Clinical Briefs in Primary Care™

Evidence-based updates in primary care medicine

By Louis Kuritzky, MD

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CV Hope for the Exercise-Disinclined

Source: Kearney TM, et al. *J Am Soc Hypertens* 2014;8:117-126.

The favorable relationship between exercise and cardiovascular health has been announced, and reannounced, and reannounced for decades. Nonetheless, only a minority of Americans participate in regular vigorous exercise, and the numbers of adult Americans who are categorized as overweight or obese continues to climb. Does one have to be an athlete to claim the rewards of physical activity? Maybe not.

Kearney et al performed a study among overweight adult men and women who acknowledged being essentially sedentary. Subjects randomized to exercise were compared to subjects performing stretching activities, with the outcome of interest being the effects on vascular health as measured by arterial stiffness (reflected in pulse wave velocity) and production of nitric oxide.

It is the novelty of the applied exercise program that might strike clinicians as having potential for widespread use: The exercise subjects were asked to engage in three 10-minute sessions of brisk walking on 5 days of each week. Brisk walking was described as sufficient to produce slight shortness of breath but not impede the ability to hold a conversation. Outcomes were measured at the end of the 6-month intervention, and 4 months after the intervention ended.

At study end, as well as 4 months post-intervention, there was a statistically significant difference in pulse-wave velocity and nitric oxide production in the exercise group compared to the stretching group. Even for those with too-busy schedules, lack of athletic prowess, and distaste for overly strenuous activity, a menu of brief episodes of brisk walking for only 5 days per week might be an attractive option. ■

The Elbow Sign for OSA

Source: Fenton ME, et al. *Chest* 2014;145:518-524.

Obstructive sleep apnea (OSA) is garnering ever-growing respect from clinicians who recognize it is responsible for diverse toxicities beyond simple sleep disruption: hypertension, cardiac arrhythmia, auto accidents, and excessive daytime sleepiness among them. Clinicians tend to uncover OSA when persons of "typical" phenotype (overweight mid-life men and women) present with associated symptoms. Sometimes, the consequence of OSA triggers an evaluation, even in the absence of overt OSA symptoms, such as the recent observation that among persons with resistant hypertension and no history or overt stigmata of OSA, sleep studies were positive for OSA in more than 80%!

Not everyone can afford a sleep study, so clinicians would like to identify simple methods to refine the pretest probability of OSA. The elbow sign may be just such an intervention.

Fenton et al provide data on asking patients referred for a sleep study two questions: 1) Does your bed partner ever poke or elbow you because you are snoring? or 2) Does your bed partner ever poke or elbow you because you have stopped breathing?

Persons who answered affirmatively to either question were 4-6 times more likely to emerge with sleep studies that were positive for OSA. Correction for other OSA-related items (body mass index, Epworth Sleepiness Scale, etc.) did not alter this relationship.

These two simple questions may help identify patients most likely to benefit from a sleep study investigation. ■

Another New and Under-recognized Psoriasis Comorbidity

Source: van der Voort EA, et al. *J Am Acad Dermatol* 2014;70:517-524.

Upon encountering the word psoriasis, clinicians typically first think "skin," and might next reflect on "joints," and perhaps even "nails," but rarely does the internal intellectual discussion go any further. It is only in the last decade that an immunologically related disorder — rheumatoid arthritis — has been recognized to be associated with marked increase for cardiovascular (CV) disease. More recently, an association between psoriasis and CV disease has also been confirmed, and although the mechanism by which either of these inflammatory disorders induces vasculopathy is unclear, their common immunologic underpinnings suggest shared pathology.

According to a report by van der Voort et al, we should consider adding nonalcoholic fatty liver disease (NAFLD) to the list of comorbidities related to psoriasis. Reflecting on earlier case-control studies that indicated an increased prevalence

of NAFLD among psoriasis patients, the authors studied a large population of persons enrolled in the Rotterdam Study (n = 2292) who underwent hepatic ultrasound. The prevalence of NAFLD was more than 30% greater in psoriasis subjects than controls (46.2% vs 33%).

The mechanism by which NAFLD is induced by psoriasis is unclear, although specific culprit genes are suspected. Because most of these patients did not have severe psoriasis, clinicians should be vigilant for the potential development of NAFLD, even in psoriatic patients with mild-moderate disease. ■

Is There a Difference Between Dutasteride and Finasteride for Male Pattern Baldness?

