GI Symptoms, Energy Balance and Nutrition Assessment in Parkinson's disease

Ann Gaba*
Hunter College, CUNY School of Public Health, 2180 Third Avenue, New York 10035, USA

Abstract
As demographics in many countries shift towards older populations, disorders affecting primarily older people have garnered increasing attention. One such disorder is Parkinson's disease (PD), which after Alzheimer's, is the second most prevalent neurodegenerative disorder, and is most commonly diagnosed in people greater than sixty years of age.

While attention is typically paid to the visible symptoms of the movement disorder, non-motor symptoms of PD can significantly detract from quality of life for affected individuals. Many of these non-motor symptoms impact the gastrointestinal (GI) system, with concurrent impact on nutritional status. This paper will describe the nature of these problems as described in research literature, and offer some suggestions as to how these issues may be addressed.

ABBREVIATIONS

INTRODUCTION
Parkinson's disease (PD) is the second most prevalent chronic neurodegenerative disorder. Dorsey et al. [1] estimated that the incidence of PD would increase from about 4.1 to 4.6 million worldwide in 2005, to between 8.7 and 9.3 million by 2030. Onset is most frequent in people over 60 years of age. With demographics in many countries shifting towards older populations, the care of individuals affected by this disorder is becoming of increasing importance.

The three primary symptoms of PD are tremor, rigidity, and bradykinesia. Although these symptoms create the definition of this disorder, additional non-motor symptoms are commonly seen, including taste and smell changes, gastroparesis, and constipation. Sleep disturbances, anxiety and depression are also not uncommon. These non-motor symptoms have been shown to have a significant impact on quality of life [2-4]. In addition to the individual costs to individuals and their families, the increasing costs of medical care, as well as indirect social costs make the management of this disorder of importance to society at large [5]. Therefore, any means of alleviating this should be explored.

These secondary symptoms are the most likely to impact, and be impacted by, dietary intake and nutritional status. Therefore nutrition evaluation should be an important part of case management. Furthermore, about one-quarter to one-half of patients taking levodopa, the primary drug used to treat the movement disorder of PD, develop motor fluctuations after about five years. This is the so-called "on-off syndrome". Treatment focuses on trying to improve absorption of the drug, altering timing of doses, and prolonging the effect of every dose. A high protein meal can reduce levodopa absorption in the gut [6] and limit its ability to cross the blood-brain barrier [7], management of which also calls for nutritional evaluation and assistance.

TASTE AND SMELL CHANGES
The aroma and taste of foods are among the most significant indicators of palatability, and strongly influence both the desire to eat, and food choices [8]. Changes in the sense of taste [9], and the more often reported changes in the sense of smell, [10] affect many individuals with PD. Indeed decreased sense of smell has been identified as one of the earliest symptoms of PD, preceding motor symptoms often by many years [10]. The predominant theory explaining these phenomena is the Braak hypothesis [11], according to which the pathological or toxic agents responsible for triggering PD enter the body through the nasopharyngeal cavity and/or the gastrointestinal tract thus initiating the earliest symptoms of PD at these sites. While this seems plausible, the cellular and molecular mechanisms underlying olfactory and GI dysfunction in PD remain unknown.
Loss of the ability to smell may contribute to decreased food intake, and weight loss that is common in PD [12]. Sharma and Turton [13] describe two different phenotypes of PD, one characterized by more severe loss of olfaction, higher initial body weight, and significant weight loss as the disease progresses, and a higher risk of dyskinesia, and the other with less severe loss of olfaction, lower initial body weight, minimal weight changes with disease progression, and a lower risk of dyskinesia. In either case, these symptoms are related to duration and severity of disease [3] and reported quality of life [2].

GASTROINTESTINAL DYSFUNCTION

In addition to taste and smell aberrations, gastrointestinal symptoms are also a common feature of PD. Virtually all parts of the gastrointestinal tract can be affected, in some cases early in the disease course [14]. Abnormalities of function may occur at virtually all levels of the gastrointestinal tract. Weight loss, dental deterioration, salivary excess, dysphagia, gastroparesis, decreased bowel movement frequency, and anorectal dysfunction may occur [15]. Many authors have described these symptoms with PD, most especially Pfeiffer [14] and Edwards [16]. In examining this literature, most available data suggests that the primary neurological disorder within PD is the main cause of GI dysfunction in this patient population [17]. In other words, the neuropathological process creating the well recognized motor symptoms of PD may be carrying out similar damage to nerves in the GI tract, thus causing the GI symptoms.

