Memory Care Monthly

Supporting Healthcare Professionals in Caring for the Aging July 2007

New Study Highlights the Efficacy of the MCI Screen in Primary Care Practice

A new study included in the June issue of *Journal of Alzheimer's Disease* highlights the unsurpassed ability of the MCI Screen, a technology and mathematics based memory assessment to accurately and efficiently detect very early signs of abnormal memory loss in a fast-paced primary care setting. Furthermore, the study makes the clinical justification for regularly assessing the memory of individuals over the age of 65. The study was conducted by Dr. Douglas Trenkle, a primary care physician at Maine Coast Memorial Hospital, as a part of the Hancock County Aging Project.

Entitled *Detecting Cognitive Impairment in Primary Care: Performance Assessment of Three Screening Instruments*, the study compared the MCI Screen to the two most widely used pen-and-paper assessments, the Mini-Mental Status Exam (MMSE) and the Clock Drawing Test (CDT). Patients over 65 without previous diagnosis of memory disorders were assessed using the MCI Screen, MMSE, and the CDT. Those found to be impaired with any of the three assessments received a standard diagnostic workup including blood tests and brain imaging. The MCI Screen was 96% accurate in detecting patients with impairment, while the MMSE was 72% accurate and the CDT 57%. The MCI Screen detected memory disorders from a variety of conditions ranging from Alzheimer's disease (43%) to cerebrovascular disease (36%) to depression (3%). Two-thirds of patients diagnosed with an underlying condition had no subjective complaints of impairment.

Reference: Trenkle D et al. JAD (2007) 11(3):323-35.

Conference Presentation: MCI Screen Helps Detect Silent Stroke

Stroke is the third leading cause of death in the United States. Each year, about 700,000 people suffer a stroke. About 500,000 of these are first attacks, and 200,000 are recurrent attacks. With the aging of the US population and increase in risk factors such as heart disease and diabetes, the number affected with stroke will increase greatly.

Analysis of the data from the Hancock County Aging Project led by Dr. Douglas Trenkle, a primary care physician at Maine Coast Memorial Hospital, found 36% of patients with memory impairment had an underlying diagnosis of cerebrovascular disease or stroke. Of those found to be impaired, two-thirds had no outward signs of impairment or complaints of impairment. In other words, these individuals were at risk for developing major strokes and would not have been identified if they were not screened by the MCI Screen. This finding greatly supports routine memory screening of patients at risk for stroke, in primary care settings.

Results of the study will be presented at annual conference for The International Society for Vascular Behavioural and Cognitive Disorders, Vas-Cog 2007 held in San Antonio from July 11-14, 2007

Update on Beta-Amyloid Lowering Agents

Beta-Amyloid Lowering Agents (BALA) are a class of medications that lower beta amyloid 1-42 brain levels in various ways. There are approximately 17 drugs in FDA phase I-III clinical trials which lower beta amyloid 1-42 levels in the brain. An illustrative example of the BALA class of drugs is Flurizan (tarenflurbil), which has four years of FDA phase II and III clinical data, and has already closed enrollment for their final phase III study.

Flurizan selectively modulates gamma secretase cleavage of the amyloid precursor protein to lower beta amyloid 1-42 production which reduces neuritic plaque formation. To date, Flurizan daily doses of 800-1,600 mg have been used to treat approximately 1,600 patients with mild to moderate Alzheimer's disease (AD) for up to four years[1]. Flurizan is well tolerated with possible adverse effects of anemia, eosinophilia, mild hypertension, lower respiratory tract infections, rash, and mild cardiac conditions occurring more commonly than placebo. However, more serious vascular adverse effects of stroke and myocardial infarction did not occur more commonly than placebo. Flurizan can increase bleeding when given with Coumadin because it increases prothrombin time. Cognitive, functional and global severity tests showed that Flurizan, 1,600 mg daily, is more effective when started earlier in the course of AD. Over a two-year course on this dose vs. placebo of 800 mg daily, there were mean 2- vs. 8-point, 2- vs. 3-point, and 8- vs. 12-point declines on the ADAS-Cog, CDR sum of the boxes, and ADCS-ADL scales respectively. The study has demonstrated a reduction in the rate of decline in patients who were given a higher dose of Dlurizan when compared to those given a lower dose. Likewise, there has also been a statistically significant treatment reduction in the rate of decline in patients treated for 24 months with Flurizan when compared to patients initially treated with placebo for 12 months then switched to Flurizan for 12 months. The Flurizan example of the BALA class of AD medications demonstrates that early detection, diagnosis and treatment of AD will become increasingly important. FDA approval for the BALA medications, Alzhemed (Neurochem Inc.) and Flurizan (Myriad, Inc.) is anticipated to be in 2008-9.

