

Lessons Learned in Antibiotic Stewardship: Fluoroquinolone Use in Pediatrics

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The use of fluoroquinolones differs dramatically between adult and pediatric patients. For adults, they are the leading class of antibiotics prescribed in ambulatory care visits whereas in children, they are the least frequently prescribed class. The reasons for this difference in practice likely relate to perceptions of their potential for harm. This highlights the impact of physicians' perception of direct patient harm in antibiotic decision making which has implications for antibiotic stewardship.

Key words. antibacterial agents; drug resistance; physician's practice patterns.

Overuse and misuse of antibiotics has contributed to the public health crisis of antibiotic resistance and the specter of untreatable infections [1]. Although local and national campaigns have contributed to declines in antibiotic prescribing for viral conditions such as colds and acute bronchitis where they confer no benefit, overuse for these conditions remains unacceptably high [2]. Another dimension of the overuse problem has emerged: rampant overuse of antibiotic classes with a relatively broad-spectrum of activity (particularly macrolides and fluoroquinolones) instead of guideline-recommended, narrower-spectrum alternatives that are usually equally effective. Some strategies, including education and benchmarking, show promise in reducing overuse [3]. Comparing fluoroquinolone prescribing patterns for children to adults may provide further insight into how to be more effective antibiotic stewards.

WHAT DO PRESCRIBING PATTERNS FOR FLUOROQUINOLONES REVEAL ABOUT STRATEGIES TO IMPROVE ANTIBIOTIC USE?

Data from the National Ambulatory and National Hospital Ambulatory Medical Care surveys indicate that fluoroquinolones are the leading class of antibiotics prescribed during adult ambulatory care visits, resulting in over 25 million prescriptions annually [4]. It is easy to understand why: they have convenient dosing regimens, high bioavailability, and the broad spectrum of activity targets

the most important pathogens that cause common bacterial infections including community-acquired pneumonia and urinary tract infections. The use of fluoroquinolones is dramatically different among children. Although they are the most frequently prescribed antibiotics for adults, fluoroquinolones are the least frequently prescribed class for pediatric patients, accounting for under 2% of all antibiotics prescribed during ambulatory visits [4]. The extremely limited use in children has remained unchanged for over a decade (Figure 1). This low use of fluoroquinolones is despite the fact that the bacteriology of respiratory tract infections and urinary tract infections is very similar in adults and children.

WHY DON'T PHYSICIANS PRESCRIBE FLUOROQUINOLONES FOR CHILDREN?

The most likely explanation for why prescribing patterns for fluoroquinolones differ between children and adults is the perception of their potential for harm. A generation of physicians was trained to avoid prescribing fluoroquinolones to children. This practice was due to concerns about potential toxicity to developing cartilage, based largely on animal studies conducted in the 1970s that demonstrated damage to articular cartilage of weight-bearing joints in juvenile beagle dogs exposed to high doses [5]. In children, extensive review of safety data suggests that musculoskeletal adverse events, predominantly arthralgias, may occur slightly more often in

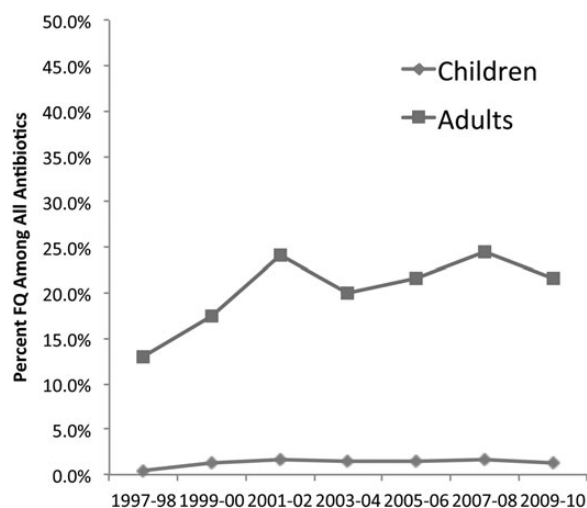


Figure 1. Annual percentage of all antibiotics prescribed accounted for by fluoroquinolones (FQs) during ambulatory care visits in the United States. Source: The National Ambulatory Care and Hospital Ambulatory Care Surveys.

