Official Title: Dental Appliance for Parkinson's Disease

NCT Number: 04082663

Document Date: April 23, 2019

I. SPECIFIC AIMS

The primary objective of this study is to determine if the use of a dental mouthpiece can improve gait and motor signs and symptoms, sleep, or quality of life for people with Parkinson's disease (PD). We will conduct a pilot study with participants who have been diagnosed with PD recruited from the community. For this study, participants will have one in-person study visit where they will be fitted with a dental mouthpiece and complete motor tests while wearing the mouthpiece and while not wearing the mouthpiece. Participants will also complete sleep questionnaires and quality of life questionnaires. Participants will then be asked to take the mouthpiece home and wear it at night while they sleep and during the day, except while eating, for one month. At the end of the month, they will complete the same sleep and quality of life questionnaires administered remotely by mail and answer questions about their experience with the dental mouthpiece.

Specific Aim 1: To determine the immediate effect of a dental mouthpiece on Parkinsonian gait and motor symptoms. A 4.8m GAITRite (CIR Systems, Inc., Franklin, NJ) will be utilized to quantify gait mechanics with and without mouthpiece use. Gait and balance tasks will be assessed.

Hypotheses:

a. People with PD will show improvements in gait speed with the mouthpiece in place compared to without.
b. People with PD will show improvements in balance with the mouthpiece in place compared to without.

Specific Aim 2: To determine the longer-term feasibility of use and effect of dental mouthpiece on sleep and quality of life (QOL) for people with PD.

Hypotheses:

a. People with PD will show improvements in sleep quality and duration after one month of wearing the mouthpiece as compared to baseline.
b. People with PD will show improvements in health-related quality of life after one month of wearing the mouthpiece as compared to baseline.

II. BACKGROUND AND SIGNIFICANCE

For people with Parkinson's disease (PD) advances in medical treatments have increased lifespans but have not effectively mitigated the decline in function and the characteristic signs and symptoms of the disease.[1, 2] People with PD often report disturbances in sleep, activities of daily living, and general quality of life. Gait and balance dysfunction are known to negatively affect quality of life in this patient population and are considered risk factors for falls.[3] Walking ability appears to be particularly important in this population, as impairments in ambulation tend to precede impairments with other gait-dependent activities.[4]

Several clinical reports and case studies have shown assorted benefits from use of a dental mouthpiece in people with PD. Specific characteristics of these mouthpieces differ somewhat across cases, but the mouthpieces are typically modeled after those used for temporomandibular joint disorder. A clinical report for one woman with PD showed improvements in grip strength and subjective improvements in motor function and quality of life while using a mouthpiece.[5] This report relied on observation for determining improvements in motor function and did not report a formal quality of life measure or questionnaire. In another case report, a participant subjectively reported use of a bruxism splint improved their sleep quality and fatigue levels.[6] However, again, no quality of life or sleep measures were reported.[6]

A more recent case study found some objective improvements in selected gait and balance measures in a participant with PD while using a dental mouthpiece.[7] The Four Square Step Test and grip strength in the non-dominant hand showed significant improvements with the mouthpiece compared to the patient's baseline condition without the mouthpiece. Additionally, this participant reported significant increases in quality of life while using the mouthpiece, as evidenced by significant improvements in Parkinson Disease Questionnarie-39 (PDQ39) and Global Rate of Change Scale. The researchers reported the participant's gait mechanics differed with use of the mouthpiece, with the participant holding his arms closer to midline.[7]

The mechanism underlying the mouthpiece's effect on gait and motor function is not well understood. It is possible that because afferent inputs from the trigeminal nerve project to the nucleus raphe of the reticular formation, abnormal input from the mandibular branch of the trigeminal nerve may affect rhythmic motor function and balance.[8] Stimulation of the nucleus raphe can produce rhythmic contractions of muscle groups which could potentially affect gait and posture.[8] A mouthpiece may function to promote a more optimal maxillomandibular vertical interrelationship and reduce irritation or abnormal feedback from the mandibular branch of the trigeminal nerve, or more specifically the auriculotemporal nerve, to the nucleus raphe.[9]

Current knowledge regarding the effects of a mouthpiece on motor function and quality of life in people with PD is limited by slight variance in design between mouthpieces and by the small number of participants studied thus far. Our understanding of the topic is based on a small handful of clinical reports and case studies. By conducting an exploratory pilot study, we will examine whether a mouthpiece can affect motor symptoms and gait in a larger group of participants with PD. Additionally, we will determine whether use of a mouthpiece can improve sleep and quality of life in people with PD. Donald R. Moeller, DDS, MD, MA, ThM will custom fabricate the mouthpieces for this study. Dr. Moeller has authored several peer-reviewed, journal-published studies in which he fabricated mouthpieces to treat various symptoms resulting from neurological disorders.[10,11]

III. METHODS

Participants

Participants will be recruited from the community.

