

Clinical Briefs in Primary Care

The essential monthly primary care update

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Daily vs As-Needed Steroids for Asthma

Source: Boushey HA, et al. *N Engl J Med.* 2005;352:1519-1528.

MANAGEMENT OF ASTHMA IN America remains problematic, with as many as 5,000 deaths annually in recent years. Current guidelines suggest that for anyone with any degree of persistent asthma, maintenance anti-inflammatory medication is appropriate. The first-line recommended anti-inflammatory medication is inhaled corticosteroids (ICS), which are generally prescribed for daily use. Despite clinician advice to use ICS daily, prescription patterns indicate that this advice is often not heeded.

Reflecting upon the observed pattern of ICS administration, Boushey and colleagues randomized 225 adult asthmatics to receive 1) daily ICS, or 2) daily zafirlukast, or 3) brief steroid bursts with worsening asthma symptoms (10 days ICS or 5 days oral steroids), but no daily asthma maintenance medications. Subjects were followed for one year.

The primary end point of the study, change in morning peak expiratory flow rate, did not differ amongst the 3 groups. As anticipated, ICS did provide more favorable effects upon pulmonary inflammatory cellular changes (eg, degree of sputum eosinophilia). The number of asthma exacerbations did not differ between the groups. Although the daily administration of ICS did result in a greater number of symptom-free days than other regimens (26 days per year), this must be counterbalanced with the lack of impact of ICS upon exacerbations. Boushey et al caution that their results should be considered preliminary; larger studies would be required before such an approach could be endorsed. ■

Intensive Lipid Lowering with Atorvastatin

Source: LaRosa JC, et al. *N Engl J Med.* 2005;352:1425-1435.

THE VASCULOPATH—ANYONE WITH established vascular disease such as previous MI, stroke, PAD, or type 2 diabetes—is known to be at increased risk for subsequent vascular events and mortality. A large body of encouraging data of late have indicated that use of statins to lower lipids has favorable effects in diverse populations, including primary and secondary prevention, and even impressive results in acute coronary syndromes (ACS). Statin data from the ACS studies may not accurately reflect risk reductions that might be attained in stable patient populations. Additionally, although the PROVE IT trial suggested that lower lipid levels achieved were responsible for more favorable outcomes in a pravastatin vs atorvastatin trial, there still remained the possibility that there was some inherent difference between statins. So, 2 critical questions remained: Is lower better? Do persons with stable coronary disease benefit similarly to other populations?

Patients with stable demonstrated coronary heart disease and modest levels of LDL (< 130 mg/dL mean) were enrolled and randomized to 10 mg or 80 mg of atorvastatin daily for a median of 4.9 years (n = 10,00).

The relative risk reduction in the primary end point (first major cardiovascular event) was 22% (absolute risk reduction 2.2%). These favorable effects were achieved with a mean LDL of 77 mg/dL on 80 mg/dL atorvastatin, vs an LDL of 101 mg/dL on 10 mg/d. Lower is better. ■

The Polymeal: Natural Strategy to Reduce CVD

Source: Franco O, et al. *BMJ.* doi:10.1136/bmj.329.7480.1447.

YOU MAY RECALL SPIRITED DISCUSSION prompted by commentary in the *British Medical Journal* (Wald NJ. *BMJ.* 2003;326:1419-1423) that in theory, a sound public health measure would simply be to administer to everyone at age 55, regardless of health status, a multicomponent pill containing a statin, HCTZ, and ACE inhibitor, Beta Blocker, and Folic acid, all at half-standard dose. Administered population-wide, such a 'polypill' could conceivably provide radical reductions in cardiovascular disease end points.

Franco and colleagues believe there is perhaps a better, less expensive, less adverse effect-laden method that is substantially more palatable: The Polymeal. Based upon their literature review of favorable data on individual components of diet, the following ingredients of the Polymeal would have a beneficial effect: wine (150 mL/d), fish (114 g 4x/week), dark chocolate (100 g/d), fruits and vegetables (400 g/d), garlic (2.7 g/d), and almonds (68 g/d).

Based upon the Framingham life table data, Franco et al calculate the Polymeal reducing cardiovascular disease by 76%. Omitting any component might reduce the benefits; for instance, simply by omitting the wine, one might lose 11% of that benefit! They also calculate a 4.8 years (women), 6.6 years (men) increase in life expectancy from the Polymeal. Cost, of course, will be highly variable depending upon one's tastes in wine and chocolate, but could certainly conform to the most modest of economic settings. Bon appetite! ■

Hemochromatosis and Iron-Overload Screening

Source: Adams PC, et al. *N Engl J Med.* 2005;352:1769-1778.

