Family Medicine Clinical Pharmacy Forum
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Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

Contents

Spring into allergy season—recommended therapies

- Nasal corticosteroids (Flonase®, Beconase®, etc) are the most effective treatment for allergic rhinitis. Suggest the new generic fluticasone for patients who want to save money.
- For patients experiencing mild to moderate nasal symptoms plus itchy, watery eyes oral antihistamines are the agent of choice. Second-generation antihistamines (fexofenadine, loratadine, etc) work as well as older antihistamines for allergic rhinitis and are better tolerated, taken less often, and are also somewhat effective for congestion.
- For nasal symptoms and congestion, azelastine spray is an option. For congestion alone, pseudoephedrine is the best option. With sales restrictions on pseudoephedrine, phenylephrine (Sudafed PE®) is being used as an alternative, but it doesn't seem to work as well.
- Other tips: Nasal decongestant sprays are only for short-term use. Montelukast (Singulair®) is not any more effective than antihistamines or pseudoephedrine for allergic rhinitis. Ipratropium nasal spray (Atrovent®) can alleviate runny nose symptoms, but not congestion or sneezing.

To summarize, suggest starting with an antihistamine and/or decongestant for mild to moderate symptoms lasting less than a month. Recommend a nasal corticosteroid for more severe or persistent symptoms.

Emsam®—the first patch for depression

Emsam® (selegiline) will be used as an alternative to oral MAO inhibitors in patients who do not respond to other antidepressants. Oral selegiline is selective for MAO-B at the low dose used for Parkinson's, but it's nonselective at higher doses needed for depression.

Emsam® patches come in 6, 9 and 12 mg strengths and are applied once daily. Giving selegiline transdermally allows for inhibition of MAO-A and MAO-B in the brain with minimal inhibition in the gut

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and liver. This means patients on the lower 6 mg patch don't have to worry about the usual dietary restrictions associated with oral MAOIs. For now, tell patients using these higher-strength patches to avoid tyramine-containing foods such aged cheeses, salami, draft beer, red wine, sauerkraut, etc.

Drug interactions are still are concern with Emsam®. Emsam® should not be used with other antidepressants, buspirone, cyclobenzaprine, dextromethorphan, meperidine, methadone, propoxyphene, tramadol, or St. John's wort due to increased risk of serotonin syndrome. Amphetamines, pseudoephedrine, or phenylephrine should also be avoided because of risk of increased blood pressure.

The Role of MSM in Osteoarthritis

Traditional treatments for osteoarthritis (OA) such as acetaminophen, nonsteroidal anti-inflammatory agents, and cyclo-oxygenase-2 inhibitors often do not provide adequate pain relief leading patients to turn to alternative agents. A recent pilot clinical trial indicates that MSM may be another possible alternative for the treatment of osteoarthritis pain.

MSM or methylsulfonylmethane is a derivative of DMSO, or dimethyl sulfoxide, and is found naturally in various fruits, vegetables, grains, and animals. Due to its sulfur content, it is thought to have many useful properties such as chemoprevention, anti-inflammation, the ability to inhibit prostacyclin synthesis, and to help maintain normal connective tissue.

The double-blind pilot study provided 12 weeks of 3 grams of MSM taken twice daily vs. placebo in 50 men and women with OA of the knee. Patients taking MSM had significantly better pain (P=0.041) and function scores (P=0.045). Patients in the treatment group also experienced significant improvement in the physical activities of daily living (P= 0.045). Adverse effects reported by patients taking MSM including bloating, insomnia, and fatigue, but the incidence of these adverse effects was not significantly different than placebo. Adverse effects of MSM seen in previous studies, but not reported in this trial, include increased bruising, bleeding time, and increased hepatic enzymes.

Although the results are preliminary, MSM appears to be a reasonable treatment option given the questionable effectiveness of glucosamine and chondroitin and the possible adverse effects associated with the use of NSAIDs and COX-2 inhibitors. However, future studies are warranted to further explore the safety and efficacy of MSM for the treatment of osteoarthritis.

References:
Osteoarthritis and Cartilage 2006; 14 (3); 286-94.
APhA Drug Info Line Feb 2006.

Tramadol- A Low Abuse Risk Alternative to Opioids?

Tramadol (Ultram®) is a central-acting analgesic structurally related to morphine and codeine. Its' affinity for μ receptors is about 10-fold less than codeine and 6000 fold less than morphine. The inhibitory effects of tramadol on spinal cord pain transmission are enhanced due to its' inhibition of seretonin and norepinephrine reuptake.

Tramadol withdrawal has been seen in patients who abruptly discontinue therapy. Symptoms of withdrawal are similar to that of opioid withdrawal.[1] Following several FDA case reports and a 3-year post-marketing cohort study[2,3,4], Ortho-McNeil Pharmaceuticals (OMP) amended their package insert to include "Tramadol may induce psychic and physical dependence of the morphine type (mu-opioid). Dependence and abuse, including drug-seeking behavior and taking illicit actions to obtain the drug are not limited to those patients with prior history of opioid dependence. The risk for patients with a history of substance abuse has been observed to be higher."[5] Despite this disclaimer, tramadol continues to be a non-scheduled drug often overutilized and misused in the community setting.

