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Investigation of food preference in Alzheimer patients; Assessment of glycemic index and glycemic load of their diet

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Abstract

In this study, our objective was to investigate the food preferences of patients with Alzheimer's-type dementia and healthy individuals of the same age and to compare the glycemic index and glycemic load of the preferred foods. This study was conducted with 55 patients, who were diagnosed with Alzheimer's-type dementia by a neurologist, and 57 healthy individuals at the same age interval as the control group. The cognitive functions of the participants were assessed with the Standardized Mini-Mental State Exam (SMMSE). The food consumption preferences were determined following the obtainment of the three-day food consumption records and then the glycemic index and glycemic load of the diets was calculated. The carbohydrate amount consumed by Alzheimer's patients, the energy content of the diet, and the glycemic load were significantly higher ($p<0.05$) compared to the control group. The comparison of Alzheimer's patients, who were divided into two groups, mild dementia (SMMSE=18-23) and severe dementia (SMMSE≤17) according to the SMMSE scores, showed that patients with severe dementia consumed significantly more carbohydrates and the energy content of their diet was higher ($p<0.05$). We determined that Alzheimer's patients consumed more carbohydrates and sugar compared to the control group. The daily carbohydrate intake increased as the severity of the disease increased, however, the quality of the consumed carbohydrate remained the same.

Keywords: Alzheimer's disease, carbohydrate consumption, glycemic load, glycemic index

1. Introduction

Glucose is the main energy source of the brain. Glucose is necessary for the supply of the precursors used in the neurotransmitter synthesis, the activities of adenosine-triphosphate (ATP), and other energy needs of the brain (1). The biggest portion of the energy demand of the brain, which increases during mental activity, is needed for computation and information processing (2). Under normal conditions, the energy consumption decreases gradually with the aging of the brain (3). The age-dependent cognitive changes are associated with the neuro-anatomical changes manifested by the decrease in the grey-matter volume. It is not a pathological process (4). The decline in the volume, glucose and oxygen metabolism of the brain cells observed during the normal aging process is more prominent in neurodegenerative diseases like Alzheimer's Disease (AD) (5). On the other hand, despite this decline in the glucose metabolism, which is more significant in Alzheimer's patients, and cortical and hippocampal regions, studies showed that Alzheimer's patients consumed carbohydrate-rich food more than the healthy individuals at the same age (6). The answer is not yet clear why Alzheimer's patients consume more carbohydrates than the same age group.

Studies have proven that the pathogenesis of AD is not limited to neuronal damage, but is also related to immunological mechanisms and glial cells in the brain (7). Microglia and astrocytes are macrophages of the central nervous system (CNS) that provide neuroprotection and repair of damaged neuronal tissue under normal conditions. It becomes activated when exposed to neuroinflammation and amyloid plaques (AP). Activated microglia further exacerbate the neuroinflammatory response by releasing cytotoxic molecules such as cytokines, interleukins and nitric oxide, and their numbers gradually increase (8). Similarly, the pathological events accompanying AD seem to be related CNS insulin resistance (9). Insulin has also been shown to affect hippocampal functions and molecular structures related to cognition and memory (10). There are studies showing that acute increases in insulin levels under healthy metabolic

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conditions have a positive effect on cognition (11). In this study, our objective was to investigate the food preferences of Alzheimer's patients and to compare the glycemic index and glycemic load of the consumed carbohydrates. Our objective was also to determine whether the consumed carbohydrate amount and glycemic index and load of these carbohydrates were changing with the severity of the disease.

2. Materials and methods

2.1. Study design

This prospective study has a cross-sectional design. All participants were selected from patients who applied to our hospital, a tertiary healthcare institution, in 2012. All participants and legal representatives were informed about the study procedures before their inclusion in the study and their written consent was obtained.

