PREVALENCE OF DIETARY SUPPLEMENT USE

OF INDIVIDUALS WITH

PARKINSON'S DISEASE

by

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ABSTRACT

Parkinson's disease (PD) is an incurable, progressive neurological disease that appears with motor and non-motor symptoms such as tremors, muscle rigidity, impaired gait, mood disorders, constipation, and sleep disorders.[1,2] Although its etiology is unknown, oxidative stress is believed to be involved in the development and progression of PD. This has prompted interest in dietary supplements with antioxidant functions as a potential strategy to mitigate these processes.[2] However, individuals with PD may self-medicate with dietary supplements that are poorly regulated.[3,4,7] The primary aims of this study were to explore the prevalence of dietary supplement use among individuals with PD and to identify the most common supplements being taken. This cross-sectional study utilized a questionnaire that was administered through Qualtrics to those with PD via support group websites. Dietary supplement users were also asked if they spoke with a healthcare professional about their supplement use. In addition to descriptive statistics, Mann-Whitney U, Fischer's Exact, and chi-square tests were used to determine differences in demographic characteristics between supplement users and non-users. Spearman's correlations were used to identify possible associations between demographic variables and dietary supplement use. The percentage of respondents who reported using at least one dietary supplement in the past thirty days was 83.4% (171/205). The most commonly used dietary supplements were vitamin D, multivitamins, vitamin B12, fish oil, melatonin, CoQ10, and calcium. However, 94 different supplements were identified. More than one in four respondents reported that they had not discussed their supplementation with a physician or other healthcare professional. These results demonstrate a high prevalence of dietary supplement use among

individuals with PD as well as a wide variety of supplements being taken. This study's findings also indicate the need for better dialogue between patients and healthcare providers regarding the use of dietary supplements.

DEDICATION

This thesis work is dedicated to the memory of my mother, Vicki Miller, who was always my biggest supporter. Her strength and humility have been a constant source of inspiration. I would not be where I am today without her.

LIST OF ABBREVIATIONS AND SYMBOLS

CoQ10	Coenzyme Q10
DSHEA	Dietary Supplement Health and Education Act of 1994
FDA	Food and Drug Administration
GMP	Good Manufacturing Practices
IP	Internet Protocol
IRB	Institutional Review Board
MoCA	Montreal Cognitive Assessment
NAC	N-Acetyl Cysteine
NDSR	The Nutrition Data System for Research
NHANES	National Health and Nutrition Examination Survey
PD	Parkinson's disease
PHI	Protected Health Information
PRO-PD	Patient-Reported Outcomes in PD
REM	Rapid eye movement
SNAP	Supplemental Nutrition Assistance Program
UPDRS-III	Unified Parkinson's disease Rating Scale Part III
USP	US Pharmacopeial Convention
<	Less than
>	Greater than
=	Equal to

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CHAPTER 1

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease that is characterized by motor symptoms such as tremors, muscle rigidity, and impaired gait, but it also includes non-motor symptoms such as mood disorders, sleep disorders, weight changes, and constipation.[1,2] PD is one of the most common neurological disorders primarily affecting older adults with an average age of onset of 40-70 years old.[1,2] Although oxidative stress has been linked with PD onset, a decrease in dopaminergic neurons is what ultimately leads to the decline in motor function and the appearance of non-motor symptoms.[3] While PD is incurable, medical treatment includes pharmacological, surgical, and physical therapy approaches.[2] The prescription medication levodopa is the primary treatment for PD. Because older adults and patients with other neurodegenerative diseases have reported more frequent use of dietary supplements compared to other groups[1-3], it is plausible that patients with PD may also self-medicate with dietary supplements.[1-3] Existing research on individuals with PD and their use of dietary supplements is limited and dated. Specifically, it is not clear if dietary supplement use is common in this population, nor is it known what types are being taken. The purpose of this research was to determine if individuals with PD are taking dietary supplements and if so, to identify the specific supplements they are taking.

CHAPTER 2

LITERATURE REVIEW

The following review of the literature will define the types of products that are available over-the-counter as dietary supplements, summarize the evidence base regarding which supplements may pose benefit or harm to individuals with PD, explain why individuals with PD may be motivated to self-supplement with these products, and summarize the existing evidence related to use of specific dietary supplements by patients with PD.

Overview of Disease

PD is a type of neurodegenerative disease that presents with motor and non-motor symptoms.[2] Common motor symptoms include tremors, muscle rigidity, and impaired gait; in addition, examples of non-motor symptoms are cognitive impairment, mood changes, constipation, dysphagia and weight changes. The substantia nigra is responsible for producing dopamine in the brain. The neurons in the substantia nigra are impaired in PD, which ultimately leads to the presence of these symptoms. Both genetic and environmental factors have been linked with the onset of PD.[4] While it is more common in Caucasian men, it affects people of both genders and all ethnicities.[2] PD typically presents between the ages of 40-70 years old, and once diagnosed, it is estimated that at least 50% of individuals are classified as disabled within five years. The most common medical treatment for PD is levodopa medication, specifically Sinemet®, which contains levodopa and carbidopa, which are both dopamine promoters.[1]

Although effective, adverse side effects of levodopa medication have been observed, such as anorexia, weight loss, gastrointestinal distress, and insomnia.

