Clinical Briefs in Primary Care™

The essential monthly primary care update

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Lumbar Disk Herniation: Is Surgical Treatment Superior to Conservative Management?

Source: Weinstein JN, et al. *JAMA.* 2006;296:2441-2450.

The SPORT (Spine Patient Outcomes Research Trial) trial enrolled over 1,000 adults with lumbar disk disease-herniated disk, spinal stenosis, or spondylolisthesis-to compare outcomes between persons who were assigned to surgical treatment vs medical therapy. All study subjects underwent imaging to confirm pathology consonant with symptoms (97% had MRI).

The surgical intervention performed was open diskectomy; medical therapy included exercise, education, and use of NSAIDs. The primary outcome measures were bodily pain and physical function (as measured on the SF-36) and degree of disability (as measured by the American Academy of Orthopedic Surgeons Oswestry Disability Index). End points were assessed at baseline, 3 months, 1 year, and 2 years.

For primary end points (by intention-to-treat analysis) there was no statistically significant difference between groups at any point during the study period. Although this would seem to confirm that surgery does not have advantage over conservative treatment, it must be recognized that the intention-to-treat analysis used in this trial does not necessarily function well because a large number of persons (40-45% in either group) originally assigned to one intervention ultimately crossed over to receive the other; ie, many patients randomized to surgery did not ultimately receive it, and vice versa. If one just looks at the data from the perspective of dividing the population into the treatment they actually received, outcomes favored surgery, but this does not reflect the original randomization process, and is hence subject to confounding. ■

Rimonabant: An Answer to Overweight in Diabetes?

Source: Scheen AJ, et al. *Lancet.* 2006;368:1660-1672.

Overweight is a cause, concomitant, and consequence of diabetes. Clearly, overweight status increases the likelihood of developing diabetes, and is present at the time of diagnosis in most type 2 diabetics. Similarly, pharmacotherapy is often associated with weight gain, and diabetic consequences such as painful neuropathy may result in reduced activity levels, further exacerbating weight control dilemmas. Some weight loss agents such as orlistat (xenical) have shown favorable effects in diabetic subjects, but may be limited by tolerability.

Rimonabant (RBT) has been shown to produce statistically significant weight loss in non-diabetic overweight and obese subjects. Additionally, the weight loss has been noted to impact the critical abdominal visceral fat compartment. Scheen, et al, investigated the impact of RBT in overweight diabetic subjects.

Overweight/obese subjects with type 2 diabetes (n = 1,047) were randomized to receive RBT or placebo. All subjects were counseled in regard to diet and exercise, and followed for 1 year.

RBT at 5 mg/d or 20 mg/d was superior to placebo for weight loss at 1 year (2.3 kg or 5.3 kg vs 1.4 kg, respectively). RBT has shown a statistically significantly greater weight loss than diet and exercise alone in type 2 diabetics. ■

Renin Inhibitors: A new Class of Antihypertensive Agents

Source: Vaidyanathan S, et al. *Int J Clin Pract.* 2006;60(11):1343-1356.

Despite a diverse array of antihypertensive agents, less than half of Americans with hypertension (HTN) are aware of their condition, on treatment, and controlled to a BP of less than 140/90. New treatments, hence, are welcomed.

Aliskiren (ALISK) is the first potential member of a new class of oral agents: renin inhibitors. Although drugs like ACE inhibitors and ARBs impact the renin-angiotensin-aldosterone system, they typically induce a compensatory increase in renin. Combination of ACE/ARB and ALISK, on theoretical grounds, is sensible and appealing. Vaidyanathan, et al report on four open-label studies (n = 87) evaluating the efficacy, safety, and tolerability of ALISK in combination with a representative agent from each of the 4 most commonly used antihypertensive classes: calcium channel blocker (amlodipine), ARB (Valsartan), diuretic

(HCTZ), and ACE inhibitor (ramipril). It was anticipated that ALISK was unlikely to have significant drug interactions, since it is hepatically eliminated unchanged (ie, no p450 interactions), does not inhibit p450 enzymes, and is not highly protein bound.

ALISK therapy was not associated with any clinically relevant tolerability or safety issues. Mild headache, dizziness, and GI symptoms were reported, but differed minimally from adverse effect profiles seen with the other classes of agents when used as monotherapy. ALISK is currently pending FDA approval. ■

Is There a Link between Coffee and Diabetes?

Source: Smith B, et al. *Diabetes Care.* 2006;29:2385-2390.

The relationship between coffee and diabetes is complex. For instance, even though cohort studies suggest less risk of diabetes in coffee drinkers, similar results have been seen in data evaluating decaffeinated coffee consumption, suggesting that some other component than caffeine might be responsible. Another limiting factor of previous studies is the inclusion of subjects based upon definition of diabetes by self report, rather than as confirmed by oral glucose tolerance testing (OGTT).

Smith, et al followed middle-aged adults (n = 910) for 8 years, comparing coffee drinkers with non-coffee drinkers. The population was also compartmentalized into persons with and without prediabetes as baseline. New development of diabetes was confirmed with OGTT.

The odds ratio for development of new-onset diabetes was 0.36 for coffee drinkers compared to non-drinkers. Similar risk reduction was seen in the population who were prediabetic at baseline. There was no relationship between the amount of coffee imbibed daily with outcomes. Coffee drinkers have about a 60% reduced risk of developing diabetes than non-drinkers. Persons with prediabetes enjoy similar reductions in risk as persons with normal glucose metabolism. ■

Is it Time to Start Screening for Lung Cancer?

Source: The International Early Lung Cancer Action Program Investigators. *N Engl J Med.* 2006;355:1763-1771.

Trials of screening for lung cancer have not provided robust support, and major consensus groups do not endorse lung cancer screening. Because the burden of lung cancer is epidemiologically compelling, and the volume of at risk-individuals is equally prominent, investigators have sought to determine whether progressively more sensitive tools (ie, capable of detecting lung CA at smaller size) might provide advantage.

The Early Lung Cancer Action Program enrolled at-risk asymptomatic men and women over the age of 40 (n = 31,567). Participants were considered at increased risk for lung cancer due to cigarette smoking, occupational exposure (eg, asbestos), or second-hand smoke exposure. After a baseline low-dose spiral CT (and appropriate followup if suspicious lesions were discerned) 21,456 participants underwent annual low-dose spiral CT for up to 12 years.

Most of the cancers were detected at the initial baseline screen (over 80%). Utilizing combined strategies of a baseline screen and annual followup, most of the cancers were identified at Stage 1, where the 10 year survival rate was 88%. The authors suggest that the detection rate of lung cancer in this trial compares favorably with rates of breast cancer detected by mammography. ■

Can Ramipril Prevent Progression from Pre-Diabetes to Diabetes?

Source: The DREAM Trial Investigators. N Engl J Med. 2006;355:1551-1562.

Some cardiovascular trials, like the HOPE trial, have shown that ACE inhibitors such as ramipril (RAM) can reduce the incidence of new onset diabetes (DM). Whether similar effects might be seen in specifically in a population known to be at high risk for development of diabetes—persons with known prediabetes—has received little study. Prediabetes is defined as either a fasting glucose 110-125 mg/dL or glucose 2 hours post glucose-load of 140-199.

The DREAM (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication) trial enrolled prediabetic adults (n = 5,269) and randomized them to ramipril (15 mg/d target dose) or placebo for 3 years. In contrast to the HOPE trial, subjects had to be free of CV disease and diabetes at entry. This same trial also examined the impact of rosiglitazone, reported in a separate publication.

After 3 years, there was no difference between ramipril and placebo in the incidence of diabetes among persons with prediabetes. ■

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