2.2. Study Group

This study was conducted with 55 patients, who had been diagnosed with Alzheimer's type dementia, and 57 healthy individuals as the control group. The diagnosis of AD was made according to DSM IV diagnostic criteria (12). The patient group included patients over the age of 60 who were diagnosed with Alzheimer's type dementia and had a Standardized Mini-Mental State Exam (SMMSE) score <24/30. The control group consisted of healthy individuals in the same age group with an SMMSE score of 24/30 and above. The SMMSE test applied to the patients in the study group was graded according to the Folstein system (13). The cut-off value of this grouping system for Turkish society has been found to be valid and reliable (14). Participants in both groups were capable to make their food choices. The exclusion criteria were as follows: History of cerebrovascular disease, other neurodegenerative brain diseases excluding Alzheimer's type dementia, diabetes, severe psychiatric disease, other known neurological diseases affecting sense of smell and taste, severe food allergies, and gastrointestinal system diseases. These patients were excluded from both groups. We took also into consideration whether the participants in both groups were following any particular diet or using food supplements and whether they were capable to decide what to eat.

2.3. Procedure

The demographic characteristics and body weight measurements were recorded. Patients and their relatives were asked to record food and drinks consumed in three days (2 weekend days, 1 weekday). We used a photo catalog of food sizes and portions for an accurate determination of food and drink consumption. We did not interfere with the type and amount of food choices. Participants were briefed to use certain measurements such as slice for bread, count or portion for fruits, a portion for foods, and glass for drinks to standardize the records. The study dietitian collected the 3-day records from all participants. The energy and macronutrient consumption were analyzed with the Food Code and Nutrient Data Base (BEBIS 6.1, Germany). The consumed carbohydrate, fat and protein amounts were calculated in grams. Dietary mean glycemic index (GI) and the global dietary glycemic load (GL) were calculated using the three-day food logs, and equations stated below (15):

$$\text{Mean dietary GI} = \frac{\sum_{i=1}^{n} GIi \; x \; CHOi}{\sum_{i=1}^{n} CHOi}$$

$$\text{Global dietary glycemic load} = \sum_{i=1}^{n} GIi \; x \; CHOi / \; 100$$

Gli: GI of food "i"; CHOi: carbohydrate content of food "i" (gram/day); n: number of daily consumed food. GI values for all food types were collected from the last editions of the national (16) and international (17) GI charts and the online database "Sydney University Glycemic Index Research" (18).

2.4. Evaluation of the Blood Parameters

The fasting blood samples were collected between 08:00 and 09:00 AM. Serum fasting glucose, insulin, HbA1c, thyroid-stimulating hormone (TSH), and vitamin B12 levels were determined with a paramagnetic particle chemiluminescent immunoassay method.

The insulin resistance was evaluated with HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) = Fasting insulin (uU/mL) x fasting glucose (mg/dL) (19). There is no universally accepted HOMA-IR threshold for insulin resistance (20). In a study including 3331 Turkish participants, a cut-off value of 3 was determined for HOMA-IR (21). In another study, the determined cut-off value was 2.46 (22). The calculated HOMA-IR values in both studies had a positive correlation to elevated insulin resistance.

2.5. Statistical Analysis

Data analysis was performed with a statistical software package (IBM SPSS Statistics for Windows 11). Normality was assessed with the Shapiro–Wilk test. Regarding the normally distributed data, descriptive statistics were given in mean ± standard deviation values, while the median (interquartile range) was used for the non-normally distributed data. The intergroup comparison was done with the Student's T-test for normally distributed data, while the Mann Whitney-U test was used for the non-normally distributed data. Categorical variables were analyzed with the Pearson's Chi-Square or Fisher's Exact Chi-Square test where appropriate. A p-value smaller than 0.05 was considered statistically significant.

3. Results

The study included 55 Alzheimer's patients (male: 37 (67.3%), female: 18 (32.7%) and 57 healthy volunteers (male: 35 (61.5%), female: 22 (38.5%)). The average age of Alzheimer's patients was 72.8 ± 8.2 years, and the average age of the control group was 69.9 ± 7.0 years.