Definition and Regulation of Dietary Supplements

The Food and Drug Administration (FDA) regulates dietary supplements under the Dietary Supplement Health and Education Act of 1994 (DSHEA).[4] DSHEA defines dietary supplements as:

> "a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin, (B) a mineral, (C) an herb or other botanical, (D) an amino acid, (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A),(B),(C),(D), or (E) … [and] is not represented for use as a conventional food or as a sole item of a meal or the diet." [5(p2-3)]

The FDA is responsible for enforcing the regulations established by DSHEA. However, unlike medications, the FDA does not investigate a product classified as a dietary supplement until after the product has reached the market and has been reported as being misbranded or adulterated. Therefore, there is little oversight of a dietary supplement prior to reaching the market.[6] Manufacturers of dietary supplements may hire third party testers such as US Pharmacopeial Convention (USP) to verify the quality, safety, and claims of the product; however, this is not required. Moreover, third party companies use different methods of testing supplements and have different standards. Consumers may not be aware if dietary supplements have been tested to verify the quality and safety of the product. Some dietary supplements may contain unknown or potentially harmful substances if not properly tested.

Rationale for Dietary Supplement Use

Using data from the National Health and Nutrition Examination Survey (NHANES) from 2011-2014, Gache et al. found that older adults represent the largest age group in the United States to use dietary supplements.[7] Use of complementary and alternative medicine, including dietary supplements, is also higher among those with incurable, progressive diseases.[3] In addition, those with higher income and education level, private insurance, and Caucasian race have also reported higher rates of dietary supplement use.[7]

Some studies have shown that patients with PD are more likely to become vitamin D and coenzyme Q10 (CoQ10) deficient, so there may be an indication for the use of these dietary supplements.[8-10] Furthermore, because oxidative stress is thought to play an underlying role in neurodegeneration, dietary supplements with antioxidant function may be helpful in reducing inflammation and oxidative stress in individuals with PD.[2] However, there is conflicting evidence regarding the risks and benefits of individual dietary supplements for PD, and this is an area that warrants further research.[1,3,4,7-11]

Individual Dietary Supplements and PD

Vitamin D

A few studies have investigated the potential for vitamin D to ameliorate the complications of PD.[11] Evatt et al. concluded that individuals with PD may have an increased risk of vitamin D deficiency and decreased bone mineral density, which could lead to osteoporosis and increased risk of fractures.[3,8,12] Although vitamin D is best known for its effect on bone health, vitamin D receptors are widespread throughout the body.[11] Notably, receptors for the active form of vitamin D, calcitriol, are found in the substantia nigra neurons in the brain that

produce dopamine. It is known that the neurons' functions in the substantia nigra are impaired in PD, so there may be a relationship between circulating vitamin D levels and substantia nigra function.[2] Suzuki et al. conducted a randomized, double-blind, placebo-controlled trial in Japan that evaluated the effects of vitamin D supplementation on PD progression.[8] Among a cohort of 114 patients with PD, they found that 12 months of supplementation with a 1200 IU daily dosage of vitamin D significantly decreased PD motor and non-motor symptom severity compared to a placebo. In addition, the supplements were well-tolerated without any adverse events. The investigators found that different genetic variants may also influence sensitivity to vitamin D supplementation. Conversely, in a separate study, no associations were observed between vitamin D supplementation and PD symptoms.[11] In light of conflicting results between these two studies, more research needs to be conducted on the relationship between vitamin D and symptom severity in patients with PD.[8,11]

Coenzyme Q10 (CoQ10)

CoQ10 is a vitamin-like compound that functions as an antioxidant while also playing a key role in regulation of the electron transport chain, which produces energy in the body.[9] Because part of the underlying etiology of PD may be due to oxidative stress, the antioxidant properties of CoQ10 could hold promise for neuroprotection.[2,3,8-10] Furthermore, individuals with PD are at an increased risk for CoQ10 deficiency, which could be an indication for supplementation.[9] CoQ10 is a dietary supplement commonly used by older adults; however, there have been conflicting results to support its efficacy among individuals with PD.[1,3,4,7,9,11]

The Parkinson Study Group QE3 Investigators conducted a multicenter, randomized, double-blind, placebo-controlled study to evaluate the effects of high dose CoQ10

supplementation among 267 patients in the early, untreated stage of PD.[10] The study was originally planned to have a duration of 16 months; however, it had to be terminated early due to a large number of participants being prescribed PD medication, a predefined exclusion criterion for study participation. The average follow-up time was approximately 10 months, and the available data showed no significant differences in the Unified Parkinson's Disease Rating Scale among patient groups receiving 1200 mg/d CoQ10, 2400mg/d CoQ10 or placebo. It was noted that the high doses of CoQ10 supplements were safe for the participants; however, there were several instances of adverse events such as gastrointestinal symptoms, mood worsening, difficulty sleeping, and vertigo. The instances of adverse events were not significantly different among the three groups, leading investigators to conclude that CoQ10 supplementation was safe. Although supplementation was deemed safe at dosages of up to 2400 mg/d, there were no significant results indicating it delayed PD progression or reduced severity of symptoms.

