



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 practice-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

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New UK Guidelines for Hypertension do not Include Beta-Blockers

The British guideline development group conducted a meta-analysis of different medication classes used to treat hypertension and concluded that beta blockers were usually less effective than the comparator drug in decreasing the incidence of major cardiovascular drugs. Atenolol was the beta-blocker used in the majority of these studies, and with insufficient data on other beta-blockers, it is unclear whether the conclusion applies to all beta-blockers. The guidelines maintain that for patients 55 and older, calcium channel blockers and thiazide diuretics are the initial treatments of choice for hypertension. In patients under the age of 55, ACE inhibitors are the initial treatment of choice. When multiple drugs are required, the guidelines recommend adding an ACEI in patients over the age of 55, or adding a calcium channel blocker or thiazide diuretic in patients under age 55 who are already taking an ACEI. If a third drug is required, the guidelines recommend the combination of a thiazide diuretic, ACEI and calcium channel blocker, with beta blockers being the fourth drug class for consideration. The authors suggest that clinical benefit is least likely with beta-blockers, especially for stroke prevention.

Beta blockers are not a preferred initial choice for hypertension, but could be considered in patients intolerant to ACEIs and ARBs, women of child-bearing age, and patients with increased sympathetic drive. If therapy is initiated with a beta-blocker and additional medications are needed, calcium channel blockers are recommended over thiazide diuretics to decrease the risk of diabetes. The guidelines recommend in patients who are not at goal blood pressure and on a regimen that includes a beta-blocker, the regimen should be revised according to the treatment algorithm provided. However, if a patient has good blood pressure control on a regimen that includes a beta-blocker, there is no absolute need to replace the beta-blocker.

Authored by:

Jim Hoehns, Pharm.D, BCPS

Northeast Iowa Family Practice Program

Waterloo, IA

(special thanks this edition also to contributors: Jess Purcell, Pharm.D., M.P.H (pharmacy resident),, Ginelle Schmidt and Jackie Stark (PharmD candidates at The University of Iowa.)



NICE/BHS. Hypertension: management of hypertension in adults in primary care. June 28, 2006. Available at www.nice.org.uk/CG034

Chantix-Newest Aid for Tobacco Cessation

Chantix (varenicline tartrate) is the newest prescription medication to be approved by the FDA. Chantix acts as a partial agonist by binding to a sub-type of the nicotinic receptor providing agonist activity, while at the same time preventing nicotine from binding to these same receptors. Varenicline stimulates the alpha4,beta2 nicotinic receptors at a much lower level than nicotine, while simultaneously blocking accessibility of these receptors to nicotine, thus blocking the reward and reinforcement experience of smoking.

To date, they have completed six trials with 3600 smokers (>10 cigarettes/day). In all studies, abstinence was determined by patient self-report as well as measurements of exhaled carbon monoxide at weekly visits. In comparison studies with bupropion SR, Chantix was superior with 12-week quit rates of 44% compared to 30% in the bupropion SR group and 17% in placebo. Additionally, 29% of Chantix patients were continuously abstinent from one week after the established quit date through the end of treatment compared to 21% of the bupropion group and 11% of placebo patients. Continuous abstinence across 52 weeks ranged from 14-29% for Chantix patients, 14-16% for bupropion patients and 4-10% for placebo patients.

Chantix is available in 0.5mg and 1mg tablets with a recommended dose of 1mg BID following a 1-week titration of 0.5mg daily on days 1-3, 0.5mg BID days 4-7 and 1mg BID day 8-end of treatment. Day 8 should be the patient's smoking quit date to ensure patients have achieved steady state prior to their quit date. Treatment should last 12 weeks and if a patient has successfully quit after 12 weeks, an additional 12 weeks of therapy may help to enhance the chances for long-term abstinence. Patients who do not successfully quit after 12 weeks, or who relapse, should be encouraged to make another attempt once contributing factors to the failure have been identified and addressed. No clinically meaningful drug-drug interactions have been identified and combination therapy with bupropion has not been studied. The most common side effects experienced (>5%) were nausea, flatulence, sleep disturbance, and vomiting. When combined with nicotine replacement therapy, higher rates of adverse effects were observed, including nausea, headache, vomiting and dizziness, although there was no effect on nicotine pharmacokinetics.

A 12-week supply of Chantix costs around \$350.

United States Food and Drug Administration. "FDA approves novel medication for smoking cessation." Accessed 7/15/06. Available at www.fda.gov/bbs/topics/NEWS/2006/NEW01370.html.