children treated with fluoroquinolones. However, serious toxicity, including tendon rupture, is exceedingly rare and almost certainly substantially less likely than in adults. In a 2011 statement, the American Academy of Pediatrics concluded “fluoroquinolones are reasonably safe in children,” and it outlined conditions in which the use of fluoroquinolones was justified [5]. Nonetheless, the perception of risk remains high. It is not uncommon as pediatric infectious disease physicians consulting on patients with infections where fluoroquinolones are the only option to have the referring physician state “I thought we couldn’t prescribe those drugs to children.” As a consequence of very limited use, fluoroquinolone resistance for several important organisms has remained very low in children compared with adults.

CHANGE THE MESSAGE: FOCUS ON PREVENTING HARM AND ADVERSE EVENTS

Over the last decade there has been, in effect, a natural experiment of strategies to control fluoroquinolone prescribing. In adults, conventional messaging through guidelines and educational efforts has emphasized the risk of resistance and the limited benefit of antibiotics for many common conditions. The impact on behavior has been modest. In children, the message has been that fluoroquinolones can harm children and the risks may outweigh the benefit. The impact has been striking. Maybe this should come as no surprise. In 1 study, concern about promoting antibiotic resistance was rated as the least important factor contributing to physician decision making about whether to prescribe an antibiotic [6].

Perhaps, as demonstrated by the experience with fluoroquinolones, efforts to curtail antibiotic overuse should

more broadly incorporate a stronger focus on reducing direct patient harm, rather than the less tangible (although critically important) issue of antibiotic resistance. There is plenty of harm to consider. Adverse reactions to antibiotics are costly, including causing over 600 000 visits to offices and emergency departments annually [7]. Extended-spectrum β -lactams and cephalosporins, often used unnecessarily for respiratory tract infections, are strongly linked to increased risk of *Clostridium difficile* infection (CDI), and the rates and severity of CDI are increasing including community-onset cases [8, 9]. Multiple antibiotic classes can cause serious allergic reactions including Stevens Johnson syndrome [10], and macrolides are linked to an increased risk of sudden cardiac death [11]. There is more. As our understanding of the human microbiome advances, it is becoming evident that early and often unnecessary exposure to antibiotic therapy may be linked to an increasing number of chronic diseases such as inflammatory bowel disease [12], asthma [13], and even obesity [14]. The evolving evidence base for the direct patient harm of antibiotic exposure is compelling.

To develop new messages related to antibiotic-associated adverse events, the Centers for Disease Control and Prevention’s Get Smart: Know When Antibiotics Work program conducted in-depth interviews with primary care physicians. Physicians reported not discussing the potential for adverse events or side-effects with parents or patients unless asked and perceived that the risk of antibiotic-associated adverse events was low. These findings are reinforced by evidence that physicians sometimes prescribe antibiotics for placebo effect [15].

CONCLUSION

Physicians are taught to weigh risks and benefits, and they are more likely to consider the immediate risk and benefit to the patient in front of them as opposed to future risk, or the more intangible public health threat of antimicrobial resistance. In the case of fluoroquinolone use in children, the true risk may have been lower than the perceived risk, but the impact on behavior is telling. If we better communicate the true risks and benefits of antibiotic use and overuse to patients and physicians, they are likely to make better decisions, especially when treating conditions where the benefits of treatment are modest or nonexistent. Most antibiotics prescriptions for children are for upper respiratory tract infections, the majority of which are viral. Although both physicians and patients have concerns about “missing” a bacterial infection, even for diagnoses in which antibiotics are usually indicated (eg, sinusitis or otitis media), the major benefits are limited to symptom

resolution, not prevention of serious sequelae [16]. Sometimes “therapies,” such as chicken soup for colds, are worth trying because they “can’t hurt.” Unlike chicken soup, antibiotics can hurt. The lesson of the fluoroquinolone experience—physicians treating children are responsive to concerns about direct patient harms that result from antibiotic use—can be harnessed and broadly applied as a core stewardship strategy.

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