Review article

Dietary interventions in Parkinson's disease: An update

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ABSTRACT

Parkinson's disease (PD) is a progressive neurodegenerative disorder mostly affecting the elderly population. Nutritional status, dietary habits, and physical activity are closely associated with PD clinical symptoms. Based on scientific evidence, lifestyle adjustments are being considered as therapy approaches in various chronic diseases. Dietary modifications are an additional treatment strategy for managing motor and non-motor symptoms in PD. This review focuses on the latest nutritional interventions with protein restriction, Mediterranean and ketogenic dietary modification, probiotic utilisation, and their impact on PD.

Keywords: Ketogenic diet; Mediterranean diet; Parkinson's disease; probiotics; protein restriction diet.

INTRODUCTION

arkinson's disease (PD) is a multifactorial neurodegenerative disorder resulting from a complex interplay between aging, genetics, and environmental factors. Pathophysiology of PD is triggered by the accumulation of alpha-synuclein (asyn) on exposure to environmental toxins and bacterial lipopolysaccharides. The gastrointestinal tract and nasal cavity are the two main vulnerable sites for exposure to environmental toxins (1). Braak hypothesis indicates the Lewy pathology is initiated in the gut and accumulated α -syn misfolding is propagated to substantia nigra via the vagal nerve (2). This prompts the degeneration of the dopaminergic neurons, which occurs decades before the onset of cardinal motor symptoms of PD, as revealed by Baark staging (3). Hyposmia, sleep disorder, constipation, and other gastrointestinal symptoms are prodromal non-motor symptoms, whereas resting tremors, bradykinesia, rigidity, and postural variability are the key motor symptoms of PD (4).

An intact gastrointestinal system is essential for digesting and absorbing ingested nutrients and maintaining energy balance. The gastrointestinal tract also provides a large surface for exposure to environmental risk factors that can trigger intestinal inflammation, leaky gut, exposure to bacterial pathogens and endotoxins, immune response, neuroinflammation, and eventually Lewy pathology in PD (5). Consumption of artificial sweeteners, alcoholic beverages, fried foods, and processed foods are associated with disrupting intestinal integrity, leading to barrier dysfunction and malabsorption (6–8). Diet is one of the several environmental risk factors closely linked with PD pathology and disease progression. A metanalysis by J. Fu et al. reports a higher incidence of malnutrition in PD, mainly in developing countries, and relates Hoehn-Yahr (H&Y) staging, Unified Parkinson's Disease Rating Scale (UPDRS) score, higher levodopa equivalent daily dose (LEDD), and disease duration with inadequate nutrition (9). Most of the available data on the nutritional status of PD is limited to either cross-sectional or prospective cohort observational epidemiological studies. Researchers have analysed the risk factors associated with the consumption of the food groups and related with either PD pathology or progression.

Though levodopa remains the drug of choice in treating PD, it is associated with motor fluctuation and dyskinesia, and it has less impact in managing the non-motor symptoms (10,11). New therapeutic approaches are being considered to treat motor fluctuations and non-motor symptoms. Diet manipulation is one such approach that has been in the limelight lately. We summarize the available data on clinical trials on dietary interventions in PD, highlighting protein restriction, Mediterranean and keto diets, and probiotic usage and their outcomes since the past decade.

Dietary intervention

Dietary interventions or clinical trials are carried out to understand the role of modifying the food habits of an individual or group of subjects. Adjusting nutritional habits by educating PD patients with malnutrition or under risk of malnutrition has positively impacted the

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quality of life and motor and non-motor symptoms. Patients were recommended a balanced diet, considering sufficient intake of fibers, fluids, and macro and micronutrients based on the daily nutritional or calorie requirement (12). Tobias *et al.* observed bowel cleansing for eight days with dietary intervention on an ovo-vegetarian diet for two weeks improved the motor symptoms and reduced the levodopa dosage in a year on follow-up in PD patients. In their study, vegetarian diet intervention consisted of vegetables, fruits, cereals, spices, herbs, nuts, seeds, olive oil, and vinegar, including milk and egg products. Patients were on a butyrate-rich diet that included ghee in most dishes, which influenced microbial density and diversity (13).

