Clinical Briefs in Primary Care™

The essential monthly primary care update

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Does Screening for Type 2 Diabetes Pay Off?

Source: Simmons RK, et al. Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): A cluster-randomised controlled trial. *Lancet* 2012;380:1741-1748.

IT IS EASY TO ENVISION THAT EARLIER DIAGnosis of type 2 diabetes (DM2) might lead to an opportunity for earlier, intensified interventions that might translate into improved outcomes. So far, however, we only *think* that, we don't actually *know* it. Simmons et al followed patients from general practices in England (n = 11,737) who enrolled in pathways of 1) screening for DM2 plus intensive multifactorial interventions, 2) screening for DM2 plus routine care, and 3) a "no screening" population. The mean age of the population was 58 years.

The practices in which multifactorial intervention groups were enrolled received educational and logistical support for attaining glucose, blood pressure, and lipid goals. Recent data in the United States suggest that currently fewer than 15% of type 2 diabetics are achieving simultaneous goal attainment in all three of these.

Over an interval of approximately 10 years' follow-up, there were no significant differences seen between unscreened vs screened subjects in regards to all-cause mortality, cardiovascular mortality, cancer mortality, or diabetes-related death.

Explanations for failure to reduce risk include the following: 1) screening for diabetes became more routine in the non-screened group over time; 2) routine care is improving, such that intensive intervention may not be as dramatically different than routine care, and 3) the duration of follow-up was insufficient. ■

Surgical Treatment of Diabetes

Source: Vetter ML, et al. Comparison of bariatric surgical procedures for diabetes remission: Efficacy and mechanisms. *Diabetes Spectrum* 2012;25:200-210.

THE LINK BETWEEN OBESITY AND TYPE 2 diabetes (DM2) is widely acknowledged. Certainly, weight gain is associated with increased incidence of DM2, and weight loss improves insulin sensitivity, as well as other cardiovascular risk factors. Surgery produces prompt and dramatic reductions in excess body weight, yet it appears that rebalancing of the disturbed metabolic homeostasis seen in DM2 varies among the different bariatric surgical interventions. Additionally, it appears that weight loss alone cannot fully explain the metabolic restorations seen post-surgically. Favorable metabolic changes are especially prompt, intensive, and durable when surgery involves bypassing or elimination of much of the small intestine from the digestive path.

In their review of the DM2 bariatric surgery trials, Vetter et al conclude that the primary driving force for DM2 remission appears to be weight loss. Since diversionary procedures are associated with greater and more durable weight loss, they would be anticipated to produce greater benefits for DM2 and they do. Overall adjustable gastric bypass is reported to result in remission in 57% vs 95% in biliopancreatic diversion surgery. The long-term relapse rate is not insubstantial: One very long follow-up of diversionary surgery (up to 16 years) noted relapse in 43%.

There are distinct hormonal changes that differ between the surgical interventions. For instance, gastric banding does not affect incretin activity, but bypass surgeries are associated with increased secretion of incretins. Evidence continues to accumulate that corroborates the efficacy, safety, and durability of bariatric surgical intervention for DM2. ■

Benefits and Consequences of Aldosterone Antagonists for HF

Source: Hernandez AF, et al. Associations between aldosterone antagonist therapy and risks of mortality and readmission among patients with heart failure and reduced ejection fraction. *JAMA* 2012;308: 2097-2107.

CLINICAL TRIAL DATA HAVE CONCLUSIVELY demonstrated improved mortality and cardiovascular outcomes in chronic heart failure (CHF) patients who receive aldosterone blockade (ALD) with spironolactone or eplerenone in addition to standard of care treatment. Clinical trial populations, however, are different from practice settings in which patients may not enjoy the same risk:benefit balance as the often highly selected subjects who enroll in clinical trials.

To evaluate outcomes among patients

with newly administered ALD *not* enrolled in a clinical trial, Hernandez et al reviewed 2005-2010 Medicare data on older (mean age, 78 years) patients who had received a new ALD prescription on discharge from the hospital for CHF (n = 5887). They looked at all-cause mortality, cardiovascular readmission, heart failure readmission, and hyperkalemia.

