

Clinical Briefs in **Primary Care**TM

The essential monthly primary care update

By Louis Kuritzky, MD

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

VOLUME 10, NUMBER 9

PAGES 17-18

SEPTEMBER 2005

Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment

Source: Petersen RC, et al. *N Engl J Med.* 2005;352:2379-2388.

MILD COGNITIVE IMPAIRMENT (MCI) is a term used to designate a level of cognitive change in between normalcy and dementia. Alzheimer's disease (ALZ) continues to be an individually and epidemiologically compelling disorder, with only modest therapeutic advances in the previous decade. ALZ might be preventable, and an appropriate high-risk population to study would be subjects with MCI, amongst whom as many as 10-15% per year progress to ALZ.

Based upon the hypothesis that oxidative damage might contribute to ALZ, and that cholinesterase inhibition has shown some symptomatic improvement in ALZ, both agents were considered of merit for intervention in MCI patients. In a randomized, double blind fashion, subjects (n = 769) were assigned to vitamin E (2000 IU/d), donepezil 10 mg/d, or placebo. The primary end point, assessed by intention-to-treat analysis, was development of ALZ (possible or probable).

Over the 3-year study period, there was no demonstrable difference between either Vitamin E, donepezil, or placebo. At an early assessment point (12 months) the donepezil group demonstrated reduced ALZ development, but this improvement was not sustained to the end of the trial.

Neither Vitamin E nor donepezil appears effective over the long term (3 years) in

forestalling ALZ amongst individuals with MCI. ■

Foot Small Muscle Atrophy Before the Detection of Clinical Neuropathy

Source: Greenman RL, et al. *Diabetes Care.* 2005;28:1425-1430.

DIABETIC PERIPHERAL NEUROPATHY (DPN) is costly to diabetics in that it is associated with subsequent disability and limb loss, not to mention the frequent problematic neuropathic pain. Small muscle atrophy (SMA) is felt to be a primary contributor to derangements in musculoligamentous foot mechanics which foster structural changes (eg, clawing of the toes). Ultimately, the combination of insensitivity from sensory neuropathy, SMA, and alteration of foot mechanics conspire to induce foot ulcers.

MRI scanning can be used to quantify phosphorus metabolism in muscle. Healthy muscles subjected to ischemia quickly restore phosphorus metabolism to normal, whereas unhealthy muscle does not. Greenman and colleagues studied a population of non-diabetics, diabetics with DPN, and diabetics without DPN to evaluate the use of MRI-phosphorus scanning.

Subjects with DPN were identified using typical tools such as a biothesiometer for vibration perception threshold and Semmes-Weinstein monofilament testing.

MRI-phosphorus testing indicated a statistically significant lower level of viable muscle tissue in the feet of DPN patients

than diabetics without DPN.

However, even diabetics without DPN demonstrated reductions in muscle tissue compared with normal controls. These data indicate that SMA is occurring prior to the advent of overt DPN in diabetics, and becomes more progressive as DPN becomes evident. ■

Statins and the Risk of Colorectal Cancer

Source: Poynter JN, et al. *N Engl J Med.* 2005;352:2184-2192.

NSAIDS HAVE SHOWN CONVINCING benefits for prevention of colon cancer (CCA) in high-risk populations. The toxicity of NSAIDs, including GI bleeding and cardiovascular events, has recently been highlighted and includes the here-to-fore-considered 'safer' COXIBs. Hence the search for additional CCA chemopreventive agents continues. Statins have theoretic potential benefits for CCA since HMG-CoA reductase (the enzyme upon which statins impact) is overexpressed by CCA cells, and in vitro data support increased CCA cell apoptosis stimulation by statins.

To evaluate potential benefits from statin therapy, a population from the Molecular Epidemiology of Colorectal Cancer study (n = 1,953) was studied using a case-control method. Participants had received a diagnosis of CCA between 1998-2004, vs their case controls, who did not have a diagnosis of CCA.

Use of statins for at least 5 years was associated with a 0.5 odds ratio for CCA risk (approximately 47% relative risk reduc-

tion). Contributing to the evidence that the statin effect is class specific, use of fibrates in this same population was not associated with reduced risk. Poynter et al suggest that the role of statins in CCA chemoprevention is worthy of further study. A large prospective interventional trial would be ideal. ■

Screening for Abdominal Aortic Aneurysms: Single-Center Randomized Controlled Trial

Source: Lindholt JS, et al. *BMJ USA*. 2005;5:222-224.

