Fluoroquinolones and the Risk of Serious Arrhythmia

To the Editor—We read with great interest the recent article by Lapi et al in the January 2012 issue of Clinical Infectious Diseases, which aimed to address the clinical conundrum regarding the risk of serious arrhythmia attributed to fluoroquinolone exposure [1]. In this article the authors concluded that fluoroquinolones, in particular gatifloxacin, moxifloxacin, and ciprofloxacin, are associated with increased rates of serious arrhythmia. We believe readers should interpret these conclusions cautiously as the authors’ conclusions are not supported by the methods employed and the results presented.

In practice, the clinical significance of QTc prolongation associated with fluoroquinolone use, especially when administered with concomitant QTc-prolonging medications, is commonly questioned because of the rapid onset and grave consequences of a prolonged QTc interval. Oftentimes, clinicians feel compelled to switch to alternative antibiotics or perform repeated electrocardiograms (ECGs) because of the fear of serious arrhythmias. These measures are often taken because of the acute effect fluoroquinolones appear to have on cardiac potassium channels [2]. For example, in a study of healthy individuals, investigators found a significant prolongation of QTc interval in just 1 hour after a single dose of moxifloxacin compared to placebo [3]. As such, an observational study which demonstrated the temporal association between current fluoroquinolone use and the risk of arrhythmia would help clinicians safely and effectively treat patients.

In the study by Lapi et al, the RAMQ (Régie de l’assurance maladie du Québec) database used to define exposure only provides information regarding outpatient therapy. Therefore, fluoroquinolones and arrhythmogenic medications such as certain opioids, antiemetics, and antiarrhythmics that may have been administered during hospitalization are unaccounted for. Interestingly, the authors highlight the importance of immeasurable time bias and claim to account for it by use of sensitivity analysis that excludes patients who had been hospitalized during the “current” time window (within 14 days of index date) of exposure [4]. Unfortunately, this does not address the underlying possibility that cases were exposed to fluoroquinolones and arrhythmia-inducing agents during their hospitalization, which would be of greatest concern given the acute nature for which fluoroquinolones appear to affect ECGs. Clearly, the most immediate concern regarding a patient’s risk of arrhythmia would be for those currently taking a fluoroquinolone, not for patients who had been exposed weeks or months prior.

Although International Classification of Diseases, Ninth Revision and Tenth Revision codes were used to define cases of ventricular arrhythmia or sudden/unattended death in this study, the authors have overlooked patients who may be hospitalized for an unrelated illness, who develop arrhythmia or experience sudden cardiac death after exposure to fluoroquinolones, arrhythmia-inducing drugs, and/or physical states such as dehydration that ensue during hospitalization. Similarly, the study does not control for confounders (eg, electrolyte imbalances, ischemia, inflammation, and hypokalemia) that often occur during hospitalizations, which would contribute to the development of these arrhythmias. The results, therefore, can only infer associations between previous, not “current,” use of fluoroquinolones and the risk of serious arrhythmia. Thus, readers should proceed cautiously when using this information for clinical decision making and patient care.

Note
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