ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Is there a relationship between hypertension and cognitive function in older adults?

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Midlife hypertension is associated with impaired cognition and dementia later

A: Yes. There is also evidence suggesting that treatment of chronic hypertension can reduce cognitive decline later in life and even decrease the incidence of dementia due to Alzheimer disease.

EPIDEMIOLOGY

The incidence of both hypertension and Alzheimer disease increases with age.

The rise of hypertension in the population precedes that of dementia by about 30 years. The prevalence of hypertension increases rapidly between the ages of 30 and 50, then slowly after age 60.[1]

The prevalence of Alzheimer disease is very low before age 60, but increases rapidly after age 75.[2]

However, the relationship between blood pressure and dementia is not linear. Blood pressure may become lower and more variable at the time of clinical manifestation of dementia. This finding has been described in persons with established Alzheimer disease and other types of dementia, such as vascular dementia.[3,4]

PROPOSED PATHOPHYSIOLOGY

The influence of long-standing hypertension in middle age on cognition late in life may be multifactorial.

Hypertension is associated with cerebrovascular disease, which is in turn associated with dementia. For example, multiple small strokes or one unfortunately situated stroke can result in vascular dementia.

Stroke may also affect the course of Alzheimer disease, which is more common in the United States than vascular dementia. Clinical manifestations of Alzheimer disease may be accelerated by cerebral infarcts. For instance, subjects in the Nun Study[5] who met the neuropathologic criteria for Alzheimer disease and had brain infarcts had poorer cognitive function and a higher prevalence of dementia than those without infarcts. Subjects with lacunar infarcts in the basal ganglia, thalamus, or deep white matter had an especially high prevalence of dementia.

Abnormalities in cerebral autoregulation seen in chronic hypertension may impair perfusion, causing impairments in psychomotor function, attention, short-term and long-term memory, and speed of responses.

There may be one or more genetic links, such as the gene for apolipoprotein E4, associated with both cardiovascular disease and Alzheimer disease.

OBSERVATIONAL STUDIES AND COGNITION

Several large observational studies demonstrated a strong relationship between long-standing hypertension and cognitive impairment, especially with untreated hypertension (TABLE 1).[6–13] In the Framingham cohort, the relationship was even stronger in diabetic persons with hypertension.[7]

However, the relationship between blood pressure and cognition is complex.[8,9] Blood pressure may decrease to low or normal levels before Alzheimer disease becomes clinically manifest.[14] Studies suggest that this decrease may be a dysregulation resulting from dementia, although a causal relationship cannot be excluded.

There may also be an association between blood pressure variability in hypertensive

TABLE 1

Hypertension and risk of cognitive impairment or dementia: Large prospective cohort studies

STUDY*	NO.	AVERAGE AGE AT STUDY ONSET (YEARS)	DURATION (YEARS)	FINDINGS
LPS[6]	382	70	15	Increased risk of dementia at age 79–85 with high SBP at age 70 or high DBP at age 70 or 75
FHS[7]	1,811	67	28–30	Increased risk for falling below 25th percentile on immediate and delayed memory and word fluency with DBP > 90 mm Hg Subgroup with diabetes had even higher risk
EPESE[8]	3,657	74	6–15	15% more errors in the SPMSQ if SBP > 160 mm Hg compared with SBP 130–139 mm Hg Suggestion of U-shaped association of errors with lowest blood pressure
EPESE subset with Alzheimer disease[9]	634	72	6–15	No association of Alzheimer disease with hypertension 13 years before diagnosis Inverse association of Alzheimer disease with SBP 4 years before diagnosis Inverse association of Alzheimer disease with pulse pressure 4 years before diagnosis
Hisayama[10]	828	74	7	Elevated SBP was an independent predictor of vascular dementia but not Alzheimer disease
Honolulu-Asian[11]	3,735	53	23–28	5% increased risk of cognitive impairment for every 10 mm Hg increase in SBP
Western Collaborative[12]	717	45	38	Decreased verbal memory in those with persistent hypertension throughout the study
Twin Study[13]	392	47	25	Subgroup with highest midlife SBP had largest decline in psychomotor speed and smallest increase in verbal fluency over 10 years This group also had decreased brain volume and increased white matter hyperintensities on MRI

*LPS = Longitudinal Population Study in Göteborg, FHS = Framingham Heart Study, EPESE = Established Populations for the Epidemiologic Study of the Elderly, SPMSQ = Short Portable Mental State Questionnaire, SBP = systolic blood pressure, DBP = diastolic blood pressure, MRI = magnetic resonance imaging

patients and impaired cognition. In an extension of the Systolic Hypertension in Europe (Syst-Eur) study in older people,[15] blood pressure variability at baseline was positively correlated with the incidence of dementia during the study. This variability may reflect central nervous system dysregulation or occult injury to the prefrontal autonomic centers, occurring just before the clinical manifestation of dementia.

DOES TREATING HYPERTENSION PREVENT DEMENTIA?

Secondary analyses of two major studies of hypertension in older adults evaluated the risk of dementia in the groups receiving active treatment and placebo.

In the Syst-Eur study,[16] 21 new cases of dementia were found in the 1,180 patients in the placebo group, vs 11 cases in the 1,238

patients receiving the calcium channel blocker nitrendipine, a statistically significant 50% difference. The investigators calculated that treating 53 people for 5 years would prevent 1 case of dementia. Of the incident cases of dementia, 23 were Alzheimer disease, 2 were vascular dementia, and the other 7 were felt to be a mixed dementia.

On the other hand, in the Systolic Hypertension in the Elderly (SHEP) study,[17] no difference in the incidence of dementia was found between the groups receiving the diuretic chlorthalidone (1.6%) and placebo (1.9%).

The difference in findings between these two major studies raises the question of whether the effect on cognitive outcome depends on the drug, or perhaps on the differences in the risk factors between subject populations in the two studies. Interestingly, in a prospective but nonrandomized study of 1,301 hypertensive adults older than 75 years,[18] those receiving diuretic monotherapy had a 40% lower incidence of dementia over 3 to 5 years compared with those receiving no treatment.

The relationship between hypertension treatment and incidence of dementia may be clarified further when the results of the SCOPE trial (Study on Cognition and Prognosis in the Elderly) become available. The study is comparing an angiotensin-receptor blocker with placebo.[19]

RECOMMENDATIONS

- Consider treating chronic hypertension in older adults, not only to prevent cardiovascular and cerebrovascular disease, but also for the possible cognitive benefits.
- The goal for treatment of chronic hypertension in a person without diabetes is 140/90 mm Hg, according to guidelines from the sixth Joint National Committee (JNC VI).[20] For people with diabetes, the goal is 130/85 mm Hg.
- Neither the optimum target blood pressure nor the drug of choice once dementia is diagnosed is known. The JNC VI criteria remain appropriate guidelines for elderly as well as middle-aged adults.

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