

Clinical Briefs in Primary CareTM

The essential monthly primary care update

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

VOLUME 12, NUMBER 12

PAGES 23-24

DECEMBER 2007

Benefits of Coronary Prevention: WOSCOPS

Ford I, et al. *N Engl J Med.* 2007;357(15):1477-1486.

THE PREPONDERANCE OF EVIDENCE supporting lipid modulation for reduction of coronary heart disease (CHD) springs from secondary prevention trials comprised largely of mid-life individuals with prior history of diabetes, stroke, or MI. Much less evidence is available to confirm the benefits of primary prevention through lowering of LDL. The West of Scotland Coronary Prevention Study (WOSCOPS) enrolled a population (n = 6,595) of men with elevated cholesterol who had NOT sustained an MI, and randomized them to pravastatin 40 mg/d (PRAV) or placebo for 5 years. Inclusion criteria required LDL at baseline to be at least 174 mg/dL. At the conclusion of the trial the composite endpoint (CHD death plus nonfatal MI) was reduced by 30% in the PRAV group compared with the placebo group. Whether the 5-year PRAV intervention might result in continued benefit beyond the initial clinical trial period was the subject of this report by Ford, et al.

Five years after the WOSCOPS trial completion, the two arms of the trial started to look fairly similar: almost equal percentages of each were receiving a statin (PRAV group = 38.7%, placebo group = 35.2%).

Endpoint ascertainment 10 years after close of the clinical trial still showed a significant advantage for study subjects originally assigned to PRAV. For instance, for the endpoint of fatal + nonfatal MI, there was still a 37% relative risk reduction seen in the PRAV group ($p = 0.001$). Considering the high number of persons in the placebo group who ultimately ended up on statins in the post-trial interval, these long-term benefits of PRAV treatment may even be an underestimate. ■

Topiramate for Alcohol Dependence

Johnson BA, et al. *JAMA.* 2007;98(14):1641-1651.

COMPLEX NEUROCHEMICAL MECHANISMS support the potential role of topiramate (TOP) for enhancing abstinence from alcohol (ABST). For instance, TOP has two different pathways by which it can reduce CNS dopamine release, thereby decreasing reinforcing aspects of alcohol ingestion. Indeed, favorable effects have already been seen in a short pilot trial.

This 14-week double-blind placebo controlled trial randomized 183 men to 300 mg/d TOP or placebo. Participants fulfilled DSM-IV criteria for alcohol dependence, and imbibed a minimum of 4 drinks/day (women) or 5 drinks/day (men). One drink was defined as 10 oz. beer, 4 oz. wine, or 1 oz. of 100-proof liquor.

The primary efficacy endpoint was number of days of heavy drinking, defined as more than 5 drinks/d for men, or 4 drinks/d for women. Secondary outcomes included the percentage of days of successful total abstinence, and weekly average number of drinks.

At the 14 week study endpoint, TOP was associated with a statistically significant reduction in the primary endpoint; the placebo group continued to engage in heavy drinking on 52% of days, vs 44% of days for TOP subjects. Similarly, the TOP group was over two times more likely to maintain at least 28 days of continuous abstinence than the placebo group. Differences between TOP and placebo were seen early (by 4 weeks), and were maintained throughout the trial. TOP appears to be a reasonable consideration to enhance alcohol abstinence. ■

Job Strain and Recurrent CHD

Aboa-Eboule, et al. *JAMA.* 2007;298(14):1652-1660.

ALTHOUGH THE EVIDENCE IS BY NO means incontrovertible, many clinicians concur with clinical trials which suggest job strain is a risk factor for and contributor to myocardial infarction (MI). Whether a second coronary event might also be related to job strain has been far less studied, and the trials addressing this question have been in very small populations.

Hospitals in Quebec, Canada, supplied study subjects for this large trial (n = 1,191) of relatively young adults (age < 60) who had sustained an acute MI, and returned to work within 18 months after the index event. The primary outcome was incidence of new CHD events, including fatal and nonfatal MI, and angina. The Karasek Job Content Questionnaire, a validated metric for psychological demands of the work environment, was used.

After 2 years of follow-up, risk of a second cardiac event was more than twice as great among persons with the highest levels of job stress.

