity index scores of I–IV and therefore did not meet the inclusion criteria is incorrect. As described in the Methods section of our paper [1], the inclusion criterion for severe CAP was either being in pneumonia severity index class V, meeting American Thoracic Society criteria for severe pneumonia [4], or being hospitalized in the intensive care unit (ICU) during the first 24 hours after presentation. Although the pneumonia severity index has been demonstrated to be the best risk adjustment tool for CAP [7], it was designed to help determine which patients may be treated as outpatients, and not which patients should be admitted to the ICU [8]. Therefore we used it only as one of several definitions of severe CAP. Our study also points out the limitation of the pneumonia severity index in identifying those patients who require ICU care.

Second, Dr Agarwal expresses concern that prolonged time to initial receipt of antibiotics (>8 hours) might have co-occurred with use of fluoroquinolones. As stated in the Methods section of our report, a dichotomized variable of whether or not a patient received an initial dose of antibiotics within the currently recommended 4 hours was included in our multivariable model. Also, as shown in Table 2 of the

report, there were no significant differences with respect to initial receipt of antibiotics within 4 hours between the different antibiotics, and neither was there a significant difference between antibiotic groups in administration within 8 hours (59% versus 56%; $P = 0.72$).

Third, Dr Agarwal criticizes the use of pipericillin–tazobactam as part of the initial antimicrobial treatment in 25% of the patients included in our cohort. According to the clinical practice guidelines published by the Infectious Diseases Society of America and the American Thoracic Society [4,9], the use of these antimicrobials is part of the recommended regimens for those with severe CAP, especially those who have a history of structural lung disease, who are nursing home residents, or who are at risk for *Pseudomonas aeruginosa*. Because 31% of our patients had a history of chronic obstructive pulmonary disease and 10% were from a nursing home, we consider usage of this regimen to be quite appropriate.

Finally, regarding the recent MOXIRAPID study [6], that study is not comparable to ours. First, the MOXIRAPID study enrolled hospitalized patients with CAP without severe disease. The mortality rate was 3% as compared with about 30–40% for previous studies of severe CAP [1,10,11]. Only four patients included in that study had a pneumonia severity index class V, and no information on the number of patients who met American Thoracic Society criteria for severe pneumonia [4] or the number of patients who required ICU admission was provided. Therefore, it is highly unlikely that this population included a significant number of patients with severe pneumonia. In addition, the MOXIRAPID study primarily compared antibiotic regimens that are not considered guideline-concordant for severe CAP, and nowhere in the report presenting the results of the study [6] can we find separate information on the patients who were treated with erythromycin and ceftriaxone (which would be the only guideline-concordant regimen for severe CAP studied). Also, nowhere in the literature could we find any reports indicating that more rapid resolution of fever is associated with improved outcomes for patients with CAP. Therefore, although the MOXIRAPID study is an important addition to the literature regarding care for patients hospitalized with CAP who have low mortality rates, it bears no relation at all to the findings of our study.

These views are those of the authors (EMM, MIR, AA and JP) and do not necessarily represent the views of the Department of Veterans Affairs (South Texas Veterans Health Care System, TX, USA) with which the authors are affiliated.

Competing interests

The author(s) declare that they have no competing interests.

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