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Assessment of Dietary Antioxidants Intake in Relation to Dementia

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Abstract: *Background: The generation of oxygen free radicals is involved in the pathogenesis of dementia.The purpose of this study is to find out if there is a link between the dietary intake of antioxidants (vitaminE, vitaminC, β-carotene and selenium) and risk of dementia. Methods: In this study we used an age and sex matched case control method, consisting of 120 men and women of 50 years (± 2) of age and older. Data were collected at 'Iran Alzheimer Association', Tehran, in 2013. The experimental cases (with dementia) and controls (normal) (n = 60) were randomly selected. Dietary data were collected using food frequency and 24-hour recall questionnaire and analyzed using the food processor Nutritionist IV. The SPSS version 19.0 for Windows software program, was used for all statistical. Logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence interval (CI) for dietary intake of antioxidants and risk of dementia. Results: The mean intake of antioxidants from food sources, before adjustment and After adjustment for confounfing factors, was significantly lower among dementia patients; There was observed no differences in risk of dementia by decreasing of antioxidants intake. Conclusions: The findings of this study suggest no link between lower level of antioxidants intake (vitamin E, vitamin C, β-carotene and selenium) from food sources and risk of dementia. Maintaining a high level of these antioxidants through the consumption of specific foods is a viable option to prevent dementia occurrence and progression.*

Keywords: *Dementia, VitaminE, VitaminC, β-carotene, Selenium, Dietary*

INTRODUCTION

According to the World Alzheimer Report, there were 35.6 million people living with dementia worldwide in 2010, a number that will increase to 115.4 million by 2050 unless effective means of reducing disease incidence are found (Association, 2013). Reactive oxygen species (ROSs) are generated in the body as a consequence of cellular metabolism and are involved in many physiological functions, such as vasodilatation and cellular proliferation (Lester, Manfred and Enrique, 2010).

Since ROSs are potent oxidant compounds, they must be maintained within a certain range to avoid the oxidation of biomolecules, including DNA, lipids, and proteins, which leads to cell damage and death (Lester, Manfred and Enrique, 2010). Although organisms are endowed with protective mechanisms to prevent

oxidative damage, certain situations can shift the oxidant/antioxidant balance toward ROS production, known as oxidative stress. In brain aging, oxidative stress is increased, and this may contribute to the onset and progression of neurodegenerative disorders, such as dementia and AD (Zhu et al., 2007; Smith et al., 2010).
Much support for the role of oxidative stress in the etiology of Alzheimer's disease and vascular dementia has emerged from the identification of several potential neurodegenerative mechanisms in experimental and clinical studies (Danielle et al., 2004). Consequently, the effects of intake of antioxidants, including carotenoids (beta-carotene), ascorbic acid (vitamin C), tocopherols (vitamin E) and selenium, in the prevention of cognitive impairment and dementia have been investigated in a number of studies, To date the evidence is inconsistent (Wengreen et al., 2007; Danielle et al., 2004; Luchsinger et al., 2003; Laurin and Masaki, 2002). The hypothesis that antioxidant nutrients in the human diet may protect against the degenerative disease of aging, has become popular in recent years.

Objectives

It is of interest to study the examination of associations between dietary intake of antioxidant nutrients from food sources and risk of dementia among men and women 50 years and older of Iran Alzheimer Association members.

Materials and Methods

In this study, 60 Cases of histologically confirmed dementia and 60 healthy subjects (controls) from the healthy participants in accordance to the Aging Survey of the Alzheimer's Association were selected. They were of 50 years of age and older; according to the inclusion criteria were randomly selected from Iranian Alzheimer Association (in 2013). The subjects were matched based on their age and sex. The study inclusion criteria was:1) age range 50 years and older, 2) diagnosis of dementia, 3) lack of any diet and, 4) absence of neurologic disease or other medical conditions that might affect the cognitive functions such as acquired immunodeficiency syndrome, epilepsy, brain trauma, neoplasms, and cerebrovascular disease and 4) no use of antioxidative supplements. Baseline interviews included self report of demographic variables, medical history, as well as information about their usual dietary intake. For the dementia patients group data was collected through patient's relatives interviews, including their families and caregivers.

