Clinical Briefs in Primary Care™

The essential monthly primary care update

By Louis Kuritzky, MD

Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports.*

VOLUME 15, NUMBER 10 PAGES 19-20 OCTOBER 2010

Male pattern baldness treated with oral dutasteride

Source: Eun HC, et al. Efficacy, safety, and tolerability of dutasteride 0.5 mg once daily in male patients with male pattern hair loss. *J Am Acad Dermatol* 2010;63:252-258.

More than three-fourths of men have some degree of male pattern hair loss by age 70. The unwanted hair loss seen in male pattern balding is stimulated by dihydrotestosterone. Clinical trials of low-dose oral finasteride (Propecia® 1 mg/d) have shown that blockade of 5-alpha-reductase (5AR), the enzyme responsible for converting testosterone to dihydrotestosterone, is effective for producing new hair growth.

There are two different 5AR enzymes: Type 1 5AR functions primarily in skin, and type 2 5AR is expressed predominantly in hair follicles and the prostate. Finasteride only blocks type 2 5AR, whereas dutasteride blocks both type 1 and type 2 5AR. The potential utility of dutasteride as a treatment for male pattern hair loss is bolstered by data from large, long-term clinical BPH and prostate cancer trials, which demonstrate excellent tolerability.

Eun et al performed a randomized, double-blind, placebo-controlled, 6-month trial in adult men (n = 153) of dutasteride 0.5 mg/d for male pattern hair loss. At the end of the trial, hair counts were statistically significantly improved in the active treatment group, with more than 70% of men self-assessing hair growth to be improved. The safety profile of dutasteride was excellent, with no serious drug-related adverse events.

Theoretically, dutasteride might provide better hair growth results than finasteride because the dual blockade mechanism of the former produces lower DHT plasma levels. Since both agents block type 2 5AR, which is thought to be the primary culprit in male pattern hair loss, and there are no comparison trials between finasteride and dutasteride, it remains uncertain which treatment is superior. ■

Home-based diagnosis of sleep apnea

Source: Skomro RP, et al. Outcomes of home-based diagnosis and treatment of obstructive sleep apnea. *Chest* 2010;138:257-263.

Clinicians are increasingly aware of the adverse outcomes associated with obstructive sleep apnea (OSA), including hypertension, cardiac arrhythmia, stroke, MI, and overall CV mortality. Overnight polysomnography (OPSG) in a sleep laboratory has been recognized as the gold standard for diagnosis, but because this process is expensive, time-consuming, and not readily available in all settings, other methodologies, if sufficiently accurate, would be welcome.

Skomro et al compared home-based OSA diagnosis and treatment with OPSG in 102 Canadians referred for evaluation of potential OSA due to associated symptoms (e.g., daytime sleepiness) and/or signs (e.g., snoring). Outcomes included the Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index, SF-36, and adherence to CPAP after 1 month.

Home diagnosis was performed with Embletta™, a portable battery-operated device that records position, activity, leg movement, oxygen saturation, pulse, oral flow, and respiratory events. Confirmation of OSA was followed by auto-CPAP for 1 week, followed by further fixed CPAP derived from auto-CPAP measurements.

After 1 month, outcomes in the subjects diagnosed and treated with home methodology were essentially the same as those diagnosed by means of OPSG. Technical factors led to the need to repeat Embletta in a small subset (16.6%). These data support a role of home methodologies for diagnosis and management of OSA. ■

What is the risk of bariatric surgery?

Source: Birkmeyer NJ, et al. Hospital complication rates with bariatric surgery in Michigan. *JAMA* 2010;304:435-442.

Bariatric surgery has become the second most common abdominal surgical procedure in the United States. Both the likelihood of a favorable outcome and the frequency of adverse surgically related events may be linked to the frequency with which a particular surgery is performed. To that end, the American College of Surgeons and the American Society for Metabolic and Bariatric Surgery have established criteria for accreditation as a Center of Excellence in bariatric surgery.

Birkmeyer et al report upon surgical outcomes in 25 hospitals throughout the state of Michigan, including more than 15,275 bariatric surgeries reported from 2006 to 2009. Two of the 25 hospitals had Center of Excellence status.

Mortality (within 30 days of surgery) was very low (< 0.2%), and serious adverse events were similarly infrequent (1.6%-3.5%). Adverse outcomes were inversely

related to hospital case volume, but did not differ significantly between Centers of Excellence and hospitals without such designation. Hospitals with at least 300 cases/year and individual surgeons with experience of least 100 procedures/year had the fewest adverse outcomes.

Bariatric surgery is a generally safe and effective tool. Although adverse outcomes are infrequent, they are related to the volume with which the procedure is performed. ■

Comparing insulin and incretins

Source: Horton ES, et al. Weight loss, glycemic control, and changes in cardiovascular biomarkers in patients with type 2 diabetes receiving incretin therapies or insulin in a large cohort database. *Diabetes Care* 2010;33:1759-1765.