There was no significant difference between the Alzheimer's patients and the control group in age, gender, and body weight. The mean SMMSE scores of Alzheimer's patients and the control group were 17.4 ± 5.8, and 26.4 ± 2.2, respectively. A significant difference was detected between them ($p<0.05$) (Table 1). We compared the amount of

macronutrient intake, blood parameters, glycemic index and glycemic load between Alzheimer's patients and the control group. In the comparative analysis, the average daily carbohydrate consumption of the control group was 226.5 ± 51.1 grams (g) and the average daily carbohydrate consumption of the Alzheimer's group was 297.2 ± 40.4 g, and the difference between them was significant ($p<0.05$). The average daily carbohydrate consumption of the mild dementia group was 261.3±31. g, the average daily carbohydrate consumption of the severe dementia group was measured as 338.3±32.7 g and the difference between them was significant ($p<0.05$).

Table 1. Characteristics of the participants

Variables	Control (n=57)	Alzheimer's patients (n=55)
Age (year)	69.9 ± 7.0	72.8 ± 8.2
Gender		
Men	35 (61.5%)	37 (67.3%)
Women	22 (38.5%)	18 (32.7%)
Body weight (kg)	70.2 ± 6.7	69.1 ± 7.9
SMMSE score	26.4 ± 2.2	17.4 ± 5.8*

*p<0.05

Daily energy consumption of the control group was measured as 1767.8±73.8 kcal, and that of the Alzheimer's group was 2190.6±109.6 kcal, and the difference between them was significant ($p<0.05$). Daily energy consumption of the mild dementia group was measured as 2001.4 ± 111.5 kcal, and that of the severe dementia group was 2407 ± 189.4 kcal, and the difference between them was significant ($p<0.05$). The glycemic load of the control group was measured as 162.8 ± 49.3, and that of the Alzheimer's group was 210.8 ± 35.5, and the difference between them was significant ($p<0.05$). The glycemic load of the mild dementia group was measured as 182.5±21.5, and that of the severe dementia group was 243.1±39.2, and the difference between them was significant ($p<0.05$). Daily protein consumption was measured as 75.6 ± 16.5 g in the control group and 61.1 ± 15.5 g in the Alzheimer's group, and the daily protein consumption of the control group was significantly higher ($p<0.05$). In summary, we compared the amount of macronutrient intake, glycemic index and glycemic load between Alzheimer's patients and the control group. The consumed carbohydrate amount, the energy content of the diet, and glycemic load were significantly higher in Alzheimer's group ($p<0.05$). On the other hand, protein consumption was significantly higher in the control group ($p<0.05$). The comparison of the subgroups in the Alzheimer's patient group according to the SMMSE scores mild dementia (SMMSE=18-23) and severe dementia (SMMSE≤17) showed that patients with severe dementia consumed more carbohydrates and the energy content of their diet was higher ($p<0.05$). The decline in the SMMSE score had a positive correlation to the carbohydrate and sugar consumption and glycemic load of the diet. In blood biochemical and hormone analyses, there was no significant difference between the groups in terms of fasting blood sugar, TSH, HbA1c, insulin and vitamin B12 levels (Table 2).

Table 2. Dietary macronutrient consumption, glycemic variables, and blood parameters of the participants regarding the presence of disease

Variables	Control (n=57)	Alzheimer's patients (n=55)	Mild Dementia SMMSE=18- 23 (n=29)	Severe Dementia SMMSE≤17 (n=26)
Carbohydrates (g)	226.5 ± 51.1	297.2 ± 40.4[a]	261.3 ± 31.5	338.3 ± 32.7[b]
Protein (g)	75.6 ± 16.5	61.1 ± 15.5[a]	62.0±12.7	59.8±10.3
Fat (g)	68.6 ± 14.6	77.7 ± 13.2	74.3±19.9	81.5±26.9
Sugar (g)	57.9 ± 12.0	78.6 ± 18.9	54.5±18.3	76.2±16.8[b]
Energy (kcal)	1767.8 ± 73.8	2190.6 ± 109.6[a]	2001.4 ± 111.5	2407± 189.4[b]
Glycemic Index	67.8 ± 11.7	69.3 ± 10.7	66.8 ± 9.9	67.7 ±11.6
Glycemic Load	162.8 ± 49.3	210.8 ± 35.5[a]	182.5 ± 21.5	243.1 ± 39.2[b]
Fasting Glucose (NR: 75-100 mg/dL)	99.0 (90-110)	102.0 (91-115)	101.5 (92-115)	104.0 (90-115)
Fasting Insulin (NR: 2-25 mIU/mL)	7.5 (9.8-12.7)	7.6 (3.9-10.1)	6.9 (3.9-10.1)	8.0 (4.6-11.7)
HOMA-IR	1.7 (0.2-3.8)	2.7 (1.1-11.9)	2.0 (0.2-3.3)	2.5 (0.8-3.6)
HbA1c (NR: 3.5-6 mmol/mol Hb)	6.0 (5.8-6.4)	5.9 (5.7-6.3)	6.0 (5.8-6.3)	5.8 (5.6-6.3)
TSH (NR: 0.35-5.5 IU/L)	1.7 (0.9-2.4)	1.5 (0.8-2.3)	1.4 (0.7-2.1)	1.5 (0.8-2.7)
Vitamin B12 (NR: 190-911 pg/mL)	343 (204-487)	340 (262-393)	321 (225-358)	281 (225-394)

