Food consumption in patients with Parkinson's disease and its impact on disease prognosis and drug therapy

Consumo alimentar em pacientes com doença de Parkinson e o seu impacto sobre o prognóstico e a terapia medicamentosa

Danielly Zilma de Sousa¹, Ana Carolina Landim Pacheco¹, Gilberto Santos Cerqueira¹, Paulo Michel Pinehiro Ferreira¹, Ana Paula Peron¹, Iana Bantim Felicio¹

¹Universidade Federal do Piauí, Piauí, Brasil.

* Correspondência: ianacalou@gmail.com

ABSTRACT
This study evaluated the dietary intake of patients with Parkinson’s disease in a small city of Brazil’s Northeast. To assess food consumption, was applied the 24-hour recall which uses the RDA 1989 as a benchmark. Was observed that patients, not having access to nutritional information, do not know about the limitation and food requirements imposed by the disease. All parameters analyzed: total energy, macronutrient, minerals and vitamins intake as well as protein intake throughout the day, were in disconformity with what is recommended by the RDA and discord with the own needs with this group of patients. Was noted that the exemption of the professional nutritionist to health care triggers improper actions that may worsen the patient's physical condition and their quality of life besides likewise not be benefited with nutriments that could alleviate the symptoms of the disease, what ends up burdening further the public health system. Keywords: Neurodegeneration; diet; pharmacotherapy

RESUMO
Este trabalho avaliou a ingestão alimentar de pacinetes com Parkinson em uma pequena cidade do nordeste do Brasil. Para avaliar o consumo alimentar, foi aplicado o recordatório de 24 horas, que usa a RDA 1989 como ponto de referência. Foi observado que os pacientes, não tendo acesso à informação nutricional, desconhecem as limitações e as necessidades alimentares impostas pela doença. Todos os parâmetros analisados: energia total de macronutrientes, minerais e vitamina, bem como a ingestão de proteína ao longo do dia, estavam em desconformidade com o que é recomendado pela RDA e em discordância com as necessidades próprias deste grupo de pacientes. Observou-se que a isenção do profissional nutricionista aos cuidados de saúde desencadeia ações impróprias que podem piorar a condição física do paciente assim como sua qualidade de vida, além de não obterem os benefícios nutricionais que poderiam aliviar os sintomas da doença, o que acaba por onerar ainda mais a saúde pública sistema. Palavras-chave: Neurodegeneração; dieta; farmacoterapia
INTRODUCTION

Parkinson's disease (PD) is a progressive and incurable neurodegenerative disorder affecting 1% of the older adult population, and its characterized by progressive and relentless loss of dopaminergic neurons of the substantia nigra (pars compacta), resulting in decreased dopamine production and destruction of nigrostriatal pathway. This loss of dopaminergic impulse is the mechanism responsible for the onset of rigid akinetic syndrome and is often associated with tremor and postural instability, typical of the disease (ABBOTT, 2010).

The nutritional elements can affect patients with PD, being determinants for their quality of life. The basic characteristics of the disease, its progression and the therapeutic approach, are not the only factors that should be considered in treatment. Several complications of stamp nutrition affect these patients and a diet that takes into account the peculiar needs of the pathology is essential to minimize future problems (BARICHELLETA et al., 2009).

In general, it has not been paid attention to the effects of interactions between neural elements and nutrients in the prognosis of patients with PD. The non-participation of the dietitian and its communication with a pharmacist in primary care to the patients can be harmful to their health and quality of life. This study evaluated the dietary intake of patients with Parkinson's disease in the city of Picos, a Brazilian Northeast city where nutritional nether pharmaceutical care are available for patients in the Health Public System, and its impact on their quality of life proposed by pharmacologic treatment.

METHODS

The study was conducted in Picos, state of Piauí, in 2012, with all 10 patients enrolled in the Parkinson's Drug Delivery System at the Municipal Department of Health that received, as major therapy, Levodopa. To collect data, we used the 24-hour recall, analyzed by the program NutWin version 1.5 of the Department of Health Informatics, Federal University of São Paulo (ANCÃO et al., 2006), which uses the RDA 1989 (Recommended Dietary Allowance) as a benchmark. Foods that were not included in the program had their nutrient composition verified based on the Food Composition Table. A survey containing clinical information about pharmacotherapy, symptoms, complementary therapies and nutritional counseling was carried out.

