Antihypertensive Therapy and Cognition
More Questions Than Answers
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A
n article in this issue of *Stroke* by Peila et al., that duration of antihypertensive therapy seems to correlate with a reduced risk for both dementia and nondementing cognitive decline in elderly men, revisits a number of tantalizing questions, some of which are specifically mentioned by the authors and some not. What, pathophysiologically, is subsumed under the term “vascular dementia”? Can hypertension impair cognition by causing small vessel disease and widespread microinfarction in the absence of clinical stroke? Is such a process reflected in cerebral white matter hyperintensities on MRI? How specific are such abnormal signals for microvascular disease, and to what degree do they correlate with cognitive decline? Can hypertension damage neurons independently of vasculopathy? Does vasculopathy contribute to Alzheimer disease? Is hypertension a risk factor for Alzheimer disease or does it simply add to the cognitive decline by superimposing microvascular lesions? Might certain antihypertensive drugs protect against dementia by mechanisms other than blood pressure–lowering?

Peila et al’s 848 subjects, from the Honolulu-Heart Program/Honolulu-Asia Aging Study, had a mean age of 77 years and had been hypertensive from midlife. Some had never been treated; others had been treated, variably, from <5 years to >12 years. Dementia-free at baseline cognitive assessment, they were periodically reassessed for up to 7 years. Four hundred and forty-six normotensives served as controls. During follow-up 108 subjects became demented, 65 with Alzheimer disease, 19 with vascular dementia, and 24 with dementia from other causes.

For each year of antihypertensive treatment there was a 3% reduction in the risk for dementia, including both Alzheimer disease and vascular dementia. Treatment was also associated with reduction in cognitive decline short of dementia. As might be expected, the benefit of longer duration treatment was most evident in those whose blood pressure was best controlled. On the other hand, longer duration of treatment also produced benefit among those with “noncontrolled” blood pressure, suggesting a nonantihypertensive drug effect.

The medications used were not identified and undoubtedly varied from subject to subject and for some were changed during many years of treatment. Moreover, MRI imaging was not performed, and so whether dementia or cognitive decline was associated with white matter signals is unknown. Finally, as the authors acknowledge, definitively determining whether treating hypertension in the elderly reduces the risk of dementia or cognitive decline would require a prospective, randomized controlled trial, yet widespread agreement that antihypertensive therapy is indicated in such persons makes it unlikely that such a study can be performed.

Reference

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