Update on Fluoroquinolones

Charles Krasner, M.D.
June 16, 2016
Antibiotic Stewardship Program - ECHO
Potential fluoroquinolone side-effects

- Increased risk, greater than with most other antibiotics, for causing *C. difficile* colitis
- **Acute Tendonitis** - particularly Achilles tendinitis and rupture, can be unilateral or bilateral, and can occur at any time with these antibiotics
- **QT prolongation** - can cause Torsades. Some fluoroquinolones have been taken off the market because of this problem.
- **Peripheral neuropathy** - may be irreversible
- **Central nervous system toxicities** - particularly in older patients
FDA Drug Safety Communication- FDA advises restricting use for certain uncomplicated infections. Posted May 12, 2016

- FDA recommends that:
- □ Serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (UTI) who have other treatment options.
- □ For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.
- □ Providers should instruct patients to contact their health care professional immediately if they experience any serious side effects while taking fluoroquinolone medicine such as tendon, joint and muscle pain; a “pins and needles” tingling or pricking sensation; confusion; and hallucinations.
- □ Providers should stop systemic fluoroquinolone treatment immediately if a patient reports serious side effects, and switch to a non-fluoroquinolone antibacterial drug to complete the patient’s treatment course.
77 year old male with ampicillin allergy seen for infected dog bite

- 4 days prior to admit bite in thenar aspect of hand when separating 2 dogs
- Came to ER c/o progressive onset redness and swelling of hand and arm
- Given oral levofloxacin 750mg daily for 2 days, not better so consulted on by me
- Eschar and cellulitis up to elbow. Admitted to hospital
- Given 2 doses of ceftriaxone – improves
- Discharged, told to finish off the remaining 3 Levaquin tabs he has at home
- Two days later – severe unilateral Achilles tendonitis. Uh-Oh!
56 year old female with asymptomatic bacteruria

- 56 year old female has pre-op evaluation prior to elective hip replacement
- Noted on urinalysis to have bacteruria and positive culture but no symptoms
- Surgeon prescribed one week of ciprofloxacin, completed day before surgery
- Uneventful surgery, discharged
- Readmitted next day with fulminant c.diff colitis and dies
Why treat Acute cystitis?

- ***Rarely** progresses to severe disease even if untreated:
  
  **Goal of treatment is to ameliorate symptoms**

  In selecting therapy, efficacy as well as “ecologic collateral damage” (selecting for antibiotic resistant bacteria, causing C. difficile colitis) should be considered equally- fluoroquinolones should be avoided, except in pyelonephritis

  **Therefore use First line agents whenever possible:**

  Trimethoprim/sulfa (Bactrim) for 3 days

  Nitrofurantoin (Macrodantin) for 5 days

  Fosfomycin for one dose
Diagnosis of Uncomplicated Cystitis

- **Symptoms only**: +dysuria, +frequency, no discharge or irritation:
  
  ***90% chance of cystitis***

- **Dipstick**: leukocyte esterase + and/or nitrite + only 75% sensitive, so symptoms more important for diagnosis even if dip is negative

- **Culture**: $10^5$ (100,000) bacterial CFUs – traditional criterion for UTI– 50% sensitive – will miss up to half the cases of UTI– counts of 100 to 10,000 colonies – all at levels that may be called as “no growth” by micro lab. Least sensitive diagnostic test.

- Thomas Hooton, M.D. UTI review NEJM 3/15/2012– *don’t do dip stick, u/a or culture– can be negative or misleading– just treat on basis of classic symptoms in uncomplicated UTI*
How about treating asymptomatic bacteruria (ASB) to prevent UTI? If it ain’t broke, don’t fix it - treatment of ASB just leads to drug resistant bacteria and side-effects from the antibiotic

- Antibiotic treatment of ASB does not reduce frequency of symptomatic UTIs
- Treatment of ASB in diabetes does not reduce adverse outcomes or improve glucose control
- It does lead to untreatable drug resistant bacteria, c. difficile infection, etc
- **Only exceptions are pregnancy** where ASB is associated with pyelonephritis, growth retardation, neonatal death... and patients undergoing **urologic procedures** (such as prostate bx)
Bottom line on UTIs

- Think twice before ordering a urine culture - go by symptoms and signs. Only culture in possible pyelonephritis, unclear diagnosis, complicated cases or treatment failure.
- Consider Nitrofurantoin or Septra as first line therapy, quinolones only if ill or allergic to first line therapies.
- Mid-stream culture results with enterococcus and Group B strep can be deceiving - rarely cause of UTI. Most likely still E. coli.
- If the patient is asymptomatic – if it ain’t broke, don’t fix it!
Choosing Wisely® – Advice for Seniors – an initiative of the ABIM and American Geriatrics Society

- Many older patients get screening u/a’s and reflex cultures even when they don’t have urgency and burning symptoms. They are then treated for a “UTI”. This is a too common mistake...
- “older patients should **not be tested or treated** for UTI unless they have symptoms”
- If you are treated for a true UTI: no follow-up test of cure should be performed
- Antibiotics:
  - have side-effects
  - can cause future problems like yeast infection and colitis
  - lead to drug resistant bacteria
  - are a waste of money
Recent Study of antibiotic use in uncomplicated cystitis in 2 large private FP clinics with well insured patients

- 1546 visits—all women with any possible complicating factor were excluded—pregnancy, recurrent infection, antibiotic allergy, fever
- Prescribed Antibiotics:
  - 52% Fluoroquinolones—Cipro or levofloxacin (71% of these prescriptions were for 5 to 10 days of therapy, only 29% were for recommended 3 days)
  - 36% nitrofurantoin (70% were for one week of therapy)
  - 12% trimeth/sulfa (50% were for more than 5 days)

Conclusion—primary care physicians strongly prefer fluoroquinolones and prescribe longer courses of therapy than recommended in Guidelines
Guidelines for management of **acute sinusitis**

- Antibiotics indicated for either symptoms for >10 days, or severe symptoms with purulent nasal drainage and fever, or worsening symptoms after initial improvement.

- Empiric treatment suggestions:
  1. Augmentin / high dose in adults
  2. Doxycycline if PCN allergic. Give 200mg initial loading dose to get effective blood levels.
  3. Levofloxacin as alternative, 5 days should be adequate.

Do not use azithromycin given high incidence of resistant strep pneumoniae.
What’s on line for patients to view

- https://www.youtube.com/watch?v=73ywSGqMEPs
Bottom line

- There is growing awareness that the fluoroquinolones are potentially toxic drugs.
- I think the greatest overuse of these drugs are in treatment of uncomplicated UTIs and asymptomatic bacteruria, both in using them in the first place and then prescribing them for a longer course than indicated.
- Primary care physicians are **totally overwhelmed** with demands on their time and may not be aware of these guidelines, hopefully we can help disseminate this info to them.
- I am as guilty as anyone in overusing these antibiotics, but I am now making a concerted effort to think twice before prescribing them.