EDITORIAL

FLUOROQUINOLONES

The article "Quinolones and Tendon Ruptures" by Casparian et al[1] is part of a growing number of reports of serious side effects associated with the use of fluoroquinolones, including ciprofloxacin.[2] The fluoroquinolones are a class of synthetic antimicrobial agents that were modeled after nalidixic acid, a nonfluorinated quinolone antibiotic with a narrow spectrum of activity that was largely limited to treating urinary tract infections.

During the 1980s, modifications of the quinolone structure were made. It was discovered that a fluorine atom on the number 6 carbon, among other small changes, greatly enhanced the spectrum of antibacterial activity. Thus, as a result of their broad spectrum activity against causative pathogens resistant to older antimicrobial agents, these new 6-fluoroquinolone antibiotics have become extremely useful in a variety of infections: urinary tract, soft tissue, respiratory, and bone and joint infections, as well as typhoid fever, sexually-transmitted diseases, prostatitis, community-acquired pneumonia, acute bronchitis, and sinusitis. These broad spectrum agents have also been shown to be highly effective in treating complicated skin and skin structure infections, which are often polymicrobial, as well as for the more severely complicated infections of the feet of diabetic patients.

The newest fluoroquinolones, appearing within the past few years, are different from the earlier agents in that they have increased activity against gram-positive bacteria. Much like other antibiotics, the 6-fluoroquinolones work by inhibiting bacterial DNA synthesis; while the earlier generation of fluoroquinolones are inactive against most anaerobic bacteria, the newer available fluoroquinolones have significant antianaerobic activity.

At present, at least 18 fluoroquinolone antibiotics are used worldwide. Some of these, in alphabetical order, are Ciprofloxacin, Clinafloxacin,* Enoxacin, Fleroxacin, Gatifloxacin,* Gemifloxacin,* Grepafloxacin,† Levofloxacin, Lomefloxacin, Moxifloxacin, Nomofloxacin,* Norfloxacin, Ofloxacin, Pefloxacin,* Sitafloxacin,* Sparfloxacin, Temafloxacin,† and Trovafloxacin.**

A host of well-documented adverse reactions to fluoroquinolones have been reported.[3] The most common adverse effects of fluoroquinolones involve the gastrointestinal tract (nausea and vomiting), the skin (photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria, vasculitis, anaphylactoid reactions, etc), and the central nervous system (dizziness, convulsions, and psychoses). Although fluoroquinolone-induced arthropathy is often benign and heals without sequelae, the prognosis is not so favorable in the case of fluoroquinolone-related tendinopathy, which carries an important risk of immediate or secondary tendon rupture.

Tendinopathies as a result of fluoroquinolone therapy have been well known since 1983. Achilles tendinitis and tendon rupture are the most frequent complications of ciprofloxacin and ofloxacin therapy. The most important risk factors for tendinopathies are compromised renal function, hemodialysis and transplantation, long-term corticosteroid use, strenuous sports activities, secondary hyperparathyroidism, advanced age, and diabetes mellitus.

The latency period of these tendinopathies usually ranges from 2 to 60 days, though in one of the two cases reported in this issue, the tendon rupture appeared 6 months after the medication had been discontinued. As more people are treated with newer fluoroquinolones, the clinical incidence of tendon rupture with these agents will, perforce, increase.

The newest fluoroquinolones may benefit some patients, but their ease of use may promote indiscriminate use. The risk/benefit ratio of the fluoroquinolones should be carefully considered, and these drugs should be prescribed cautiously, since better-tolerated, less expensive drugs can usually be prescribed instead. Fluoroquinolones should be chosen for indications in which they offer a clear therapeutic advantage over other classes of antibiotics rather than as agents whose broad spectrum prompts routine empirical use. Do we need another fluoroquinolone?

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*Not yet available in the United States.
†Recalled in the United States.
**Approved only for hospital use.

References

1. Casparian JM, Luchi M, Morrat R, et al: Quinolones and tendon ruptures. *South Med J* 2000; 93:??-??
2. Fried S: *Bitter Pills.* New York, Bantam Books, 1998
3. Litt JZ: *Drug Eruption Reference Manual*. New York, Parthenon Publishing, 2000

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