Journal of
Alzheimer's Disease & Parkinsonism

Parvaresh et al., J Alzheimers Dis Parkinsonism 2016, 6:6
DOI: 10.4172/2161-0460.1000280

Thesis Open Access

Evaluation and Comparison of Dietary Patterns in Patients with Alzheimer's Disease and Healthy Controls

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Abstract

Background: Nutrition is an important modifiable risk factor that plays a role in the strategy to prevent or delay the onset of Alzheimer disease (AD). Previous studies have focused on AD and an individual nutrients or single food-based approach which does not take into account combinations of food that are consumed. Therefore, we aimed to investigate the relation between Alzheimer disease and major dietary patterns among elderly people.

Materials and methods: This case-control study was conducted on 50 elderly people who suffering from AD and 92 healthy controls (elderly people without Alzheimer disease). Usual dietary intake was assessed using a validated 168-item semi-quantitative food frequency questionnaire. Major dietary patterns were identified using factor analysis.

Results: From 12 food groups, three major nutrient patterns were identified: first, was high in milk and milk products, eggs, meat, poultry, fish, fat different than cream and butter, vegetables and fruit rich in vitamin C, vegetables and fruit rich in beta-carotene, vegetables and fruit different than mentioned source. The second pattern was high in grain, cereals, bread, butter, cream, sugar and sweets, and the third one included high amount of potato and seeds and legumes. The findings showed that individuals with the greatest adherence to the first dietary pattern were less likely to have AD compared with those with the lowest adherence in crude model and after stratification by age, sex and education (OR=0.13; 95% CI: 0.04-0.42 and OR=0.006; 95% CI: 0.00-0.218, respectively).

Conclusion: In conclusion, dietary pattern characterized by high consumption of milk and milk product, meat, fish, vegetable and fruit was associated with lower odds of Alzheimer disease. Further studies, particularly of prospective nature, are required.

Keywords: Alzheimer's disease; Dietary pattern; Cognitive function

Introduction

Alzheimer disease (AD) is a chronic and progressive neurodegenerative disorder, with multiple pathophysiological mechanisms which features mainly with memory impairment and loss of cognitive function [1]. In 2015, about 48 million people suffering from Alzheimer disease throughout the world, approximately [2]. According to the latest WHO data published Alzheimer's/Dementia Deaths in Iran extended 4,011 or 1.19% of total deaths [3]. This dementia have a wide range of risk factors including genetic, vascular/metabolic and lifestyle-related indices [4,5]. Recent treatment technologies for AD have been suggested both of pharmacotherapy and non-pharmacological interventions [6]. Accumulating evidence shows nutritional interventions influence the risk of developing Alzheimer's disease (AD) and its progression [7]. Some research has indicated that caloric intake influences one's risk for AD and correspondingly, that debarment obesity/calorie intake might play an important role in delaying the AD degenerative process [8]. Other reports show that some vitamin/nutraceuticals formulation appears to be one of the successful strategies for the treatment of AD [9-11].

The most of the pervious consideration on diet and Alzheimer's disease (AD) or cognition among the elderly has focused on the role of single nutrients or foods, while available information on dietary pattern (DP) analysis, which better reflects the complexity of the diet, is sparse [12]. The reality is, a single nutrient efficacy's may be too rare to indicate or, a numerically remarkable affiliation might be simply found by chance alone [13]. In addition, the operation of the food matrix is disparate from the individual nutrients or food items, as humans usually eat meals with complex mixtures of food items or nutrients that are likely to be synergistic or antagonistic [14]. Also, food items or nutrients are extremely associate within foods, so it is difficult to investigate their single effects [13]. Therefore, this study was conducted to examine the association between Alzheimer disease and main dietary patterns identified by posterior approaches.

Methods and Materials

Population of study

This retrospective study was conducted in people with Alzheimer's disease among both male and female genders (age group >60) inhabitant in nursing home mainly (twelve nursing home in Tehran and Isfahan which was determined from State Welfare Organization of IRAN and Iran Alzheimer's Association).

Distinguish of patients with Alzheimer disease have been conducted by neurologist. The mini–mental state examination (MMSE) is the most common neuropsychological tests, which has both validity and reliability for the diagnosis and longitudinal assessment of Alzheimer's disease [15]. 34 women and 16 men were considered as cases. Healthy

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Received October 03, 2016; **Accepted** October 27, 2016; **Published** November 04, 2016

Citation: Parvaresh F, Ghiasvand R , Feizi A , Bahreini N (2016) Evaluation and Comparison of Dietary Patterns in Patients with Alzheimer's Disease and Healthy Controls. J Alzheimers Dis Parkinsonism 6: 280. doi: 10.4172/2161-0460.1000280

subjects in the control group, who had a regular brain and healthy mental function, were selected mainly from nursing home.

