Hypertension and Cognitive Function

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Abstract

Persistent hypertension is a modifiable risk factor for stroke, cognitive impairment, and dementia. Cognitive impairment and dementia may be due to acute or recurrent strokes secondary to hypertension or due to chronic structural changes in the brain induced by chronic hypertension.

Key words: Hypertension, cognitive, dementia.

Introduction

Hypertension is known to damage many organs in the body, including the brain. Persistent hypertension is a modifiable risk factor for stroke, cognitive impairment, and dementia. Hypertension is linked to the development of both vascular dementia and Alzheimer’s disease (AD), which are the two most common forms of dementia. Cognitive impairment and dementia may be due to acute or recurrent strokes secondary to hypertension or due to chronic structural changes in the brain induced by chronic hypertension.

Observational Studies

Several long-term observational studies have provided strong evidence for a relationship between hypertension and cognitive dysfunction.[1-4] A study of 1301 persons aged 75 years or more without dementia who were followed up for 3 years showed that the incidence of dementia reduced by 30% in persons with hypertension who were treated with antihypertensive drugs.[1] In a French study of persons aged 59–71 years, the risk of cognitive impairment was increased 2.8 times at 4-year assessment in persons with hypertension.[2] A community-based study of persons with a mean age of 72 years showed poorer cognitive function associated with increased blood pressure (BP) variability.[4] In the Rotterdam study, 7046 elderly persons who were free of dementia at baseline were followed for about 2 years. The incidence of dementia decreased by 24% in persons on antihypertensive drug therapy, vascular dementia risk decreased by 30%, and AD decreased by 13%.[5]

A few studies showed a strong association between midlife hypertension and cognitive impairment and dementia.[6-11] Executive function and processing speed were the cognitive domains more affected, whereas memory was less affected. As far as late-life BP was concerned, the risk of dementia increased only with extremes of BP.[12] A couple of recent studies yielded further evidence for an association between midlife systolic hypertension and cognitive impairment two decades later.[13,14]

Supportive Evidence

Neuroimaging and autopsy studies which have looked at the relationship between BP and cognitive dysfunction provide further evidence. Magnetic resonance imaging showing cerebrovascular disease and atrophy, quantitative analysis of Aβ deposition on positron-emission tomography, and autopsy studies of pathological correlates of dementia constitute this evidence.

Hypertension is the main risk factor for chronic ischemic white matter lesions in the brain, which are associated with cognitive dysfunction.[13] Radiological studies using magnetic resonance imaging have shown 2.3–3.4 times higher incidence of ischemic white matter lesions in persons with hypertension.[16]

A meta-analysis showed that higher BP levels are associated with smaller total, cortical, and hippocampal brain volumes,
regardless of treatment with antihypertensives. There is also evidence linking BP and AD pathology. The deposition of vascular Aβ leading to cerebral amyloid angiopathy is a risk factor for AD, microhemorrhages, macrohemorrhages, microinfarction, and vascular cognitive dysfunction. Positron-emission tomography studies have shown that the extent of Aβ deposition in the brain positively correlates with higher pulse pressure and higher systolic and diastolic BP. Autopsy studies have shown evidence of neurofibrillary tangles and neuritic Aβ plaques, typical of AD pathology, in the brains of hypertensive older adults.

**Randomized Controlled Trials**

Many randomized controlled trials have provided evidence that treatment of hypertension reduces the incidence of stroke. However, randomized controlled trials that studied the role of antihypertensive treatment in preventing dementia have yielded mixed results. While some studies showed a benefit of antihypertensive therapy in reducing incidence of dementia, others failed to do so. The Systolic Hypertension in Europe trial, Perindopril Protection Against Recurrent Stroke Study, and Heart Outcomes Prevention Evaluation study all showed decrease in the incidence of dementia, whereas the Systolic Hypertension in the Elderly Program and the Hypertension in the Very Elderly Trial showed insignificant improvement in cognitive dysfunction.

Possible explanations for the negative results could include methodological issues. Many of these studies did not have prevention of cognitive dysfunction as a primary endpoint and looked at cognitive dysfunction among secondary end points. Consequently, appropriate parameters were not considered when assessing cognitive functions. Most studies have not considered the duration of hypertension, which is thought to be a more important risk factor than age itself. A recent study demonstrated that midlife hypertension modifies the relationship between late-life hypertension and brain function. In persons without midlife hypertension, higher systolic and diastolic BPs in late life were associated with cerebral small vessel disease, whereas in persons with midlife hypertension, lower late-life diastolic BP was associated with more atrophy and cognitive dysfunction. Another reason could be the non-inclusion of dementia biomarkers. It is known in AD that tau and Aβ biomarkers precede the onset of clinical features of dementia by several years. The effect of individual antihypertensives also needs to be considered. The beneficial effects on cognition were found to be highest for the angiotensin receptor blockers, followed by calcium channel blockers, beta-blockers, diuretics, and angiotensin-converting enzyme inhibitors (ACEIs).

The Systolic BP Intervention Trial (SPRINT) focused on the effect of intensive (systolic BP <120 mmHg) versus standard (systolic BP <140 mmHg) BP control on cardiovascular outcome. The trial was stopped early because of the cardiovascular benefit, but collection of data on cognitive functions in persons aged 75 years or more was continued as the SPRINT MIND study which was presented at the Alzheimer’s Association International Conference. Lowering systolic BP to a target of 120 mmHg or less in people with cardiovascular risk factors reduced the risk of primary end point, probably all-cause dementia by 17% which was not statistically significant. However, it reduced the risk of secondary end points of mild cognitive impairment (MCI) by a statistically significant 19% and combined secondary endpoint of MCI and probable dementia by a significant 15%.

The imaging part of the study of 454 subjects had brain MRI at baseline and 4 years later. Although there was no change in total brain volume, those receiving intensive BP lowering had 18% lower white matter lesion load than those in the standard care group, statistically a significant reduction.

Animal studies have shown that angiotensin II type 1 receptor blockers (ARBs) and ACEIs reduce the amount of AD-like pathology and improve cognitive performance in most mouse models of AD. This beneficial effect seen in animal studies is supported in secondary outcomes of clinical trials of various ARBs and ACEIs, as well as in epidemiological studies where the prevalence of AD was reduced.

**Conclusion**

The available evidence suggests that hypertension is strongly associated with cognitive impairment and dementia. Midlife hypertension and duration of hypertension correlate better with cognitive dysfunction in later life. While there is enough evidence to show that hypertension is associated with vascular dysfunction, cerebrovascular disease, and Aβ deposition, there is a lack of consistent data from randomized controlled clinical studies evaluating the effect of lowering BP on dementia.

**References**


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How to cite this article: Murgod U. Hypertension and Cognitive Function. Hypertens 2018;4(3):154-156.

Source of support: Nil
Conflict of interest: None