Clinical Briefs in Primary Care

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Evidence-based updates in primary care medicine

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A Link Between Obesity and Asthma Severity

SOURCE: Bhatt NA, Lazarus A. Obesity-related asthma in adults. *Postgrad Med* 2016;128: 563-566.

Asthma, like hypertension, may be more than one entity. That is, more than one underlying pathophysiology may lead to similar phenotypic expression. Just as hyperaldosteronism may present with hypertension that is otherwise indistinguishable from "essential hypertension," might the clinical presentation of asthma reflect various underpinnings?

It perhaps has been underappreciated that risk for development of asthma increases as body mass index increases over 25 kg/m^2, that obese asthmatics may be more treatment resistant, and that obese asthmatics experience higher rates of asthma-related hospitalizations (with worse outcomes).

Mechanistically, obesity-related asthma (ORA) is characterized by less occurrence of atopy and eosinophilia. Perhaps this helps explain the observation that steroid responsiveness is lower in ORA patients. Other pathways of inflammation differ in ORA vs. atopic asthma, such as interleukin levels.

Determining which aberrant inflammation circuitry in ORA deserves intervention to improve ORA outcomes is not yet clear. On the other hand, there are very encouraging prospective randomized trial data confirming improvements in asthma achieved through weight loss in obese patients. Clinicians should be aware that individualization of treatment for ORA may need to include attention to weight reduction to optimize outcomes. ■

Low-dose OTC Proton Pump Inhibitor for GERD Relief

SOURCE: Peura D, Le Moigne A, Pollack C, et al. A 14-day regimen of esomeprazole 20 mg/day for frequent heartburn: Durability of effects, symptomatic rebound, and treatment satisfaction. *Postgrad Med* 2016;128:577-583.

Esomeprazole is available over the counter as Nexium 24 (20 mg) and by prescription as Nexium 40 mg. More than 75% of patients with uncomplicated gastroesophageal reflux disease (GERD) enjoy symptomatic relief with a four- to eight-week course of prescription esomeprazole 40 mg daily, and many of the remainder find improvement with twice-daily dosing.

Might even a lower esomeprazole dose over the short term be effective? To test this hypothesis, Peura et al performed two clinical trials in which they randomized subjects to 20 mg esomeprazole or placebo daily for two weeks. The remarkable thing about the patient population is that subjects were excluded if they received a confirmed diagnosis of GERD or erosive esophagitis or were on a prescription for GERD medications. One might perceive such patients as those with insufficiently burdensome symptoms to seek clinician care for relief. Study subjects reported frequent heartburn at least two days/week for the past month.

Daily low-dose esomeprazole (20 mg) was statistically significantly superior to placebo for symptom relief during 14 days of administration and the week following discontinuation, without evidence of rebound. When patients do not achieve satisfactory symptomatic relief from GERD with low-dose treatment, appropriate courses of action include increasing the dose, switching to another proton pump inhibitor, adding an H_2 antagonists, or adding an alginate. ■

Home BP Monitoring Associated with Better BP Control

SOURCE: Erden S, Mefkure Ozkaya H, Banu Denizeri S, Karabacak E. The effects of home blood pressure monitoring on blood pressure control and treatment planning. *Postgrad Med* 2016;128:584-590.

Intuitively, incorporation of home blood pressure monitoring (HBPM) into the regimen of BP control interventions should improve outcomes. Encouraging patients to take ownership of their BP management, elimination of white-coat hypertension, and the ability to detect overtreatment by identification of episodes of hypotension at home could improve outcomes of hypertensive patients. But does HBPM improve outcomes?

Erden et al retrospectively evaluated charts of 1,006 hypertensive Turkish adults, of which 40% participated in HBPM. They compared several outcomes: office BP, percent achieving BP control (defined as < 135/85 mmHg), and vascular health (cardiovascular [CV] events and retinopathy).

The HBPM group was statistically significantly more likely to achieve BP control

(85% vs. 56%). More difficult to explain is the polarity of vascular results: CV events actually were statistically significantly *more* common in the HBPM group, whereas retinopathy was *less* common. While the HBPM group, on average, had been treated for hypertension for a substantially longer duration (nine years vs. seven years), this would not reconcile why one vascular compartment (retina) showed favorable effect, whereas CV events did not, especially since a ponderous amount of clinical trial data shows a consistent relationship between office BP lowering and CV outcomes. ■

Linking Psoriasis to Vascular Health

SOURCE: Chiu HY, Lo PC, Huang WF, et al. Increased risk of aortic aneurysm (AA) in relation to the severity of psoriasis: A national population-based matched-cohort study. *J Am Acad Dermatol* 2016;75:747-754.