Chantix prescribing information. Accessed 7/15/06. Available at http://www.pfizer.com/pfizer/download/uspi_chantix.pdf.

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Poison Ivy, Poison Oak and Sumac Treatments

With the summer comes boating, swimming, hiking, along with seasonal illnesses such as contact dermatitis from exposure to poison ivy (poison Urushiol the common allergen in found in the leaves, stems and roots of these plants). Nearly 70% of the population is sensitive to the urushiol released from these plants. Even indirect contact from clothes, pets or even the burning leaves of these plants can produce a reaction. Fluid from lesions is not sensitizing to others, however thorough washing with soap and water should take place as soon after exposure as possible to minimize spread to other areas of the body. All contaminated clothes should be removed and washed as soon as possible. Frequent baths with colloidal oatmeal can be soothing as well as application of cool compressed or diluted aluminum acetate solution or calamine lotion.

Management should include thorough washing with soap and water, preferably within 10 minutes of exposure, as this may prevent dermatitis. Corticosteroids are the mainstay of treatment due to their ability to stop lymphocyte proliferation and decrease cytokine production. Mild to moderate dermatitis can be treated with topical steroids applied twice daily for two weeks. If the dermatitis is particularly severe, systemic corticosteroids can be used. These will produce a dramatic rapid response, but therapy must be tapered slowly to avoid rebound dermatitis. Oral prednisone is usually dosed at 1mg/kg/day for several days followed by a 2-week taper. Alternatively, Brodell et al suggest 60mg days 1-4, 50mg on days 5-6, 40mg on days 7-8, 30mg on days 9-10, 20mg on days 11-12 and 10mg on days 13-14. Oral antihistamines may provide some anti-pruritic and sedative effects, although they are nominal at best. Regardless, any reduction in itching and scratching limits the incidence of secondary infections, and therefore may be beneficial.

Brodell RT, Williams L. Taking the itch out of poison ivy: are you prescribing the right medication? Postgrad Med 1999;106(1):69-70

Lee NP, Arriola ER. Poison ivy, oak, and sumac dermatitis. WJM November/December 1999;177:354-5.

New Drug: Exubera (insulin human [rDNA origin])

- In January 2006, the FDA approved Exubera, a human insulin inhalation powder and the first non-injectable insulin for the treatment of hyperglycemia in adult patients with diabetes mellitus. It is anticipated to arrive on pharmacy shelves in August.
 - Type 1 Diabetes mellitus: Exubera plus longer-acting insulin
 - Type 2 Diabetes mellitus: Exubera by itself or in combination with oral agents or longer-acting insulins.
- Exubera has a more rapid onset of action compared to regular insulin, a duration of action comparable to regular insulin and should be administered no more than 10 minutes prior to each meal.

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- Exubera comes in blister packs that contain a 1 mg (\equiv 3 IU of regular human insulin) or a 3 mg dose of insulin (\equiv 8 IU of regular human insulin).
- The Exubera blister is inserted into the inhaler, the patient pumps the handle of the inhaler and presses a button to pierce the blister pack. The insulin inhalation powder is released into the chamber, allowing for the patient to inhale the powder.
- Initial pre-meal doses are based on patient body weight using the following formula: [body weight (kg) X 0.05 mg/kg = pre meal dose (mg)] rounded down to the nearest whole milligram number.
- Exubera is contraindicated in patients who smoke or have smoked in the past 6 months, or who have unstable or poorly controlled lung disease. It is not recommended for use in patients with underlying lung disease, such as asthma, COPD, bronchitis, or emphysema
- Baseline lung function tests (FEV₁ and DL_{CO}) are recommended before treatment and every 6 months to 12 months thereafter due to the fact that trials showed small, non-progressive declines in pulmonary function with Exubera.
- Common side effects include hypoglycemia, cough, shortness of breath, sore throat, and dry mouth.
- Blister packs should be stored at controlled room temperature, not frozen or refrigerated. Once the foil overwrap is opened, it must be protected from moisture and used w/in 3 months. The Exubera inhaler can be used up to 1 year from the first date of use, but the Exubera Release Unit in the inhaler should be replaced every 2 weeks.
- The exact cost of inhaled insulin is not known at this time.
 - NDA 21-868 / EXUBERA ® US Package Insert, Version Date: 2006-01-27
 - First inhaled insulin product approved. *FDA Consum.* 2006 March-April; 28-9.
 - Bellary S, Barnett A. Inhaled insulin: a new technology, new possibilities. *Int J Clin Pract.* 2006 June; 60(6): 728-734.