Reference: 1. Flurizan Clinical Update. Myriad Investigators Meeting. New Orleans. May 18, 2007.

Research Updates

Early Treatment of Stroke Reduces Risk of Recurrent Stroke

A new study led by Peter Rothwell, MD, PhD from University of Oxford, United Kingdom found that aggressive treatment of first ischemic attack (TIA) or minor ischemic stroke reduces the risk of recurrent stroke. The Expressive Preventive Strategies for Stroke (EXPRESS) study is a 5 year population based study. Current standard management in a group of TIA and minor stroke patients over 30 months was compared with early, aggressive management in a second, consecutive 30-month period in similar group of patients. Treatment protocol was the same for both groups of patients. Researchers concluded that relative risk of recurrent stroke was reduced by more than 90% among patients who received early, aggressive treatment of first stroke.

Reference: Presented at 16th European Stroke Conference, in Glasgow, Scotland

Type 2 Diabetes Increases Risk of Stroke 2-Fold

Individuals with type 2 diabetes are twice as likely to suffer from a stroke within the first 5 years of diagnosis compared to the general population. Researchers found a 10% absolute risk for stroke within five years of a diabetes diagnosis versus a 4.5% absolute risk in the general population. Thomas Jeerakathil, MD, MSc from the University of Canada, Alberta, studied data from health databases from the province of Saskatchewan. Stroke hospitalizations are documented annually by age and sex. 12,272 people aged 30 or older were included in the diabetes cohort.

Reference: Jeerakathil T et al. Stroke (2007) 38(6):1739-43.

Type 2 Diabetes Linked to Loss of Brain Tissue

According to a recent study type 2 diabetes is associated with brain atrophy in the frontal and temporal regions. Cerebral blood flow (CBF) was examined in 26 diabetics (aged 61.6 +/- 6.6 years) and 25 comparable controls (aged 60.4 +/- 8.6 years) using continuous arterial spin labeling (CASL) imaging during baseline, hyperventilation, and CO2 re-breathing. Regional gray and white matter, cerebrospinal fluid (CSF), and white matter hyperintensity (WMH) volumes were also measured on a T1-weighted inversion recovery fast-gradient echo and a fluid attenuation inversion recovery MRI.

The diabetic group had smaller global white and gray matter and larger cerebrospinal fluid volumes than the controls. Also regional differences were observed for white matter and CSF in the frontal region, and for gray matter and CSF in the parieto-occipital region. Baseline regional CBF ($P = 0.006$) and CO2 reactivity ($P = 0.005$) were reduced in the diabetic group.

These findings may have implications for cognition and balance in elderly subjects with diabetes.

Reference: Last D et al., Diabetes Care. (2007) 30(5):1193-9.

Personality Traits May Aid in Diagnosis of Dementia

Taking an inventory of a patient's personality traits may help distinguish patients between two leading causes of dementia: Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). James E. Glavin, MD, MPH, from the Washington University School of Medicine in St. Louis, Missouri conducted a longitudinal study with 290 participants who were followed up to autopsy. Annual caregiver interviews were conducted and information about changes in personality, interests and drives were gathered using the Blessed Dementia Scale.

The study found that personality traits such as decreased emotional responsiveness, giving up hobbies, increased apathy, and purposeless hyperactivity, most likely are manifested in DLB than AD. Any changes in personality were often associated with the presence of visual hallucinations common to DLB.

Reference: Glavin, H et al., Neurology. (2007) 68(22): 1895-1901.

