

Is there much risk in using fluoroquinolones in children?

Evidence-based answer

No, the risks seem to be minimal. Arthralgias and myalgias have been observed clinically in children and adolescents exposed to fluoroquinolones, but they're transient, disappear when the drug is discontinued, and appear to be no more prevalent than with other antibiotics (strength of recommendation [SOR]: **B**, 1 structured review and 2 prospective cohort studies). No apparent long-term

risk of developmental skeletal growth delay is associated with fluoroquinolone exposure (SOR: **B**, 1 prospective controlled study). Fluoroquinolone use in children isn't associated with tendonopathy (SOR: **B**, 1 prospective controlled study), but it probably carries a very low risk of tendon rupture (SOR: **C**, extrapolation from a national passive postmarketing monitoring system study predominantly in adults).

Clinical commentary

Be judicious

Just because you can do something doesn't mean you should. It's reassuring that quinolones can be given to pediatric patients if necessary inasmuch as the drugs don't appear to cause long-term skeletal side effects, and the infrequent arthralgias and myalgias they produce

seem to be transient and benign. However, in an era of increasing microbial drug resistance and escalating pharmaceutical costs, we should strive for rational prescribing and reserve quinolones for patients who truly need them.

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Evidence summary

Few short-term joint complaints, no long-term skeletal harm

A 1997 database review compiled reports of skeletally immature patients ranging in age from 4 days to 26 years who were exposed to quinolones.¹ Thirty-one reports met search term criteria, for a total of 7045 patients. No incidences of quinolone-associated arthralgia were documented in 30 reports (>5000 patients). The review didn't report the incidence of tendonopathy. One report of 1795 pediatric patients documented a small inci-

dence of arthralgias (~1.5%), which was considered to be reversible and no more than expected for a comparable quinolone-naïve population.

Follow-up data on safety and adverse findings, from as long as 12 years after treatment, were reported for 530 (28%) of the 7045 patients. Changes in skeletal growth were evaluated using various diagnostic techniques. Clinical observation was the most common method of assessment (N=357), however. The follow-up data revealed no arthropathy or abnormal skeletal growth

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FAST TRACK

The FDA ordered a Boxed Warning for increased risk of tendonitis and tendon rupture with fluoroquinolone use, but made no comments about children

FAST TRACK

Arthralgias and myalgias are transient and appear to be no more prevalent than with other antibiotics

(rate=0%; estimated 95% confidence interval [CI]=0%-0.04%).

A prospective study published in 2006 monitored joint toxicities (swelling, tenderness, or restricted movement) during acute treatment with ciprofloxacin as well as skeletal growth at follow-up based on physical examination.² Preterm neonates with septicemia were treated with either ciprofloxacin (n=48) or other antibiotics (n=66). Forty infants in the ciprofloxacin group completed an average of 28 months of follow-up. No complaints or physical findings of osteoarticular joint abnormalities or skeletal growth delay were noted in either group during acute treatment or at follow-up. The incidence of tendonopathy was not reported.

Arthralgias, myalgias are transient

A large multicenter, prospective, non-blinded cohort study evaluated adverse effects in children receiving fluoroquinolones versus other antibiotics.³ Duration of fluoroquinolone use was 1 to 23 days. Arthralgias or myalgias, which were only evaluated clinically, occurred more often in children receiving fluoroquinolones—10 of 276 children (3.6%) vs 1 of 249 (0.3%), respectively (odds ratio [OR]=9.3; 95% CI, 1.2-195; $P=.02$). All events occurred within the first 2 weeks of fluoroquinolone treatment and resolved within 20 days. No tendonopathies were reported.

Tendon rupture is rare, especially in children

A 1996 study reported the incidence of tendon disorders related to fluoroquinolones using drug surveillance data from the general population. The average age of the patients was 55 years.⁴

The author estimated the risk of tendon rupture associated with norfloxacin or ofloxacin to be 1 case per 23,130 days of treatment and only 1 case per 779,600 days of ciprofloxacin treatment. The estimated risk would likely be even lower in children, the author noted, because the risk of tendon rupture increases with age.

Recommendations

Ciprofloxacin is the only fluoroquinolone approved by the US Food and Drug Administration for pediatric indications. The FDA recently ordered the addition of a Boxed Warning to fluoroquinolones regarding the increased risk of tendonitis and tendon rupture. The FDA made no comments specifically about children or adolescents, and stated that the risks are increased in people older than 60.

The American Academy of Pediatrics recommends limiting fluoroquinolone use to children with infections caused by multidrug-resistant pathogens or children for whom parenteral therapy is not feasible and no other effective oral medication is available.⁵

The Agency for Healthcare Research and Quality (AHRQ) recommends fluoroquinolones as first-line treatment for children with uncomplicated gonorrhea who weigh more than 45 kg,⁶ and second-line therapy for children with bacterial meningitis,⁷ nongonococcal urethritis, chlamydia,⁶ or pelvic inflammatory disease.⁸ ■

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