Exclusion criteria included taking medication except for dysfunction neurology, and obey particular dietary pattern. At last total of 50 Alzheimer cases and 92 controls participated in the study. The sample size is determined based on the use of factor analysis. For each food items (12 groups), at least five subjects are considered.

Written informed consent was obtained from all caregivers. The ethical committee of Isfahan University of Medical Sciences, Isfahan, Iran, approved the study.

Dietary intake assessment

Data on usual dietary intake was assessed by using a previously validated 168-item semi-quantitative food frequency questionnaire (FFQ) [16] as well as factor analysis was conducted to identify major dietary patterns. The FFQ included a list of typical Iranian foods with standard serving sizes. Consumption frequencies of each food item were put into nine categories which participants could reported their average dietary intake during the previous year by choosing one of the following choices: never, 1-3 times per month, once a week, 2-4 times per week, 5-6 times per week, once daily, 2-3 times per day, 4-5 times per day and 6 or more times a day. Portion sizes of each food item were converted into grams by using standard Iranian household measures [16]. Then frequencies of consumed foods were transformed into daily intakes. The nutrient composition of all foods was derived by using modified nutritionist IV software. To do dietary pattern analysis, food items were grouped into 12 different categories based on the similarity of their nutrients profiles. Patients and their caregivers as well as controls were presented with food frequency questionnaire, asked them about their diet earlier in life to make an analysis more reliable in determination diet pattern as a risk factor. Because of the small number of subjects relative to the number of food items, classification is collapsed into 12 predefined food groups.

Anthropometric assessment

Weight was measured using a standard digital Seca scale (made in Germany), while participants wearing light clothes without shoes. Measurements were recorded to the nearest 100 g. Height was measured using a mounted tape in a standing relaxed shoulder position with no shoes to the nearest 0.5 cm. We calculated body mass index (BMI) using weight in kilogram divided by height squared in meters. Waist circumference (WC) and hip Circumference (HiC) were measured by using an un-stretched tape in standing position over the light clothes. Waist was positioned as the narrowest circumference between the costal margin and the iliac crest and hip as the maximum level between the waist and thigh. All measurements were recorded to the nearest 0.5 cm. Waist to hip ratio (WHR) was calculated as WC in centimeters divided by HiC in centimeters. A trained dietician did all measurements in order to reduce error.

Assessment of other variables

A self-reported questionnaire was distributed to gather information on age, educational status (lower than diploma, diploma, Bachelor and higher than bachelor), job's patient (Employee, Non-employee), smoking status (yes or no), duration of the disease and long life at nursing home, current use of medications (yes or no) and some other medical history. Data on physical activity was obtained by a short form of validated international physical activity questionnaire (IPAQ) (http://www.ipaq.ki.se) [17], which was presented as metabolic equivalent-minutes per week (MET-min/week) and physical activity level as high, moderate and low [18].

Statistical Analysis

We conducted factor analysis to identify the major dietary patterns based on 12 food groups totally previously described. Also, for statistical analysis of the statistical methods T2 Hoteling, two independent samples (or multivariate ANOVA), chi-square test (and, if necessary, Fisher's exact test) and logistic regression was being used. Dietary patterns using factor analysis and varimax rotation was be extracted. We obtained the score for subjects by summing the consumption of each food group weighted by the correlation coefficient of each factor score.

Results

The mean ages of participants were 69.47 ± 14.15 in healthy controls group (group 1) and 83.51 ± 9.16 in Alzheimer' disease group (group 2). Also, frequency of male and female were 36.5% and 63.5% in group 1 and 36.4% and 63.6% in group 2, respectively. From 12 food groups, 3 major dietary patterns were extracted by using factor analysis test and the factors were rotated by varimax rotation. Base on weigh of food group in each dietary pattern, the first was high in milk and milk products, eggs, meat, poultry, fish, fat different than the source mentioned, vegetables and fruit rich in vitamin C, vegetables and fruit rich in beta-carotene, vegetables and fruit different than mentioned. The second pattern was high in grain, cereals, bread, butter, cream, sugar and sweets and the third one include high amount of potato, seeds and legumes. Altogether, these three dietary patterns explained 45% of primary variable information in this population. The results of factor loadings analysis are presented in (Table 1). General characteristic of participant was presented in (Table 2). No significant different was observed in term of WC and physical activity between 2 groups but not in age and BMI. There was significant difference between Alzheimer' disease group and healthy control group in intake of grain, cereals, bread, butter and cream, fat different than butter and cream (FD), vegetables and fruit rich in vitamin C, vegetables and fruit different than above mentioned (VD). Also, participants were older than those in G1. No further significant different was found between G1 and G2. Characteristics of dietary intake base on 12 food groups were presented in Table 3.

