an Ounce of Prevention

ALZHEIMER'S PREVENTION THROUGH DELAY *SUMMER 2009*

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FEATURED ARTICLE

KNOW THE 10 SIGNS: EARLY DETECTION MATTERS

In March 2009 issue of Alzheimer's & Dementia, the journal of National Alzheimer's Association, thought leaders contributed to lay a clear roadmap for preventing Alzheimer's disease by the year 2020. The vision and recommendation featured in the journal is based on 3 think-tank meetings held in 2007 and 2008, and represents collective thoughts from over 70 leaders worldwide in the areas of Alzheimer's disease and dementia.

Following this effort, the National Alzheimer's Association has recently launched an educational campaign called "Know the 10 Signs: Early Detection Matters," along with an updated version of their 10 warning signs of Alzheimer's. This is to encourage early detection of Alzheimer's disease (AD) in the community. The new "10 signs" include more descriptive symptoms of AD ranging from memory changes affecting daily life, to decreased or poor judgment, and to changes in mood and personality. They are also compared with typical state for these functions among the healthy.

Recent studies provide more evidence for the importance of early detection. Early detection not only allows the maximum benefit of currently available treatments, but also gives patients an opportunity to participate in the planning of their future care and personal matters.

For more information, please visit:
http://alz.org/alzheimers_disease_know_the_10_signs.asp

Also available at their site is a memory questionnaire for doctors visits, a 10 warning signs check list, and principals for a dignified diagnosis.

WHAT'S NEW?

FOR MORE TIMELY NEWS, VISIT OUR BLOG: "BRAIN TODAY"

Myriad news reports about brain health are published every day. The news covers many related topics such as memory loss, Alzheimer's disease, drugs and treatments, risk factors, diagnostic tests, and published discoveries across the field. Some of the news is objectively reported, some is over-sensationalized, and some is intentionally misleading. This blog is devoted to interpreting the daily news and distilling its true value.

http://braintoday.blogspot.com

RESEARCH UPDATES

TREATMENT PRACTICE OF MILD COGNITIVE IMPAIRMENT IN CALIFORNIA ALZHEIMER'S DISEASE CENTERS

"Real world" treatments for patients with mild cognitive impairment (MCI) were examined at the California Department of Public Health, Alzheimer's Disease Research Centers of California. This study was lead by Dr. Kristine Yaffe from UC San Francisco and VA Medical Center San Francisco.

Of 578 patients with MCI, 166 patients (28.7%) were taking anti-Alzheimer's medications, and this treatment was associated with greater functional impairment, higher education, certain MCI subtypes and older age. 252 patients (43.6%) were taking statins, and the use was associated with diabetes mellitus, hypertension, myocardial infarct, male gender, and MCI subtype. 115 patients (19.9%) were taking anti-oxidants, and the use were associated with higher education and diabetes mellitus and varied according to site. 37 patients (6.4%) were taking folic acid, and the use were associated with nonwhite race, male gender, and greater functional impairment.

This study also suggested that the patients with MCI are frequently being treated "off label" with cholinesterase inhibitors, memantine, and/or other cognition enhancing drugs.

Weinstein A et al. JAGS. 2009; 57(4):686-90.

UNCONTROLLED DIABETES INCREASES THE RISK OF ALZHEIMER'S

Researchers from the Karolinska Institute, Stockholm, Sweden, have investigated the association of diabetes with different dementing disorders taking into account glycaemic control, and the link between glucose dysregulation and neurodegeneration. They found that uncontrolled diabetes increases the risk for both Alzheimer's (AD) and vascular dementia (VaD).

A dementia-free cohort (n=1,248) aged >/=75 years was longitudinally examined to detect dementia due to AD and VaD cases. The AD diagnoses were further classified into AD with stroke and AD without hypertension, heart disease and stroke. Diabetes was ascertained based on medical history, hypoglycaemic medication use, or a random blood glucose level >/=11.0 mmol/l while borderline diabetes was defined as a random blood glucose level of 7.8-11.0. Cox models were used to estimate the hazard (risk) ratios (HRs).

During the 9 year follow-up, 420 individuals developed dementia including 47 VaD and 320 AD. Of AD cases, 78 had previous, temporally unrelated stroke, and 137 had no major vascular comorbidities. Overall diabetes was only related to VaD (HR 3.21). Undiagnosed diabetes lead to an HR of 3.29. Diabetic patients with <7.5 mmol/l had no increased dementia risk. Uncontrolled and borderline diabetes were further associated with AD without vascular comorbidities.

Xu WL et al. Diabetologia. 2009; March [Epub Ahead of Print].

VASCULAR RISK FACTORS ACCELERATE THE PROGRESSION OF ALZHEIMER'S

Vascular risk factors include medical history (heart disease, stroke, diabetes and hypertension), smoking, and pre-diagnosis blood lipid measures (cholesterol: total, high-density lipoprotein, low-density lipoprotein [LDL-C], and triglyceride concentrations), and these factors may predict how Alzheimer's disease (AD) will progress.