Diagnosis of dementia

After baseline assessment, Dementia diagnosis were obtained via neuropsychologist through clinical evaluations and cognitive function tests (Abbreviated Mental Test Score (0-6 score), Mini Mental State Examination (0-24 score) and Alzheimer's Disease Assessment Scale-Cognitive Subscale (30-70 score).

Dietary Assessments

Dietary data were collected using food frequency questionnaires that included major food sources of vitaminE, vitaminC, ß-carotene, selenium and 24-hour food recall questionnaire. Participants were asked to report the frequency of consumption of each food item. To calculate intake of a these nutrients, the nutrient content of each food was multiplied by the frequency of consumption of it and then summed over all food items. The food processor nutrition analysis program was used (Nutritionist IV). Nutrients intake was adjusted for total energy intake using analysis of Covariance models (ANCOVA).

Confounder Factors Assessment

Nondietary variables were collected at participants baseline in interview and included the followings: diabetes mellitus (self reported history of disease or antidiabetic medication use), heart disease (self reported history of myocardial infraction or digitalis use or angina pectoris), hypertension (self reported history or blood pressure ≥ 120 mm Hg systolic or ≥ 85 mmHg diastolic or use of antihypertensive medications), stroke (self-reported history), cigarette smoking (self-reported history /ever or never), depression (self repoted history), alcohol consumption (self repoted history). Information on medications was based on interview inspection.

Statistical Analysis

The SPSS version 19.0 for Windows software program, was used for all statistical analysis. Mean, percentage, and mean ± standard deviation were provided as descriptive statistics. In order to compare dementia patients and healthy subjects, chi-square test was used for qualitative variables; even so, independent t-test was used for quantitative variables. Moreover adjustments for total energy intake, analysis of covariance models (ANCOVA) and for confounding factors, Multi-way Analysis of variance models (MANOVA) were used. We also used regression logistic models to compute the Odd Ratios (OR) and 95% confidence intervals [95% CI]. P-value of less than 0.05 were considered statistically significante.

Results

Based on research findings, there were 37 female (61.7%) and 23 male (38.3) in dementia patients and healthy subjects. The mean age of dementia patients was 74.58±8.19 years. The mean duration of disease was 2.5±1.19 years and the average age of onset of disease was 72 years old. According to the DSM-IV criteria, dementia patients consisted of 71.7% Alzheimer disease, 15% cognitive impairment and 13.3% mixed dementia (AD+PD or AD+Vas.D).

Demographics and clinical characteristics of the study, was shown in Table1; subjects in 2 groups (dementia and healthy subjects) and 3 subgroups (Alzheimer disease, cognitive impairment and mixed dementia). No significant differences between the mean age of dementia patients and healthy subjects, history of diabetes, hyperlipidemia and hypertension was observed (Table 1). Dementia patients had cardiac disease (P=0.029), stroke (P<0.001), depression (P<0.001), smoking (P=0.019) and drinking (P=0.008) more than healthy subjects.

Intake of vitamin E, vitamin C, beta-catotene, selenium from food sources between groups was compared (Table2). Results showed that the mean intake of these nutrients was significantly lower in dementia patients than those of in healthy subjects (before and after adjustment for daily total calory intake and other confounding factors).

Table 3 shows that the mean intake of vitamin E, selenium from food sources in compare to RDA. Dementia patients significantly consumed vitamin E and selenium lower than RDA. No significant differences was found for other nutrients in compare to RDA.

Results in multi-adjusted logistic models that tested for associations between dementia and dietary intake of antioxidants, were shown in Table 4. The significant increased risk of dementia was not observed in subjects with the lower intake of vitamin E, vitamin C, beta-carotene and selenium.

