Limiting the use of quinolone antibiotics

The following questions can be used as discussion points for peer groups or self-reflection of practice.

It is strongly recommended that the linked article is read before considering the questions. "**Limiting the use of quinolone antibiotics**"

Quinolones (e.g. ciprofloxacin, norfloxacin) are associated with increasing antimicrobial resistance and rare, but potentially harmful, adverse effects. Their use should be reserved for specific indications involving serious bacterial infections, in order to protect their effectiveness. It is therefore recommended that quinolones only be used to treat people with serious, life-threatening or difficult-to-treat infections, when other antibiotics cannot be used due to allergy, intolerance or when the pathogen is resistant to alternative antimicrobial agents. Antimicrobial resistance to quinolones is prevalent globally and includes both Gram-negative and Gram-positive strains. In New Zealand, resistance has been shown in many infections, including those caused by *Haemophilus influenzae*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and *Shigella*.

There are few situations where quinolones are recommended first-line. **Ciprofloxacin** is indicated first-line for the treatment of patients with prostatitis, epididymo-orchitis (if a urinary tract infection pathogen is suspected) and severe cases of salmonellosis. It is also indicated for the treatment of gonorrhoea (if known to be susceptible) and severe cases of shigellosis (if known to be susceptible and the patient is unable to take the first-line treatment), *Campylobacter enterocolitis* (second-line) and some eye and ear infections. Ciprofloxacin can be considered for the treatment of patients with uncomplicated urinary tract infection that is unresponsive or resistant to a first-line treatment. Ciprofloxacin should not be used for pneumococcal pneumonia or travellers' diarrhoea. **Moxifloxacin** is indicated (unapproved) for *Mycoplasma genitalium* infection if first-line treatment with doxycycline followed by azithromycin has failed or there is known macrolide resistance. Moxifloxacin is also an approved treatment for multi-drug resistant tuberculosis. **Norfloxacin** is no longer recommended for the treatment of patients with uncomplicated urinary tract infection due to the potential for bacterial resistance. It has no recommended uses in a primary care setting.

In general, these medicines are well tolerated, with the most common adverse effect being gastrointestinal disturbance. Less frequently, people using quinolones may experience central nervous system effects (e.g. headache, insomnia, dizziness anxiety, restlessness, tremor), crystalluria, rash or photosensitivity. In rare circumstances, serious adverse effects can occur, including tendinitis and tendon rupture, progression or rupture of an aortic aneurysm or aortic dissection, QT prolongation, retinal detachment, CNS excitation and seizures. The risk of serious adverse effects seems to be greater with later generation quinolones (i.e. moxifloxacin) than with earlier generations (i.e. ciprofloxacin and norfloxacin).

Patients prescribed quinolones should be advised about the risk of these rare but serious adverse effects so that they can prevent or minimise the impact if they occur. Many of the adverse effects associated with quinolones occur more frequently in people with pre-existing risk factors, or in certain at-risk groups, including older people and those with epilepsy. When ciprofloxacin and norfloxacin are prescribed, dose adjustment is required for patients with impaired renal function. Quinolones can interact with a number of other medicines, such as those that reduce seizure threshold, prolong the QT interval, warfarin and medicines metabolised by common pathways in the liver.

Tendon rupture is one of the rare serious adverse effects associated with quinolones that has generated much interest in both medical and non-medical literature. A number of toxicological studies have confirmed that quinolones damage the collagen within tendons, which on rare occasions can result in tendinitis and tendon rupture, particularly affecting the Achilles tendon with bilateral involvement possible. This can occur even after a single dose of quinolone and the risk can persist for months. The risk is increased in people aged 60 years or over, who are taking oral corticosteroids, have chronic kidney disease, a prior history of tendon damage or a history of kidney, heart or lung transplant. There is also some evidence that athletes are also included in the higher-risk group.

Questions to consider:

1. Quinolones are an effective, well tolerated antibiotic medicine and as such they are at risk of being over-prescribed. However, their association with increasing antimicrobial resistance and rare, but potentially harmful, adverse effects means that a balance has to be struck when considering use. Thinking about quinolone use, and after reading this article, do you think they are being prescribed appropriately by yourself and within your practice? If not, do you feel that there are changes that can be made so that quinolone prescribing is closer to the recommendations?
2. There are some conditions where quinolones are no longer recommended as a first-line choice, e.g. norfloxacin in people with uncomplicated urinary tract infection (UTI) and ciprofloxacin in travellers' diarrhoea. What antibiotic treatment do you usually prescribe for UTI? Were you aware that norfloxacin should not be used? How would you usually manage a case of travellers' diarrhoea? What antibiotic, if any, do you prescribe?
3. Prior to reading the article were you also aware that ciprofloxacin does not cover *Streptococcus pneumoniae* adequately and therefore should not be used in pneumococcal pneumonia? What is your usual choice of antibiotic when prescribing for an adult with pneumonia?
4. Can you think of the last time you prescribed ciprofloxacin or another quinolone: what was the indication in that situation and was it appropriate?
5. Were you aware of the risk of serious adverse effects associated with the use of quinolone antibiotics? Although the current number of patients in New Zealand who have been affected by serious adverse effects is small, the consequences for patients can be significant. Does the risk of a severe adverse effect change the way you choose an antibiotic? How do you convey these kinds of risk to patients?
6. Thinking in general terms now, prescribing antibiotics to patients who may not need them increases the risk of adverse effects and increasing antibiotic resistance, however, the decision to prescribe, or not, is not always clear cut. Do you have a "process" in place in your practice that helps you make these decisions? Do you consult evidence-based guidance to help you make your prescribing choice? What additional tools or resources could help guide your prescribing?

Extra: In most DHBs in New Zealand, the dispensing of ciprofloxacin and norfloxacin has been decreasing. In the article we presented data showing the number of patients dispensed each of these quinolones by DHB. Looking at the DHB you practice in, consider how that area is performing in terms of reduction in use. If you are in a DHB where use remains quite high, can you think of reasons why this might be? If your DHB has reduced dispensing numbers, can you think of strategies that have been put in place to support this?