A cross-sectional study conducted by Mischley et al. evaluated the relationship between self-reported CoQ10 supplementation and disease progression among a cohort of 1053 patients with PD.[11] The primary investigator developed a Patient-Reported Outcomes in PD questionnaire (PRO-PD) to assess different aspects of each participant's level of functioning and PD-related symptoms. Another questionnaire was administered to participants to inquire about their use of dietary supplements over the previous six months. Results showed that CoQ10 supplementation was correlated with decreased severity of PD symptoms as assessed by the PRO-PD questionnaire ($p=0.026$). However, after adjusting for income, results were no longer statistically significant.

While there is not sufficient evidence to support CoQ10 supplementation, current evidence suggests that a moderate dosage of CoQ10 (no more than 2400 mg/d) is not harmful to

older adults with PD.[10] However, the long-term side effects of CoQ10 supplementation are unknown. Larger clinical trials and prospective observational studies are needed to determine whether CoQ10 supplementation may be beneficial for patients with PD.[3]

Melatonin

Melatonin is a hormone produced by the pineal gland that is involved in many processes in the body. It is known to improve sleep quality and immune function, while displaying antioxidant and neuroprotective properties.[13] The prevalence of sleep disorders is higher in older adults with PD compared with age-matched individuals, so it is not surprising that melatonin has been investigated in relation to PD.[14] The cross-sectional study previously described by Mischley et al. found that melatonin use was associated with advanced disease progression per their PRO-PD questionnaire.[11] A plausible explanation for this is that melatonin was mainly used by individuals in later stages of PD with more severe symptoms, including insomnia, rather than supplementation causing more rapid progression of the disease. After adjusting for reported insomnia, melatonin supplementation was not significantly associated with PD progression. Additionally, it has been suggested that melatonin supplementation could improve rapid eye movement (REM) sleep disorders that are common in patients with PD.[13] However, more studies are needed to determine whether supplementation may benefit patients with PD who suffer from insomnia.

Fish Oil

Fish oil has the potential to be beneficial to individuals with PD.[3,11] Not only has the increased intake of omega-3 fatty acids been linked to reduced oxidative stress, it may also have

a therapeutic role in reducing the rate of neurodegeneration.[15] Notably, a cross-sectional study reported that fish oil supplements were associated with significantly reduced PD symptom severity.[11] More studies have shown promise for the protective effects of omega-3 fatty acids, from food or dietary supplements, in Alzheimer's disease.[16] However, while it may be beneficial in the prevention and treatment in another progressive, neurological disease, there have not been enough clinical trials to support or negate the supplementation of omega-3 fatty acids in fish oil for PD.

B Vitamins

Folate, vitamin B_6, and vitamin B12 supplementation may decrease circulating homocysteine.[3] Elevated homocysteine levels may increase the risk of depression and potentially decrease cognitive function. Additionally, supplementation of these vitamins could be particularly helpful to patients with PD since levodopa medication has been shown to increase homocysteine production.[3] However, the research on B vitamins in relation to the development and progression of PD is scarce.[17] The aforementioned cross-sectional study by Mischley et al. did not find any significant associations between B vitamin supplementation and PD symptoms.[11] Thus, supplementing B vitamins for PD is not indicated at this time.

Mucuna Pruriens

Mucuna pruriens is a legume that is a natural source of levodopa, and it could possibly exhibit antioxidant functions as well.[18] It has been shown to have a greater tolerability than artificial levodopa medication, and limited data suggest promise for improving PD symptoms. A double-blind, randomized, controlled, crossover study found that a high dose of mucuna pruriens

was just as effective in reducing motor-related symptoms as levodopa treatment, and it had greater tolerability with fewer side effects.[18] While these results are encouraging, more clinical trials are warranted before recommendations for supplementation can be made.

Iron

Iron has been shown to decrease levodopa absorption; therefore, it could render the medication to be less effective.[3] If an adult with PD also has iron deficiency anemia, the timing of the iron supplement should be considered so as not to interact with levodopa. Iron is also known to be highly susceptible to oxidation in the brain. Excessive amounts of iron from supplements has the potential to worsen PD-related symptoms due to its potential for increasing oxidative stress.[11] This could lead to the production of proinflammatory cytokines, increased systemic inflammation, and further neurodegeneration.[4]

N-Acetyl Cysteine

N-Acetyl Cysteine (NAC) is the precursor for cysteine, which is involved in the regulation of glutathione synthesis.[19] Low glutathione levels in PD patients have been associated with increased oxidative stress, which may accelerate disease progression. There is a limited body of research related to the effects of NAC on human subjects with PD.[20] Evidence has shown increased levels of glutathione following IV administration of NAC; however, oral supplementation may not yield similar effects due to reduced bioavailability.[21]

To determine if NAC crosses the blood-brain barrier, a two-day study conducted by Katz et al. measured the effects of oral NAC on cerebrospinal fluid.[19] Twelve participants were divided into groups of three and were administered doses of 7 mg/kg, 35 mg/kg, or 70 mg/kg of NAC in capsulated form. Three participants were given comparable doses of NAC in liquid form

for comparison. The treatment was given for two days, and lumbar punctures were taken at baseline and after the treatment period. The Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) and Montreal Cognitive Assessment (MoCA) were used to assess changes in PD symptoms. The results indicated there was a dose-dependent response in cerebrospinal fluid for both forms of NAC ($p<0.001$). This suggests that oral NAC has the bioavailability to be absorbed and used by the brain. The oral forms of NAC were well tolerated by all participants, and the capsulated form was preferred. There were no detectable changes in PD-related symptoms, but this is likely due to the short study duration.

