Clinical Briefs in Primary Care™

The essential monthly primary care update

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Food Allergy in IBS: Patch Testing

Source: Stierstorfer MB, et al. Food patch testing for irritable bowel syndrome. *J Am Acad Dermatol* 2013;68:377-384.

We have, as yet, no fully satisfactory etiologic explanation for the symptom complex recognized as irritable bowel syndrome (IBS). Yet, demonstration of various derangements — hypersensitivity to neurogenic stimuli, altered bowel flora, dysregulation of serotonin — has been seen in subgroups of persons with typical IBS. Results from IBS trials of non-systemic antibiotics (e.g., rifaximin) demonstrate improvements in IBS symptoms and support bacterial flora imbalance in some, but not all, IBS subjects.

IBS patients commonly report foods that exacerbate symptoms. Could these food sensitivities represent actual food allergy, and contribute etiologically to IBS? A variety of commonplace foods and food additives have been documented to cause allergic *cutaneous* contact dermatitis (type-4 hypersensitivity). Could similar responses lead to inflammatory changes in the gut and symptoms of IBS?

Stierstorfer et al performed patch testing in IBS subjects (n = 51) using up to 40 different foods or food additives that have been previously recognized as implicated in food hypersensitivity. Fifty-eight percent of subjects had one or more patch test results indicating possible food sensitivity, and when the "offending" food was eliminated from the diet, about two-thirds of subjects reported symptomatic improvement. Food allergy may play a more important role in IBS than previously recognized. ■

A Relationship Between Atrial Flutter and Sleep Apnea

Source: Bazan V, et al. Obstructive sleep apnea in patients with typical atrial flutter: Prevalence and impact on arrhythmia control outcome. *Chest* 2013;143:1277-1283.

Commonly recognized consequences of obstructive sleep apnea (OSA) include increased risk for hypertension, cardiovascular events, and arrhythmias, the most common of which is atrial fibrillation (AFib). Less well understood is the relationship between atrial flutter (AF) and OSA. Even though invasive treatment through catheter ablation is highly effective for AF, over the long term, as many as one-third of AF ablation patients develop postoperative AFib, which of course has its own toxicities.

Bazan et al evaluated a preoperative population of AF patients with polysomnography, none of whom had previously been diagnosed with or suspected of OSA. Overall, 82% of subjects were diagnosed with OSA, almost half of whom were graded as severe OSA.

Over the ensuing 12 months, use of continuous positive airway pressure (CPAP) in OSA patients who had received catheter ablation for AF resulted in a dramatic reduction in new postoperative AFib: from 46% (untreated) to 6% (treated).

OSA appears to be more commonplace in AF than previously recognized. Although a much larger randomized clinical trial will be necessary for confirmation, this small study suggests that for AF patients with OSA who are undergoing catheter ablation, CPAP substantially reduces the likelihood of postoperative AFib. ■

Beyond Hypertension: Metabolic Effects of Telmisartan

Source: Takagi H, et al. Telmisartan as a metabolic sartan: The first meta-analysis of randomized controlled trials in metabolic syndrome. *J Am Soc Hypertens* 2013;7:229-235.

It has not gone unnoticed that angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (ARBs) can sometimes have a favorable effect on glucose metabolism in diabetics and prediabetics. Experts have opined that it is perhaps vascular dilation in the skeletal muscle compartment from renin-angiotensin-aldosterone system blockade that produces increased glucose utilization. One of the ARBs, telmisartan, in addition to its blood pressure-lowering effect, has been noted to have peroxisome proliferator-activated receptor (PPAR)-gamma activation activity, distinct from the other members of this drug class. PPAR-gamma activation could favorably impact metabolic syndrome, but individual clinical trials of telmisartan have been inconclusive in this regard.

Takagi et al performed a meta-analysis of clinical trials (n = 10) of telmisartan in patients (n = 546) with metabolic syndrome. Favorable effects were seen for

fasting glucose, insulin, and A1c. Of the 10 trials analyzed, only three included data on adiponectin, but results were also favorable for this metric.

Large clinical trials of telmisartan in patients with established vascular disease (e.g., TRANSCEND, n = 5926) have shown a nonsignificant trend toward less new onset diabetes, but the number of metabolic syndrome subjects in this trial was not specified.

