Original article

Do Nutrition Habits Influence the Clinical Presentation of Parkinson's Disease?

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Abstract

Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder characterized with alpha-synuclein pathology. For the majority of patients, except for some genetic forms, etiology is still unknown. There are some implications that food intake and gut microbiota could contribute to PD.

Aim: The aim of this paper is to analyze the influence of protein, fruit and vegetable intake on the clinical presentation of idiopathic Parkinson disease

Patients and methods: Patients with idiopathic PD were surveyed for demographic data and nutritional habits in regards to protein, fruit and vegetable intake. Motor symptoms were evaluated using the Unified Parkinson Disease Rating Scale (UPDRS) part III and IV, cognitive impairment using Mini Mental State Examination (MMSE) and depression using Beck Depression Inventory (BDI).

Results: We have analyzed data of 96 patients. Patients using fewer dairy products have more often tremor type of PD ($p<0.040$). We did not find any differences in severity of motor symptoms, disease stage, age when disease start, frequency of motor complications and fluctuation of therapy, depression and cognitive impairment according to protein, fruit and vegetable ingestion.

Conclusion: Higher intake of dairy products could influence the appearance of less favorable forms of Parkinson's disease (rigor type). Protein, fruit and vegetable intake do not influence the disease appearance, severity of motor symptoms, motor fluctuation and complication of therapy, disease stage, the appearance of cognitive impairment nor depression in Parkinson's disease patients.

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Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder characterised by alpha-synuclein pathology [1]. For the majority of patients, the etiology of the disease is still unknown. Some recent studies in PD patients are addressing food and its influence on gut microbiota [2]. It is known that PD patients have altered gut microbiota with abundance in proinflammatory and reduction in anti-inflammatory microbes [3]. Those changes can promote alpha-synuclein pathology in the enteric nervous system, which could spread in a prion-like manner to the brain [4]. Many studies have been done in order to explore the influence of various types of nutrition on the risk of Parkinson's disease. There have been papers reporting an increased risk associated with diets rich in animal fat [5,6], dairy foods [7,8], raw meat [9], and carbohydrates [10], while some other studies have not found a strong correlation between nutrition and the risk of PD [2, 11-13]. It has been shown that some nutrients could decrease the risk of developing PD in many ways. Monounsaturated (MUFAs) and polyunsaturated fatty acids (PUFAs) are known to have anti-inflammatory effects and they can reduce oxidative stress and inhibit apoptosis [14,15]. Vitamin A, B6, B9, B12, D and E have been proven to have protective effects and decrease the risk of PD [16-20]. Early post-treatment (after 6- hydroxydopamine toxicity) with retinoic acid in the animal model is able to provide protection from neurodegeneration in nigrostriatal dopaminergic neurons [16]. Decreased levels of vitamins B6, B9 and B12 lead to elevated levels of homocysteine. Hyperhomocysteinemia damages the DNA, depletes energy reserves and subsequently induces neuron apoptosis [21]. Calcitriol (vitamin D) reduces neuronal toxicity, while vitamin E has the ability to reduce MPTP-induced (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) toxicity in dopaminergic neurons [22,23]. Using food with anthocyanin- and proanthocyanidin-rich substances improves the mitochondrial function and reduces the level of neurodegeneration [24].

This paper aims to analyse the influence of protein, fruit and vegetable intake on the clinical presentation of idiopathic Parkinson's disease observed through several parameters: the age when the disease was diagnosed, severity of motor symptoms, type of Parkinson`s disease, appearance of motor fluctuations and complication of therapy, depression and cognitive impairment.

