



Fluoroquinolones and the Risk of Kidney Damage

Kidney injury isn't usually a top consideration when prescribing fluoroquinolones, even though reports of acute kidney injury have been published and the product label includes renal failure as a rare but possible adverse reaction. But oral fluoroquinolones more than doubled the risk of acute kidney injury, severe enough to require hospital admission in adult men, according to researchers from the Department of Health and Human Services in Silver Spring, Maryland; the University of Florida in Gainesville; the University of British Columbia in Vancouver and McGill University Health Center in Montréal, Quebec, both in Canada; and the University of Washington in Seattle.

They evaluated data on 1,292 men aged 40 to 85 years admitted to the hospital with acute kidney injury and 12,651 matched controls admitted for other diagnoses. The researchers focused on outpatient-dispensed preparations: ciprofloxacin, gatifloxacin, gemifloxacin,

levofloxacin, moxifloxacin, and norfloxacin. They also selected 2 common oral antibiotics—amoxicillin and azithromycin—as control drugs. Ciprofloxacin and levofloxacin were the most commonly used fluoroquinolones and were used most often to treat respiratory or genitourinary infections.

The researchers found an increased risk of acute kidney injury with current use of oral fluoroquinolones (adjusted relative risk [RR], 2.18; 95% confidence interval [CI] 1.74-2.73), and no change in risk with either recent (adjusted RR, 0.87; 95% CI 0.66-1.16) or past (adjusted RR 0.86; 95% CI 0.66-1.12) use. They found no association between the use of amoxicillin or azithromycin and acute kidney injury.

When the researchers stratified their analysis by product, they found the largest RR for ciprofloxacin (2.76; 95% CI 2.03-3.76), followed by moxifloxacin (2.09; 95% CI 1.04-4.20) and levofloxacin (1.69; 95% CI 1.20-2.39).

The researchers also found an interaction between the combined use of fluoroquinolones and renin-angio-

tensin-system blockers, amounting to a more than 4-fold increase in the RR for acute kidney injury with active use of both drugs. They found a similar increased risk for dual use of fluoroquinolones and either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.

Previous evidence of acute kidney injury with fluoroquinolone use comes from case reports, the researchers say, most of which resulted from an allergic or hypersensitivity reaction termed *acute interstitial nephritis*. They noted that fluoroquinolones have also been implicated in cases of granulomatous interstitial nephritis, crystalluria, and acute tubular necrosis. Although most published case reports are of ciprofloxacin use, they add, that might be an artifact of its high use.

Although this study was done in adult men, there is no reason to suppose that the increased risk is limited to middle-aged and elderly men, the researchers caution, advising further study in other patient groups. ●

Source: Bird ST, Etrinan M, Brophy JM, Gartzema AG, Delaney JAC. *CMAJ*. 2013;185(10):E475-E482. doi: 10.1503/cmaj.121730.