In despite limited, depending on the patient's memory, the 24-hour recall perfectly serves the purpose of the study to assess the degree of patients' awareness about their food and the need for more information on the impact of nutrition on disease.

Ethics

Patients who accepted to participate in this study signed consent form for the beginning of the study which was previously approved by the Ethics Committee of the Federal University of Piauí (no. Protocol 0258.0.045.000-10). All studies were performed in accordance with Brazilian research guidelines (Law 196/96, National Council of Health) and with Declaration of Helsinki.

RESULTS AND DISCUSSION

The treatment of Parkinson's disease goes beyond the pharmacological therapy and requires a multidisciplinary team to minimize the symptoms that are usually associated with increased mortality and poor quality of life (LANG & LOZANO, 1998).

Several inadequacies in nutrition of patients with PD were observed in this study. Firstly, the total energy (TE) was considered low for 80% of participants. Individuals with PD often present loss of weight and malnutrition. The involuntary movements related to the illness cause increase of energy consumption, changes in appetite, dysphagia, constipation as well as nauseas and vomiting induced dopaminergic therapy, that can contribute to a poor dietary intake. Emotional factors and motor difficulties as muscle rigidity, tremor of the hands and difficulty swallowing also collaborate for a low TE (DESPORT et al., 2013).
Some complementary therapies may be effective and, when properly used, can improve the patient's clinical condition without reducing the benefits of dopaminergic therapy (ZESIEWICZ & EVATT, 2009). In this study, we found that the only patient with normal TE, besides pharmacotherapy, used other forms of self-care, indicating that he probably had better information and was concerned about his general health status.

The consumption of carbohydrates and lipids showed no balance, characterized with low intake, in 20% of patients. Despite adequate in all patients, protein consumption did not obey, in either case, the special requirements imposed by the disease, such as the protein redistribution scheme, essential for successful therapy with levodopa.

Since its advent, levodopa remains the gold standard in the treatment of PD (ABBOTT, 2010), and nutrition plays a primary role in its effectiveness. In this study, all participants are treated with levodopa. Then, it is necessary a dietary guideline implementation that provides a better nutritional profile and allows a reduction of the adverse effects which appear with disease progression and drug therapy (DESPORT et al., 2013).

The patients in use of levodopa shows postprandial motor block due to competition between the drug and amino acids from diet for absorption. Thereby A diet with protein redistribution, concentrating the protein intake during the night, can improve the pharmacokinetics of levodopa, ensuring more stable drug plasma levels and reducing the severity of feared motor fluctuations (CEREDA ET AL., 2010). Study subjects were not instructed about the redistribution of protein in the diet than probably affected with a therapy rich on adverse effects without the expected pharmacological action.

It was found that many patients consume low amounts of polyunsaturated fatty acids (PUFA) and high amounts of animal fat and saturated fatty acids (SFA) (Table 1), an unhealthy association for them (de LAU et al., 2005). An adequate intake of PUFA is, which has been corroborated by several clinical and preclinical studies that show even the neuroprotective role of omega-3, important to protect neurons from the oxidative stress (CALON, 2007). Already over-consumption of animal fats and SFA is related to deleterious effects that may contribute to oxidative stress predisposing to neurodegenerative process (CHEN et al., 2003). This relationship, despite not established on its entirety, is being increasingly cited and must have been taken into account in the design of PD patients' care. Three patients who underwent consultations with nutritionist, by itself, with targeted information for the DP, showed less intake of saturated fatty acids, highlighting the importance of nutritional counseling.

Table 1. Adequacy of the RDA among participants about intake of saturated, monounsaturated and polyunsaturated fats by patients with PD.

<table>
<thead>
<tr>
<th></th>
<th>Over</th>
<th>Appropriate</th>
<th>Under</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFA</td>
<td>40%</td>
<td>60%</td>
<td>-</td>
</tr>
<tr>
<td>MFA</td>
<td>10%</td>
<td>90%</td>
<td>-</td>
</tr>
<tr>
<td>PUFA</td>
<td>10%</td>
<td>40%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Legenda: SFA = saturated fatty; MFA = monounsaturated fatty and PUFA = polyunsaturated fats

Some controversies persist regarding prevention or reduction of the progression of Parkinson's disease combined with a healthy diet, especially in relation to micronutrients (MIYAKE et al., 2011b). In this study, all patients showed deficiencies in mineral intake indicating inadequate and deficient nutrition (Table 2).