Source: Harcha WG, et al. *J Am Acad Dermatol* 2014;70:489-498.

In the United States, the two approved pharmacologic agents for treatment of male pattern hair loss are topical minoxidil (Rogaine) and systemic finasteride 1 mg/d (Propecia). The mechanism by which finasteride enhances hair growth is related to its activity as a 5-alpha-reductase inhibitor (5-ARI), which prevents the conversion of testosterone in the skin to its active derivative dihydrotestosterone (DHT). Since DHT is believed to be the primary culprit inducing male pattern hair loss, diminution of its activity results in reduced hair loss and allows better unrestrained hair regrowth.

The 5-ARI activity of finasteride is designated as type 2. Because there are multiple 5-ARI isoenzymes (types 1, 2, and 3), the potential role of dutasteride — which is active at both type 1 and type 2 tissue sites — is of interest. Indeed, dutasteride is already approved in Korea for treatment of male pattern baldness.

A placebo-controlled, randomized, head-to-head (no pun intended, honest) trial compared hair growth in men with male pattern baldness treated with finasteride 1 mg/d vs dutasteride 0.02-0.5 mg/d for 6 months (n = 917).

At the end of the trial, although both active agents were superior to placebo, there was a significant difference favoring dutasteride for both absolute hair count as well as hair width compared to finasteride. Dutasteride may become a viable alternative to finasteride for male pattern hair loss. ■

Best Management of Superficial Thrombophlebitis in the Lower Extremities

Source: Di Nisio M, et al. *JAMA* 2014; 311:729-730.

The consequences of superficial thrombophlebitis (STBP) of the lower extremities are not as well recognized as those of deep venous thrombosis (DVT). Similarly, there is some uncertainty among clinicians about best management. Choosing treatment wisely is important because untreated STBP can extend to DVT; indeed, even treated STBP can progress or recur in as many as 10% of patients.

Although other consequences are important (extension of STBP, recurrence), the most concerning sequel of STBP is DVT. Although trials of fondaparinux found a significant reduction in risk for DVT when administered for 45 days (an 85% risk reduction), data from studies with low-molecular-weight heparin (LMWH) and nonsteroidal anti-inflammatory drugs (NSAIDs) did not confirm venous thromboembolism risk reduction.

LMWH and NSAIDs provided lower rates of STBP recurrence than placebo, but based on equivocal results for VTE reduction, fondaparinux should be the preferred treatment. ■

Is There a Role for Pregabalin in Restless Legs Syndrome?

Source: Allen RP, et al. *N Engl J Med* 2014;370:621-631.

The impact of restless legs syndrome (RLS) can range from nuisance symptomatology requiring modest interruption of sleep to major decrements in quality of life for the patient and/or bed partner. Although dopaminergic medications have become the mainstay of therapy, they are sometimes associated with "augmentation;" a worsening of symptom intensity, symptom frequency, or increase in areas of the body involved with symptoms, over long-term treatment. Since there is no known cure for RLS, many patients require lifelong treatment, necessitating alternatives in the event that RLS augmentation occurs. To complicate the picture further, not everyone agrees that augmentation is a pharmacologically related issue; instead, the worsening of symptoms over time may simply reflect disease progression in susceptible individuals.

Allen et al performed a randomized, double-blind trial to compare the initial success rate for RLS symptoms (over 12 weeks) as well as frequency of augmentation over an additional 40 weeks of treatment with either pregabalin (300 mg/d), pramipexole (0.25 or 0.5 mg/d), or placebo (n = 719).

Both active treatments were effective in reducing RLS symptoms, although only higher dose pramipexole (0.5 mg) and pregabalin were statistically significantly superior to placebo. For the endpoint of augmentation, pregabalin was superior to both placebo and pramipexole 0.5 mg.

The underlying assumptions prompting treatment choices for RLS presume dopaminergic deficits. Since pregabalin has no known dopaminergic activity, and was found to be as effective as the dopaminergic treatment (pramipexole), the current understanding of the pathophysiologic basis for RLS has been challenged. ■

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Executive Editor: Leslie Coplin.
Editor: Stephen Brunton, MD.
Managing Editor: Neill L. Kimball.

Subscriber Information
Customer Service: 1-800-688-2421
E-Mail Address: neill.kimball@ahcmedia.com
World Wide Web: www.ahcmedia.com
Address Correspondence to: AHC Media, One Atlanta Plaza, 950 East Paces Ferry Road NE, Suite 2850, Atlanta, GA 30326.

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