Enzyme That Links Alzheimer's to Brain Injury Identified

Researchers have identified an enzyme essential in the production of amyloid-beta protein which may explain the link between brain injury and Alzheimer's disease (AD). The beta-site APP-cleaving enzyme (BACE) is essential in the production of amyloid-beta. Brain injuries lead to increased BACE levels which increase the risk of AD. The research team, led by Dr. Guideppina Tesco of Massachusetts General Hospital and colleagues, found increased levels of BACE in AD patients. Although researchers had known of the link between brain injury and AD, this study furthers the understanding of the cause of dementia in brain injury patients.

Reference: Tesco G et al. Neuron, (2007) 54(5):721-37.

CPAP Therapy Helps Alzheimer's Patients with Sleep Apnea

According to a new study, patients with Alzheimer's disease (AD) and sleep apnea may benefit from treatment of continuous positive airway pressure (CPAP). The study included 48 patients with AD and sleep apnea; subjects were randomized and assigned to either a 6 weeks CPAP group or a 3 week placebo group. After 3 weeks of treatment with CPAP, subjects in the first group had significant improvement in sleep as measured by reduced amount of time spent awake during the night, increased time spent in deeper levels of sleep, and improved oxygenation.

Reference: SLEEP 2007, 21st Annual Meeting of the Associated Professional Sleep Societies

Clinical Trial Updates and FDA Approvals

Clinical Trial Update: Alzhemed by Neurochem

Tramiprostate (Alzhmed) developed by Neurochmen, currently in phase III trial, has experienced difficulty in data analysis due to variation between data from the 67 centers included in the study. The trial included 1052 patients and was designed to evaluate the efficacy, safety, and disease modification effect of tramiprostate which reduces amyloid-beta levels in cerebrospinal fluid (CSF) of Alzheimer's patients. Factors that were inconsistent among trial sites and influenced result of the treatment with tramiprostate included use and duration of other medications such as memantine. Researchers are now working to account for these site differences before analyzing the data.

Reference: Presented at the Alzheimer's Association 2007 International Conference on Prevention of Dementia

Clinical Trial Update: LY450139 by Eli Lilly & Company

LY450139 is a drug that deactivates gamma-secretase, an enzyme involved in amyloid-beta synthesis. According to phase II trials, the drug seems to be safe and reduces the plasma concentrations of amyloid-beta in Alzheimer's disease patients. Eli Lilly & Company in collaboration with the Alzheimer's Disease Cooperative Study are conducting the study.

Reference: Presented at the Alzheimer's Association 2007 International Conference on Prevention of Dementia

Clinical Study Follow-up: AN1792 by Elan Pharmaceuticals

Alzheimer's disease patients who participated in a clinical trial which was stopped due to safety concerns were followed-up. 4.5 years prior, subjects were immunized with a synthetic amyloid-beta peptide (AN1972) developed by Elan Pharmaceuticals as part of the clinical trial. The original study included 372 subjects, 300 of whom were immunized with AN1792 and 72 with a placebo. 59 of the 300 subjects developed IgG antibody titers of 1:2,200 or greater and were classified as responders. The study was discontinued when some of the subjects developed encephalitis.

The follow-up study included 159 of the original patients, 30 of whom were vaccinated with the placebo. 25 had been identified as responders and 17 still had detectable antibody titers. Responders scored significantly better than placebo subjects on cognitive assessments.

Reference: Presented at the Alzheimer's Association 2007 International Conference on Prevention of Dementia

FDA Approval: Exelon Patch

On July 9, 2007, the Federal Food and Drug Administration (FDA) approved the Exelon Patch developed by Novartis Pharmaceuticals for treatment of Alzheimer's disease and mild to moderate Parkinson's dementia. The Exelon Patch delivers treatment through a skin patch which is applied to the back, chest or upper arm and maintains steady drug levels in the bloodstream, improving tolerability and allowing a higher proportion of patients to receive therapeutic doses of medication, with potential improvements in efficacy.

MEDICAL CARE CORPORATION

Medical Care Corporation
Simple and Accurate Memory Assessment
19782 MacArthur Blvd. #310, Irvine, CA 92612
www.mccare.com • (888) 565-5535