Approximately 15,000 people per year die in the United States from ruptured abdominal aortic aneurysms (AAA). The commonly recognized risk factors for AAA include hypertension, smoking, male sex, and age. While the link between inflammatory disorders, such as rheumatoid arthritis and psoriasis, and coronary vascular disease has received increasing attention in the last decade, little cognizance exists of a relationship between psoriasis and AAA.

To define this relationship further, Chiu et al reviewed the medical records of 34,301 patients with psoriasis in a Taiwanese database. When age and sex matched with controls (n = 137,204), a surprisingly strong association between psoriasis and risk for AAA emerged.

Patients with psoriasis were almost twice as likely (hazard ratio = 1.8) to be diagnosed with AAA as controls. Further substantiating the relationship, psoriasis severity was associated linearly with increasing risk for AAA. The strong association was independent of the already recognized risk factors for vasculopathy such as hypertension, smoking, and dyslipidemia. The authors suggested consideration of screening for AAA in psoriasis patients because of increased risk. Current U.S. Preventive Services Task Force guidelines suggest a one-time ultrasound screening for men between 65-75 years of age who are ever smokers (≥ 100 lifetime cigarettes). ■

Secondary Prevention of Stroke by Pioglitazone in Prediabetes

SOURCE: Inzucchi SE, Viscoli CM, Young LH, et al. Pioglitazone prevents diabetes in patients with insulin resistance and cerebrovascular disease. *Diabetes Care* 2016;39:1684-1692.

The Insulin Resistance After Stroke (IRIS) trial randomized patients with recent ischemia stroke or transient ischemic attack to pioglitazone (PIO) or placebo for approximately five years. The rationale for selecting PIO was that these patients were all prediabetic, as defined by the homeostatic model assessment-insulin resistance score, further supported by their mean A1c (5.8). To be clear: diabetics were *excluded* from the trial; only prediabetics were included.

The primary endpoint of the IRIS trial indicated a significant 24% reduction in new stroke with PIO. This follow-up report detailed the ability of PIO to prevent development of diabetes in this population of prediabetics.

Over a five-year interval, 7.7% of placebo recipients progressed from prediabetes to diabetes, compared with 3.8% of the PIO group (hazard ratio = 0.48). Predictably, those prediabetics with the greatest degree of fasting blood glucose perturbation and highest baseline A1c showed the greatest degree of benefit.

PIO reduces vascular events in insulin-resistant stroke victims, as well as reduces risk of progression from prediabetes to diabetes by > 50%. ■

10-year Outcomes for Localized Prostate Cancer

SOURCE: Hamdy FC, Donovan JL, Lane JA, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016;375:1415-1424.

For the past three decades, the majority of prostate cancer (PRCA) detection has resulted from prostate-specific antigen (PSA) screening. As compared to pre-PSA modes of detection, the population of PSA screening-detected PRCA is prominently comprised of earlier, prostate-localized disease. Is there a clear advantage to one path of long-term intervention than another in long-term management of localized PRCA?

From a population of 84,429 PSA-screened men in the United Kingdom, 2,664 were diagnosed with localized PRCA and randomized to active surveillance vs. radical prostatectomy vs. external beam radiation. Although prostatectomy and external beam radiation probably are self-explanatory, the method of "active surveillance" differs from the "watching waiting" in two other prostate cancer trials. That is, active surveillance entailed PSA measurement every three months for a year, and then every six to 12 months going forward. Any 12-month PSA increase of 50% or greater prompted a case review and reconsideration of intervention; ultimately, 56 men in the active surveillance group ended up receiving an intervention secondary to increases in PSA.

At 10 years of follow-up, there was no statistically significant difference in either PRCA-specific death or all-cause mortality between the three groups. Although these results are heartening in that the three methods demonstrated similar (and low) levels of mortality, the relatively younger age of these men (mean age = 62 years) and the fact that disease progression over 10 years was more common in the surveillance group indicates that even longer-term follow-up will be needed to fully inform men on how to make optimum choices. ■

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