[a] *p<0.05*. Control vs. dementia groups; [b] *p<0.05*. Mild vs severe dementia.
Abbreviations: SMMSE: Standardized Mini-Mental State Examination. NR: normal range

4. Discussion

In this study, we evaluated the distribution of macronutrient intake, carbohydrate content (glycemic index), and amount (glycemic load) in Alzheimer's patients and compared the results with a control group consisting of healthy individuals in the same age group. In addition, we investigated the potential effect of dementia on glucose metabolism (fasting glucose, fasting insulin, HbA1c), and parameters related to general

metabolism (TSH) and vitamin B12). We hypothesized that the glycemic index and glycemic load are associated with Alzheimer's disease and its stages. We determined that the carbohydrate intake and glycemic load of the diet were significantly increased among Alzheimer's patients compared to the control group. There was no significant difference between the groups for glycemic index. The stage of dementia had a positive correlation to the glycemic load of the diet, which indicated that patients with severe dementia consumed more carbohydrates and sugar and consequently had a higher glycemic load. Although Alzheimer's patients consumed more carbohydrates and sugar than the control group, there was no significant difference in their fasting blood sugar and HbA1c values compared to the healthy control group. These results made me think that the consumed carbohydrates and sugar may be used somewhere else that we don't know yet. İn this article, we wanted to discuss where excessive amounts of sugar and carbohydrates may be used.

Various studies had demonstrated that energy consumption declines with the aging of the brain (3). It was reported that the decline in the glucose metabolism in Alzheimer's patients was more prominent in the frontal, parietal, and temporal cortexes (23). These studies reporting a decline in cerebral glucose metabolism were mostly focused on the cerebral cortex and neuronal metabolism (24). However, pathological changes emerge in both grey and white matters (24). It was conclusively demonstrated that the pathogenesis of AD was not limited to neuronal damage but was related to the immunological mechanisms in the brain and glial cells (23, 7). It was proven that there is an over-activation and glucose overuse in the cerebral immune cells along with a decline in neuronal metabolism (24). Under normal conditions, microglia and astrocytes, which provide neuroprotection and repair the damaged neuronal tissue, are activated when they are exposed to neuroinflammation and AP (8). It was demonstrated that the activated microglia migrated to the newly developed AP (25). These microglia, whose number and functions are increased in AD, release cytotoxic molecules such as cytokine, interleukin, and nitric oxide and hence the neuroinflammatory response, which emerges with the physiological aging, is aggravated (8, 26). Continuous exposure to the pro-inflammatory cytokines causes an unstoppable hyperactivation in microglia and astrocytes (8).

The glucose uptake of microglia, which are the resident histiocyte-like macrophages of the central nervous system, was investigated with positron emission tomography (PET) following F-18 fluorodeoxyglucose (FDG) application (27). These studies, which were conducted with F-18 FDG and PET, showed that the metabolism of the white matter was 15.3% higher in Alzheimer's patients compared to healthy subjects. Furthermore, it was determined that this increase in glucose metabolism was negatively correlated to the cognitive parameters (24). In other words, the glucose metabolism in the white matter of Alzheimer's patients had a negative correlation to the SMMSE score. Moreover, it was found that glucose uptake had a strong and positive correlation to amyloid accumulation. Particularly microglia, which are induced by the AP and activated by the neuro-inflammation, seem to increase the glucose consumption in order to mediate the inflammatory process (24). In our study, we thought that the mechanism related to the higher carbohydrate intake in Alzheimer's patients compared to healthy individuals and the increase in carbohydrate consumption with the increase in the severity of dementia might be related to microglia activation.