Discussion

The findings of this study suggest that, lower dietary antioxidants intake from food sources appear unrelated to increase risk of dementia. Our data showing a greater effect of vitamin E than other antioxidants; vitamin E, a fat –soluble nutrient, readily donates electrons to neutralize reactive oxygen species (ROS) and may be especially important in protecting of lipid membranes in the oxygen rich environment of the brain. Several studies indicate that high antioxidants intake may be partly counteracted with the excess risk of dementia for smokers and cardiac patients. This is supported by the evidence which indicates an increase of free radical loads in smokers and cardiac patients, (Marianne et al., 2002; Mitra et al., 2011). Several biological mechanisms could explain a possible relationship between antioxidants from food and dementia. First, antioxidants may decrease the level of oxidative stress in the brain. Antioxidants may thereby reduce the

amount of DNA damage, neuronal cell death, and the aggregation of ß-amyloid within the brain (Castellani, Perry and Smith, 2006). These phenomena are all important in neuropathological features of cognitive decline; the risk of dementia might be reduced by preventing the genesis of these features. Second, because Alzheimer disease and dementia is associated with both atherosclerosis and oxidative process, these are involved in atherogenesis process (Mitra et al., 2011). So high intake of antioxidants could also decrease the risk of dementia by reducing the risk of atherosclerosis (Mitra et al., 2011), which may activate the receptor for advanced glycation end products (RAGE) and contribute to endothelial and neuronal damage in addition to encourage lipid proxidation of plaque formation of low-density lipoproteins, path ways likely related to progresse of vascular dementia (P kovacic, 2012). Thus antioxidants may protect against cognitive impairment by influencing several different metabolic pathways.

Results from cross-sectional and large prospective studies provide inconsistent evidences of associations between dietary antioxidants and cognitive function. For example, cross-sectional analysis of data from Rotterdom study (Jama et al., 2010) found that, low intake of beta-carotene (but not vitamin E or vitamin C) was associated with cognitive impairment, but additional prospective analysis found only higher intakes of vitamin C and vitamin E (but not beta-carotene) were associated with risk of dementia (Engelhart et al., 2002). Engelhartet et al (2005) from the Rotterdom study reported no association between plasma levels of vitamin A or vitamin E in incidence of Alzheimer disease or cognitive decline. A prospective analysis, Ber et al (2010) showed that low plasma levels of selenium was associated with increased risk of dementia over a follow up period of 4 years.

In our study, inverse relationship between intake of vitamin E, vitamin C, beta-carotene and selenium was not observed, maybe because of the common antioxidant sources (e.g fruits, vegetables and vitamin supplements) are sources for other beneficial vitamins, minerals and other compounds too; so the health effects of specific antioxidants maybe differ to identify. In adition, life-time exposture to antioxidants seems to be the most likely factor affecting in the late-life cognition, Laurin er al (2002) found no association between mid-life dietary of antioxidant intake and late life cognitive function.

Another prospective study from the Chicago Health and Aging Project (CHAP) found that 36% reduction in the rate of cognitive decline among participants in the highest quintile of vitamin E intake from both foods and supplements, but little evidence of associations with vitamin C or carotene intake from either foods or supplements was found (Morris et al., 2002).

Several studies have examined the relationship between dementia and intake of vitamin C and vitamin E from supplements (Luchsinger et al., 2003; Morris et al., 2002; von Arnim et al., 2012; Masaki et al., 2000). A case-control study (von Arnim et al., 2012) reported, high dietary intake of vitamin C and E were associated with lower risk of the disease, but a prospective study in men (Masaki et al., 2000) showed no association between supplements intake and cognitive decline. Another prospective study found that use of supplements,in particular vitaminC but not vitamin E was associated with a lower risk of Alzheimer disease (Morris et al., 2010).

This study showed, the mean intake of vitamin E (13.32 ± 5.12) mg/d, vitamin C (84.68 ± 37.75) mg/d, beta-carotene (994.27 ± 901.91) µ/d, selenium (0.042 ± 0.013) µ/d from food sources, was lower in dementia patients in compare to healthy subjects. Results in intake from foods may not be comparable with those of supplements used and risk of dementia. Antioxidants from foods are always consumed together with other nutrients in a certain proportion, whereas antioxidants from supplements are consumed in a very high dose either with or without other substances. This may lead to differences in absorption or biological activity

between antioxidants from food sources and antioxidant supplements, though little is yet known on these issues.