The General Electric Centricity research database contains EMR information on more than half a million adults with DM2. Of course, therapeutic choices for DM2 vary widely among this large population. Because the incretin class of medications (DPP4 inhibitors and GLP-1 agonists) has been associated with weight loss (or at least weight neutrality), the resultant changes in CV risk factors usually seen with weight reduction could ultimately influence CV outcomes. Horton et al studied CV biomarkers (BP, lipids) and markers of glycemic control in subjects that had received incretins and compared these same markers in subjects treated with insulin. All subjects (total n = 44,539) had to be treated for at least 1 year.

Exenatide, the only GLP-1 agonist available at the time this study was reported, was associated with a 3 kg weight loss, compared to a 1.1 kg weight loss for the sitagliptin group and a 0.6 kg weight gain for the insulin group. SBP improved in all 3 groups, but only very slightly (1-2 mmHg). LDL improved modestly in all three groups (5%-6% reduction). The absolute reduction in A1c was greater with insulin (1.0% A1c reduction) than incretins (0.5% A1c reduction); however, the baseline A1c was higher in the insulin group (8.8%) vs the incretin group (7.7%).

Similar improvements in SBP, LDL, and A1c were seen in this database. Whether the more advantageous impact on weight seen with incretins will ultimately impact CV outcomes remains to be determined. ■

Which is better: COX2 or NSAID plus PPI?

Source: Chan FK, et al. Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR). *Lancet* 2010;376:173-179.

The GI toxicity of NSAIDs is well recognized, with a 1998 report suggesting that as many as 16,500 deaths that year were attributable to NSAID-induced GI bleeding. One of the reputed benefits of the development of cyclo-oxygenase selective NSAIDs was the belief that their relative lack of effect on COX1 would obviate much of the GI toxicity seen. Some patients will continue to use maintenance therapy with anti-inflammatory agents for protracted periods; hence, determination of which GI protection technique is most beneficial is a critical issue. To that end, Chan et al studied *Helicobacter*-negative patients with osteoarthritis and/or rheumatoid arthritis (n = 4484) to compare GI adverse events (the primary outcome) seen with celecoxib vs a traditional NSAID (diclofenac) plus PPI (omeprazole). Utilization of aspirin was a study exclusion.

At 180 days, the celecoxib group showed a statistically significantly lesser GI event rate than the diclofenac plus omeprazole group (0.9 % vs 3.8%). Tolerability, as measured by treatment discontinuation, of celecoxib (200 mg bid) was superior to diclofenac 75 mg bid plus omeprazole 20 mg qd (6% vs 8%).

For patients requiring maintenance anti-inflammatory treatment, GI consequences of celecoxib are fewer than if a traditional NSAID is combined with a proton pump inhibitor, although cost considerations may preclude universal application of this preferred treatment. ■

Combination therapy to prevent DM2

Source: Zinman B, et al. Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial). *Lancet* 2010;376:103-111.

Clinicians are increasingly presented with the tasks of addressing not only a burgeoning population of type 2 diabetics, but an equally voluminous group of prediabetics. It has been clearly established that numerous interventions can prevent the development of DM2 in prediabetes, including metformin, diet, exercise, thiazolidinediones, alpha-glucosidase inhibitors, and pharmacologically induced weight loss. Typically, 7%-10% of prediabetes will progress to overt DM2 per year if untreated. Pharmacotherapy, diet, and exercise have each been shown to reduce the incidence of DM2 by more than 50% among prediabetics, but each of the pharmacotherapy trials has been based on monotherapy.

Zinman et al report on the CANOE trial (Canadian Normoglycemia Outcomes Evaluation), which randomized 207 prediabetics to either low-dose metformin (500 mg bid) plus low-dose rosiglitazone (2 mg qd) or placebo. Subjects were followed for 3.9 years.

Relative risk reduction for development of DM2 was impressive: 66%. As has been seen in earlier diabetes prevention trials, in the placebo group almost 40% of prediabetics had developed DM2 over the 4-year interval of study. Tolerability of the low-dose regimen was excellent, with only 4 patients discontinuing medication for adverse effects possibly linked to medication. Low-dose combination treatment offers another reasonable choice to offer patients with prediabetes. ■

Clinical Briefs in Primary Care™ is published monthly by AHC Media LLC.

Associate Publisher: Coles McKagen. **Editor:** Stephen Brunton, MD. **Senior Managing Editor:** Paula Cousins. This is an educational publication designed to present scientific information and opinion to health professionals, stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for the layman.

Subscriber Information
Customer Service: 1-800-688-2421
E-Mail Address: paula.cousins@ahcmedia.com
World Wide Web: www.ahcmedia.com
Address Correspondence to: AHC Media LLC 3525 Piedmont Road, Building Six, Suite 400 Atlanta, GA 30305.

AHC Media LLC