Protein restriction diet

Diet has an effect on levodopa metabolism. PD patients are recommended to avoid a protein-rich diet during the day and are suggested to consume meat or proteins only during the evening meals (Omni diet), as protein metabolism leads to the production of amino acids that could compete with the specific amino acids carrier substrates (larger neutral amino acid transporters) responsible for crossing levodopa through the blood-brain barrier and entering the brain. A plantbased dietary intervention of 12 weeks that restricted patients from consuming meat (protein) showed a significant reduction in the severity of symptoms and stage in PD. Here the patients were on a balanced diet where they also received an adequate daily requirement of proteins with legumes and vitamin B12 (14). A systematic review on a protein restriction diet also reports a reduction in motor impairment or improvements in fluctuations in PD (25).

Ketogenic diet

In a regular or normal diet, 30% of calories are obtained by fat intake, whereas in the keto diet, which is rich in fat, fat contributes 90% to the calorie intake (16). Keto diet activates dopaminergic centres of the central nervous system (26). It induces ketosis that increases the level of ketone bodies in the tissues. Increased utilisation of ketone bodies by the brain improves cognitive function (27).

A randomised dietary intervention for eight weeks with a low-fat, high carbohydrate diet and a keto diet with high-saturated fat and low carbohydrate diet has shown a drastic fall in the motor and non-motor scores in PD, confirming the improvement in the symptoms. The ketogenic diet also reduced motor complications and most non-motor symptoms more efficiently than the low-fat-high carb diet (15). Another study reports an improvement in voice quality of the PD patients after a three-month keto diet intervention (16). Tidman *et al.* report a positive impact of the ketogenic diet on the biomarkers of health BMI, weight, waist circumference, fasting insulin, and triglycerides. Though they have not found an influence on depression in PD, they report a significant decrease in anxiety after a 12-week intervention (17).

Mediterranean diet

Lately, the Mediterranean diet has earned prominence since it has been associated with reduced risk of cancer, cardiovascular, and neurodegenerative diseases. It's a food pattern of inhabitants residing around the Mediterranean Sea, consisting of fresh vegetables, whole grains, and legumes as a staple food with fresh fruits, moderate fish and wine, low dairy products, and infrequent red meat, while olive oil, nuts, and seeds are fat sources (28).

Cross-sectional studies report adherence to the Mediterranean diet during mid-age, lower risk of developing PD (29), delayed early onset of prodromal symptoms of PD (depression, constipation, morning drowsiness) (30), and associated with later onset of disease (31) but do not correlate with disease duration or difficulty in swallowing (32). Clinical intervention with the Mediterranean diet reduced constipation (20), lowered UPDRS score and severity, improved activity of daily living (18), and cognitive function in PD (19).

Mediterranean diet is a rich source of omega 3, polyphenols, beta-carotene, vitamin E, and Vitamin C, which have antioxidant properties that possibly suppress oxidative stress and inflammation and are associated with neuroprotection in PD (18,29).

Probiotics

Gastrointestinal dysfunction is one of the commonest non-motor symptoms experienced by PD patients. Lower GI dysfunction such as decreased bowel movement, excessive straining evacuation, incomplete evacuation are prominent symptoms of constipation in PD (33). A combination of prebiotics and probiotics have been recommended for functional constipation of neurological origin (34). A study on PD reports the beneficial effect of one such synbiotic therapy consisting of prebiotic and multiple strains of probiotics improved complete bowel movement in PD (22). Synbiotic therapy is recommended treatment by movement disorder society evidence-based guidelines for non-motor symptoms in PD (35).

Using various combinations of strains as probiotics for treating constipation in PD has also shown positive results (24). Yet another study confirms an improvement in abdominal pain and bloating on clinical trial subjects with gastrointestinal symptoms in PD. However, they have reported conflicting results with respect to resolving constipation and incomplete evacuation (21). Omid et al. have observed an improvement in clinical symptoms of PD on intervention with probiotics (23).