Whether favorable changes seen in metabolic syndrome patients treated with telmisartan are sufficient to improve "hard" outcomes (myocardial infarction, cerebral vascular accident, diabetes mellitus) would require a very large clinical trial. ■

Risk of New Onset Diabetes with Statins

Source: Danaei G, et al. Statins and risk of diabetes: An analysis of electronic medical records to evaluate possible bias due to differential survival. *Diabetes Care* 2013;36:1236-1240.

The oft-quoted "9% increase in new onset diabetes (NODM) due to statins" sounds pretty scary. What is left out of the aforementioned quote, however, is that the increased risk is a *relative*, not *absolute*, increase. To make the issue more concrete: In one of the largest meta-analyses (n = 91,000), we learned that statins increase risk for diabetes. Among 45,521 statin-treated patients, there were 2226 NODM cases (compared to 2052 of 45,619 placebo recipients); the incidence of NODM then was 4.89% in the statin group, compared to 4.5% in the placebo group, for an underwhelming risk increase of 0.39%. This would translate into a number needed to treat of 250 patients receiving a statin to induce one new case of diabetes. Not nearly so scary, huh?

The most recent analysis of NODM compiled data from the electronic medical records of 500 United Kingdom general practices (n = 285,864). Similar to the above mentioned meta-analysis, the absolute annual incidence in the United Kingdom dataset was 1.59% in statin users compared to 1.13% in nonusers.

Statins can cause NODM, but in trials of secondary prevention, risk of NODM is far outweighed by risk reduction for cardiovascular events. ■

Perimenstrual Asthma: A High-Risk Phenotype

Source: Rao CK, et al. Characteristics of perimenstrual asthma and its relation to asthma severity and control: Data from the severe asthma research program. *Chest* 2013;143:984-992.

Some women with asthma note a worsening of asthma related to onset of menses. In the National Heart, Lung, and Blood Institute Severe Asthma Research Program (SARP), 17% of women (92/483) reported that menses were a trigger for their asthma symptoms. Exploration of perimenstrual asthma (PMA) as a distinct phenotype has been prompted by the recognition of an association between PMA and asthma acuity. Indeed, near-fatal and fatal asthmatic events have been linked to PMA.

Evaluation of women identified with PMA from SARP found that nearly twice as many PMA subjects met criteria for classification as severe asthma than women without PMA. In addition, levels of asthma control were worse in PMA subjects, and they experienced greater urgent health care utilization. Aspirin sensitivity was found three times more often in PMA patients (30% vs 10%), as were nasal polyps (16% vs 5%).

At the current time, PMA is not a widely appreciated entity. In the United States, there are still approximately 5000 asthma deaths per year. Any phenotypic prototype that can help to identify an asthma population at greater risk of fatal or near-fatal asthma might be a step toward reducing the mortality burden of asthma. ■

What's the Durability of Lifestyle Change in Type 2 Diabetes?

Source: Jakicic JM, et al. Four-year change in cardiorespiratory fitness and influence on glycemic control in adults with type 2 diabetes in a randomized trial: The Look AHEAD trial. *Diabetes Care* 2013; 36:1297-1303.

Embarking on lifestyle change is widely reinforced early on by numerous incidental happenstances. First, response to diet is most prominent in the early weeks of dieting. Second, relative gains in fitness and strength are most obvious in the early weeks of dieting. Third, most support programs providing advisors for diet, exercise, and psychological aspects are "front-loaded" (greater frequency/intensity at first) to try and establish optimum patterns early on. Fourth, as one gains positive initial steps, observers and friends tend to be avid supportive "cheerleaders," a response that diminishes as the going gets tougher, occasional ground is lost, or ground gained is less visible.

Jakicic et al report on the outcome at 4 years in the Look AHEAD Research Group trial. Overweight or obese type 2 diabetics (n = 3942) were randomized to intensive lifestyle intervention (ILI) or standard care. ILI included weekly instructional/support sessions × 24, continuing with lesser (but still frequent) support on diet and exercise throughout 4 years time. Goal exercise time was 175 minutes a week of brisk walking or the equivalent. As perhaps is intuitive, the intervention group achieved and maintained better fitness levels, better A1c, and better weight control. Structured ILI programs can provide sustained benefits in overweight and obese type 2 diabetics. ■

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