Woitalla and Goetz [18] explain that “the enteric nervous system is a subdivision of the autonomic nervous system, controlling and regulating gastrointestinal function. Spinal, enteric and vagal afferent pathways transmit information ascending from the gut to the brain. The complexity of this regulation may predispose the GI tract to pathological conditions affecting any of the neurotransmitter systems.”

Gastroparesis

Gastroparesis, a slowing in gastric motility and delay in gastric emptying, that can produce various symptoms in patients with PD and may cause erratic absorption of medications [14]. L-dopa is absorbed in the proximal duodenum; therefore delayed gastric emptying will slow the uptake of the drug [19]. Gastroparesis has the potential to affect nutrition and quality of life. Unfortunately, as Heetun and Quigley [20] concluded, that “while gastric emptying has been reported to be frequently delayed in PD, the existing data do not permit definitive conclusions concerning the true prevalence, relationship to the underlying disease process, relevance to PD management, or the optimal therapy of related GI symptoms.”

Constipation

Of all the various GI manifestations of PD, the most commonly mentioned are severe constipation and defacatory dysfunction [21]. Constipation is usually defined as less than one bowel movement in 3 days, whereas defacatory dysfunction is the term for straining with stools and/or a sense of incomplete bowel evacuation. While incidence of constipation increases with advancing age, it is disproportionately prevalent in individuals with PD. A study by Kaye et al. [22] found that by a variety of standardized criteria, people with PD reported more constipation the people of the same age without neurological disorders. Furthermore, they noted a disproportionate impact on quality of life, in that individuals with PD not only reported increased incidence of constipation, but were also more likely to report being bothered by these symptoms.

Ueki and Otaka [23] reported that about 60 to 80% of PD patients suffer from constipation, which appears about ten to twenty years prior to motor symptoms. They found that intake of water was significantly decreased in PD patients from early life, and associated with their constipation. Decreased thirst sensation with concurrently decreased fluid intake, may be a factor contributing to constipation with PD. Although Gage et al. [24] found that constipation with PD was not related to diet of lifestyle factors. Prolonged colonic transit time, likely related to the disease process, is another contributing factor to constipation [16], while weakness in the pelvic floor musculature may create to defecatory dysfunction [25]. Devos et al. [26] Described colonic inflammation in PD patients, with a measure of pro-inflammatory cytokines similar to those observed with irritable bowel syndrome (IBS). Tan et al. [27] found that about twenty-five percent of a sample of PD patients had small intestinal bacterial overgrowth (SIBO). This was related to worse motor function, but not to constipation or tenesmus. SIBO may be due to decreased immune function. These findings together indicate a possible role for altered immunological response in GI symptoms in PD. In spite of increased understanding of these issues, there remains insufficient evidence to recommend any one mode over another in management of neurogenic bowel function in any particular patient group [28].

MEDICATION INTERACTION OF L-DOPA WITH DIETARY PROTEIN

Dopamine is a key neuropeptide in the regulation of movement. Levodopa (L-dopa) is a dopamine pro-drug and is the primary drug used to treat the movement disorder symptoms of Parkinson’s disease [29]. The pharmacokinetics of this drug greatly affects its efficacy [30]. When serum levels of Levodopa fluctuate, the symptoms of the movement disorder can wax and wane, causing alternation between muscle rigidity, normal movement, and fast twitching or jerking motions. These symptoms are known to negatively impact quality of life for PD patients [31].