In conclusion, our data suggest that, vitamin E, vitamin C, beta-carotene and selenium intake from food sources in dementia patients were insufficient and inverse association with risk of dementia was not found. The observed average intake of dietary vitamin E and selenium in dementia patients of our study was less than RDAs. Since, most of the compounds are readily available from a normal diet and supplements; thus, maintaining levels through the consumption of specific foods and supplements is a viable option for dementia patients. General recommendations to increase these micronutrients intake in order to reduce risk of dementia are supported. Studies that include examining dietary antioxidants, associated serum biomarkers in relation to risk of dementia with adequate power and follow-up time would be a significant step to clarify any possible link involved.

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Table 1. Demographic, clinical characteristics of the study groups [1]

	Dementia patients (Cases)					
	AD n=43	MCI n=9	Mixed dementia [2] n=8	Total n=60	Healthy n=60	P-value
Demographic characteristics						
Age (yr)	75.2 ± 7.2	69.3 ± 11.5	76.4 ± 7.4	73.18 ± 8.5	74.6 ± 8.2	0.165
Sex (% female)	9.5	32.4	8.2	50	50	<0.001
Clinical characteristics [3]						
Disease duration (yr)	4.2 ± 1.3	1.8 ± 0.6	6 ± 1.6	4.07 ± 1.7		
Diabetes	27.9	33.3	37.5	30	36.7	0.689
Heart disease	51.2	55.6	50	51.7**	31.7	0.124
Hyperlipidemia	65.1	55.6	50	61.7	51.7	0.579
Hypertension	65.1	33.3	87.5	63.3	55	<0.001
Stroke	32.4	11.1	75	35*	1.7	<0.001
Depression	86	77.8	100	86.7*	40	<0.001
Smoking use	32.6	0	37.5	**28.3	13.3	0.002
Alcohol use	14	11.1	0	11.7**	1.7	0.034

[1] Mean ± SD (all such values), Subgroups and controls were compared by ANOVA.

[2]Mixed dementia: AD+VaD/AD+PD.

[3] Confounders between Cases and controls were compared by chi-square test.

* Significantly different from control subjects, P < 0.001 (Cases and controls were compared by Independent-sample T-test).

** Significantly different from control subjects, P < 0.05 (Cases and controls were compared by Independent-ample T-test).

Table 2. Mean intake of vitaminE, vitaminC, ß-carotene and selenium in cases and controls

	Cases (n=60) Mean ± SD	Controls (n=60) Mean ± SD	P-value
VitaminE (mg/d)	13.36 ± 5.12	16.03 ± 4.83	0.003
adjusted for:			
Total -energy (kcal/d)	13.42 ± 0.67	15.93 ± 0.67	0.013
Diabetes	13.34 ± 0.74	16.13 ± 0.70	0.011
CVD	13.38 ± 0.68	16.35 ± 0.73	0.005
Hyperlipidemia	13.41 ± 0.69	15.89 ± 0.68	0.016
HTN	13.51 ± 0.70	15.88 ± 0.68	0.022
Strokes	13.28 ± 0.71	14.98 ± 2.55	0.528
Depression	13.73 ± 0.99	15.91 ± 0.68	0.081
Smoking	13.30 ± 0.72	17.59 ± 0.95	0.001
VitaminC (mg/d)	84.67 ± 37.75	167.16 ± 56.23	<0.001
adjusted for:			
Total -energy (kcal/d)	83.68 ± 6.49	168.16 ± 6.49	<0.001
Diabetes	86.38 ± 7.08	165.96 ± 6.74	<0.001
CVD	84.72 ± 6.48	166.02 ± 7.001	<0.001
Hyperlipidemia	86.24 ± 6.59	167.16 ± 6.44	<0.001
HTN	86.59 ± 6.72	167.90 ± 6.50	<0.001
Strokes	83.42 ± 6.83	148.38 ± 24.57	<0.001
Depression	76.59 ± 9.41	167.12 ± 6.50	<0.001
Smoking	81.95 ± 7.12	164.99 ± 9.33	<0.001
ß-carotene (µ/d)	994.27 ± 901.91	1861.31 ± 889.73	<0.001
adjusted for:			
Total -energy (kcal/d)	917.11 ± 119.13	1938.47 ± 119.13	0.030

