Pharmacy Times

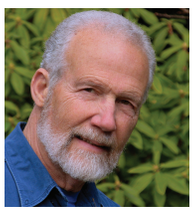
MORE @ PHARMACY TIMES.COM

For references, go to PharmacyTimes.com/publications/issue.

Fluoroquinolones and Steroids: An Achilles Heel Interaction

John R. Horn, PharmD, FCCP, and Philip D. Hansten, PharmD

John R. Horn, PharmD, FCCP



Philip D. Hansten, PharmD

Tendinopathy has been recognized as an uncommon, but potentially disabling, adverse effect of fluoroquinolones. Fluoroquinolones demonstrate excellent tissue penetration, with their concentrations in tissue often exceeding those in plasma. Muscle cells have high fluoroquinolone concentrations, and tendons receive some of their blood supply from the myotendinous junction, which may predispose tenocytes to elevated drug exposure.[1] Signs and symptoms of tendon injury include pain, edema, warmth, and reduced joint motility. The mechanism of fluoroquinolone-induced tendon toxicity has not been determined. Several pathologic changes have been noted, including inhibition of collagen and proteoglycan synthesis, increased intracellular oxidative stress, swelling and dilation of cell mitochondria and endoplasmic reticulum, a decrease in tenocyte proliferation, and cell necrosis.

Risk Factors

Patients who experience fluoroquinolone-induced tendinopathy typically have an onset of symptoms 9 to 17 days following the initiation of the fluoroquinolone, with about 50% of patients having symptoms within 6 days. The Achilles tendon accounts for more than 90% of the affected sites.[2,3] The risk of fluoroquinolone-induced tendinopathy can be increased by concurrent disease and drug exposure.

TABLE: ADJUSTED ODDS RATIO FOR ACHILLES TENDON INJURY WITH FLUOROQUINOLONE

Study	Patient Age Group	FQ OR	FQ + Steroid OR
Wise et al[4]	<60 yr	1.6	9.1
	≥60 yr	8.3	
Corrao et al[5]	All	4.1	43.2
van der Linden et al[6]	All	4.3	17.5
	60-79 yr	6.4	
	≥80 yr	20.4	

FQ = fluoroquinolone; OR = odds ratio.

Risk factors associated with an increased risk of tendinopathy include renal dysfunction, a renal transplant, rheumatic disease, gout, being older than 60 years, male gender, and the use of high fluoroquinolone doses.[2-4]

Several studies have examined the contribution of concurrent steroid administration to the risk of tendinopathy and rupture associated with fluoroquinolones.[4-6] The results of these studies are summarized in the Table. It is apparent that the risk of Achilles tendon injury increases with age and markedly so with concurrent steroid use. This probably represents a pharmacodynamic drug interaction because steroids alone have reportedly increased the risk of Achilles tendon rupture by about 2-fold.[5] In one report, 50% of patients with fluoroquinolone-induced tendon rupture received concurrent steroids.[2]

As noted above, fluoroquinolone-induced tendon injury is dose-dependent and more common in patients with renal dysfunction. Because fluoroquinolones are eliminated by the kidneys, patients with renal insufficiency will be exposed to elevated concentrations of fluoroquinolones if the doses are not appropriately reduced. The predictable reduction in renal function with increasing age may be partly responsible for the increased risk of fluoroquinolone-induced tendinopathy in the elderly.

Summary

The potential interaction between fluoroquinolones and steroids may be unlikely, but the risk of a tendon injury during concurrent administration is much greater than that reported with either drug alone. Achilles tendon rupture often results in significant disability, especially in the elderly. All patients receiving systemic steroid therapy who are prescribed fluoroquinolones should be carefully monitored for any signs of tendon injury. Discontinuing the drugs and minimizing activity are suggested until symptoms resolve. It would be prudent to avoid the combination of steroids and fluoroquinolones in elderly patients, particularly those with renal dysfunction or other known risk factors.

Drs. Horn and Hansten are both professors of pharmacy at the University of Washington School of Pharmacy. For an electronic version of this article, including references, visit hanstenandhorn.com.