Table 2 – Percentage adequacy of the RDA among participants on micronutrient intake:

<table>
<thead>
<tr>
<th>Micronutrients</th>
<th>Consumption</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Over</td>
</tr>
<tr>
<td>Iron</td>
<td>40%</td>
</tr>
<tr>
<td>Zinc</td>
<td>-</td>
</tr>
<tr>
<td>Magnesium</td>
<td>-</td>
</tr>
<tr>
<td>Calcium</td>
<td>20%</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>70%</td>
</tr>
</tbody>
</table>

Legend: intake of iron, zinc, magnesium, calcium and phosphorus in accordance with RDA

As an essential mineral micronutrient for normal neurological development, iron is
involved in some pathological processes of PD, such as formation of Lewy bodies (SIPE et al., 2002; KAUR & ANDERSEN, 2004). The increased intake of iron observed in this study can predict a worse prognosis, considering that iron supplementation is related to a decrease activity of superoxide dismutase in the substantia nigra, contributing to the oxidative stress and increasing neuronal damage (NIIZUMA et al., 2009). Zinc is also involved in oxidative stress and neuronal death (MOCCHEGIANI et al., 2005) but was not ingested in excessive amounts by study participants.

The dopamine depletion observed in the caudate nucleus has been linked to a diet with deficiency in magnesium. In a rat PD model whtg culture of ventral mesencephalic-striatal cells with 1-methyl-4-phenylpyridinium (MPP+), an increase in the concentration of magnesium from 0.8 mM to 1.2 mM significantly inhibited the toxicity of MPP+, and a concentration of 4.0 mM completely prevented any decrease in the number of dopaminergic neurons. This mineral have also played a crucial role in inhibiting induced-Ca2+ excitotoxicity, process involved in the dopaminergic neurons deficit (MIYAKE et al., 2011b). In this study, 70% of participants had deficient intake of Mg2+, confirming previously outcomes found in North American and European metabolic studies (SEELIG, 1981). In addition, it is important to consider that the senility process increases the demand for this mineral, which requires readjusting of the diet to slow the disease progression (TRAMONTINO et al., 2009).

Bradykinesia, postural instability and as well as the empairement of anticipatory control of grasp during obstacle crossing experienced by Parkinson’s patients predispose them to frequently falls, with serious consequences such as hip fractures and worsening of the mobility (GRAY & HILDEBRAND, 2000; MCISAAC et al., 2012). The maintenance of bone mass is essential in the reduction of such injuries, though this work revealed a low intake of calcium and magnesium associated with high intake of phosphorus, which increases the serum levels of parathyroid hormone and contribute to the decrease bone density (MAHAN & ESCOTT-STUMP, 2010).

Oxidative stress already has its undoubted role in the final mechanism of cell death in many neurodegenerative disorders. The brain contains a high amount of phospholipids and polyunsaturated free fatty acids which are vulnerable to oxidants. Oxidative stress is one of the contributors in the loss of dopaminergic neurons in PD. For this reason, maintaining a diet rich in antioxidants is critical for brain integrity and the role of antioxidant vitamins in neurodegenerative processes has been increasingly studied clinically and experimentally (SURENDRAN & RAJASANKAR, 2010).

In this study, it was observed that the intake of the antioxidant vitamins C and E was inadequate in the majority of the patients (Figure 1). Reports have demonstrated the neuroprotective effect of vitamin E in PD (ZHANG et al., 2002; ETMINAN et al., 2005; MIYAKE et al., 2011a), though direct effects have not been described yet. Then, since it is believed that PD is a chronic condition, early dietary supplementation with vitamin E could promote a preventive action against Parkinson (FARIS & ZHANG, 2003). The protector properties of vitamin C was not observed in PD, since it has difficulty to cross the blood-brain barrier (ETMINAN et al., 2005).

**Figure 1. Percentage adequacy of the RDA among participants on vitamin intake.**

Nevertheless, supplementation using the combination of vitamins E and C have been used and studied in patients with neurodegenerative diseases due to the important role of vitamin C in maintaining the vitamin E appropriate levels (HATHCOCK et al., 2005). Additional studies have found that
the combination of both vitamins was also useful to improve levodopa therapy, delaying its onset (AYUSO-PERALTA et al., 1997).