Despite evidence of its bioavailability, there is conflicting research regarding the efficacy of administering NAC supplements orally for individuals with PD. A clinical trial conducted by Coles et al. evaluated the effects of 6000 mg/day dosage of NAC on five PD patients and three healthy controls.[21] Half of the participants experienced notable adverse events that resolved after cessation of the high dose supplement. Therefore, safe and tolerable dosages of NAC have yet to be determined, and the long-term effects of supplements are unknown.

Prevalence of Dietary Supplement Use among Patients with PD

Little is known about the prevalence of dietary supplement use among patients with PD. In a study by Wolfrath et al., investigators conducted in-person interviews with 120 patients with PD to inquire about dietary supplement use.[14] They also asked questions regarding disease progression, demographic information, and socioeconomic data. Investigators discovered that not only did 63% (76/120) of the participants with PD take $\geq$1 supplement, fewer than 50% (36/76) discussed their dietary supplement use with a physician or other health professional. However, this survey research was conducted from 2000-2001. At that time, commonly used supplements

among individuals with PD were multivitamins, vitamin C, calcium, and vitamin E. It is currently unknown whether these products represent the most commonly used supplements nearly two decades later given the additional research that has been done since then.

Gaps in the Literature

There are many gaps in the literature regarding dietary supplements and PD. Although limited data supports the benefits of certain dietary supplements such as fish oil and CoQ10, evidence is lacking to make firm recommendations for supplementation.[2,3,8-11,15] Moreover, some studies suggest that iron supplementation may pose more harm than benefit in this population.[3,11] As a first step toward establishing an evidence base for dietary supplements and PD, it is imperative to determine which supplements patients are currently taking. This study will add to the body of research and will provide a foundation for future research that aims to examine individual dietary supplements and their effects on PD.

CHAPTER 3

METHODOLOGY

Introduction

The current prevalence of dietary supplement use of individuals with PD is not well known since existing data are limited and dated.[14] Oxidative stress likely plays a role in the progression of neurodegeneration; therefore, it is plausible that certain antioxidant supplements may hold promise for PD.[9] The use of other dietary supplements has also been hypothesized to improve common PD symptoms and/or decrease the rate of neurodegeneration.[3,8,9,11] The aim of this research was to identify individual dietary supplements that are currently being used by this population. Additionally, this study aimed to elucidate possible demographic predictors of dietary supplement use. In addition to providing a foundation for future research, results of this study will be important to gain better insight about the health behaviors of this population in order to guide clinicians and investigators in future patient or participant interactions.

Hypotheses

1. Dietary supplement use among those with PD is high (greater than 50%).
2. Higher education level and income are correlated with dietary supplement use.
3. The most commonly used supplements among individuals with PD will be multivitamins, coenzyme Q10, melatonin, and fish oil.

Questionnaire Development

NHANES is a validated national survey designed to collect health and nutrition information. It contains a section about dietary supplement use. NHANES interviews are conducted both in-person and over the phone.[19] The Nutrition Data System for Research (NDSR) is widely used to collect nutrition intake data.[20] NDSR is formatted for in-person or over the phone interviews, and it has a questionnaire section for dietary supplements. Thus, both NHANES and NDSR have developed validated surveys to assess dietary supplement use in the general population. These tools in addition to a thorough review of the literature were used to develop this study's questionnaire.

The questionnaire was designed to collect demographic information, dietary supplement use or non-use in general, and information about individual supplements taken. The sociodemographic information included age, gender, date of onset of PD, zip code, insurance status, and a brief question inquiring about medications. Internet Protocol (IP) addresses were collected to assess for duplicity. However, no protected health information (PHI) was collected.

If participants responded that they had used one or more dietary supplements in the past 30 days, then they were prompted to answer thirteen additional questions. The questions were formatted to be multiple choice with yes or no options. The individual dietary supplement questions asked about multivitamins, vitamin D, calcium, mucuna pruriens, CoQ10, vitamin B_6, vitamin B12, folic acid, melatonin, vitamin E, iron, fish oil, and NAC. The existing literature indicates that these supplements are either commonly used by older adults or may have potential positive or negative effects on PD. If participants responded that they had taken any of the individual dietary supplements, they were prompted to answer two additional questions. The first question assessed whether they took the supplement for PD or for another reason. The second

question inquired about whether the participant was taking the supplement before or after their PD diagnosis. Another question asked about any other dietary supplement use, and if the participant selected "yes," there was an open text box allowing a free text response. The last question asked if the participants who had used dietary supplements had spoken with a physician or other healthcare provider about their supplements at any time.

Participant Characteristics

Anyone age 18 years and older with a diagnosis with PD was eligible to take this survey. Those with severe motor symptoms that may impair their ability to complete the online survey could receive assistance from their caregivers, family members, or friends. All participants were recruited through online support groups. Participants whose residence was outside of the United States were excluded from this study.