Restarting warfarin in patients after intracranial hemorrhage (ICH)?

Patients with atrial fibrillation and mechanical heart valves (MHV) have clear indications for lifelong Coumadin to decrease the risk of stroke. This clear indication, however, becomes blurred when these patients experience intracranial bleeds. In patients who have had a previous ICH, the risk of recurrence is approximately 2-3% per year. On the flip side, the annual risk of thromboembolism is roughly 5% in untreated patients with Afib (12% if previous ischemic stroke) and up to 4-22% in untreated patients with a MHV. For patients with mechanical heart valves the benefit of reinitiating anticoagulation may outweigh the risks of recurrent ICH, in contrast to patients with Afib where the risks of ICH and clotting are similar.

Location of the ICH can help determine the risk of recurrent hemorrhage. In general, ICH occurs in two areas of the brain; lobar hemorrhages, involving the cerebral cortex, which appear to carry a higher risk of recurrence (15%) and are most commonly related to amyloid angiopathy vs. deep hemispheric hemorrhages which reoccur only at a rate of 2.1% and are most commonly related to hypertensive vasculopathy, a modifiable risk factor. Outcomes from a prospective cohort study

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of 435 patients with Afib and previous ICH were utilized in a Markov decision analysis study. The base case focused on a 69 y.o. man with a history of ICH and newly diagnosed nonvalvular Afib. The investigators looked at risk of stroke and determined the quality-adjusted life years (QALYs) which considered both mortality & disability. In patients with a prior lobar ICH, withholding anticoagulation was strongly preferred due to the high risk of recurrent ICH and an increase in life expectancy of 1.9 QALYs. In patients with deep ICH, withholding anticoagulation resulted in a smaller gain in QALY (0.3), therefore one must weigh the risk/benefit of restarting Coumadin.

General Recommendations:

- For **primary prevention** of ischemic stroke in most elderly patients with **Afib**, the long-term high risk of recurrent ICH usually **does not warrant re-initiation of anticoagulation**.
- For patients with **prosthetic heart valves or for secondary prevention** in patients with Afib, the risks of thromboembolism in the absence of anticoagulation are much higher, and the **risk/benefit assessment appears to favor use of anticoagulation**.
- **Optimal timing:** warfarin can be restarted in appropriate patients in **7-14 days**. In patients whose INR was corrected using prothrombin complex concentrate, it seems reasonable to begin low dose SQ heparin or LMWH 48 hours after ICH onset if they are at particularly high risk of thromboembolic stroke.
- If warfarin is to be given to an ICH survivor, a **target INR of 2** is sensible, representing the lower end of the recommended INR of 2-3.
- **Aggressive control of blood pressure** is particularly critical

Eckman MH et al. Stroke 2003;34:1710-16.

Gardasil (human papillomavirus vaccine)

This new quadrivalent, HPV-like particle vaccine has been approved by the FDA for use in girls and women 9-26 years old to prevent diseases associated with HPV types 6, 11, 16, and 18, including cervical cancer, genital warts, and vaginal or vulvar lesions. HPV types 16 and 18 are associated with more than 70% of cervical cancers. Types 6 and 11 cause 90% of genital warts.

One randomized, double-blind, placebo-controlled 3 year trial of a quadrivalent HPV vaccine (equivalent to Gardasil) in women 16-23 yrs old resulted in a 90% reduction in persistent HPV infection or cervical or genital HPV-associated disease.

A randomized, placebo-controlled trial of Gardasil in more than 12,000 women evaluated its efficacy in preventing HPV 16/18-related CIN and cervical cancer. At 2 yrs there was no HPV 16/18-related CIN among the 5301 women who were vaccinated and 21 cases among the 5258 who received placebo. One case of genital warts was observed in those who were vaccinated

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versus 59 cases among those receiving placebo. Adverse reactions were mostly related to the injection site including pain, swelling, erythema, and pruritus.

The ACIP recommends vaccination in all girls and women 11-26 years old. Girls aged 11-12 yrs old can receive the vaccine in conjunction with the Tdap and meningococcal vaccine. The ACIP has suggested vaccination could be started as early as age 9 at the discretion of the health care provider. Gardasil should not be given to pregnant women.

Gardasil is given as 3 IM injections at 0,2, and 6 months. Each dose costs about \$120.

Medical Letter , Vol 48, August 14/28, 2006.
Koutsky LA et al. N Engl J Med 2002;347:1645.

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