Theories trying to explain the pathophysiology of Parkinson's disease stipulate that the disease is a consequence of obvious and correctable metabolic disorders, marked by the deficiency of vitamin B2, which has a role in the conversion of glutathione in its reduced state, decreasing local oxidative stress as a precursor of FAD⁺ (SAYRE et al., 2008). The administration of high doses of the B2 vitamin has been associated with beneficial effects and contrary to the disease. A hypervitaminosis is not recommended, but the normalization of FAD⁺ by increasing the absorption of its precursor, riboflavin, that shows poor absorption during advanced age (COIMBRA & JUNQUEIRA, 2003). Half of the patients in this study showed poor intake of vitamin B2 and none of them made use of supplements to elevate it levels.

Mitochondrial dysfunction and energy depletion are involved in the dopaminergic neurons death in substantia nigra. Oxidative stress may cause pore opening in mitochondrial membrane, modifying mitochondrial permeability and leading to a significant loss of NAD⁺'s inventory with subsequent cell injury and activation of the cascade of apoptosis (HAELTERMAN et al., 2014). In this context, niacin, being a precursor of NAD⁺, has demonstrated neuroprotective effect in preclinical models of PD (LI et al., 2006; ANDERSON et al., 2008). The care for patients with PD considers that the peripheral carboxylase inhibitors used in combination with levodopa increases niacin needs (BENDER et al., 1979), demanding an adequate diet. In this study, 4 patients had inadequate intake of niacin. A case study showed that niacin supplementation decreased the patient muscle rigidity and bradykinesia, improving greatly their quality of life. However, nicotinamide excessive exposure can cause self-intoxication precipitating diseases, among them, the Parkinson disease (ALISKY, 2005).

The deficiency of tiamine, which is involved in cell energy apparatus maintenance, may impair important brain structures involved on modulation and integration of motor responses, such as the striatum (SJÖQUIST et al., 1998). By acting as a cofactor of key enzymes related to the cellular energy metabolism, even a partial deprivation of its triggers biochemical alterations, as ATP reduction, preceding death of nervous cells in PD, adding latent mitochondrial dysfunctions and making worse the prognosis (BERG et al., 2004).

Lipid peroxidation is selectively increased in the substantia nigra of patients with Parkinson, being a consequence of the increase in homocysteine plasmatic levels. The use of levodopa has been related to hyperhomocysteinemia (BELCASTRO et al., 2010) affecting the cognitive performance (LEWERIN et al., 2005). Studies conducted by Valkovic et al (2005) demonstrated that folate and vitamins B6 and B12 supplementation can significantly reduce plasma concentrations of homocysteine in patients and has been shown to increase the catabolism of homocysteine in patients on levodopatherapy (LEWERIN et al., 2005). Folate deficiency raises homocysteine plasma concentration and is associated with diseases in central nervous system. In this regard, folate and vitamins B6 and B12 operate in debug cycle of homocysteine, preserving the integrity of central nervous system and being important for cognitive and motor function (HAGHDOOST-YAZDI et al., 2012). In this study was observed low intakes of vitamins B6, B12 and folate in 40, 20 and 90% of patients, respectively. However, despite the beneficial effect of vitamin B6 on homocysteine metabolism, it can nullify the levodopa effects by increasing the peripheral decarboxylation of the product, preventing the central action (FUCHS & WANNMACHER, 2010). The vitamin B6 intake was higher than that recommended on the half of patients, which probably reduces the effectiveness of therapy and provokes adverse events.

CONCLUSIONS

The aspect of food and nutrition is cardinal for a comprehensive health care of patients with Parkinson's disease. The action of the dietitian comprises the improvement of nutritional status and mitigation of symptoms as well as the side effects of treatment, fitting
the demands of the disease and its carrier, specifically.

The benefits of pharmaceutical and nutritional assistance to patients with parkinson are widely evident. There are several Nutrition Support Groups in divers' centers around the world, responsible for addressing issues related to food, nutrition and metabolism of various diseases, integrating a multidisciplinary team of health and promoting a more adequate assistance for the patients. Such strategies should be encouraged by the government, since dietitians deletion of health’s teams associated with an ineffective pharmaceutical assistance, besides providing sub-optimal treatment for patients, increase public spending on health and worsens the quality of life of patients.

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