

Memory Care Monthly

Supporting Healthcare Professionals in Caring for the Aging

April 2007

Hypertension and Cognitive Impairment

Hypertension significantly increases the risk of developing cerebral white matter lesions, which themselves increase the risk of developing stroke, cognitive impairment and dementia due to Alzheimer's or cerebrovascular disease [1]. Both diastolic and systolic elevations of blood pressure in hypertensives can increase these risks. Diastolic blood pressures above 90 mm Hg among hypertensive patients correlate with worsened cognitive performance [2]. In elderly patients with systolic hypertension who were exposed to cold, exercise, or other events that stimulate the sympathetic nervous system, blood vessels did not react normally, and increased the patient's risk of stroke and cognitive impairment [3].

In Alzheimer's disease patients, the presence of cerebral white matter lesions worsens their cognitive performance [4]. Small arteries and arterioles supply blood to the white matter. Prolonged exposure to hypertension produces inelasticity, hardening and calcification in these small arteries and arterioles and are important factors in the pathophysiology of cognitive impairment and dementia due to hypertension-mediated cerebrovascular disease [5].

Treating hypertension has a profound effect on the degree of cognitive impairment and the risk of Alzheimer's disease among patients with memory loss. Among 1,241 elderly hypertensive patients with memory complaints, those who received treatment that controlled their blood pressure had better cognitive function than untreated patients, even after adjusting for age, sex, education and diagnosis (Mild Cognitive Impairment, Alzheimer's Disease, or Vascular Dementia). Furthermore, the risk of having Alzheimer's disease was twice as high in the untreated vs. treated hypertensive patients [6].

The type of antihypertensive treatment also matters. Patients treated with calcium channel blockers had higher cognitive function than those treated without calcium channel blockers, and the improvement was independent of blood pressure level [6].

Hypertension is also one of the many factors (weak grip strength, obesity, hyperglycemia, smoking, and excessive alcohol consumption) associated with longer life expectancy and reduced morbidity if it is prevented or well controlled during midlife [7].

References

1. Sierra C, Coca A. White matter lesions and cognitive impairment as silent cerebral disease in hypertension. *ScientificWorldJournal*. 2006;6:494-501.
2. Imarhiagbe F, Ogunrin O, Ogunniyi A. Cognitive performance of hypertensive elderly Nigerians: a case control study. *Afr J Med Med Sci*. 2005; 34:269-73.
3. Castellani S, Bacci M, Ungar A, Prati P, Di Serio C, Geppetti P, Masotti G, Neri Serneri GG, Gensini GF. Abnormal pressure passive dilatation of cerebral arterioles in the elderly with isolated systolic hypertension. *Hypertension*. 2006;48:1143-50.
4. Burns JM, Church JA, Johnson DK, Xiong C, Marcus D, Fotenos AF, Snyder AZ, Morris JC, Buckner RL. White matter lesions are prevalent but differentially related with cognition in aging and early Alzheimer disease. *Arch Neurol*. 2005;62:1870-6.
5. Pantoni L, Simoni M. Pathophysiology of cerebral small vessels in vascular cognitive impairment. *Int Psychogeriatr*. 2003;15 Suppl 1:59-65.
6. Hanon O, Pequignot R, Seux ML, Lenoir H, Bune A, Rigaud AS, Forette F, Girerd X. Relationship between antihypertensive drug therapy and cognitive function in elderly hypertensive patients with memory complaints. *J Hypertens*. 2006;24:2101-7.
7. Willcox BJ, He Q, Chen R, Yano K, Masaki KH, Grove JS, Donlon TA, Willcox DC, Curb JD. Midlife risk factors and healthy survival in men. *JAMA*. 2006;296:2343-50.

Amyloid Beta Ratio May Predict Risk of Alzheimer's Disease

Researchers led by Dr. Neill R. Graff-Radford of Mayo Clinic in Jacksonville, FL studied plasma levels of amyloid beta protein (Abeta40 and Abeta42) and their link to developing mild cognitive impairment (MCI) or Alzheimer's disease (AD). They found that Abeta42 and Abeta40 levels, individually, were not associated with the risk of AD or MCI. However, a low ratio of amyloid beta protein42 (Abeta42) to 40 (Abeta 40) in plasma levels was associated with an increased risk of developing MCI and AD. Those with ratios of Abeta42/Abeta40 in the lowest quartile were more than 3 times as likely to progress to MCI or AD in comparison to those in the highest quartile.