Research Design

This research used a cross-sectional survey to assess dietary supplement use by individuals with PD and identify the individual supplements being taken. A description of the study and a link to the survey was posted to online support groups' websites. Potential participants were not contacted directly to complete the survey. An informed consent page was included prior to the beginning of the survey detailing the content of questions asked, time to complete survey, risks or benefits to participants as well as a confidentiality statement. The University of Alabama's Institutional Review Board (IRB) approved this study prior to survey distribution. Qualtrics software (Provo, UT, 2018) was used to administer the questionnaire to participants.

Statistical Analysis

This study utilized a convenience sample from online support groups for PD; therefore, sample size could not be determined a priori. Primary measures included dietary supplement use or non-use and the types of individual dietary supplements used. Secondary measures included the reason for dietary supplement use, if the participant started taking dietary supplements before or after PD diagnosis, and if a health professional was consulted at any point about their dietary supplement use.

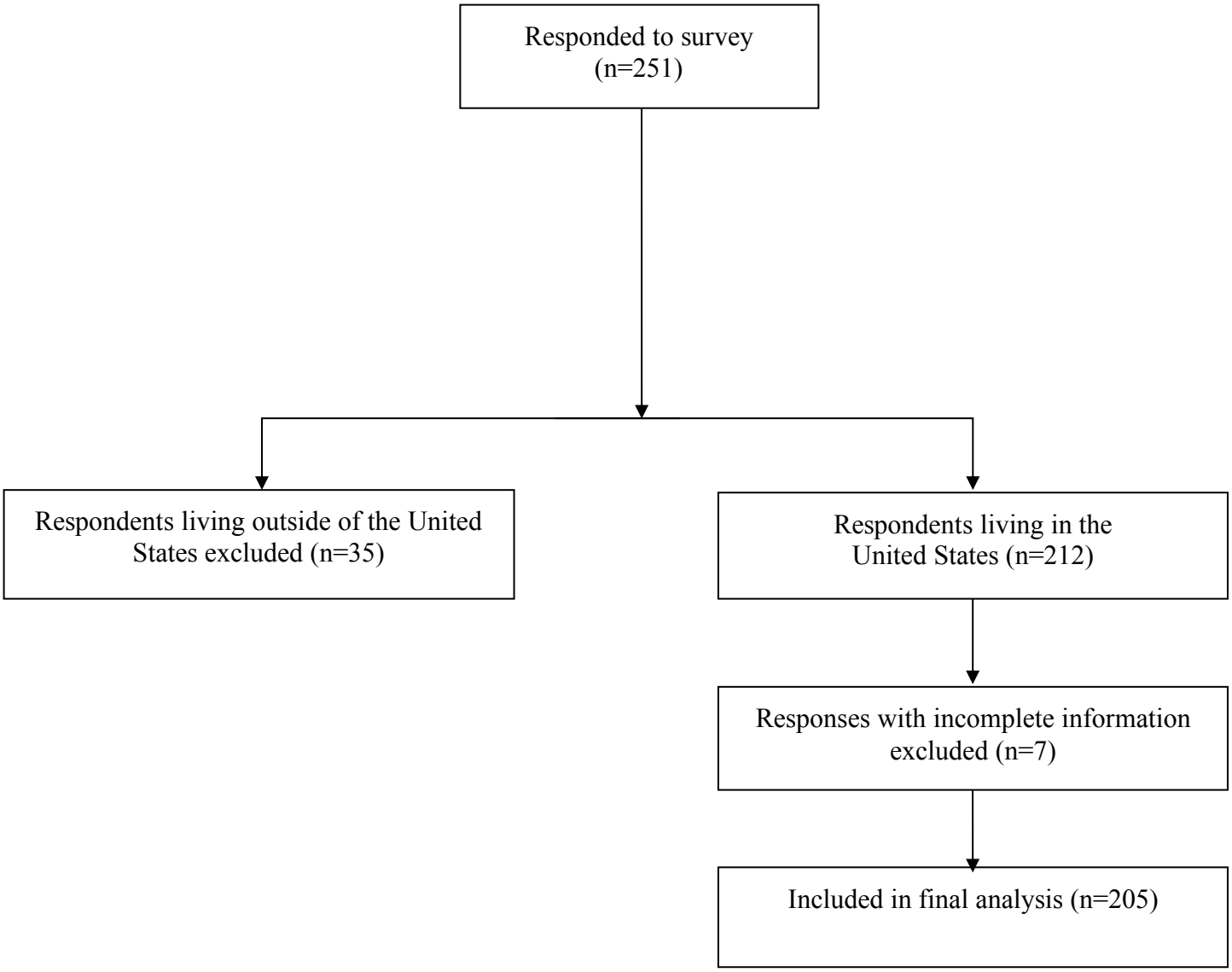
Frequencies were calculated to describe dietary supplement use or non-use, discussion of dietary supplement use with a healthcare professional, assistance used to complete survey, and types of individual dietary supplements taken. Mann-Whitney U, Fischer's exact, and chi-square tests were used to detect differences between users and non-users of dietary supplements. Spearman's correlations were applied to evaluate relationships between supplement use and demographic variables. Analyses were performed using SPSS Version 25. A p-value <0.05 was considered statistically significant.