Diabetes	879.69 ± 130.80	1948.02 ± 124.64	<0.001
CVD	925.35 ± 120.35	1919.58 ± 129.95	<0.001
Hyperlipidemia	947.06 ± 122.92	1930.58 ± 119.89	<0.001
HTN	916.65 ± 124.66	1935.33 ± 120.71	<0.001
Strokes	927.89 ± 125.29	1586.77 ± 450.91	0.166
Depression	1061.48 ± 172.50	1916.76 ± 119.22	<0.001
Smoking	851.95 ± 129.51	2060.74 ± 169.63	<0.001
Selenium (µ/d)	0.041 ± 0.013	0.059 ± 0.022	<0.001
adjusted for:			
Total -energy (kcal/d)	0.042 ± 0.002	0.059 ± 0.002	<0.001
Diabetes	0.043 ± 0.003	0.059 ± 0.003	<0.001
CVD	0.042 ± 0.002	0.058 ± 0.003	<0.001
Hyperlipidemia	0.042 ± 0.005	0.059 ± 0.002	<0.001
HTN	0.042 ± 0.003	0.059 ± 0.002	<0.001
Strokes	0.042 ± 0.003	0.040 ± 0.009	0.862
Depression	0.042 ± 0.004	0.059 ± 0.002	<0.001
Smoking	0.042 ± 0.003	0.061 ± 0.003	<0.001

† Mean ± SD (all such values).

†† Total energy intake was adjusted by ANCOVA and confounder factors were adjusted by MANOVA analyses

Table 3. Mean intake of vitaminE and selenium of dementia patients (cases) in comapare to RDA[1]

	RDA	Cases (n=60) (Mean ± SD)	P-value
VitaminE (mg/d)	15	13.36 ± 5.12	0.014
Selenium (µ/d)	55	0.041 ± 0.013	<0.001

[1] Mean ± SD (all such values)

Table 4. Odd ratios (95% CIs) for lower intake of food antioxidants

	VitaminE (mg/d)	P-value	VitaminC (mg/d)	P-value	Beta-carotene (mic/d)	P-value	Selenium (mic/d)	P-value
Unadjusted	0.33 (0.16, 0.70)	0.004	0.33 (0.16, 0.70)	0.001<	0.08 (0.03, 0.18)	0.001<	0.13 (0.059-0.29)	0.001<
Adjusted for:								
Total energy intake (Kcal/d)	0.64 (0.27, 1.5)	0.304	0.33 (0.16, 0.70)	0.001<	0.05 (0.02, 0.15)	0.001<	0.11 (0.042-0.27)	0.001<
Diabetes	0.29 (0.14, 0.65)	0.002	0.33 (0.16, 0.70)	0.001<	0.07 (0.03, 0.18)	0.001<	0.13 (0.059-0.30)	0.001<
Heart Disease	0.29 (0.13, 0.64)	0.002	0.33 (0.16, 0.70)	0.001<	0.08 (0.03, 0.19)	0.001<	0.13 (0.058-0.30)	0.001<
Hyperlipidemia	0.34 (0.16, 0.72)	0.005	0.33 (0.16, 0.70)	0.001<	0.07 (0.03, 0.18)	0.001<	0.13 (0.056-0.29)	0.001<
Hypertension	0.32 (0.15, 0.69)	0.003	0.33 (0.16, 0.70)	0.001<	0.08 (0.03, 0.18)	0.001<	0.13 (0.058-0.29)	0.001<
Stroke	0.35 (0.15, 0.79)	0.011	0.33 (0.16, 0.70)	0.001<	0.07 (0.03, 0.19)	0.001<	0.12 (0.056-0.33)	0.001<
Depression	0.34 (0.15, 0.80)	0.013	0.33 (0.16, 0.70)	0.001<	0.09 (0.04, 0.25)	0.001<	0.15 (0.063-0.38)	0.001<
Use smoking	0.34 (0.16, 0.72)	0.005	0.33 (0.16, 0.70)	0.001<	0.08 (0.03, 0.19)	0.001<	0.12(0.053-0.28)	0.001<
Supplements users excluded	0.31 (0.15, 0.67)	0.003	0.33 (0.16, 0.70)	0.001<	0.07 (0.03, 0.17)	0.001<	0.13 (0.060-0.30)	0.001<