Graff-Radford et al., Arch. Neurol., 64(3), 354-62, 2007.

Number of People with Alzheimer's in the U.S. Reaches 5 Million

According to a new report by the Alzheimer's Association, more than 5 million people in the United States have Alzheimer's disease (AD), an increase from 4.5 million. This number is expected to rise with the aging of the population. The report also said that annually, there were 400,000 new cases of Alzheimer's each year. The report also mentioned that in 2005, Medicare spent \$91 billion on beneficiaries with Alzheimer's and other dementias. This number is projected to double to \$189 billion by 2015. New treatments and diagnostic tools will help ease the economic burden of this debilitating disease.

The full report can be found at: http://www.alz.org/national/documents/Report_2007FactsAndFigures.pdf

Cholinesterase Inhibitors May Help Manage Behavioral and Psychological Symptoms of Dementia

Cholinesterase inhibitors may be helpful in the management of behavioral and psychological symptoms of dementia (BPSD). Depression, anxiety, delusions and agitation are some of the symptoms of BPSD. Psychotropic medications including antipsychotic, antidepressants, and hypnotics are currently used to treat these symptoms. However, cholinesterase inhibitors, which prevent the breakdown of neurotransmitter acetylcholine, may also help manage symptoms of BPSD, enabling physicians to reduce or stop use of psychotropic drugs.

Mohad Shamsi, MD, a resident in psychiatry at the University of Missouri in Columbia, conducted a retrospective chart study and compared two groups diagnosed with dementia. The first group (n=62) took cholinesterase inhibitors, while the other group (n=62) did not. Those who did not take cholinesterase inhibitors were twice as likely to have a prescription for psychotropic drugs. 61.3% of patients in the cholinesterase inhibitor group were not taking psychotropic drugs, while 62.9% of those not on cholinesterase inhibitors were taking other psychotropic drugs. This initial study did not examine doses, compliance issues, severity of symptoms, or specific psychotropics.

Study presented at American Association of Geriatric Psychiatry 2007 Annual Meeting: Abstract 49

Imaging Compound May Detect Amyloid Beta

A case study of a 76 year old man recently published in the Archives of Neurology confirms that PET imaging with a compound called Pittsburgh Compound B (PiB) can detect amyloid-beta in living patients. The subject was diagnosed with dementia with Lewy bodies. The patient underwent PET imaging with PiB three months before his death. The PET with PiB imaging revealed amyloid-beta in certain regions of the brain. The presence of amyloid-beta was confirmed by autopsy. The case study was published by Dr. John Growdon of Massachusetts General Hospital in Boston.

Bacsikai et al., Arch. Neurol., 64(3):431-4, 2007.

High Adiposity Linked With Increased Risk for Dementia

Dr. Jose A. Luchsinger and colleagues from Columbia University College of Physicians and Surgeons in New York studied the link between adiposity and dementia. In the study, adiposity measured by body mass index (BMI), waist circumference, and weight change was associated with dementia, probable Alzheimer disease (AD), and dementia associated with stroke (DAS). The researchers followed 893 subjects with BMI data, 907 with waist circumference data and 709 with a second weight measurement. At baseline, none of the subjects had dementia. After 5 years, 181 had incident dementia, 112 had Alzheimer's disease, 53 had DAS. The mean patient age was 77 years.

When compared to the first quartile of BMI group, the third BMI quartile had lower dementia and AD risk, while the second BMI quartile group had a lower DAS risk. The association between BMI and dementia resembled a U-shape in those younger than 76 years, while dementia risk decreased with higher BMI in those 76 years and older. The fourth quartile of waist circumference was related to a higher DAS risk in the whole sample, and to dementia and AD in persons younger than 76 years. Weight loss was related to a higher dementia and DAS risk, and weight gain was related to a higher DAS risk only.

These results show that an association between adiposity and dementia differs depending on the anthropometric measure used, and is modified by age, and would explain why there are various conflicting reports.