Although there was no difference in total mortality, the addition of ALD to the treatment regimen was associated with lower heart failure readmission. On the other hand, patients treated with ALD were statistically significantly more likely to be readmitted with hyperkalemia over the next year (1.5-2.5 times more likely). ALD treatment offers some positive outcomes, but clinicians must be vigilant for hyperkalemia when ALD treatment is chosen. ■

Long-term Prevention of Recurrent DVT

Source: Brighton TA, et al. Low-dose aspirin for preventing recurrent venous thromboembolism. *N Engl J Med* 2012; 367:1979-1987.

Current guidelines for management of venous thrombosis (e.g., the Antithrombotic 9 guideline published by the American College of Chest Physicians in 2012) suggest that after an initial episode of unprovoked deep venous thrombosis (DVT), it is reasonable to provide at least a 3-month course of anticoagulation, with consideration of a longer interval on a case-by-case basis. Usually, anticoagulation is not continued long-term. But the risk of DVT recurrence after cessation of coumadin is not insignificant.

Aspirin (ASA) is easy to administer and has a generally favorable risk profile. After cessation of coumadin, Brighton et al compared DVT patients treated with aspirin vs placebo for approximately 3 years. Although numerically fewer recurrent DVT episodes occurred in the ASA group, the numbers did not achieve statistical significance (4.8%/yr vs 6.5%/yr; P = 0.09). On the other hand, ASA produced a reduction in secondary composite outcomes, which included myocardial infarction, stroke, and cardiovascular death. Hence, even though ASA did not produce a statistically significant reduction in DVT, the potential reduction in other cardiovascular adversities might tip the balance toward benefit. Because the primary endpoint of the trial was not met, secondary endpoints, however, must be considered hypothesis generating rather than conclusive. ■

Marijuana and the Risk of Schizophrenia

Source: Evins AE. The effect of marijuana use on the risk for schizophrenia. *J Clin Psychiatry* 2012;73:1463-1468.

The recent legalization of marijuana in two states has brought the discussion of potential toxicity to the fore. Although it is unclear what impact legalization will have on epidemiology of marijuana use, most experts agree that more widespread and heavier marijuana use would not be at all surprising. The psychiatry community has particular concern about marijuana use because observational data suggest that early (during adolescence) marijuana use is associated with an increased risk for an earlier onset of schizophrenia.

Most schizophrenia is genetic in origin (80%). Hence, if marijuana is a contributor to schizophrenia, it occurs in a minority of cases. On the other hand, some genetic predilection for development of schizophrenia can be seen in carriers of the Met allele of the COMT gene, who appear especially likely to develop psychosis subsequent to cannabis use in adolescence.

At the current time, experts suggest advising parents that marijuana use in adolescence, especially heavy use, may increase the risk of future schizophrenia, and for persons with existing psychosis, may make symptoms worse. ■

Losartan Improves Erectile Function in Diabetics

Source: Chen Y, et al. Losartan improves erectile dysfunction in diabetic patients: A clinical trial. *Internat J Impot Res* 2012; 24:217-220.

Animal studies have shown that high levels of angiotensin II (ANG2) in the corpora cavernosa of the penis extinguish erections, the effect of which can be blocked by losartan, an ANG2 receptor blocker. Whether losartan might have a favorable effect on erectile dysfunction (ED) in diabetic humans has not been definitively confirmed.

Chen et al studied diabetic adults with ED (n = 124) who were randomized to receive either LOS 50 mg/d alone, tadalafil 5 mg/d (TAD) alone, the combination of LOS + TAD, or no treatment for 12 weeks. Persons with poorly controlled hypertension were excluded from the trial.

At the conclusion of the trial, TAD and LOS provided comparable significant improvements in erectile function scores, but the LOS + TAD combination was significantly better than either monotherapy. The control group experienced no significant improvement in erectile function. LOS was very well tolerated, and tolerability was not compromised by combining LOS + TAD. Clinicians might consider the addition of LOS to patients with insufficient ED response to TAD alone. ■

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