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From the Front Lines

AlixaRx Clinical Pharmacists Address Everyday Challenges in Long-Term Care

Colds, Coumadin, and Carefully Examining Drug Interactions

In this issue:

As the leaves begin to fall and the temperatures get colder, colds and respiratory infections begin to rise. An increase in respiratory infections ultimately results in an increase in the prescribing of antibiotics.

Although antibiotics can be helpful when treating bacterial infections, they can also cause some unintended side effects and drug interactions.

Many of our patients receive Coumadin (warfarin). As we know, warfarin has many drug interactions. In fact, the popular website www.drugs.com reports that there are a total of 803 medications that interact with warfarin. Unfortunately, many of the most commonly used antibiotics are among those medications that cause problems with warfarin. Since our patients often take 9 or more medications, they are at increased risk for drug interactions.

In 2001, AMDA (American Medical Directors Association) established a list of the Top 10 Particularly Dangerous Drug Interactions in Long Term Care. Three of these top 10 interactions involve warfarin and an antibiotic.

These interactions and suggested management are listed below:

1. Coumadin and Macrolides:
    - Erythromycin, Clarithromycin, Azithromycin
    - Potential increased effect of warfarin due to inhibition of warfarin metabolism.
    - Concomitant use should be avoided unless absolutely necessary
    - INR should be monitored every other day.
    - Effect is unpredictable and may not occur in all individuals (dental article)
2. Coumadin and Fluoroquinolones
    - Although caution may be warranted when using warfarin with all quinolones, problems have been documented especially with ciprofloxacin, ofloxacin, and norfloxacin. In addition, some INR elevations with levofloxacin have been reported.

- Potential increase effect due to a combination of inhibition of warfarin metabolism and decrease in Vitamin K producing intestinal flora.
- INR should be monitored every other day during the use of the Fluoroquinolone antibiotics.

3. Coumadin and Sulfa drugs
    - Bactrim, Septra, Sulfamethoxazole/Trimethoprim
    - Potential increased effect of warfarin due to inhibition of warfarin metabolism
    - If use of sulfamethoxazole/trimethoprim is required, it is recommended to reduce the current dose of warfarin by 50% and monitor INR every other day during antibiotic treatment and for 7 days following completion of the antibiotic.

Other antibiotics that may significantly interact with warfarin, but not listed in the AMDA top 10 interactions include:

1. Warfarin and Metronidazole
    - Potential increased effect due to inhibition of warfarin metabolism
    - If concomitant use cannot be avoided, a dose reduction of warfarin by 1/3 to ½ of the current dose is recommended.
    - INR should be monitored closely during metronidazole therapy.
2. Warfarin and Azole Antifungals (Fluconazole, Ketoconazole, Miconazole)
    - Potential increased effect due to inhibition of warfarin metabolism
    - INR monitoring every other day is recommended during azole antifungal therapy.

Almost all antibiotics have the potential to interact with warfarin. Routine monitoring for signs and symptoms of active bleeding is recommended for any patient receiving warfarin and an antibiotic. Your AlixaRx Clinical Pharmacist can provide more information on the best antibiotics to use in patients receiving warfarin and how to manage drug interactions.

References: 1. www.drugs.com – accessed December 3, 2015 2. https://www.amda.com/tools/clinical/m3/topten.cfm - accessed December 3, 2015 3. Rice, PJ, Perry, RJ, et al. Antibacterial prescribing and warfarin: A Review. British Dental Journal 2003; 194: 411–415. 4. Baillargeon, PJ; Holmes, Holly, et al. Concurrent use of Antibiotics and the Risk of Bleeding in Older Adults. Am J Med. 2012 February ; 125(2): 183–189.

Probiotics for the Prevention of Clostridium Difficile Infection

Are probiotics effective at preventing Clostridium difficile (C. Diff) infection in patients receiving antibiotic treatment? According to a recently published study, they are.

A meta-analysis of 19 different studies, published from 1986-2016 revealed a significant decrease in C. Diff infection rates in patients that received probiotics as compared to those who received a placebo.

In all, results for over 6000 hospitalized patients receiving antibiotics were evaluated. The probiotic strain, species, formulation or dose did not have any effect on the rate of infection, however, the timing of administration did. Patients who started treatment with probiotics within 2 days of starting

the antibiotic had lower rates of C. Diff infection than patients whose probiotic treatment was started later during the course of antibiotic therapy. There were no reports of probiotic-related sepsis in any of the studies reviewed.

This analysis indicated that no further study was needed to establish the efficacy of probiotics for the prevention of C. Diff infection, but "further study is needed to identify optimal dose and strains."