CHAPTER 4

RESULTS

The analytic sample (n = 205) included data from individuals who provided answers to all of the questions and lived within the U.S (Figure 1).

Figure 1. Participants included and excluded



The majority of respondents were female (60.0%) and Caucasian (94.1%) with an average age of 60 years old (Table 1). Ninety-two percent of respondents reported attending college, and 30.7% had completed post-graduate degrees. Fifteen respondents received assistance to complete the questionnaire (7.3%).

The percentage of respondents reporting use of at least one dietary supplement in the past thirty days was 83.4% (171/205). Of dietary supplement users, 95 took between one and five dietary supplements. Forty-three percent of dietary supplement users reported taking six or more different supplements per day.

Most respondents (54.6%) were in the early stages of PD, which was classified as disease duration of less than five years. Of those who used dietary supplements, 56.1% were in the early stages of PD. There was no significant difference in dietary supplement use among middle (5-10 year disease duration) and late stages of PD (greater than 10 year disease duration; $\chi 2=4.092$, $p=0.129$). Type of insurance was not correlated with dietary supplement use ($p=0.171$). Of those that receive government financial aid (10.2%), only 9.9% reported using dietary supplements.

Frequencies of types of dietary supplements used can be found in Table 2. More than half of participants taking dietary supplements (n=171) took multivitamins, vitamin D, and vitamin B12 (52.6%, 74.3%, and 56.1%, respectively). In addition to the 13 supplements that were included in the questionnaire, participants reported use of 81 additional types of dietary supplements in the free text question. Additional dietary supplements that were used by at least three people are shown in Table 2. Other less commonly reported supplements can be found in Supplemental Table 1. Of respondents taking dietary supplements, 70.8% (121/171) discussed their use of dietary supplements with a healthcare professional.

Frequencies were used to assess percentages of dietary supplement users who were taking each supplement for PD or for other health reasons; additionally, they were asked if they started taking each supplement before or after PD diagnosis. For those taking CoQ10, mucuna pruriens, folate, vitamin B12, vitamin B6, melatonin, and NAC, over half of respondents reported using these specifically for PD (Table 3). Those taking these dietary supplements were also more likely to take them after diagnosis of PD. Spearman's correlations for associations between supplement use and demographic variables showed no significance.

Table 1. Demographic characteristics of individuals with PD who have or have not used dietary supplements within the past 30 days

Variable	Total respondents (n=205)	Users of dietary supplements (n=171)	Nonusers of dietary supplements (n=34)	P Value
Sex, n (%)				0.512
Male	81	68 (39.8)	14 (41.2)	
Female	12	103 (60.2)	20 (58.8)	
Age, average (SD)	60.0	60.6 (10.3)	59.4 (11.4)	0.538
PD duration, n (%)				0.129
Less than 5 years	112	96 (56.1)	16 (47.1)	
Between 5 and 10 years	62	53 (31.0)	9 (26.5)	
Greater than 10 years	31	22 (12.9)	9 (26.5)	
Education, n (%)				0.324
High school certificate or less	17	13 (7.6)	4 (11.8)	
Some college or bachelor's degree	125	102 (59.6)	23 (67.6)	
Post graduate education	63	56 (32.7)	7 (20.6)	
Ethnicity, n (%)				0.296
European American	193	160 (93.6)	33 (97.1)	
African American	3	2 (1.2)	1 (2.9)	
Other	9	9 (5.3)	0 (0)	
Use of government financial aid, n (%)				0.473
Yes	21	17 (9.9)	4 (11.8)	
No	184	154 (90.1)	30 (88.2)	
Use of Medications, n (%)				
Levodopa	156	128 (74.9)	28 (82.4)	0.349
Ropinirole	28	19 (11.1)	9 (26.5)	0.027

Table 2. Types of dietary supplements used by individuals with PD

Dietary Supplement	Overall Use N (%)
Vitamin D	127 (74.3)
Multivitamin	90 (52.6)
Vitamin B12	96 (56.1)
Fish Oil	78 (45.6)
Melatonin	74 (43.3)
Coenzyme Q10 (CoQ10)	71 (41.5)
Calcium	62 (36.3)
Vitamin B6	53 (31.0)
Vitamin E	35 (20.5)
Magnesium	34 (19.9)
Folate (Vitamin B9)	33 (19.3)
Iron	24 (14.0)
Turmeric	18 (10.5)
N-Acetyl Cysteine (NAC)	16 (9.4)
Mucuna Pruriens	12 (7.0)
Vitamin C	11 (6.4)
Potassium	10 (5.8)
Choline	9 (5.3)
Probiotic	8 (4.7)
Glutathione	7 (4.1)
Tyrosine	5 (2.9)
Curcumin	5 (2.9)
Cinnamon	5 (2.9)
Niacin (Vitamin B3)	4 (2.3)
Zinc	3 (1.8)
Milk Thistle	3 (1.8)
Selenium	3 (1.8)
Saw Palmetto	3 (1.8)
Lithium	3 (1.8)
Lion's Mane	3 (1.8)
Ginseng	3 (1.8)
Biotin	3 (1.8)