Patients and Methods

The study was conducted on patients with idiopathic Parkinson's disease diagnosed during a regular check-up at the outpatient clinic at Osijek Clinical Hospital Centre. Their consent of participation in this study was obtained and the study was approved by the local Ethics Committee. The patients were surveyed for age, sex, disease duration, the age when the disease was diagnosed and nutrition habits pertaining to protein, fruit and vegetable intake for 3 months prior to the examination (part of the Mini Nutritional Assessment, source Nestlé Nutrition Institute). Motor symptoms were evaluated using the Unified Parkinson Disease Rating Scale (UPDRS) Part III (range from 0 to 103 points) and IV (range from 0 to 23 points), cognitive impairment symptoms were evaluated using the Mini Mental State Examination (MMSE; range from 0 to 30 points) and depression was evaluated using the Beck Depression Inventory (BDI; range from 0 to 63 points). According to the UPDRS Part III, patients were divided into 2 groups – rigor-dominant and tremor-dominant. Categorical data were presented as absolute frequencies and percentages, while the differences between nominal variables were tested by the Fisher's exact test. Numerical data were tested with the Shapiro-Wilk test for normality of data distribution. Afterwards, numerical data were presented with the mean and standard deviation in the case of normal, and with the median and interquartile range in the case of abnormal distribution. The comparison between nominal and numerical variables with normal distribution was tested using the One-way ANOVA or Student's t-test, while for numerical variables with abnormal distribution, the Mann-Whitney and Kruskal-Wallis tests were used. Statistical significance was defined as α=0.05, while the statistical analysis was conducted with STATISTICA 13 (StatSoft Inc., Tulsa, Oklahoma, USA).

Results

A total of 96 patients were analysed, of whom 57 (59.4%) males and 39 (49.6%) females, with the mean age of 70.22±8.598. Regarding the type of Parkinson's disease, 50 (52.1%) patients had the tremor-dominant type, while 46 (47.9%) patients had the rigor-dominant type. Table 1 shows the data about disease duration, disease stage, the age of onset, UPDRS III, MMSE and BDI score.

Table 1. Demographic data, UPDRS III, MMSE, BDS data

	mean/median	std. dev./25th-75th	min/max
Age	70.22	±8.598	48/80
Disease duration	4.00	(2.00-10.00)	1/16
Age when disease started	64.64	±9.730	36/81
Updrs Iii	16.50	(10.25-23.75)	3/83
Mmse	26.00	(23.00-28.00)	15/30
Bds	13.60	±8.992	0/44

UPDRS III – Unified Parkinson`s Disease Rating Scale part III; MMSE – Mini Mental State Examination; BDS – Beck

Table 2 presents the frequency of nutrition intake. The majority of the patients eat meat every day (40.6%) or every other day (37.5%). More than two-thirds (71.9%) of the patients consume dairy products every day, while 68.8% of them consume two or more legumes and eggs per week. Half of them eat meat, fish and poultry every day and more than 2 pieces of fruit and vegetable per day (Table 2).

Table 2. Frequency of protein, fruit and vegetable intake

Food	N	%
Protein intake		
• once per week	4	4.2
• twice per week	17	17.7
• every other day	36	37.5
• everyday	39	40.6
Dairy products one per day		
• yes	69	71.9
• no	27	28.1
Legumes or eggs two or more per week		
• yes	66	68.8
• no	30	31.2
Meet, fish, poultry every day		
• yes	46	47.9
• no	50	52.1
Fruit or vegetable ≥2 per day		
• no	43	44.8
• yes	53	55.2

The UPDRS III and IV results were compared with the nutrition habits of PD patients, but no significant difference was found. The comparison is shown in Table 3.

Table 3. Difference in UPDRS part III and motor complications and fluctations of therapy according to protein, fruit and vegetable intake

	UPDRS III		„OFF"		DYSKINESIA	
	median	p	yes/no (N)	p	yes/no (N)	p
Protein intake						
• once per week	19.50		1/3		0/4	
• twice per week	22.00		10/7		2/15	
• every other day	17.00		15/21		5/31	
• everyday	15.00	0.580	17/22	0.572*	9/30	0.614*
Dairy products one per day						
• yes	17.00		30/39		11/58	
• no	16.00	0.925	13/14	0.820*	5/22	0.766*
Legumes or eggs two or more per week						
• yes	17.00		29/37		11/55	
• no	14.50	0.351	14/16	0.828*	5/25	1.000*
Meet, fish, poultry every day						
• yes	15.00		20/26		10/36	
• no	18.50	0.334	23/27	0.840*	6/44	0.275*
Fruit or vegetable ≥2 per day						
• no	17.00		19/25		6/37	
• yes	16.00	0.487	24/28	1.00*	10/42	0.656*

Differences in the age of disease diagnosis, MMSE and BDI score regarding the patients' nutrition habits were also observed, but there were no statistically significant differences, as shown in Table 4.