Dietary amino acids, specifically phenylalanine, leucine and isoleucine, compete with Levodopa for absorption in the GI tract, and, once absorbed, to cross the blood-brain barrier, thus exacerbating this problem [7]. Several studies experimentally demonstrated the role of plasma amino acid concentration and its relationship to levodopa absorption [32-34]. In an effort to reverse this problematic competition for transport of L-dopa, trials of low-protein diets were conducted to demonstrate benefits in drug bio-availability [35-37]. In order to maintain nutritional status and prevent sarcopenia, strictly low-protein diets were modified to maintain a low protein intake during day-time hours, with most of the day’s protein allowance being consumed in the evening when reduced drug activity was less problematic [38-41]. Overall diet recommendations from these studies include delimiting of dietary protein from breakfast.
and lunch (intake of <10 grams) and protein consumption to meet estimated needs beginning after 5pm. Specialized low-protein diet foods have been developed and tested to ease adherence to this type of diet [42].

Another approach to managing the competition between L-dopa and dietary amino acids was put forth by Berry et al. [43]. In examining the effects of dietary carbohydrate intake in this setting, they compared three different therapeutic diets, high-protein-low carbohydrate, low-protein-high carbohydrate, and five to one carbohydrate to protein mixtures. They found that the five to one ratio of carbohydrate to protein intake was also effective in maintaining stable plasma levodopa levels. This approach may be preferred by some patients. In yet another variation, Cerda and Barichella [44] recommended small meals at frequent intervals based on a Mediterranean-like model.

**ENERGY BALANCE, WEIGHT CHANGES, AND MALNUTRITION**

With all of the various limitations that may be imposed by the symptoms of the disease and its management, individuals with PD are at significant nutritional risk. A commonly employed method of nutritional risk assessment is to follow changes in body weight and body composition.

**Weight Changes**

Many studies have observed lower body weights or BMIs of PD patients when compared with controls [45,46] including a meta-analysis [47]. This decreased weight may begin several years before diagnosis [48]. While weight loss may be due to metabolic changes, it may also be due to a decreased oral intake, which itself can be due to a host of factors, that may or may or may not be directly related to the PD disease process in any given individual. For example, decreasing BMI may also be predictive of dementia [49]. Differences in body composition have also been observed for weight loss with PD [50,51]. Specifically, there is a decreased ratio of lean to fat mass in PD [52], Vikdahl et al. [53] found an increase in central obesity in early-stage PD. They note that the course of PD may include periods of weight gain and weight loss, varying with stages of the disease. Bachmann and Trenkwalder [54] noted that low BMI is also correlated with low bone mineral density a significant risk factor for hip fractures. It is important that PD patients’ intake include sufficient amounts of vitamin D and calcium to reduce the risk of hip fractures and bone thinning and vitamin D deficiency [62].

PD patients have been observed to lose weight, even with apparently normal, or higher than estimated calorie needs. This may be indicative of an increased metabolic rate [55], or the involuntary movements associated with PD may result in increased energy expenditure [56]. Patients may also gain weight with dopamine replacement therapy, or following surgery for subthalamic nucleus deep brain stimulation (STN-DBS). With successful disease management the rate of obesity in PD patients approaches that of the general population [57].

**Energy Balance/REE**

Weight loss is commonly observed in individuals with PD [50]. Several studies have examined the possibility of changes in resting energy expenditure (REE) as a possible etiology of this change. Markus et al. [58] and Levi et al. [59] both observed the resting energy expenditure in patients with Parkinson’s disease was significantly higher than in healthy subjects. However the increase in REE may have been due to the symptoms of PD, such as rigidity and/or involuntary movements rather than an essential change in basal metabolic rate. However, Toth et al. [60] found that daily energy expenditure was lower in PD patients compared to healthy elderly, primarily due to reduced physical activity energy expenditure. Capecci et al. [61] found that REE was higher in patients with advanced PD, and that dopaminergic treatment significantly reduced REE. These results argue against the hypothesis that elevated daily energy expenditure contributes to weight loss in PD.

**Assessment for Malnutrition**

Symptoms of Parkinson’s disease (PD), related to both the cognitive and movement disorder, can impact nutritional status. Weight loss and feeding problems including dysphagia must be addressed in nutrition evaluations.