Multivariable-adjusted odds ratios for Alzheimer across tertile dietary pattern category are provided in Table 4. There were significant association between first dietary pattern and Alzheimer in crude model and after stratification by age, sex and education (OR=0.13; 95% CI: 0.04-0.42 and OR=0.006; 95% CI: 0.00-0.218, respectively). Result remained significant after adjustment of another confounder (BMI) (OR=0.05; 95% CI: 0.00-0.22). No relation was observed between second or third dietary pattern and odds of Alzheimer in crude and adjusted model.

Discussion

In this case- control study we found a significant protective effect of adherence to dietary pattern including: milk and milk products, eggs, meat, poultry, fish, FD, vegetables and fruit rich in vitamin C, vegetables and fruit rich in beta-carotene, VD and odds of Alzheimer.

Some studies evaluate single-nutrient or food on risk of AD. In similar of our results, Barberger-Gateau et al. [19] reported consumption fish is associated with lower risk of AD. Also, animal study showed Docosahexaenoic Acid (DHA) has reverse association

Food group	1	2	3
Grain, Cereals, Bread	0.251	0.487	0.227
Milk and milk products	0.691	0.219	0.237
EGGS	0.444	-	-
Meat, Poultry, Fish	0.530	0.497	-
Butter and Cream	-	0.736	-
Fat different than the above	0.314	-	-
potato	-	-	0.862
Vegetables and Fruit rich in vitamin C	0.565	-	0.245
Vegetables and Fruit rich in beta-carotene	0.699	-	-
Vegetables and Fruit different than above	0.740	-	0.252
Seeds and Legumes	-	-	0.802
Sugar and Sweets	-	0.666	-
other	0.583	-	-

Values <0.2 were omitted for simplicity

Table 1: Factor loading matrix for the major dietary patterns.

Demographic variable		G1	G2	p-value
Age		69.47 ± 14.15	83.51 ± 9.16	<0.001
WC		92.52 ± 24.06	86.63 ± 17.15	0.55
BMI		24.04 ± 5.49	26.26 ±4.7	0.02
Sex	male	36.5%	36.4%	
	female	63.5%	63.6%	
Education	low	23.3%	13.3%	
	middle	31.7%	70.0%	
	high	45.0%	16.7%	
Past medical history				

Data are presented as mean ± SD
P-value<0.05 was significant, data was analysis by T-Test. WC: waist circumstance

Table 2: Participant characteristics.

Food groups	Healthy Control group	Alzheimer disease group	P-value*
Grain, Cereals, Bread	454 ± 271 374 (75-1857)	617 ± 337 582 (20-1362)	0.002
Milk and milk products	706 ± 523 524 (30-2239)	620.38 ± 447 536 (68-2628)	0.327
EGGS	27.88 ± 36.69 22.92 (3-321)	21.11 ± 16.32 22.92 (3.56-53.50)	0.218
Meat, Poultry, Fish	136 ± 147 95 (18-642)	124.77 ± 160.21 77.06 (8-901)	0.668
Butter and Cream	55.12 ± 49.65 40.70 (4-266)	119.31 ± 94.97 106.82 (3-368)	<0.001
Fat different than the above	26.77 ± 25.66 16.25 (2-107)	11.89 ± 15.14 6.93 (0.26-69.00)	<0.001
potato	47.78 ± 50.10 39.42 (4-260)	29.74 ± 24.79 17.4 (4-104)	0.028
Vegetables and Fruit rich in vitamin C	254 ± 178 220 (43-878)	127.82 ± 124.03 93.06 (11-685)	<0.001
Vegetables and Fruit rich in beta-carotene	70.61 ± 62.39 48.05 (4-312)	50.72 ± 95.03 22.84 (1-555)	0.136
Vegetables and Fruit different than above	1101 ± 619 1043 (293-2848)	665 ± 436 561 (116-2378)	<0.001
Seeds and Legumes	66 ± 97 29 (1-570)	36.14 ± 83.51 15.37 (1-547)	0.074
Sugar and Sweets	819 ± 449 758 (173-2486)	993 ± 527 808 (13-2227)	0.041
other	21.48 ± 26.93 13.70 (1-198)	16.32 ± 24.32 7.87 (1-107)	0.309

Data are presented as Mean ± SD and Median (min-max)
P-value obtained from independent sample t-test

Table 3: Dietary intake in Alzheimer and control group.