Table 4. Difference in age when disease start, type of Parkinson`s disease (tremor vrs rigor), MMSE and BDI according to protein, fruit and vegetable intake

	Age when disease started		Type of PD		MMSE		BDI	
	mean	p	t/r (N)	p	median	p	mean	p
Protein intake								
• once per week	68.00		2/2		25.50		18.50	
• twice per week	68.71		8/9		24.00		16.00	
• every other day	64.86		22/14		26.00		12.53	
• everyday	62.31	0.126	18/21	0.574*	26.00	0.179	13.05	0.274
Dairy products one per day								
• yes	65.29		31/38		26.00		14.45	
• no	62.96	0.295	19/8	**0.040***	25.00	0.993	11.44	0.072
Legumes or eggs two or more per week								
• yes	65.27		35/31		25.00		12.82	
• no	63.23	0.344	15/15	0.828*	27.00	0.348	15.33	0.388
Meet, fish, poultry every day								
• yes	62.24		22/24		26.00		13.28	
• no	65.00	0.704	28/22	0.540*	25.00	0.323	13.90	0.991
Fruit or vegetable ⩾2 per day								
• no	63.60		23/21		26.00		14.09	
• yes	65.31	0.399	27/25	0.835*	25.00	0.219	12.56	0.383

PD – Parkinson`s disease; t/r – tremor vrs. rigor type; MMSE - Mini Mental State Examination; BDI – Beck Depression Inventory

The analysis of influence of nutrition habits of PD patients showed that the tremor-dominant group of PD patients consumed dairy products less frequently, while there were no statistically significant differences in other nutrition habits of patients with tremor-dominant and rigor-dominant Parkinson's disease (Table 5).

Table 5. Comparison between type of Parkinson disease and nutritional habits of Parkinson disease patients

	Type of PD

	t/r (N)	p
Protein intake		
• once per week	2/2	
• twice per week	8/9	0.574*
• every other day	22/14	
• everyday	18/21	
Dairy products one per day		
• yes	31/38	**0.040***
• no	19/8	
Legumes or eggs two or more per week		
• yes	35/31	0.828*
• no	15/15	
Meet, fish, poultry every day		
• yes	22/24	0.540*
• no	28/22	
Fruit or vegetable ≥2 per day		
• yes	23/21	0.835*
• no	27/25	

