Clinical Briefs in Primary Care™

The essential monthly primary care update

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Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports.*

VOLUME 16, NUMBER 11 PAGES 21-22 NOVEMBER 2011

How Often Do You Really Have to See Patients on Warfarin?

Source: Rose AJ, et al. *Chest* 2011;140: 359-365.

IT HAS BEEN CUSTOMARY TO ASK PATIENTS on warfarin, once controlled and stable, to return on a monthly basis for recheck. This interval has been based on tradition, rather than any firm scientific basis. Frequent visits in otherwise stable patients present a significant burden of time, cost, inconvenience, and even the opportunity for overzealous "fine tuning," and may not enhance the amount of time spent in the therapeutic range. It would, therefore, be desirable to have better insight into whether stable patients might be safely allowed longer intervals without risking either toxicity of supratherapeutic warfarin dose, or thrombotic risk of subtherapeutic levels.

Rose et al report on data obtained from a large population of persons receiving anticoagulation from the U.S. Veterans hospital system (n = 104,451). By comparing the interval between an in-range international normalized ratio (INR) and the next INR measurement with the likelihood of being in the therapeutic range on follow-up visit, they were able to discern that the first two visits after a therapeutic INR measurement are time sensitive: that is, extending the time until next follow-up beyond 4 weeks was associated with progressively greater likelihood of finding an out-of-range INR at the next visit. This relationship, however, was not seen in persons with consistently in-range INR readings, i.e., if a patient had experienced three consecutive INR in-range visits, extending the length of time until next follow-up was not associated with greater likelihood of an out-of-range INR.

At the current time, another trial comparing monthly with quarterly INR monitoring is underway. Pending results from that trial, this evidence suggests that until patients have at least three consecutive stable INR measurements, the traditional 4-week return policy is best. After that, a longer interval until next INR measurement is acceptable, but has only been studied as far out as 38 days. ■

Replacing Carbohydrates with Nuts in the Diabetic Diet

Source: Jenkins DJ, et al. *Diabetes Care* 2011;34:1706-1711.

CONSUMPTION OF NUTS, ESPECIALLY WALnuts, has been associated with favorable health outcomes. For diabetics, maintenance of a healthy body weight, reduction of high-glycemic index foods, and lipid modulation through diet are each a potentially critical consideration. Because nuts have significant fat content, there has been concern that were diabetics to substitute nuts for other carbohydrates, a detrimental impact on either weight or lipids might be seen.

Jenkins et al randomized type 2 diabetics (n = 117) to substitute carbohydrates in their diets in one of three ways: mixed nut replacement, muffin replacement, or half-and-half nuts plus muffins. Based on energy requirements calculated with the Harris-Benedict equation, participants were asked to substitute their prescribed replacement supplement for whatever carbohydrate had previously comprised an equal caloric proportion of their diet. For instance, a person requiring 1600-2400 kcal/d was given 475 kcal of a replacement supplement. The trial lasted 3 months. The nut mix consisted of almonds, pistachios, walnuts, pecans, hazelnuts, peanuts, cashews, and macadamias. The muffin was whole wheat, with no sugar added. The absolute kcal content of the supplement was the same whether administered as nuts, muffin, or mixed.

The group supplemented with nuts enjoyed a statistically significant A1c reduction of 0.21%, but no significant A1c change was seen in the other two groups. Similarly, cholesterol, LDL, and cholesterol:HDL ratios were most favorably affected by the nut supplement. Nut replacement for carbohydrates has favorable effects in type 2 diabetes. ■

Hypertensive Emergency: The Prognostic Value of Elevated Troponins

Source: Afonso L, et al. *J Clin Hypertens* 2011;13:551-556.

HYPERTENSIVE EMERGENCY, CHARACTERized by marked elevation of blood pressure (typically > 180/120) associated with signs of target organ damage, is a common presenting issue in emergency departments. Since cardiac toxicity may be one of the signs of target organ damage, troponins are often measured, even though there may be no symptoms of myocardial ischemia or signs on EKG. Especially when troponins are measured in acute coronary syndromes, they have strong prognostic value. Whether they provide any discriminative value in per-

sons with hypertensive emergency has not been previously well-studied.

A retrospective analysis was done on all patients with hypertensive emergency seen at two inner-city population hospitals in Detroit (n = 567) in whom troponins had been measured. Among this group, one-third demonstrated troponin elevation (mean peak = 4.06 ng/mL). However, follow-up of these patients did not find that the presence or degree of elevation of troponins predicted subsequent mortality over the next 3 years.

