



PIC QUESTION OF THE WEEK: 11/03/08

Q: Can you summarize the relationship of fluoroquinolones and tendon-related injury?

A: The effects of fluoroquinolones on musculoskeletal tissue have been recognized since their introduction in the early 1980s. Due to a significant number of spontaneously reported cases and an FDA re-evaluation of the problem, the agency has now issued a *Black Box Warning* regarding tendon damage and this class of drugs. Most reports identify the age of affected patients as between 33 and 85 years. Clinically, these reactions usually present as tendonitis or tendon rupture. Risk factors for fluoroquinolone-associated *tendinopathy* include advanced age (> 60 years old), vigorous exercise, renal dysfunction, and concomitant use of corticosteroids. Some conditions that can increase the risk of the event include hyperparathyroidism, diabetes mellitus, gout, and rheumatic disease. Although fluoroquinolone-induced tendonitis can occur at various sites, it most commonly affects the Achilles tendon. The incidence of any adverse tendon effects is rare, occurring at a rate of 10-15 cases per 100,000 prescriptions. The reaction occurs approximately twice as frequently in men; however, women are more likely to experience actual tendon rupture. One study suggests that the rate of Achilles tendon rupture is approximately 1:6,000 patients treated with fluoroquinolones. Symptoms of *tendinopathy* may appear as early as two hours after the first dose of a fluoroquinolone, but, in one case, were reported to develop as late as six months after the conclusion of treatment. The median time for symptom onset is six days. Physicians should perform a thorough history regarding sporting activities in all patients taking fluoroquinolones. In addition, patients should avoid vigorous exercise during the early risk period. The proposed mechanism for this reaction is based on a direct dose-dependent effect of the drug on fibroblast metabolism that results in reduced cell proliferation and collagen/proteoglycan synthesis and subsequent matrix degradation. Alteration in signaling proteins may also serve as a mechanism that induces tenocyte apoptosis. Of the fluoroquinolones, perfloracin and ciprofloxacin appear to have greater potential for causing the reaction than agents such as norfloxacin, levofloxacin, and ofloxacin. Patients must be advised of this possible reaction and the drugs discontinued at the first sign of *tendinopathy*.

References:

- Karistinos A, Paulos L. Ciprofloxacin-induced bilateral rectus femoris tendon rupture. *Clin J Sport Med* 2007; 17: 406-7.
- Food and Drug Administration. Fluoroquinolone antimicrobial drugs. www.fda.gov/medwatch/safety/2008/safety08.htm#Fluoroquinolone (Accessed October 22, 2008).
- Shortt P, Wilson R, Erskine I. Tendonitis: the Achilles heel of quinolones! *Emerg Med J* 2006; 23:e63.
- Corrao G, Zambon A, Bertu L, et al. Evidence of tendinitis provoked by fluoroquinolone treatment. *Drug Saf* 2006; 29: 889-96.

Photo by: Zoemasimages: used under Creative Commons License; <http://www.flickr.com/search/?q=hurdler&page=7>
(Accessed October 22,2008)

Jennifer E. Heasley and Renee T. Phelos, Pharm.D. Candidates

The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).