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No Sex Differences Observed in Absorption of Vitamins and Polyphenols for Alzheimer's Disease Prevention

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ABSTRACT

It is estimated that 11 million deaths per year are attributed to suboptimal diets and dietary factors that contribute to several diseases, including hypertension, cancer, stroke, Alzheimer's disease (AD), and diabetes. Many clinical institutions have investigated the importance of proper nutrition for the prevention and intervention of these common diseases. As a result, fundamental principles and new concepts in nutrition and the complex relationship between dietary intake and disease prevention are beginning to emerge. In this article, we explain the preventive effects of AD through the intake of vitamins and polyphenols, as well as some unknown points.

Dr. Kishida et al.'s findings suggested that the dietary intake of fruits, vegetables, and vitamin C may reduce the risk of cognitive impairments in both men and women (1). In order to obtain evidence regarding the potential mechanisms, they investigated whether the intake of antioxidant vitamins (i.e., α-carotene, β-carotene, and vitamin C) from consuming fruits and vegetables was related to the risk of dementia (2). Thus, it was concluded that fruit and vegetable intake and the dietary intake of vitamin C may reduce the risk of disabling dementia among males and females (1).

KEYWORDS: *Vitamin C, vitamin E, antioxidant vitamin, Apolipoprotein E, KDM6A.*

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Molecular biological analyzes are also being conducted to elucidate the involvement of vitamin C intake in the pathogenesis of AD. Apolipoprotein E (ApoE), a protein involved in lipid metabolism in the central nervous system, is classified into three genetic types, E2, E3, and E4. Based on the results of clinical research to date, in particular, it has been shown that people who express the ApoE4 gene are more likely to develop AD (3). Moreover, the clinical study of Dr. Noguchi-Shinohara M in 2018 included men and women who were divided into three groups to analyze the blood levels of vitamins C and E (low, intermediate, and high) and their relationship with cognitive function (3). It was found that women with the highest blood vitamin C levels who expressed the ApoE4 gene had a reduced risk of cognitive decline of 0.10 (odds ratio) compared with women with the lowest blood vitamin C levels (3). However, it was observed that men with the highest blood vitamin E levels who did not express the apoE4 gene had a reduced risk of cognitive decline of 0.19 (odds ratio) compared with men with the lowest blood vitamin E levels (3). Based on these findings, it was concluded that for women with ApoE4 who are at a high risk of future cognitive decline, high vitamin C intake may reduce the risk of cognitive decline. These results are consistent with those of Dr. Kishida et al.

In addition, Dr. Hou and his colleagues reported associations between other dietary factors and the onset of AD. Moreover, based on the results of their clinical study, Dr. Hou et al. suggested that increased coffee and tea intake may reduce the risk of developing AD and vascular dementia (VaD). Their findings also revealed differences in the risk of developing AD and VaD depending on gender and the presence of underlying vascular diseases, such as hypertension, dyslipidemia, and diabetes (4). The research conducted by Dr. Abbel et al. also reported an association between brewed coffee intake and an increased risk of AD, which was observed only in participants who were non-ApoE4 carriers (5).

Alzheimer's Society in the UK emphasized that the physiologically active compounds contained in coffee, such as caffeine and polyphenols, may have a preventive effect on mild cognitive impairment and dementia caused by coffee consumption. A clinical study conducted by the University of South Florida in the United States and other institutions also found that among elderly people aged 65 to 88, those who did not develop dementia had a twofold increase in the caffeine level in their blood compared with those who developed dementia. Furthermore, caffeine and polyphenols have been shown to exhibit antioxidative effects.

The results of these clinical studies indicate that the intake of vitamins C and E and polyphenols may be associated with the risk of AD. However, significant sex differences in the effects of these compounds on AD were observed. Vitamin C is absorbed in the digestive tract and transported into the bloodstream. The concentration of vitamin C in the plasma reaches its peak of 1.5 to 3 hours after ingestion, and, subsequently, vitamin C is excreted in the urine and gradually decreases. Furthermore, it has been reported that 90% of ascorbic acid ingested through food is absorbed up to about 200 mg/day, but when the intake exceeds 1,000 mg/day, the absorption rate decreases to less than 50%. However, as far as we know, sex differences in gastrointestinal vitamin absorption have not been reported. While AD is more prevalent in women, men are at a higher risk of dying after developing the disease. It has been reported that the histone demethylase; Lysine Demethylase 6A (KDM6A) may be involved in this sex difference (6). Normally, one of the two X chromosomes that females possess is not activated. However, despite being an X-chromosome gene, KDM6A is not subject to inactivation and is highly expressed in the female brain (6). Furthermore, genetic polymorphisms that increase the expression of KDM6A in humans have been found to hinder the progression of Alzheimer's disease (6).

Clear gender differences have been observed in the preventive effects of vitamin C and polyphenols against the onset of Alzheimer's disease. However, no gender differences have been observed in the absorption of vitamins and polyphenols into the body. Therefore, vitamins and polyphenols may indirectly affect the activity of factors that directly act to prevent the onset of Alzheimer's disease. Based on the results of these studies, the onset of various diseases is thought to be caused by a combination of factors such as inappropriate eating habits and dietary factors, individual genetic background, and sex hormones.

Disclosure

The authors declare no potential conflicts of interest. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Data Availability Statement: The data are available and publicly available on various websites. Details are provided in the first paragraph of the Results section. Information from this clinical study and the associated transparency statement in the medical journal article are available online.

https://kyoto.hosp.go.jp/html/guide/medicalinfo/clinical research/expand/gan.html (accessed on 15 March 2025).

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