Elevation of troponins is commonly seen in patients with hypertensive emergency, but in the absence of an acute coronary syndrome, is not prognostically valuable. ■

Is Mercury Really a Bad Guy in CV Disease?

Source: Houston MC. *J Clin Hypertens* 2011;13:621-627.

Mercury has a bad rap sheet: it decreases cellular oxidative defenses, increases oxidative stress, reduces the effectiveness of metalloenzymes, induces mitochondrial dysfunction, increases vascular inflammation, and worsens endothelial function. In addition, mercury toxicity is associated with increased carotid intima-media thickness. Omega-3 fatty acids, as contained in fish, can antagonize some of the detrimental effects of mercury. However, fish in the diet are also currently the major source of human exposure to mercury.

There is no known biologic or physiologic role of mercury in the body, hence it must be regarded as a toxin.

Observational data generally, but inconsistently, find an association between tissue levels of mercury and cardiovascular disease. For hypertension particularly, numerous different populations have found a relationship between tissue mercury levels and blood pressure (systolic, diastolic, and pulse pressure). Chronic mercury toxicity may be inexpensively measured by a 24-hour urine mercury level. The author does not include mention of any trials indicating favorable effects achieved by modulation of mercury, although selenium, by complexing with mercury, may mollify some of its toxic effects. ■

Long-Term Azithromycin for Prophylaxis of COPD Exacerbations

Source: Albert RK, et al. *N Engl J Med* 2011;365:689-698.

For many patients with moderate-severe chronic obstructive pulmonary disease, acute exacerbations (AECOPD) are highly problematic. For hospitalized AECOPD, the mortality rate is approximately 10%; loss of pulmonary function that typically accompanies an AECOPD is usually not regained; mortality during the year following an AECOPD is increased. Hence, reduction and/or delay of AECOPD is an important goal.

Macrolides are often the antimicrobial agents chosen to treat AECOPD. This trial in patients with COPD randomized subjects to azithromycin 250 mg qd (n = 570) or placebo (n = 572) for 1 year. The patient's background COPD treatments were unchanged. The primary outcome of the trial was time to first AECOPD. Secondary outcomes included QOL, and scores on the St. Georges Respiratory Questionnaire. More than three-fourths of study participants were receiving background inhaled steroids, long-acting beta agonists, and/or long-acting anticholinergics during the trial.

Azithromycin prophylaxis was associated with a statistically significant prolongation of time to first AECOPD, as well as a 27% relative-risk reduction in the frequency of AECOPD. The St. George's Respiratory Questionnaire scores were improved significantly more in the azithromycin group. One adverse effect analyzed was affect on hearing function: Azithromycin was associated with a slightly higher incidence of hearing decrement than placebo. However, improvements in hearing noted on follow-up occurred whether the drug was discontinued, suggesting that perhaps the incidence of hearing decrements were initially overestimated.

Azithromycin prophylaxis may provide important benefits in COPD, especially for persons with frequent AECOPD. ■

Unintended Medication Consequences of Hospital Admission

Source: Bell CM, et al. *JAMA* 2011;306: 840-847.

Most hospitalizations have a focused agenda: heart failure, pneumonia, acute trauma, etc. It is not at all difficult to conceive that as a consequence of intensified focus on one or more often acute problems, attention can be drawn away from the issues of lesser acuity, such as maintenance medications for dyslipidemia, dysglycemia, or thyroid disease. Sometimes because of discontinuity between persons involved in the patient's hospitalization and outpatient providers, inadvertent discontinuation of necessary chronic medications can be overlooked.

Using the database of patients in Ontario, Canada (n = 396,380; age 66 and older), Bell et al examined prescription data to see whether chronic medications from five different classes experienced discontinuation subsequent to hospitalization. The five classes were: statins, antiplatelet/anticoagulants, levothyroxine, respiratory inhalers, and gastric acid inhibitors.

Hospitalization was associated with an increased incidence of discontinuation of all five classes of agents. Hospitalization, which included ICU admission, was disproportionately likely to be associated with chronic medication discontinuation. Equally distressing, the data demonstrated an increased risk for death or subsequent hospitalization in persons who discontinued their chronic medications. Gaps in continuity of care are of significant consequence to hospitalized patients. ■

Clinical Briefs in Primary Care™ is published monthly by AHC Media.

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