Correspondence

Does the Use of Fluoroquinolones for the Empiric Treatment of Pneumonia Delay Initiation of Treatment of Tuberculosis?

Str—I read with great interest the article by Dooley et al. [1], which reported that, among adults with culture-confirmed tuberculosis, initial empiric fluoroquinolone therapy for community-acquired pneumonia was associated with a delay in the initiation of appropriate antituberculous treatment. As the authors pointed out, the fact that fluoroquinolones have excellent in vitro activity against Mycobacterium tuberculosis raises the concern that the use of these agents as empiric therapy for presumed bacterial pneumonia may delay diagnosis of tuberculosis without curing the disease.

However, I find that the design of the study does not allow it to adequately address this hypothesis. Specifically, the control group (17 patients who did not receive fluoroquinolones) included 7 patients (41% of this group) who received antituberculous therapy immediately upon presentation. This makes it impossible to compare the control group with the group of patients who received empiric fluoroquinolone therapy. Because the primary outcome of interest was time to initiation of appropriate antituberculous treatment, inclusion in the control group of patients who received antituberculous therapy from the onset automatically biases results in favor of this group. This calls the authors’ conclusions into question.

The study design also renders the rest of the authors’ analyses problematic. The 7 patients in the control group who were immediately given antituberculous therapy were clearly believed to have a much higher clinical likelihood of having tuberculosis, so it would come as no surprise if these patients were found to have been evaluated and to have received diagnoses earlier. In fact, the study of Dooley et al. [1] found little difference between the 2 patient groups, either in time from presentation to performance of acid-fast bacilli (AFB) smear and culture or in the proportion of initial AFB smear results that were positive. Although Dooley and colleagues [1] did attempt to evaluate differences in clinical presentation, they found no difference between the groups except for the prevalence of shortness of breath, the significance of which is unclear. However, it is likely that these negative results are due to the small number of patients in each group and with the heterogeneous nature of the control group: 10 patients (59%) in the control group received either other (nonfluoroquinolone) antibiotics for treatment of presumed bacterial pneumonia or no antibiotics, and these patients are likely to have been similar to the patients who received fluoroquinolones in that they all presented with clinical findings that are less typical of pulmonary tuberculosis.

Clearly stated, the question that Dooley et al. [1] attempt to address is this: when clinicians initially miss a diagnosis of pulmonary tuberculosis, does the use of fluoroquinolones (instead of administration of other antibiotics or no treatment at all) for empiric treatment of presumed bacterial pneumonia further delay the diagnosis and treatment of tuberculosis? This is an important issue, both from a clinical and a public health standpoint, and although this study is to be commended for bringing attention to this question, its design leaves us no clear answer.

Reference


Reply

Sir—We appreciate the comments of Dr. Abiad [1] regarding our article [2]. He presents 2 hypotheses, one that we sought to address in the paper and one that we did not. The way in which the scientific question is framed affects the way in which it must be answered (i.e., study design). The hypothesis that he poses in his first and second paragraphs (and the one that we addressed in our study) is that administration of empiric fluoroquinolone therapy delays the initiation of appropriate antituberculous therapy. To address this hypothesis, one must assess all patients with tuberculosis who are eligible for fluoroquinolone therapy (i.e., those who present with respiratory complaints) and determine the time to initiation of appropriate therapy for patients who receive or do not receive fluoroquinolones. All such patients with tuberculosis must be included, not just the subset of patients who have delays in the initiation of therapy.

A second, different hypothesis is posed by Dr. Abiad [1] in the fourth paragraph: among persons for whom the diagnosis of tuberculosis is delayed, do fluoroquinolones...