Optimizing Protein Patterns for Skeletal Muscle Preservation and Sleep in the Medical Management of Parkinson Disease

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Study Protocol:

Background

Parkinson's disease (PD) is a complex neurological disease that affects ~6.1 million people worldwide – mostly older adults ≥60 years. The most effective treatment for PD is dopaminergic therapy, particularly levodopa (Ldopa). People with PD have variable responses to Ldopa, including degrees of motor fluctuations (MF) throughout the day. The half-life of Ldopa is ~1.5 h and therefore, dosage and timing are essential to mitigate MF. Ldopa is a large neutral amino acid (LNAA), and the bioavailability of Ldopa is compromised when simultaneously ingested with LNAA (e.g., leucine). Both Ldopa and LNAAs from food are absorbed through the same intestinal transporter, but LNAAs from food are preferentially absorbed by the enterocyte, limiting the bioavailability of Ldopa. Thus, the scientific community often recommends the protein-redistribution diet (PRD). With PRD, patients limit protein (<10 g) at the desired time of medication efficacy (daytime) and meet their protein needs during the evening meal (~70+g). There are deleterious implications of the PRD for older adults with PD; consumption of >30 g of protein, in a single meal, will not sufficiently increase muscle protein synthesis. Additionally, the impact of the PRD on skeletal muscle quality and function has not been determined, and it is unclear, based on prior studies, whether the PRD enhanced drug absorption.

Objectives

Our overarching objective is to generate preliminary data on the impact of the dietary protein pattern on markers of skeletal muscle health and drug efficacy in PD. This objective will be met with the following **Aim 1.** Quantify the effects of dietary protein pattern on skeletal muscle in Parkinson's Disease (PD). We will assess changes in (i) circulating biomarkers associated with muscle catabolism (serum GDF15 and FGF21) and (ii) muscle strength (handgrip dynamometry). **Aim 2.** Determine the effects of dietary protein pattern on sleep quality in PD. PD symptoms, including sleep, will be assessed via actigraphy.

This was a 5-week randomized crossover pilot study with n=12 participants with PD. Participants were recruited through the UAB Comprehensive Parkinson Disease and Movement Disorders Clinic, Tanner Foundation, Lakeshore Foundation, Parkinson Association of Alabama, and local PD support groups. *Eligibility to participate:* diagnosed with PD for ≥5 years, ≥45 years of age, on a stable Ldopa regimen, self-reported motor fluctuations, and no dietary restrictions that would preclude participation in this study. Eligible participants were randomized to follow a PCD (20-30g protein per meal) or a PRD (≤10g until evening meal) for 2 weeks, complete a 1-week washout period, and then follow the other respective diet for the remaining 2 weeks (Figure 1). Participants received one-on-one education and supportive materials on how to follow their assigned diets. Participants were instructed to take their medications 30 minutes before or 2 hours after a meal. As nausea is a common side effect for Ldopa medications, they were given a list of snack options without protein to take with their medication. *Outcome measures* will be assessed at weeks 0, 2 (day 14), 3 (day 21), and 5 (day 35) at Lakeshore campus.

Feasibility measures will be assessed throughout the study, including diet adherence (food records); process evaluations of study visits; time to reach recruitment goal; attrition rate; and acceptability date from exit interviews. Outcome measures, including serum GDF15 and FGF21,

handgrip dynamometry, sleep actigraphy, Parkinson's symptoms (MDS-UPDRS), and physical activity (actigraphy) will be assessed at weeks 0, 2, 3, and 5.

Statistical analysis:

This is a pilot and feasibility study that was intended to generate power and sample size calculations for a subsequent study. Outcome measures for this acute study are continuous variables that will be compared within group (paired t-test) and between groups (independent t-test)