High carbohydrate and sugar consumption in Alzheimer patients may also be related to insulin metabolism. Because insulin resistance of the central nervous system (CNS) is another pathological mechanism related to AD (9). It was demonstrated that neuroinflammation in Alzheimer's patients played an important role in the development of cerebral insulin resistance (28). It was also demonstrated that AP's suppressed the insulin expression in the astrocytes (29, 10), and there was a bidirectional correlation between the deteriorated cerebral insulin signaling and AP accumulation in AD (30). The relationship between the pathological processes accompanying AD and CNS insulin resistance led to the introduction of the term "Type 3 diabetes mellitus" for the definition of AD (9).

Under normal conditions, insulin has an important role in the development of the excitatory synapses and maintaining their continuity. It stimulates neuronal survival by inhibiting apoptosis (31) and even affects hippocampal functions, molecular structures and functions related to cognition and memory (10). It was demonstrated that the acute increases in insulin levels and glucose administration had a positive effect on cognition under physiological conditions (11, 32). It was demonstrated that intranasal insulin administration improved memory functions in both healthy individuals and patients with insulin resistance (33-35). This positive effect of insulin on cognitive functions was observed not only in healthy individuals also in Alzheimer's patients (36, 37). It was stated that the reason for the excessive carbohydrate intake in Alzheimer's patients might indicate an effort to directly stimulate mental performance (31). Taking into consideration the positive effect of insulin on cognitive functions, the high glucose intake in Alzheimer's patients may be related to an effort to increase the insulin release in response to elevated blood glucose levels (31).

There are studies showing that hypoglycemia causes impairment in executive functions in daily life, occupational functions, and a decrease in the ability to plan and organize. Hypotheses that non-severe insulin-induced hypoglycemia reduces cognitive functions have been experimentally proven (38). Consuming high amounts of carbohydrates, especially simple sugars, which will rapidly increase blood sugar, may also be an effort to increase cognitive capacity in Alzheimer's patients.

Another reason that may increase glucose use in the brain

may be cortical spreading depression (CSD). CSD is a spontaneously propagating wave of neuronal depolarization within the cortex, which is associated with various neurovascular diseases such as AD, stroke, subarachnoid hemorrhage, traumatic brain injury, Parkinson's Disease, and migraine. Cortical spreading depression causes high ATP consumption and imposes a significant energy load on brain tissues. Consecutive and chronic episodes of CSD significantly increase cerebral glucose metabolism. Successive CSD waves in the brain tissue of AD patients may be another reason that increases glucose consumption (39) and may be another answer to the question of where the glucose taken with food is used.

In conclusion, in our study, we found that Alzheimer's patients consume higher carbohydrates and sugar than healthy individuals, and that carbohydrate consumption is increased in severe dementia. We thought that high carbohydrate intake in Alzheimer's patients might be an effort to maintain the insulin-glucose balance in the brain.

Ethical Statement

In this study, all procedures were carried out in accordance with the ethical standards of the Institute and Helsinki Declaration. This study was approved by the local Ethics Committee.

Date and No. of the Ethics Committee Approval: 04.01.2012/3731. Ministry of Health, Ankara Training and Research Hospital, Committee for Training, Planning, and Coordination.

All participants provided written informed consent.

Conflict of interest

There is no conflict of interest among the authors.

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Authors' contributions

Concept: U.E., F.Y.C., L.E.İ., G.G., Design: U.E., F.Y.C., G.G., L.E.İ., A.D.L., Data Collection or Processing: F.Y.C., A.D.L., Analysis or Interpretation: A.D.L., F.Y.C., Literature Search: F.Y.C., A.D.L., Writing: F.Y.C., A.D.L.

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