Keep in mind that probiotics (Lactinex, Risa-Bid, etc) are also bacteria (or yeast, in the case of Florastor) and can be killed or have decreased effectiveness when co-administered with antibiotic therapy. Probiotics should be administered at least 2 hours before or 2 hours after any dose of antibiotic for maximal effectiveness.

Some probiotic preparations require refrigeration, while others can be stored at room temperature. Contact your AlixaRx Clinical Pharmacist if you have any questions regarding probiotic administration or storage.

Reference: Shen NT, Tmanova LL, Pino A, et al. The use of probiotics for the prevention of clostridium difficile infection (cdi) in hospitalized adults receiving antibiotics: a systematic review and meta-analysis. Paper presented at: Digestive Disease Week 2016; May 26, 2016; San Diego, CA

FDA Issues Safety Alert for Fluoroquinolones

The U.S. Food and Drug Administration is advising that serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options.

The update issued July 27, 2016, applies to the following medications: Avelox (moxifloxacin), standard- and extended-release Cipro (ciprofloxacin), Factive (gemifloxacin), Levaquin (levofloxacin) and ofloxacin.

Fluoroquinolone Side Effects:

- Tendon problems, tendinitis, tendon rupture (potentially disabling)
- Digestive distress, nausea, diarrhea, constipation, stomach pain, heartburn, vomiting; super-infections, including C. diff diarrhea
- Arthritis, muscle pain, weakness
- Headache, dizziness, anxiety, irritability, agitation, restlessness, confusion, insomnia
- Retinal detachment
- Allergic reactions, skin rash, anaphylaxis (life-threatening reaction requiring immediate medical attention!)
- Hallucinations, psychosis, seizures
- Depression, suicidal thoughts or actions
- Irregular heart rhythms, QT prolongation
- Kidney or liver damage
- Blood disorders

Symptoms of Nerve Damage from Fluoroquinolone Antibiotics:

- Pain
- Numbness
- Changes in sensation to light touch, pain or temperature, or the sense of body position
- Burning, tingling, weakness

Nursing staff should immediately report any new potential side effect to the prescriber. Consult your AlixaRx Clinical Pharmacist for advice on antibiotic treatment monitoring and alternative medications.

References: 1. http://www.peoplespharmacy.com/2016/05/12/new-fda-warning-for-popular-cipro-and-levaquin-antibiotics/ 2. http://www.healio.com/infectious-disease/antimicrobials/news/online/%7B07a3f6d2-675a-4f97-a8e1-dcca9e129a3a%7D/fda-updates-fluoroquinolone-safety-warnings

Empiric Treatment of Urinary Tract Infections (UTI) with Levofloxacin (Levaquin) or Ciprofloxacin (Cipro) – An Opportunity for De-escalation and Avoidance

If you are wondering what de-escalation means, you are not alone. While this is common practice in hospitals with infectious disease experts and onsite pharmacists, it is not common practice in the long-term care setting, but it should be. If possible broad spectrum antibiotics such as levofloxacin and ciprofloxacin should be de-escalated to a narrower spectrum antibiotic after the culture and sensitivities (C&S) are back. This process often happens during an antibiotic timeout. An antibiotic timeout is just like it sounds. At 48 hours after the decision is made to start an antibiotic for a possible UTI, the C&S is back, and antibiotic treatment should be reviewed. At this time the antibiotic can be discontinued if the urine test is negative, it can be changed if the organism is resistant to the current treatment, and it should also be changed if the organism is sensitive to a narrower spectrum antibiotic. Continuing broad spectrum antibiotics unnecessarily puts your residents at increased risk for adverse effects, including Clostridium difficile (C.diff.) and the spread of multi-drug resistant organisms (MDROs). Recent FDA warnings recommending against fluoroquinolone (Levaquin/Cipro) use to treat uncomplicated UTIs further strengthens the argument against utilizing them for initial treatment of UTI. The International Clinical Practice Guidelines, updated in 2010 by the Infectious Disease Society of America and the European Society for Microbiology and Infectious Diseases, recommends nitrofurantoin (Macrobid) 100 mg twice daily for 5 days, or trimethoprim–sulfamethoxazole (Bactrim) 160/800 mg twice daily for 3 days (if local resistance rates do not exceed 20%) for the initial treatment of UTI in the older adult. Does your facility have an antibiotic stewardship program to address these and other similar issues? Your AlixaRx Clinical Pharmacist can provide assistance in the development of an antibiotic stewardship program for your facility to reduce unnecessary antibiotic usage.

References: 1. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis.2011;52(5):e103–e120.

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