	Pattern 1			Pattern 2			Pattern 3		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
crude	1	0.19 (0.07-0.53)	0.13 (0.04-0.42)	1	2.30 (0.37-14.21)	4.5 (0.71-28.14)	1	0.81 (0.17-3.89)	0.17 (0.31-1.03)
Model 1	1	0.07 (0.003-1.32)	0.006 (0.00-0.218)	1	6.08 (0.39-94.01)	8.61 (0.60-121.76)	1	2.29 (0.07-67.37)	0.13 (0.004-4.13)
Model 2	1	0.07 (0.004-1.54)	0.05 (0.00-0.22)	1	5.97 (0.38-94.39)	5.45 (0.38-78.27)	1	2.30 (0.07-69.88)	0.15 (0.004-5.62)

Model 1: Adjusted for age, sex, education
Model 2: Model 1+BMI

Table 4: Multivariable-adjusted odds ratios of the associations between Alzheimer and dietary patterns.

with AD disease [20]. In addition to the fish and polyunsaturated fatty acid, protective dietary pattern in this study included vegetable and fruit. A population-based prospective study with 9 years' follow-up demonstrated vegetable and fruits may play protective role in onset of AD disease [21]. This study emphasized the role of anti-oxidant on risk of AD that was same our finding.

While, many study demonstrated association between nutrient and Alzheimer [22], single-nutrient or food study designs are somewhat limited for a multitude of confounding and inter-dependent factors, and people consume variety of food group together [23]. Therefore, studies with dietary patterns design may reduce methodological errors.

Gustaw-Rothenberg [24] reported a different between Alzheimer patient's dietary pattern and control group. The patients who suffer from Alzheimer, has dietary pattern with high in meat, butter and cream as well as FD, eggs, and refined sugar and low in fruit and vegetables rich in vitamin C. Although, the part of this finding was same our result including effect of protective effect of fruit and vegetable, but this study showed no significant effect of fish and polyunsaturated fatty acid on AD. Also, meat consumption was high in AD and control group. This contrast may cause for uncontrolled supplement intake in both group. Because, the protective role of B12 unsaturated fatty acid that supply from meat and from fish were emphasized in previous published [25-28].

Also, some cross-sectional [29,30] and prospective studies [31-33] reported that higher adherence to a Mediterranean-type diet (characterized by high intake of vegetables, legumes, fruits and cereals, a high intake of unsaturated fatty acids, but low intake of saturated fatty acids, a moderately high intake of fish, a low-to-moderate intake of dairy products, a low intake of meat and poultry) was associated with a lower risk for AD and lower mortality from this disease. Similar our study, this result supports the role of vegetable and fruit anti-oxidant component on AD. Although, the pathogenesis of AD is complex, some findings suggested that free radical and oxidative molecules is important pathological feature related to AD [34]. This damage takes place over the lifelong and consumption of vegetable and fruit that are beast source of anti-oxidant can be powerful protective line against oxidative damage [35-37]. Selenium, vitamin E and zinc are most frequent anti-oxidant nutrient that their positive effect was reported [38-40]. Also, studies of single-agent nutritional supplements reported variety of individual nutrient have protective effect on Alzheimer such as B vitamins [41], lutein [42], lecithin [43] and omega-3 polyunsaturated fatty acids [44,45]. Hjorth et al revealed that Alzheimer is associated with inflammation mediated by microglia and atrocities and ω3 FAs can be useful as potential treatments for it [44]. Another mechanism that suggested to association between nutrient and dietary pattern is brain insulin signaling. This mechanism, particularly act in the hypothalamus, controls several metabolic pathways in peripheral organs including controls food intake [46], hepatic glucose production [47], adipose tissue lipolysis, and de novo lipogenesis [48] and branched-chain amino acids (BCAAs) catabolism [49]. The hypothalamic insulin signaling may bypass decreased insulin transport from the circulation via the blood brain barrier to the brain improves memory in patients with AD [50,51]. Also, it reduced in cerebral cortex slices derived post-mortem from AD patients [52]. Ruiz HH reported that plasma BCAAs may serve as a marker for impaired brain insulin action in patients with AD [53].

In our knowledge, this is first study on dietary pattern and AD in Iranian population. There is some limitation should be considered. Participants in our study may have some mental disorders such as depression or anxiety might lead to changes in appetite and dietary intakes of them. Factor analysis was used to identify dietary patterns that include several subjective decisions, such as the consolidation of food items into food groups, the number of factors extracted, the method of rotation and labeling of the factors. Furthermore, because of using an FFQ, misclassification of study participants is another concern.

Conclusion

In conclusion, we found evidence indicating that a dietary pattern characterized by high consumption of milk and milk product, meat, fish, vegetable and fruit was associated with lower odds of AD while 2 pattern with high in potato and different fat, has not significant effect on this disease. Further studies, particularly of prospective nature, are required to confirm these findings and to evaluate relationships between adherence to dietary pattern during lifelong and risk of AD.

Acknowledgement

We appreciate all participants and specialists who assisted with this research. This study was extracted from an M.Sc. dissertation which was approved by the School of Nutrition and Food Sciences, Isfahan University of Medical Sciences.

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