A cohort of 156 patients with AD (mean age at diagnosis: 83 years) was followed for a mean of 3.5 (up to 10.2) years. Cognitive assessments included the domains of memory, abstract reasoning, visual-spatial orientation, language, and executive speed.

Researchers found that higher total cholesterol and LDL-C concentrations and history of diabetes were all associated with faster cognitive decline while high-density lipoprotein cholesterol and triglyceride concentrations were not associated with the rate of decline. Each 10-U increase in cholesterol and KDK-C was associated with a 0.10 standard deviation (SD) decrease in cognitive score per year of follow-up. A history of diabetes was associated with an additional 0.05-SD decrease in cognitive score per year. History of heart disease and stroke were associated with cognitive decline only in the apolipoprotein E4 gene carriers. They also found that only higher LDL-C was independently associated with faster cognitive decline.

Helzner EP et al. JAMA. 2009; 66(3):343-8.

EXAMINATION OF "GOLD STANDARD" DIAGNOSIS OF MAJOR DEPRESSION IN AGED-CARE SETTINGS

Individual clinical interviews are usually viewed as the gold standard when diagnosing major depressive disorder (MDD) and when examining the validity of self-rated questionnaires. However, this approach may not be appropriate with older people due to their tendency to under report their depressive symptoms.

Dr. Tanya Davison from Deakin University, Melbourne, Australia, and her colleagues examined the effect of including informant interview on prevalence estimates of MDD in 168 residents (mean age: 84.68 years) with normal cognitive function in low-level aged-care facilities.

They found that the estimated point prevalence of MDD rose from 16% to 22% by including informant clinical interview in the diagnostic procedure. Overall, 27% of depressed residents failed to disclose symptoms in the clinical interview.

This study supports the use of an informant interview as an adjunct when diagnosing MDD among cognitively healthy aged-care residents.

Davison TE et al. AJGP. 2009; 17(5):359-67.

USE OF STROKE SECONDARY PREVENTION SERVICES IN STROKE BELT STATES

Stroke Belt states – 11 states consisting of Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia - have been recognized by public health authorities for having an unusually high incidence of stroke and other forms of cardiovascular disease. Due to such high stroke outcomes, Dr. Joseph Ross and his colleagues from Mount Sinai School of Medicine examined whether there are disparities in the use of stroke secondary prevention services in these states.

Using the nationally representative 2005 Behavior Risk Factor Surveillance System, they examined self-reported use of 11 stroke secondary prevention services queried in the survey. They used multivariable logistic regression to examine the association between service use and age, gender, race, and Stroke Belt state residence, controlling for other socio-demographic and health care access characteristics.

Among 11,862 adults with a history of stroke, 16% were 80 or older, 54% were women, 13% were non-Hispanic black, and 23% lived within a Stroke Belt state. Overall service use varied: 31% reported post-stroke outpatient rehabilitation, 57% regular exercise, 66% smoking cessation counseling, and 91% current use of antihypertensive medications. Age 80 or older was not associated with lower use of any of the 11 services. Women were less likely to report post-stroke outpatient rehabilitation and regular exercise when compared with men, yet there were no gender-based differences in use of the 9 other services. Blacks were less likely to report pneumococcal vaccination when compared with whites, but most likely to report post-stroke outpatient rehabilitation. There were no race-based differences in use of the 9 other services. Stroke Belt state residence was not associated with lower use of any of the 11 services.

Contrary to their hypothesis, researchers found no consistent age, gender, racial or Stroke Belt state residence disparities in care.

Ross JS et al. Stroke. 2009: 40:1811-19.

ASSOCIATION OF PRIOR STROKE WITH COGNITIVE FUNCTION AND COGNITIVE IMPAIRMENT

Researchers from the Mayo Clinic investigated associations between stroke history, APOE genotype, and subtypes of mild cognitive impairment (MCI).

Randomly selected 2050 residents of Olmsted County, Minnesota, aged 70 to 89 without documented dementia were evaluated through an informant interview, a neurological evaluation, and neuropsychological testing. Neuropsychological testing included 9 tests to assess memory, attention, executive function, visuospacial cognition, and language. Subjects were diagnosed by consensus as cognitively normal or as having MCI or dementia. A stroke history was confirmed in their medical record.

Of 2050, 1640 were cognitively normal, and 329 with MCI: 241 with amnestic MCI and 88 with nonamnestic MCI. A history of stroke was associated with a higher odds ratios of nonamnestic MCI than amnestic MCI. A stroke history was also associated with impaired function in each cognitive domain except memory. The association was strongest for attention and executive function. APOE e4 genotype was associated only with amnestic MCI and with impaired memory function.

Knopman DS. Arch Neurol. 2009: 66(5);614-19.

DONEPEZIL TREATMENT OF PATIENTS WITH MCI – A 48 WEEK RANDOMINZED, PLACEBO-CONTROLLED TRIAL

In this multi-center, randomized, placebo-controlled trial, subjects with MCI entered a 3-week placebo run-in period followed by 48 weeks of double-blind donepezil (5 mg/day for 6 weeks, then 10 mg/day for 42 weeks) or placebo treatment. Primary efficacy measurements included changes from baseline in the modified ADAS-Cog and CDR-SB after 48 weeks of treatment. Secondary measurements evaluated cognition, behavior and function.

