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Widespread Use of Fluoroquinolones May Be Creating Resistant TB Strains

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August 13, 2009 — Widespread general use of fluoroquinolones may be creating a strain of fluoroquinolone-resistant tuberculosis (TB), according to the results of a retrospective case-control study reported in the August 15 issue of the *American Journal of Respiratory and Critical Care Medicine*.

"While fluoroquinolone resistance in TB strains has been reported since the mid 1990's, to our knowledge no one had investigated the direct causes of it," lead author Rose A. Devasia, MD, MPH, from Vanderbilt University in Nashville, Tennessee, said in a news release. "We wanted to determine whether and to what extent clinical practices were having an effect of creating that resistance."

The goal of this study was to examine the prevalence of and risk factors for fluoroquinolone-resistant TB in all people (n = 640) who had culture-confirmed TB, were enrolled in TennCare (Medicaid), and were reported to the Tennessee Department of Health from January 2002 to December 2006. Cases (n = 16), defined as people with fluoroquinolone-resistant *Mycobacterium tuberculosis* isolates, were compared with controls (those with susceptible isolates). Multivariable logistic regression analyses used propensity scores to control for age, sex, race, HIV serostatus, and site of disease.

TennCare pharmacy data allowed determination of outpatient fluoroquinolone exposure in the 12 months before TB diagnosis, which occurred in 116 patients (18%), including 54 patients who had more than 10 days of fluoroquinolone exposure. Of the latter group, 7 patients (13%) had fluoroquinolone resistance.

More than 10 days of fluoroquinolone exposure before TB diagnosis was associated with fluoroquinolone resistance, based on multivariable logistic regression analyses (odds ratio [OR], 7.0; 95% confidence interval [CI], 2.3 – 20.6; $P = .001$). The highest risk for resistance was seen with fluoroquinolone exposure for more than 10 days that occurred more than 60 days before TB diagnosis (20.8%; OR, 17.0; 95% CI, 5.1 – 56.8; $P < .001$ compared with no exposure).

"Patients who had undergone shorter treatment (less than 10 days) had a relatively low rate of resistance of only 1.6 percent, [but] for every additional 10 days of fluoroquinolone use, we found that patients had a 50 percent increase in the likelihood of having resistant TB," Dr. Devasia said. "Exposure to fluoroquinolones early in the course of disease may select for and allow a fluoroquinolone-resistant strain to predominate.... These findings underscore the importance of considering TB in people with symptoms consistent with it and to limit the use of fluoroquinolone in those patients until TB can be definitively ruled out and that repeated courses of fluoroquinolones for the same clinical symptoms may be an indication that TB is the real problem."

Limitations of this study include a lack of inpatient fluoroquinolone exposure data and slight differences between the study population and Tennessee patients with TB who were not in TennCare. In addition, not all patients were in TennCare for the full 12 months before TB diagnosis, which could reduce ascertainment of fluoroquinolone exposure.

In an accompanying editorial, John Bernardo, MD, from the Boston University School of Medicine in Massachusetts, and Wing Wei Yew, MB, from Grantham Hospital in Hong Kong, suggest that development of antibiotic resistance may be fueled by pressure on physicians to prescribe antibiotics inappropriately, especially in emergent settings.

"It may be possible to minimize the induction of bacillary resistance to fluoroquinolones by using higher doses of fluoroquinolones with better activity against *M. tuberculosis* in empiric anti-infective regimens, but concerns of safety and tolerance, and of cost, make this possibility rather unlikely," Dr. Bernardo and Dr. Yew write. "For now, we all need to be more careful when considering the use of these drugs in the community setting and limit the use of prolonged or repeated courses of fluoroquinolones, or even avoid them altogether, in patients who are at risk of having active TB."

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