Discussion

Nutrition habits of 96 PD patients were surveyed for the purpose of analysing their influence on the clinical presentation of the disease. The majority of the patients ingested protein in the form of dairy products, eggs and legumes and half of them in the form of meat, fish and poultry on a daily basis. No difference in the age when the disease was diagnosed, severity of motor symptoms, disease stage, frequency of motor fluctuations and complication of therapy, nor depression and cognitive impairment associated with protein, fruit and vegetable intake was found. It was only found that the patients consuming fewer dairy products more frequently suffer from tremor-dominant PD, which is a form of the disease with a favourable outcome [25]. Neuropathological studies have shown that the rigor-dominant type compared to the tremor type of PD exhibits a higher level of neuronal loss of the locus coeruleus, lateral and medial part of the substantia nigra with more severe gliosis, extra-neuronal melanin deposits and neuroaxonal dystrophy in the substantia nigra [26]. Many papers have reported a relation between dairy products and PD [27-30]. There are several possible explanations of how dairy products influence neurodegeneration and the risk of PD. One of the possible explanations is the influence of milk fat on gut microbiota. Milk fat (MF) and PUFA-rich fat had similar effects on Bacteroidetes and Firmicutes, but besides this, MF has the ability to greatly increase Bilophila wadsworthia. An increased level of Bilophila wadsworthia was associated with the pro-inflammatory T helper type 1 (T(H)1) immune response [31]. Dairy products also have the ability to reduce the uric acid level, which could cause a greater PD incidence and faster PD progression [32,33]. It is also known that they can induce insulin resistance and that this has an impact on the development of not only PD, but also of Alzheimer's disease [34,35]. People suffering from lactose intolerance and consuming dairy products are at the risk of intestinal inflammation and increased intestinal permeability. Besides that, milk could be contaminated with neurotoxic pesticides [36]. Finally, the ingestion of bovine microbiota could affect human microbiota through small intestinal bacterial overgrowth (SIBO), which could increase the risk of PD [37-39]. Marczewska et al. found in 45 advanced-stage PD patients that patients with high protein intake experience moderate to severe disease motor symptoms more frequently [40]. Serum carotenoid, retinol and tocopherol concentrations were lower in PD patients with severe motor symptoms and a more advanced stage of the disease [41]. Many studies have proved that high protein intake affects the motor response to levodopa therapy, causing the appearance of motor fluctuations [42], and that the use of a protein-redistribution diet helps with the amelioration of „on-off" fluctuations [43]. On the other hand, a protein-restricted diet (PRD) has proven to worsen the fluctuations with the worsening of dyskinesia [44]. This negative influence of proteins on the motor function is not present in early stages of PD and usually appears after 13 years of disease duration, or 8 years after levodopa was introduced in therapy [45]. No influence of protein ingestion on motor symptoms, motor fluctuations and complication of therapy was found, probably due to the fact that the study group of patients was mostly in the early stage of the disease (the median was 4.00 years), during which there is no such negative influence. The ingestion of saturated fatty acids, lower consumption of milk and dairy products and consumption of full-fat dairy products have a negative impact on age-related cognitive decline, mild cognitive impairment and vascular dementia [46]. There is limited data about the protective role of fruit and vegetable ingestion on cognitive decline, dementia and vascular dementia [46]. No differences in nutrition habits and cognitive impairment were found. The majority of our patients were diagnosed with mild cognitive impairment (MMSE median was 24.00) and were a rather homogeneous group (MMSE interquartile range from 23.00 to 28.00). Besides this, MMSE is not very sensitive to the subcortical type of cognitive impairment that is present in Parkinson`s disease [47]. Therefore, a more heterogenous patient group with more sensitive tests for subcortical cognitive impairment should be used for more conclusive results. The MIND diet (the Mediterranean-DASH Intervention for Neurodegenerative Delay diet) that emphasises intake of fresh fruit, vegetables, and legumes was not associated with the reduction of depression risk, in contrast to the Mediterranean diet [48]. Consumption of full-fat yogurt was related to a lower risk of depression, but only in women, in the study of Pernez-Cornago et al [49]. There is evidence (in large-scale and well-conducted observational studies) that the ingestion of seafood, vegetables, fruit and nuts reduces the risk of depression [50]. Unfortunately, no significant differences between nutrition habits and depression were found in this study.

Higher intake of dairy products could influence the appearance of less favourable forms of Parkinson's disease (rigor-dominant type). This study did not find any influence of protein, fruit and vegetable intake on the age of disease diagnosis, severity of motor symptoms, disease stage, motor fluctuations and complications of therapy, appearance of cognitive impairment or depression in Parkinson's disease patients. The limitation of this study is a small sample size. Furthermore, only the source of protein intake (meat, legumes or eggs, dairy) was analysed, while there are no evaluated sources regarding fruit and vegetables. For that reason, the data about the ingestion of fruit and vegetables producing antioxidant effects are limited. Therefore, the interpretation of our study results must be taken with caution. Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent: "Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article."

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Disclosure

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Competing interests. None to declare.

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