Table 3. Use of dietary supplements for PD or other reasons and timing of dietary supplement use in regard to disease diagnosis

		Started Taking Dietary Supplement	
	Use for PD	Before PD diagnosis	After PD diagnosis
Dietary Supplement	N (%)	N (%)	N (%)
Vitamin D	55 (43.3)	66 (52.0)	61 (48.0)
Multivitamin	34 (39.5)	64 (71.1)	26 (28.9)
Vitamin B12	61 (62.9)	37 (38.9)	58 (61.1)
Fish Oil	34 (43.6)	48 (62.3)	29 (37.7)
Melatonin	54 (72.0)	17 (22.7)	58 (77.3)
Coenzyme Q10 (CoQ10)	49 (69.0)	26 (36.1)	46 (63.9)
Calcium	12 (19.0)	48 (76.2)	15 (23.8)
Vitamin B6	37 (71.2)	16 (30.8)	36 (69.2)
Vitamin E	16 (45.7)	19 (55.9)	15 (44.1)
Folate (Vitamin B9)	24 (72.7)	7 (21.2)	26 (78.8)
Iron	2 (8.3)	15 (65.2)	8 (34.8)
N-Acetyl Cysteine (NAC)	14 (87.5)	2 (12.5)	14 (87.5)
Mucuna Pruriens	12 (100)	-	12 (100)

CHAPTER 5

DISCUSSION

The purpose of this study was to investigate the prevalence of dietary supplement use by individuals with PD using an online survey tool. Reasons for dietary supplement use and initiation of use were also addressed. The results support the hypothesis that dietary supplement use among those with PD is high (83.4%), but users and non-users did not differ by gender, age, education level, income level, or disease duration. As hypothesized, multivitamins, coenzyme Q10, melatonin, and fish oil were among the most common supplements reported. However, results also show the use of a wide variety of supplements.

The percentage of respondents reporting use of at least one dietary supplement in the previous 30 days was 83.4% (171/205). According to NHANES data, this is higher than that of the general U.S. population of older adults (70%).[7] This is also higher than Wolfrath et al.'s findings from 2006 reporting that 63.3% of patients with PD used nutritional supplements.[14] Among our nationwide sample, 94 total types of dietary supplements were reported. This supports the notion that those with PD often try to self-treat their PD-related symptoms and disease progression with dietary supplements.[3,8] However, because the dietary supplement industry is poorly regulated, this raises concern that there may be medication interactions with dietary supplements or other unintended side effects.[5] The body of research remains limited in supporting the use of any of these dietary supplements to improve PD symptoms and progression.

The results of this study found no statistically significant associations between dietary supplement use and the demographic variables collected. This does not support the hypothesis that higher education level and income are correlated with dietary supplement use. However, the insignificant findings regarding education level and dietary supplement use could reflect the highly-educated sample of respondents with only 8.3% (17/205) receiving a high school certificate or less. Income level was investigated by identifying those that receive government financial aid such as Supplemental Nutrition Assistance Program (SNAP). Only 10.2% (21/2015) received government financial aid, which indicates that most respondents were above the federal poverty line. Thus, statistical power was lacking to detect significant differences. These results are consistent with previous findings by Wolfrath et al. reporting that education and income were not correlated with dietary supplement use in their cohort of individuals with PD.[14] However, using NHANES data from 2011-2014, Gache et al. found both higher education and income were positively associated with dietary supplement use among the general population of older adults in the United States.[7] This could be due to having a larger sample size (n=3327) and a wider variety of education and income levels. Other demographic variables used in data analysis (gender, age, race, and disease duration) did not yield significant findings, but having PD itself may be a predictor of dietary supplement use. This is suggested by the percentages of respondents reporting use of individual supplements specifically for PD as well as initiation of supplement use post-diagnosis. However, this would need to be confirmed in future studies comparing dietary supplement use among other chronic diseases.

The most commonly used dietary supplements by at least one-third of respondents were vitamin D, multivitamins, vitamin B12, fish oil, melatonin, CoQ10, and calcium. This supports the hypothesis that the most commonly used supplements among individuals with PD include

multivitamins, coenzyme Q10, melatonin, and fish oil. In addition to the dietary supplements that were included in the hypothesis, vitamin D, vitamin B12, and calcium were among the most commonly used dietary supplements. In 2006, Wolfrath et al. found that multivitamins, calcium, vitamin C, and vitamin E were the dietary supplements most used by individuals with PD.[14] However, in the current study, only 6.4% and 20.5% of respondents reported taking vitamin C and vitamin E, respectively.

At least half of respondents reported taking vitamin B12, melatonin, CoQ10, vitamin B_6, folate, NAC, and mucuna pruriens specifically for PD. Many of these compounds have been shown to have antioxidant functions, and thus it is plausible that they may ameliorate PD disease progression by reducing oxidative stress.[2,3,8-10,13,18,19] However, to date research is lacking to establish firm recommendations for any of these dietary supplements. Future studies are warranted to determine the effects of these dietary supplements on PD progression since they are commonly taken for PD and PD-related symptoms.