HEMOCHROMATOSIS (HCRM) IS SOMETHING of an enigma to clinicians, since despite being recognized as having a gene frequency more common than any other known heritable disorder (1/10), HCRM symptoms and target organ damage are often sufficiently subtle or non-specific that the disorder goes unrecognized. Because many of the clinical consequences of HCRM are able to be reversed, or at least halted by appropriate treatment (phlebotomy), it is important to heighten clinician awareness of the disorder.

The HEIRS study (Hemochromatosis and Iron Overload Screening study) has screened for the prevalence, genetic determinants, and clinical impact of HCRM in diverse populations from 6 metropolitan areas: Washington, DC, Birmingham, Alabama, Irvine, California, Portland, Oregon, Honolulu, Hawaii, and Ontario, Canada. The population screened was comprised

of White, Native American, Hispanic, Black, Pacific Islander, Asian, and multi-ethnic individuals (n = 99,711). Laboratory data included serum iron, iron-binding capacity, ferritin, transferrin saturation, and the genetic mutation most commonly associated with HCRM (HFE C282Y).

Overall, 3 persons per thousand were homozygous for the C282Y mutation; amongst persons homozygous for C282Y (who had not been previously diagnosed with HCRM), an elevated ferritin was found in 88% of men and 57% of women. The population most frequently affected was non-Hispanic whites, although all populations had some affected persons. There remains a substantial body of individuals with undiagnosed HCRM whose clinical syndromes could be prevented or at least modified by appropriate identification and treatment. ■

RSV Infection in Elderly and High-Risk Adults

Source: Falsey AR, et al. *N Engl J Med.* 2005;352:1749-1759.

CLINICIANS MAY THINK OF RESPIRATORY syncytial virus (RSV) as a pathogen generally involved in infectious diseases of childhood. The first reports of RSV causing serious illness in older adults began in the 1970s, when RSV was recognized as the pathogen responsible for outbreaks in long-term care facilities. To obtain a clear assessment of the role of RSV infections, a population which included healthy community dwelling elders (n = 608), high-risk adults (eg, persons with underlying COPD or heart disease, n = 540), and adults admitted to the hospital for pneumonia (n = 1,388) was studied using multiple techniques (including PCR) to confirm the presence of RSV. For purposes of comparison, similar methods to identify influenza A virus were simultaneously used. The populations (in Rochester, MN) were prospectively followed for 4 winter seasons, 1999-2003.

Amongst high-risk adults, 4-10% incurred RSV infection annually. Similarly, in community dwelling elderly, 3-7% developed RSV infection annually. Overall,

RSV was responsible for 10.6% of hospitalized pneumonias, and was identified in 11.4% of COPD admissions; 5.4% of CHF admissions, and 7.2% of asthma admissions were attributed to RSV. On a comparative basis, influenza A and RSV were responsible for essentially equivalent impact upon hospital expenditures and overall mortality.

The substantial epidemiologic burden of RSV has been insufficiently recognized. An RSV vaccine could provide an important public health benefit. ■

BNP, CRP, and Urinary Albumin and Cardiovascular Events

Source: Kistorp C, et al. *JAMA.* 2005;293:1609-1616.

TRADITIONAL RISK FACTORS FOR MORTALITY and cardiovascular events such as blood pressure, lipids, and glucose provide excellent stratification opportunities for general populations. Unfortunately, not all important endpoints are directly attributable to currently recognized risk factors, and even when risk factors are effectively modified, the at-risk population is not returned to the same level of risk as persons without these same risk factors. Hence, so-called 'novel' risk factors have been sought to enhance the predictive value of available risk stratification tools.

C-reactive protein (CRP), brain natriuretic peptide (BNP), and albumin-to-creatinine ratio (ACR), have each demonstrated some predictive value in specifically defined populations. BNP levels have predictive ability even in healthy individuals.

A Danish population of 764 ostensibly healthy adults aged 50-89 was followed for 5 years, after obtaining baseline BNP, CRP, and urinary albumin-to-creatinine ratio.

Mortality risk was best predicted by BNP, with a hazard ratio of 1.96 (vs 1.88 for ACR, and 1.46 for CRP); similarly, BNP was more strongly associated with the first cardiovascular event, followed by ACR and then CRP.

Although CRP has enjoyed much more current popular discussion amongst clinicians, in healthy populations BNP and ACR provide better prognostic information. ■

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