RECENT GUIDANCE FROM THE United States Preventive Services Task Force has affirmed the evidence-based value of screening male current/ex-smokers older than age 65 for abdominal aortic aneurysm (AAA). There remains some debate about whether screening should be offered to a broader patient population, for instance to include women, male non-smok-

ers, or younger individuals. Lindholt et al studied a Danish population of men older than age 65 independent of smoking status to determine the value of AAA screening.

The study population included all men born in Viborg County, Denmark, between 1921-1929 (n = 12,639). In this cohort, half were ultrasound screened, and the other half served as the control group. An aneurysm was defined as an infra-renal aortic diameter > 3 cm. Identified aneurysms > 5 cm were referred to a vascular surgeon for elective repair; aneurysms < 5 cm were re-scanned on an annual basis. All subjects were followed for 5 years.

Ultrasound scanning identified 191 AAA subjects (4%). Screened subjects enjoyed 75% fewer emergency interventions for AAA, and an overall 67% reduction in AAA-related mortality. These data encourage consideration of more widespread screening for AAA, to include non-smoking subjects. ■

Comparison of Physical Treatments vs a Brief Pain-Management Program for Back Pain in Primary Care

Source: Hay EM, et al. *Lancet*. 2005; 365:2024-2030.

FINDING THE OPTIMUM MANAGEMENT plan to improve outcomes in low back pain (LBP) remains problematic. Generally, active treatments such as exercise and manual medicine have been found to be superior to no treatment. Increasingly, cognitive behavioral techniques have been used in an effort to enhance mobilization, reduce disability, and improve return-to-work status. Usually, cognitive behavioral techniques are applied in secondary care or referral settings.

A British patient population from 28 general practices provided adult study subjects (n = 402) with LBP of < 12 weeks duration. Subjects were randomly assigned to a brief pain management program (BPMP) or traditional physiotherapy

(which functioned as the control) consisting of exercise and manual medicine interventions. Components of the BPMP included addressing psychosocial risk factors for persistent disability, an emphasis upon returning to normal activity by means of goal setting, and strategies to overcome psychosocial barriers to recovery. Positive coping strategies—including “hurt does not mean you are inducing harm” were encouraged.

At 12 months, outcomes in both groups were equivalent. Hay and colleagues point out that providing the BPMP required fewer sessions than traditional therapy, and fewer referrals to secondary care. ■

Visit Frequency and Hypertension

Source: Guthmann R, et al. *J Clin Hypertens*. 2005;7:327-332.

DESPITE A PLETHORA OF HIGHLY effective antihypertensive agents and lifestyle modulations (eg, diet, exercise) which can favorably affect blood pressure (BP), only a minority of hypertensive individuals in America are identified, on treatment, and controlled to < 140/90. One of the factors which might influence BP control is visit frequency (VF); that is, do patients who are seen more (or less) frequently obtain better BP control?

Literature on warfarin management might provide a precedent: the more often patients are seen, the better control of INR is achieved, albeit at greater cost and inconvenience to the patient. JNC VII guidance on hypertension (HTN) suggested monthly visits until stable, then 3-6 monthly; patients with stage 2 HTN or comorbidities are suggested to be seen more frequently than monthly.

To study the relationship between VF and HTN control, data from 2 family practice patient populations were reviewed (n = 429 patients, visit n = 7,910). The median interval to return visit was 45 days. Interval to return visit was shorter if BP was uncontrolled. Overall, there was a significant correlation between shorter return visit intervals and percent change in BP. Although these data come from an observational study, it suggests that shorter intervals between visits may favorably affect likelihood of good BP control. ■

Clinical Briefs in Primary Care™ is published monthly by American Health Consultants. Copyright © 2005 Thomson American Health Consultants. **Vice President/Group Publisher:** Brenda Mooney. **Editorial Group Head:** Lee Landenberg. **Editor:** Stephen Brunton, MD. **Managing Editor:** Rob Kimball. **Associate Managing Editor:** Leslie Hamlin. 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: robert.kimball@thomson.com

World Wide Web: www.ahcpub.com

Address Correspondence to: American Health Consultants 3525 Piedmont Road, Building Six, Suite 400 Atlanta, GA 30305.

THOMSON
★
AMERICAN HEALTH CONSULTANTS