It is theorized that job strain induces sympathetic activation with subsequent enhanced thrombogenicity. Although less well supported, an additional theory about job stress is that persons under greater stress might be less adherent to medication and healthy lifestyle components. In any case, job strain does appear to exact a meaningful cardiovascular toll, which does not dissipate after the first event. ■

Sexual Dysfunction in Women with Metabolic Syndrome: Nutrition Intervention

Esposito K, et al. *Int J Impotence Research*. 2007;19:486-491.

IT HAS BEEN DEMONSTRATED THAT women with metabolic syndrome (MBS) have a higher prevalence of sexual dysfunction. Indeed, each of the individual components of MBS has been independently associated with greater frequency of female sexual dysfunction (FSD)

Clinical trials of the Mediterranean Diet as a secondary prevention intervention for MI have shown startlingly good outcomes, reducing MI by as much as 70%. Some of the benefits of the Mediterranean Diet are attributed to improved endothelial function. Whether dietary intervention in women with MBS might ameliorate sexual dysfunction was the subject of this investigation.

This study selected women with FSD and MBS. Exclusions included smokers, a prior history of CV disease, any regular

medication, and alcohol abuse. The Female Sexual Function Index (FSFI), which measures desire, arousal, lubrication, orgasm, satisfaction, and pain, was the primary trial metric.

Fifty-nine women were assigned to either Mediterranean Diet or control. The intervention group received dietary counseling, including a meeting with a nutritionist monthly for the first year, and bimonthly for the second year.

At the end of the trial, scores on the FSFI increased from 19.7 to 26.1 in the treatment group, but did not change in the control group. Each of the subcategories in the FSFI were favorably impacted. For women with MBS, utilization of the Mediterranean Diet may improve sexual dysfunction. ■

Confirming the Diagnosis of Premature Ejaculation

Symonds T, et al. *Int Jour Impotence Research*. 2007;19:521-525.

ACCORDING TO LARGE POPULATION surveys, premature ejaculation (PEJ) is the most common sexual dysfunction in America. The definition becomes problematic, however, because DSM-IV criteria lack concreteness: "ejaculation before the person wishes it," or "causing marked distress of interpersonal difficulty." These descriptors are generally appropriate, but open to a wide range of interpretation. Even the amount of time prior to ejaculation which might be used as a clinical benchmark has been much debated, but intravaginal ejaculatory latency of less than 1.0-1.5 minutes is generally accepted as PEJ.

The Premature Ejaculation Diagnostic Tool (PEDT) was developed to assist clinicians in diagnosis of PEJ. This trial compared the PEDT with DSM-IV and actual expert clinician diagnosis of PEJ. Men with complaints of PEJ (n = 102) were screened with the PEDT and individually interviewed by a clinician expert in male sexual dysfunction.

The concordance of PEDT results with

DSM-IV and expert clinician diagnosis was excellent. Although clinicians may appropriately rely on direct patient interviewing rather than formalized sexual function scales to diagnose sexual dysfunction, the PEDT provides a tool that is simple to administer and accurate. ■

A Possible Relationship Between CAD and Colonic CA

Chan AOO, et al. *JAMA*. 2007;298(12):1412-1419.

COLON CANCER AND CORONARY Artery Disease rank at the top of causes of death worldwide. A 2006 retrospective study indicated a strong relationship between them, some of which might be explicable by shared risk factors (eg, smoking, diabetes, sedentary lifestyle, obesity). A cross-sectional study of residents of Hong Kong who were being evaluated for coronary artery disease (n = 414) provided the subjects for this report. From the large group of persons selected to undergo screening for CAD, subjects were divided into those with and without CAD subsequent to evaluation. Then, subjects were compared with age/sex matched controls from the general population. Participants underwent colonoscopy within 8 weeks, or when stable if an acute coronary disorder was present.

The prevalence of any colonic neoplasm was almost twice as great (34.0% vs 18.8%) in persons with proven CAD vs no-CAD. Specifically addressing colon cancer, the prevalence among the subgroup identified with CAD was almost ten-fold greater than CAD screenees without CAD (4.4% vs 0.5%).

As has been identified in other settings, smoking and the metabolic syndrome were associated with an increased risk of colonic neoplasia. The results of this study suggest that clinicians have a high level of vigilance for colonic neoplasia in persons who have been proven to have CAD. ■

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