

Clinical Briefs in Primary Care™

The essential monthly primary care update

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Weight Loss in Type 2 Diabetes

Source: Redmon JB, et al. *Diabetes Care.* 2003;26:2505-2511.

MOST SUBJECTS WITH TYPE 2 DIABETES (DM2) are overweight. There is abundant support for the diverse benefits of weight loss in DM2, including improved insulin resistance, lipid profiles, and blood pressure, to name but a few. Unfortunately, weight loss is a very daunting challenge for most DM2 patients, often complicated by the fact that some hypoglycemic pharmacotherapies tend to induce weight gain.

In DM2, besides traditional weight loss programs, little information has been shared regarding novel dietary approaches, such as meal replacement programs (MRP) or repetitive low-calorie diets, especially in combination with pharmacotherapy.

This trial involved overweight or obese DM2 subjects (n = 61), all of whom, after calculation of daily basal energy requirement, received advice on a traditional reduced calorie diet (500-1000 Kcal reduction daily) plus exercise (recommended 30 minutes thrice weekly). Those randomized to the combination therapy received, in addition, sibutramine 10-15 mg/d and replacement meals (consisting of 900-1300 Kcal/d of meal shakes or bars, administered as 220 Kcal 4-6 times daily). Subjects were instructed to use meal replacements as their sole nutrition for 1 week every 2 months, and use the meal replacement products (calories = 340) to substitute for a single meal each day during the non-low-calorie MRP weeks.

At 1 year, weight loss in the combined treatment group was greater than the standard treatment group, including a 6.4% decline from baseline body weight. This intensive

regimen provided greater effect upon weight loss and A1C than some prior trials. Long-term maintenance of weight reduction has remained an elusive goal, and whether study subjects could maintain these favorable changes for a greater duration is unknown. ■

Dalteparin and Chronic Foot Ulcers in Diabetics with PAD

Source: Kalani M, et al. *Diabetes Care.* 2003;26:2575-2580.

THE INCREASING PREVALENCE OF type 2 diabetes (DM2) will be likely accompanied by an increase of late-onset diabetic complications, such as chronic foot ulcers (CFU). One of the limiting factors in healing CFU is the microcirculatory impairment found in DM2.

Consecutive DM2 patients with CFU (n = 87) were randomly assigned in a double-blind fashion to dalteparin 5000 units SQ daily (or a similar volume of saline). Treatment continued until the ulcer healed, or up to 6 months. Traditional ulcer care by appropriate consultants was provided to all patients.

There were 2 patients withdrawn from the study, one because of a bleeding event and one because of superficial skin necrosis at the injection sites (although concomitant insulin administration at the same sites complicates attributing etiology).

The number of patients with completely healed ulcers or markedly reduced ulcer size was much superior in the dalteparin group (29 vs 20 patients). The number of amputations in the dalteparin group was also substantially lower (2 vs 8). Dalteparin may be

considered in addition to traditional therapies for foot ulcers in DM2 patients with peripheral arterial occlusive disease. ■

Pioglitazone and LDL in Nondiabetic Hypertensives

Source: Winkler K, et al. *Diabetes Care.* 2003;26:2588-2594.

THE ROLE OF LDL IN DEVELOPMENT of arteriosclerotic disease is well established. In some patient groups, especially diabetics, the type of LDL appears to be as (or more) important than the absolute amount of LDL. That is, small dense LDL (SDDL), which is disproportionately present in type 2 diabetics (and especially when diabetes control is poor), is associated with a marked increased cardiovascular risk.

Hypertension is sometimes described as a syndrome, rather than a single physical finding, because of its frequent concomitance with dyslipidemia, insulin resistance, and obesity. As among diabetics, SDDL is disproportionately present in hypertension. Although pioglitazone (PIO) is typically considered as a hypoglycemic agent, it has previously been shown to reduce SDDL levels as well. Whether this beneficial effect might also occur with hypertensive, nondiabetic subjects was the object of inquiry in this trial.

Patients with hypertension (n = 60) were randomized to PIO 45 mg/d or placebo for 16 weeks. At the end of that time, patients on PIO enjoyed a decline of 22% in SDDL levels, with no demonstrable effect on total triglycerides, LDL, or HDL. Glitazones appear to act through the peroxisome prolif-

erators-activated receptor-gamma (PPAR-gamma) and may ultimately have a role in correcting or improving dyslipidemia associated with both diabetes and hypertension. ■

Parathyroid Hormone and Alendronate Alone or in Combination in Postmenopausal Osteoporosis

Source: Black DM, et al. *N Engl J Med.* 2003;349:1207-1215.