Luchsinger et al., Arch. Neurol., 64(3), 392-8, 2007.

Some Drugs Prescribed for Alzheimer's May Contribute to Deterioration in Patients

In Alzheimer's patients, cholinesterase inhibitors slow deterioration while antipsychotics and benzodiazepines tend to increase the rate of deterioration. Dr. J. Ellul and colleagues from the University of Patras, Greece, followed a community cohort of 224 patients with a mean age of 82.3 years with a diagnosis of probable Alzheimer's disease. The drugs used by each patient were recorded during the initial assessment and logistic regression was used to correlate disease progression with drug usage. The Global Deterioration Scale was used to measure disease progression and the subjects were followed for 12 months.

34 subjects (15%) were taking antipsychotics, 54 (24%) were taking antidepressants and 30 (13%) were taking benzodiazepines or benzodiazepine-related drugs. Those in advanced stages of the disease were more likely to be prescribed antipsychotics, tricyclic antidepressants, hypnotics or anxiolytics. 97 patients (39%) were taking drugs for dementia, one was taking Vitamin E, and 20 were taking vitamin B12 or folic acid.

Risk of deterioration was significantly higher among patients who were taking antipsychotics or sedatives compared with those who were not. Patients taking both antipsychotics and sedatives had an even higher risk of rapid deterioration. Those taking cholinesterase inhibitors or NMDA antagonists had a significantly lower risk of rapid deterioration

Ellul et al., J. Neurol Neurosurg Psychiatry, 78(3), 233-9, 2007.

Study Highlights the Link Between AD and Cardiovascular Risk Factors

A study led by Dr. Jan A. Staessen University of Leuven in Belgium reviewed the role of hypertension as a reversible risk factor in development of Alzheimer's disease (AD). A strong association between AD and cardiovascular risk factors and atherosclerosis were established. The researchers concluded that hypertension is an important risk factor for AD

Staessen et al., Hypertension, 49, 389-400, 2007.

Scientists Identify Possible Therapeutic Target for Alzheimer's

Paul Greengard, MD and colleagues at Rockefeller University in New York found that protein casein kinase 1 (CK1) may represent a therapeutic target for the prevention of beta-amyloid production, associated with Alzheimer's disease (AD).

AD is associated with accumulation of amyloid-beta (A β) produced by sequential cleavage of amyloid precursor protein (APP) by the aspartyl protease beta-secretase and the presenilin-dependent protease gamma-secretase. An increase of CK1 expression has been reported in the human AD brain.

Research, using in silico analysis, has shown that APP, beta-secretase, and gamma-secretase subunits contain, in their intracellular regions, multiple CK1 consensus phosphorylation sites. Many of these are conserved among human, rat, and mouse species. Overexpression of constitutively active CK1epsilon, one of the CK1 isoforms expressed in the brain, leads to an increase in A β peptide production. Conversely, three structurally dissimilar CK1-specific inhibitors significantly reduced endogenous A β peptide production.

By using mammalian cells expressing the beta C-terminal fragment of APP, researchers demonstrated that CK1 inhibitors act at the level of gamma-secretase cleavage. Importantly, notch cleavage was not affected.

The results of this study suggest that CK1 may possibly be used as a therapeutic target for the prevention of A β formation in AD.

Flajet et al., PNAS, 104(10), 4159-64, 2007.

Simvastatin May Reduce Risk of Alzheimer's and Parkinson's

Dr. Benjamin Wolozin, professor of pharmacology at Boston University and colleagues evaluated the incidence of Alzheimer's disease (AD) among patients taking statins. They found that use of Simvastatin for at least 7 months reduced incidence of AD by 30% and Parkinson's disease by 24%. Additionally, in people who did not have hypertension, Simvastatin reduced incidence of AD by 76% and Parkinson's disease by 65%. The researchers analyzed data from Department of Veterans Affairs pharmaceutical database which includes 4.5 million patients and more than 110 million annual medication prescriptions. Excluded from the study were individuals under the age of 65 or those with a pre-existing diagnosis of AD. Simvastatin was the only statin found to lower incidence of Alzheimer's Disease.

Presented at the annual meeting of the Society of Neuroscience



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