A greater percentage of respondents in this study reported discussing their dietary supplement use with a healthcare professional compared with Wolfrath et al.'s participants in 2006, 71% versus 47%, respectively.[14] While the reason for this increase is not known, it could be either related to healthcare professionals including discussion of dietary supplements in their assessments of patients, or it could be related to patients with PD recognizing that dietary supplements may interact with medications. Nevertheless, it is still alarming that more than one in four patients in the present study denied speaking with a healthcare professional about their supplement use. Future qualitative studies should investigate what hinders or facilitates individuals with PD to speak about dietary supplement use with healthcare professionals such as physicians, pharmacists, or registered dietitians.

Limitations of this study include the cross-sectional design, convenience sampling and inherent limitations of survey methods. Convenience sampling using an online survey tool could lead to an under-representation of certain groups of PD patients. For example, our cohort was predominantly Caucasian and highly educated. Results may not be extrapolated to individuals with PD of other ethnic groups, education levels, or older adults who may not be utilizing online support groups. Because convenience sampling was used, the population of those who received the survey could not be determined. Self-selection bias may have affected the sample of respondents, and they may have been more willing to participate in the survey if they used dietary supplements.

In conclusion, findings from this study demonstrate that dietary supplement use is widespread among individuals with PD. The most commonly used supplements in this population include vitamin D, multivitamins, vitamin B12, fish oil, melatonin, CoQ10, and calcium; however, participants reported using 94 different types of dietary supplements. Although most dietary supplement users reported speaking with a healthcare practitioner about their dietary supplement use, results reveal a need for healthcare providers to inquire about dietary supplements during their assessments. As a result of dietary supplement use being so high among those with PD, future studies are warranted to investigate the efficacy of these compounds in attenuating disease progression.

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APPENDICES

SUPPLEMENTAL TABLE

Types of dietary supplements used by individuals with PD	
Dietary Supplement	Overall Use N (%)
Taurine	2 (1.2)
Red Rice Yeast	2 (1.2)
Quercetin/Bromelain	2 (1.2)
Pyrroloquinoline Quinone (PQQ)	2 (1.2)
Lysine	2 (1.2)
Lutein	2 (1.2)
L-Carnitine	2 (1.2)
Green Tea Extract	2 (1.2)
Ginger (root)	2 (1.2)
Garlic	2 (1.2)
Fiber	2 (1.2)
DHEA	2 (1.2)
D-ribose	2 (1.2)
Astaxanthin	2 (1.2)
Alpha Lipoic Acid	2 (1.2)
5-Hydroxytryptophan (5-HTP)	2 (1.2)
Tryptophan	1 (0.06)
Trans-Resveratrol	1 (0.06)
Theanine	1 (0.06)
Sodium Bicarbonate	1 (0.06)
Serrapeptase	1 (0.06)
S-Adenosyl Methionine	1 (0.06)
Rupturewort	1 (0.06)
Rhodiola	1 (0.06)
Restore Gold	1 (0.06)
Pumpkin Seed Oil	1 (0.06)
Protandim	1 (0.06)
Osha Root	1 (0.06)
Oregon grape	1 (0.06)
Nutritional Yeast	1 (0.06)
Longan berry	1 (0.06)
L-Serine	1 (0.06)
Juniper berry	1 (0.06)
Huperzine A	1 (0.06)

Horsetail	1 (0.06)
Glutamine	1 (0.06)
Glucosamine	1 (0.06)
Ginko Biloba	1 (0.06)
Formula 303	1 (0.06)
Flaxseed Oil	1 (0.06)
Elderberry	1 (0.06)
Cysta Q	1 (0.06)
Cranberry	1 (0.06)
Collagen	1 (0.06)
Caprylic Acid Oil	1 (0.06)
Calcium D-Glucarate	1 (0.06)
Caffeine	1 (0.06)
Boswellin	1 (0.06)
Beta-carotene	1 (0.06)
Berberine	1 (0.06)
Avena Sativa	1 (0.06)
Astragalus	1 (0.06)
Ashwagandha	1 (0.06)
Arginine	1 (0.06)
ARED2	1 (0.06)
Amino Acids	1 (0.06)
Activated Charcoal	1 (0.06)

THE UNIVERSITY OF ALABAMA®
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Office for Research Compliance

April 4, 2018

Christine Ferguson
Department of Human Nutrition & Hospitality Management
College of Human Environmental Sciences
Box 870311

Re: IRB # 18-OR-143, "Prevalence of Dietary Supplement Use by Individuals with Parkinson's Disease"

Dear Ms. Ferguson:

The University of Alabama Institutional Review Board has granted approval for your proposed research.

Your application has been given expedited approval according to 45 CFR part 46. You have also been granted the requested waiver of written documentation of informed consent. Approval has been given under expedited review category 7 as outlined below:

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Your application will expire on April 2, 2019. If your research will continue beyond this date, please complete the relevant portions of the IRB Renewal Application. If you wish to modify the application, please complete the Modification of an Approved Protocol form. Changes in this study cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants. When the study closes, please complete the Request for Study Closure form.

Should you need to submit any further correspondence regarding this proposal, please include the above application number.

Good luck with your research.

Carpantato T. Myles, MSM, CIM, CIP
Director & Research Compliance Officer
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