Of 2037 patient screened, 821 were randomized into either treatment group (n=409) or placebo (n=412) and 60.8% completed the study (treatment group: 226; placebo: 273). These subjects, aged 45-90, expressed memory decline, and it was confirmed by their informant and neuropsychologic testings. Also they did not have a diagnosis of probable or possible vascular dementia or another

types of dementia, a nerulogic or psychistric disorder, a treatment with ChEI or memantine for >1 months or within 3 months of screeing, and some other conditions associated dementia risk factors.

The dual primary efficacy endpoint was not reached in this trial. However, there was a small but significant decrease in the modified ADAS-Cog scores in favor of donepezil at study endpoint. Little change from baseline in the CDR-SB and secondary measurements was observed for both groups. Patient Global Assessment scores favored donepezil at all time points except week 12. The Perceived Deficits Questionnaire scores favored donepezil at week 24. The Clinical Global Impression of Change-MCI scores favored donepezil only at week 6.

The results suggest that donepezil yields small but significant improvement on the primary measure of cognition, but there was no effect on the primary measure of global function. Most other measures of global impairment, cognition, and function were not improved, possibly due to an insensitivity of these measures in MCI.

Doody RS et al. Neurology. 2009; 72(18):1555-61.

LATE-LIFE STATIN USE DOES NOT PREVENT DEMENTIA

In 2001, the first Cochrane review was published about statin use for the prevention of Alzheimer's disease (AD) finding that there was insufficient evidence to recommend it. To expand its scope to include all forms of dementia, Dr. Bernadette McGuinness and her colleagues from Queen's University Belfast, Belfast, UK, reviewed two large, randomized controlled trials (HPS 2002 and PROSPER 2002) that included 26,340 individuals aged 40-82 years across trials.

The PROSPER 2002 included 5,804 patients aged 70-82 years who were randomized to receive a 40 mg/day of pravastatin or a placebo. All participants had risk factors for or a history of vascular diseases. During a mean follow up of 3.2-year period, cognitive function of both groups declined at the same rate. There was no significant difference between 2 groups in performance on letter digit codes, picture word learning test, Stroop and Mini Mental State Examination. There was no evidence that statins were detrimental to cognition.

The HPS 2002 study conducted in 2002 included 20,536 patients with 5806 at least 70 years old at study entry. The mean follow up period was 5-years. Participants were randomized to 40 mg/day of simvastatin or placebo. Researchers found no difference in incidence of dementia (31 cases in the simvastatin group, 31 cases in the placebo group) nor in performance on the modified Telephone Interview for Cognitive Status at final follow-up (23.7% simvastatin group cognitively impaired vs 24.2% in placebo group). There was no difference in cognition between groups either in relation to age at study entry or previous history of cerebrovascular disease.

This review suggests that statins given in late life to individuals at risk of vascular disease have no effect in preventing AD or dementia.

McGuinness B et al. Cochrane Database of Systematic Reviews 2009: Issue 2.

EFFECTS OF THE MENOPAUSE TRANSITION AND HORMONE USE ON COGNITIVE PERFORMANCE IN MIDLIFE WOMEN

Dr. Gail A. Greendale and her colleagues from UCLA examined cognitive performance during the menopause transition in 2,362 women from the Study of Women's Health Across the Nation for 4 years.

Results showed that, consistent with perceived memory difficulties reported by women in transition, perimenopause was associated with a decline in cognitive performance, characterized by women not being able to learn as well as they had during premenopause. Improvement rebounded to premenopausal levels in postmenopause, suggesting that menopause transition-related decline might be time-limited. Hormone initiation before the final menstrual period had a beneficial effect while initiation after the final menstrual period had a detrimental effect on cognitive performance.

Greendale GA et al. Neurology. 2009; 72(21):1850-7.

MEMANTINE CAUSES REVERSIBLE NEUROLOGICAL IMPAIRMENT IN MS

A research group lead by Dr. Pablo Villoslada from the Department of Neurology, Hospital Clinic, Barcelona, Spain, examined the used of memantine for cognitive impairment (CI) in patients with multiple sclerosis (MS).

The trial was designed as a 1-year, randomized, double-blind crossover study comparing memantine 30 mg/day against a placebo in 60 patients with MS with CI.

Although 19 patients were included, the trial was halted after 9 patients reported a worsening of their neurologic symptoms that deteriorated their quality of life. 7 of 9 patients in the memantine group had blurred vision, fatigue, severe headache, increased muscle weakness, walking difficulties, or unstable gait. Only 2 cases in the placebo group reported neurologic symptoms and they were related with changes in their disease-modifying treatment. These adverse events occurred on reaching the maximum dose, and after stopping medication, these symptoms reverted to their baseline disability within a few days.

Villoslada P et al. Neurology. 2009: 72(19);1630-33.

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