Adequate intake to meet protein/kcal and micronutrient needs, especially Vitamin D and Vitamin B12, should be encouraged [29,62]. Bayer et al. [50] reported that patients with Parkinson’s disease were four times more likely to report weight loss greater than ten pounds when compared to matched control subjects. The possible explanations they provide for this echo many of the difficulties described above. These include: anorexia, difficulty with chewing and swallowing, prolonged time needed to consume a meal, decreased sense of smell and taste, depression, increased energy needs due to the muscular rigidity and increased involuntary movements, and the side effects of some medications. They suggest nutritional management strategies similar to those used to address these problems singly or in aggregate in other populations.

Nutritional goals for the Parkinson’s disease patient include: improving fiber intake and reducing constipation, maintaining hydration status, and assessing for dysphagia and gastrointestinal problems, providing adequate energy to prevent weight loss or excessive gain due to lack of physical activity, and preventing bone thinning and vitamin D deficiency [62].

Using the Subjective Global Assessment (SGA), Sheard et al. [64] categorized the nutritional status of one hundred and twenty five community dwelling adults diagnosed with PD. Nineteen (15.2%) participants were moderately malnourished, while none were severely malnourished. The malnourished in this study scored more poorly on the majority of the assessments than did the well-nourished. More severe motor symptoms and more depressive symptoms were predictive of malnutrition.

While the majority of the studies discussed above took place in the United States, assessment of nutritional status in various communities also found decreased nutritional status with PD in China [65] in England [66] Australia [67] and Ghana [68] pointing out that these issues are indeed global in nature.

**DISCUSSION AND CONCLUSIONS**

Given the shifting demographics to aging populations in many countries, management of chronic diseases that are
more prevalent in older people is becoming a higher priority in healthcare practice. One such disorder is Parkinson’s disease, with the number of affected individuals projected to be as many as 9.3 million by 2030.

Non-motor symptoms may originate from the PD pathophysiological process itself, aging, or other sources. As with many disorders, the clinical presentation with PD is likely to be a combination of both symptoms due to PD and symptoms due to other factors, especially nutritional status. Since there is no known cure for PD, and existing treatments are also imperfect, diminishing the portion of symptoms due to nutritional factors is highly desirable. For example: fluid, fiber, and pre-biotics may all be helpful in managing constipation, with or without PD, and should be considered.

Evaluation of oral intake as compared to calorie needs is important in managing weight, with our without changes in metabolism. If intake is found to be inadequate, examination of potential causes, such as depression, difficulty swallowing, issues with food acquisition, or other problems can provide direction for appropriate interactions. These may or may not be directly caused by the PD disease process, but addressing them is likely to be of benefit to these patients.

Diminished sense of smell may also contribute to decreased oral intake and decreased enjoyment of foods. Modification of recipes to include higher concentrations of aromatic seasonings, or capsaicin-containing sauces may be helpful in this regard.

GI symptoms are a prominent non-motor co-morbidity with PD, and can manifest at every segment of the alimentary system. These symptoms are known to negatively impact the quality of life for these individuals, as well as contribute to decreased nutritional status. Therefore it is important that nutrition screening and assessment be a part of routine care of individuals with PD. This practice should also be incorporated into further research studies of PD to delineate optimal care strategies.

REFERENCES


27. Tan AH, Mahadeva S, Thalha AM, Gibson PR, Kiew CK, Yeat CM, et al. Evaluation of oral intake as compared to calorie needs is important in managing weight, with our without changes in metabolism. If intake is found to be inadequate, examination of potential causes, such as depression, difficulty swallowing, issues with food acquisition, or other problems can provide direction for appropriate interactions. These may or may not be directly caused by the PD disease process, but addressing them is likely to be of benefit to these patients.

Diminished sense of smell may also contribute to decreased oral intake and decreased enjoyment of foods. Modification of recipes to include higher concentrations of aromatic seasonings, or capsaicin-containing sauces may be helpful in this regard.

GI symptoms are a prominent non-motor co-morbidity with PD, and can manifest at every segment of the alimentary system. These symptoms are known to negatively impact the quality of life for these individuals, as well as contribute to decreased nutritional status. Therefore it is important that nutrition screening and assessment be a part of routine care of individuals with PD. This practice should also be incorporated into further research studies of PD to delineate optimal care strategies.