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2. Adverse Event Reporting System. Freedom of Information Report. Rockville, Md: Office of Drug Safety, Food and Drug Administration: search November 1997 to September 2004.
3. Knisely, JS, Campbell ED, Dawson KS, Schnoll SH. Tramadol post-marketing surveillance in health care professionals. Drug Alcohol Depend 2002; 68:15-22.
4. Liu, ZM, Zhou WH, Lian Z, et al. Drug dependence and abuse potential of tramadol. Zhongguo Yao Li Xue Bao 1999; 20:52-54.
5. Murray L, ed. Physicians' Desk Reference. 58th ed. Montvale, NJ: Thomson PDR; 2004:2496.

Metformin use in patients with heart failure—new evidence

Currently metformin therapy is contraindicated in patients with diagnosed congestive heart failure due to concern over the increased incidence of lactic acidosis. However, there is increasing evidence that the use of metformin in this population is not only beneficial but also safe. One meta-analysis used Saskatchewan Health databases to identify 12, 272 new users of oral antidiabetic agents. Researchers assessed the differences in all-cause mortality and all-cause hospitalization. They found that the percentage of all-cause mortality in the sulfonylurea monotherapy, metformin monotherapy, and combination treatment groups were 52%, 33%, and 31%, respectively. They also found comparable rates of all-cause hospitalizations between the three groups (70%, 69%, and 74%). This study provides evidence that the use of metformin, alone or in combination, in patients with heart failure and diabetes was associated with lower morbidity and mortality when compared to sulfonylurea therapy. Future studies with more robust methodologies will need to be run before prescribing practices and guidelines are changed, but this study certainly provides preliminary evidence that concern over the use of metformin in heart failure may be changing.

Reference:
Eurich et al. "Improved Clinical Outcomes Associated with Metformin in Patients with Diabetes and Heart Failure." Diabetes Care 28: 2345-2351.

Cymbalta® and increased risk for liver disease

Eli Lilly has recently made changes to the prescribing information for duloxetine (Cymbalta®). Patients with underlying liver disease may be at increased risk of additional hepatic injury with the use of duloxetine, and therefore, use is discouraged in this group. The changes made in October 2005, were brought about by post marketing reports of hepatic injury. These reports include hepatitis with abdominal pain, hepatomegaly, cholestatic jaundice, elevation of transaminase levels greater than twenty times the upper limit of normal with or without jaundice, reflecting a mixed or hepatocellualr pattern of liver injury. Both prescriber and patient need to be cognizant of the signs and symptoms of liver damage associated with duloxetine herapy. Patients should be informed to watch for pruritis, dark urine, jaundice, right upper quadrant tenderness, or unexplained flu-like symptoms.

Does Cranberry Juice Prevent Urinary Tract Infections?

For patients who experience recurrent UTIs, long-term antibiotic prophylaxis is commonly used, however, cranberries have been investigated as a non-antibiotic alternative for preventing these infections.

How it works:

E. coli causes about 85% of uncomplicated UTIs. Cranberries contain two compounds that inhibit the adhesion of *E. coli*, which are fructose and proanthocyanidin. Fructose inhibits the mannose-sensitive adhesins and can be found in any fruit juice. However, proanthocyanidin is only in juices from *Vaccinium* berries and is active against the mannose-resistant adhesins. This antiadherent effect starts within two hours of ingestion and continues for up to ten hours.

Does it work:

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Cranberries have been studied in clinical trials for effect on UTIs since 1966. A review article was published in 2004 by *Clinical Infectious Diseases*[1], which concluded sexually active adult women have been shown to have the most benefit with about a 20% decrease in the incidence of UTIs over six months to one year.

Might not work for:
Patients with a history of kidney stones might experience recurrent stones due to the oxalate in cranberries, which is a commonly contained in kidney stones. Diabetics should not drink large amounts of cranberry juice due to the amount of carbohydrates. Finally, reports of increased INR and bleeding episodes in patients taking warfarin and drinking cranberry juice.

See if it works:
Cranberry is available as juice, tablets, and capsules. The cost of cranberry products varies among the different dosage forms. Depending on the concentration of the tablets or capsules, the recommended dose is usually between 1-4 capsules once or twice daily.

The Journal of Family Practice[2] suggests, "a trial of cranberry juice (3 glasses daily) is reasonable for women with recurrent UTI, who are being considered for antibiotic prophylaxis." However, there are no clear guidelines on how to use cranberry juice or other cranberry products for the prevention of UTIs.

References:
1. Raz R, Chazan B, and Dan M. Cranberry juice and urinary tract infection. *Clinical Infectious Diseases* 2004;38:1413-9.
2. Kiel R and Nashelsky J. Does cranberry juice prevent or treat urinary tract infections? *J Fam Pract* 2003;52:154-55.

Medicare Part D

Medicare prescription drug coverage began on Jan 1, 2006 and many of you have experienced helping patients select plans or change their drug therapy in order to accommodate the formulary of their new plan. For additional information go to www.medicare.gov or www.iarx.org.

MAKE SURE ALL OF YOUR MEDICARE PATIENTS HAVE SIGNED UP FOR A PLAN! Patients who do not enroll by May 15, 2006 will have to pay additional fees to join later.

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