	Table 1: Dietary interventions in Pai	rkinson's disease
Study	Dietary Intervention	Beneficial Effects
Protein restriction, Plant-based diet		
Baroni et al., (14)	Plant-based diet (4 weeks)	 Improvement in Total UPDRS Score Motor Performance Modified H&Y Stage Scale
Ongun et al., (12)	Recommended dietary intervention on consultation with a dietitian as per the daily nutritional requirements of the individual subject (5 weeks)	Improvement in Nutritional Status Quality-of-life Score Motor and Non-Motor Symptom Lower UPDRS Score Anxiety Score Depression Score
Hegelmaier et al., (13)	Diet- ovo-lacto vegetarian (14days) and Enema (8 days)	Evaluation after one year Improvement in Motor Symptoms (UPDRS III Score)
Ketogenic diet		
Phillips <i>et al.</i> ,(15)	Low fat- high carbohydrate diet (8 weeks)	Improvement inNonmotor daily living experienceMotor symptoms
	Keto diet (8 weeks)	 Improvement in Nonmotor daily living experience Reduction in motor complications Decreases in Urinary problems, Pain Fatigue daytime sleepiness Cognitive impairment
Kovuncu <i>et al.</i> (16)	Keto diet (3 months)	Improvement in voice quality
Tidman <i>et al.</i> ,(17)	Keto Diet (12 weeks)	 Improvement in UPDRS, I Score (Mentation, Behaviour, Mood) Anxiety symptoms
Mediterranean diet		
Paknahad et al., (18)	Mediterranean diet (10 Weeks)	 Improvement in Activity of daily living UPDRS Score & disease severity
Paknahad <i>et al.</i> , (19)	Mediterranean diet (10 Weeks)	Improved cognitive assessment score Increased dimensions of executive function, language, attention, concentration, active memory
Rusch <i>et al.</i> , (20)	Mediterranean diet (5 Weeks)	Improvement in constipation symptoms
Probiotic intervention		
Georgescu <i>et al.</i> , (21)	Probiotics- <i>Lactobacillus acidophilus</i> and <i>Bifidobacterium infantis</i> (Daily twice for 3 months)	Improved abdominal pain and bloating
Barichella (22)	Fermented milk, containing multiple probiotic strains (<i>Lactobacillus spp</i> , <i>Bifidobacterium spp</i> , <i>Streptococcus</i> <i>salivarius, and Enterococcus faecium</i>) and prebiotic fibre (Once daily for 4 weeks)	Increase in complete bowel movements Improvement in Constipation
Tamtaji et al., (23)	Four different species of <i>Lactobacillus</i> and <i>Bifidobacterium bifidum</i> (Once daily for 12 weeks)	Decrease in MDS-UPDRS Score
Ibrahim (24)	Multi-strain probiotics (<i>Lactobacillus</i> sp and <i>Bifidobacterium</i> sp) (Twice daily for 8 weeks)	Improvement in constipation and intestinal motility by an increase in bowel opening time and reduction in gastrointestinal transit time

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H&Y : Modified Hoehn-Yahr staging; MDS: Movement Disorder Society; UPDRS: Unified Parkinson's Disease Rating Scale **CONCLUSION**

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Current research has demonstrated dietary intervention positively influence movement, can balance. intellectual ability, anxiety, and quality of life in PD. Nutritional modification can intervene in the disease progression and has eased both motor and non-motor symptoms in clinical trials. Growing evidence on the Mediterranean diet makes it the most recommended nutritional approach for neurological disorders and has been positively associated with PD. In addition, even probiotics influence mood. cognition, and gastrointestinal symptoms. On this basis, dietary changes might be considered part of a diseasemanagement strategy. A lifestyle change may also assist in delaying the progression of the disease.

"Our food should be our medicine, and our medicine should be our food"- Hippocrates.

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CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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