Extended Abstract Journal of Alzheimer's & Dementia 2021
Vol.4 No.2

Dementia-2014: Common risk factors for Alzheimer's disease and vascular dementia

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Epidemiological studies disclosed that there are common risk factors in Alzheimer's disease (AD) and vascular dementia (VaD). Theycan be classified into 4 major categories: Demographic, genetic, vascular and comorbidity risk factors. The demographic risk factor includes gender, age, past history, years in educational and occupational attainment. Male gender is a risk for VaD and stroke, whereas female gender is known as a risk factor for AD. The genetic factors for VaD may include such familial VaD as CADASIL. ApoE? 4 are known to be the possible common genetic factor for both VaD and AD. The lifestyle risk factors turn out to be obesity, lack of physical activity, cigarette smoking, excessive alcohol intake, and certain psychosocial factors. The vascular risk factors encompass hypertension in midlife, hypotension in late life, diabetes mellitus, dyslipidemia, congestive heart failure, myocardial infarction, arrhythmia, and chronic kidney disease. It is suggested that effective management of these vascular risk factors may prevent onset of dementia and cognitive decline. Randomized placebocontrolled trials of antihypertensive drugs showed that antihypertensive therapy may reduce the risk of VaD as well as AD. Low cardiac output due to hypotension and/or congestive heart failure has been regarded as a risk factor for cognitive impairment and dementia especially in elderlypatients whose autoregulation of cerebral blood flow is impaired. Although further research is needed, those evidences may support a rationale for the efficacious management of vascular risk factors in the prevention of VaD as well as AD.

Alzheimer disease (AD) and vascular cognitive impairment (VCI) are estimated to be the number one and two leading causes of irreversible cognitive impairment of late life, respectively. VCI is a relatively new nosological term that takes into account the spectrum of severity of cognitive impairment associated with vascular disease (eg, mild, moderate, and severe, or the full-blown state called vascular dementia); the underlying pathophysiological mechanism (eg, subcortical ischemic vascular disease, amyloid angiopathy, cortical infarction, etc.); and the potential for intervention and prevention based on the pathophysiological mechanism of the "brain-at-risk" stage. Because both AD and stroke show an exponential increase in frequency with age, AD and VCI may coexist as a mixed form of cognitive impairment or the existence of stroke may unmask or potentiate AD.4,5 It has been hypothesized that there may be a synergism between AD and stroke pathogenic mechanisms.6 Cerebral ischemia and amyloid may synergize to produce AD and vascular changes in the brain. Furthermore, an angiogenesis hypothesis has been proposed, which links the two pathophysiological processes. However, in a recently published neuropathological study, cerebral infarctions were shown to independently contribute to the likelihood of dementia but did not interact with AD pathology to increase the likelihood of dementia beyond their additive effect.

It has become apparent that AD might be a heterogeneous disorder now that vascular risk factors and atherosclerosis have been associated with AD. Whether this link represents a toxic effect of vascular factors on the microvasculature of susceptible brain regions, some other process, or that atherosclerosis and AD are independent but convergent disease processes remains uncertain. The treatment of one of the important atherosclerotic vascular risk factors, hypertension, has been shown to reduce the risk of dementia including AD or vascular and mixed dementias.11 Furthermore, some major midlife vascular risk factors have been linked to cognitive impairment later in life. In this paper we will review the status of risk factors for VCI and AD and the evidence for the borderland of shared vascular risk factors that may be important for prevention efforts.

In comparison to AD, VCI has been relatively understudied. Problems with operationally defining VCI, proving that AD was not the dominant form of cognitive impairment in an elderly patient with stroke, and a shift of interest and resources to the study of AD have been some of the problems that have plagued the field of VCI. It has been assumed that risk factors for VCI would be the same as those for stroke.

In the US and Europe, AD is the most common form of irreversible dementia of late life. It is estimated that the prevalence is around 1.5% at age 65 years and doubles every 4 years to reach about 30% at age 80 years. The incidence of AD increases with age and is about 1% per year but may be lower in men and in persons of African and Asian descent. However, it has been reported that VCI may be more prevalent than AD in some Asian countries.

Vascular risk factors have measurable negative effects on the brain and our cognitive abilities. Hypertension, for example, may be associated with larger volume of brain white matter disease, smaller brain volumes, silent or strategically-placed subcortical or cortical infarcts, and loss of brain volume in structures such as the thalamus or temporal lobe that are important to cognition. Not only has the vascular burden of risk factors been associated with brain changes, but it has also been associated with performance decrements in multiple cognitive domains. There are a number of traditional vascular risk factors, as discussed in the above sections, to target for prevention or treatment of cognitive impairment.1 In addition, new avenues are opening in such areas as interventions for brain insulin receptors,36 statin therapy, dietary interventions, and lowering of serum homocysteine. Interventions in midlife may provide an important window of opportunity to preserve cognitive vitality later in life. We are well positioned to develop and test hypotheses in large-scale randomized controlled trials to reduce the burden of AD and VCI, the most common forms of cognitive impairment.

Foot Note: This work is partly presented at 2nd International Conference on Alzheimer 's disease and Dementia, September 23-25, 2014 Valencia Convention Centre, Spain