THE PREVENTION AND TREATMENT OF osteoporosis (OSPS) present formidable public health issues for men and women, especially since the somewhat disconcerting results of the Women's Health Initiative have dampened enthusiasm for hormone replacement therapy in menopausal women. Bisphosphonates like alendronate (ALN) and risedronate have been demonstrated to have a favorable effect on bone mineral density (BMD) and fracture risk, mediated through decreased bone resorption.

Parathyroid hormone (PTH) has been shown to have favorable anabolic effects on BMD, which could theoretically complement benefits accrued through antiresorptive therapy with bisphosphonates.

In this study of postmenopausal women with low BMD (T score = -2.0 or less) patients were randomly assigned to PTH (n = 119), ALN (n = 60) or the PTH + ALN combination (n = 59) for 12 months. PTH was administered as 100 mg SQ QD, ALN 10 mg QD, and all study participants received 500 mg calcium (Tums) and 400 IU of vitamin D.

BMD enhancement in the lumbar spine was similarly attained with PTH, ALN, or PTH + ALN. At the hip, ALN and ALN + PTH improved BMD, but PTH alone did not. Although intellectually appealing, the combination of an anabolic bone agent (ie, PTH) with an antiresorptive agent (ie, ALN) failed to provide meaningful benefit over either agent used alone. Whether these conclusions would apply to other bisphosphonates such as risedronate is uncertain, but these results would not encourage such combination treatment until more edifying results have been obtained. ■

Dimer (DIM) testing or ultrasound imaging (USI). If the DIM was positive, USI was performed, but if negative, DVT was considered ruled-out, and no USI was performed. Patients were followed for 3 months after presentation.

A second group (n = 495) who scored high on likelihood of having DVT were randomized to DIM + USI vs USI alone. Persons with negative USI but positive DIM underwent follow-up USI for DVT confirmation 1 week later.

Results indicated that in patients identified as low likelihood of DVT based upon a clinical model scoring system, a negative DIM essentially excludes the diagnosis. ■

Exercise Testing to Predict Cardiovascular and All-Cause Death in Women

Source: Mora S, et al. *JAMA.* 2003;290:1600-1607.

IN THE MID 1970S ALMOST 3000 ASYMPTOMATIC women underwent Bruce-protocol exercise treadmill tests (ETT) as part of the Lipid Research Clinics Prevalence study. These women had entered the trial due to elevated lipids, but were free of known cardiovascular disease at the time of their ETT. The short-term prognostic value of ETT in women has suffered some criticism, but little data has been available on long-term prognosis based upon ETT.

The mean follow-up was 20.3 years, during which time 14% of subjects died; cardiovascular deaths comprised 34% of all deaths. Women with highest exercise capacity on ETT had lower overall mortality rates as well as cardiovascular deaths. For each MET decrease in exercise capacity at baseline, there was a 20% greater hazard ratio for cardiovascular death over the study observation period. On the other hand, ST segment changes did not predict subsequent cardiovascular death, in contradistinction to findings previously demonstrated in male populations. Data from ETT, specifically METs exercise capacity, is predictive of long-term cardiovascular mortality and might prove useful on a more large-scale population basis for risk stratification. ■

Evaluation of D-Dimer in the Diagnosis of Suspected Deep-Vein Thrombosis

Source: Wells PS, et al. *N Engl J Med.* 2003;349:1227-1235.

ALL STRATEGIES CURRENTLY USED FOR the diagnosis of suspected deep-vein thrombosis (DVT) are imperfect. Since investigative tools are time-consuming, can produce false-positive results leading to unnecessary hospitalizations and treatments, and are responsible for some not-insubstantial costs, refinement of strategies to improve diagnosis without sacrificing accuracy are needed.

In step one of this trial, clinicians used a clinical model for predicting pretest probability of DVT. This model scored DVT probability based upon clinical characteristics such as presence of cancer, recent immobilization, leg swelling, and history of previous DVT.

In one group, patients (n = 601) considered unlikely to have DVT based upon clinical prediction model were randomized to either d-

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