For inclusion in the study, participants must:

(1) have a diagnosis of idiopathic, typical Parkinson Disease according to the UK Brain Bank Criteria, Hoehn & Yahr stages 1-3;

(2) stable PD medications for the two weeks prior to baseline visit;
(3) be able to walk at least 10 meters at baseline with or without an assistive device;
(4) have their own teeth and/or dentures;
(5) be willing to try to wear a mouthpiece for one month;
(6) are over the age of 30; and
(7) provide written or verbal informed consent.

Exclusion criteria include:

(1) pre-existing medical conditions that would inhibit full participation in the study's tasks;
(2) absence of any dentition;
(3) cognitive impairments indicated by Mini Mental Status Exam (MMSE) score of <24;
(4) freezing of gait which moderately or severely impacts walking; or
(5) current use of an oral appliance (e.g., a dental mouthpiece, retainer, or braces).

Measures and Materials

The MMSE will be administered to ensure absence of cognitive impairment. The New Freezing of Gait Questionnaire (nFOG) includes participants watching a short video about freezing of gait and a questionnaire about whether they experience freezing of gait and if so, questions that help describe the types of freezing of gait they experience.

Mouthpiece

Each participant will be fitted with a maxillary orthotic (mouthpiece) fabricated by Dr. Moeller. The process for fabrication of the mouthpiece will be as follows:

1) The participant is seated in a normal straight-backed chair with feet on the floor.

2) A dental impression tray is sized appropriately for the participant's lower jaw to ensure that no impingement of soft tissue structures occurs.

3) A quick setting dental alginate impression material is mixed for one minute and then placed into the dental impression tray.

4) The dental impression tray is filled with the alginate material, and the tray and material are placed into the participant's mouth.

5) The tray will remain in the mouth approximately 1 to 2 minutes and will then be removed.

6) A fast setting dental stone is placed in the tray.

7) The dental stone is allowed to set for one-half hour in the alginate impression.

8) The dental stone model is removed from the alginate impression.

9) The lower jaw model is trimmed and then taken to the dental vacuum former machine where a poly-vinyl-acetate (medical-dental grade) thermoplastic sheet of material is heated to a temperature to allow deformation of the material.

10) The vacuum is turned on and the thermoplastic material is sucked down over the dental stone model. A small 5 mm wide strip of thermoplastic material is placed directly over the occlusal portion of all the mandibular teeth to act as a reinforcement.

11) The thermoplastic material is cooled to below room temperature with cold water until stiff.

12) All thermoplastic material which approximates any structure but the dental hard tissue (teeth) is removed from a height just above the attached gingival tissue so that the mouthpiece will be entirely tooth borne.

13) The occlusal material is adjusted at chairside so that an even continuous contact with the maxillary teeth is created on all teeth from the rear-most molar teeth including anterior teeth. The mouthpiece will then have the general appearance of a "horse shoe" in shape.

14) All areas which contact oral soft tissue on the perimeter of the device will be smoothed to allow placement without any trauma or discomfort to any tissue in the participant's mouth.

15) The mouthpiece will be placed in the participant's mouth for a period of about ten minutes to ensure there is no interference with any normal jaw and biting movements.

The mouthpiece is fabricated with polyvinyl ethylene acetate which is non-toxic to humans. There are similar mouthpieces sold over the counter by pharmacies for patient use without a physician/dentist's prescription.

Participants will be instructed to return the mouthpiece at the end of the study period.

Motor assessments

Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS-III) Motor subsection will be used to assess disease severity.

The GAITRite system will be used to assess gait performance. The GAITRite is a portable electronic walkway mat (600 cm long and 64 cm wide). All participants will walk along the mat so that imbedded sensors are activated by foot pressure and deactivated when pressure is released. A computer will process the footsteps for gait velocity (cm/s). The mat is located in a well-lit room, with starting and ending limits marked one meter from the mat to prevent recording acceleration and deceleration phases.

Balance will be assessed using the Mini-BESTest. The Mini-BESTest is a 14-item evaluation designed to assess a variety of balance components.

Quality-of-life questionnaires

Parkinson's Disease Questionnaire-39 (PDQ-39) contains 39 self-report items designed specifically for people with PD. There are eight subscores that are calculated along with a total score.

Parkinson's Disease Sleep Scale (PDSS) contains 15 self-report items designed specifically to assess various indicators of sleep quality in people with PD.

Participant information

Participants will fill out a demographic form, a medication form, and medical comorbidity form at the in-person visit, and note any changes in their health or medications after wearing the mouthpiece for one month.

Journal

Participants will keep a journal documenting how long they wore the mouthpiece at night and during the day, reasons for taking it out, and can make comments about the mouthpiece.

Exit questionnaires

Participants will complete an open-ended exit questionnaire regarding their experience with the mouthpiece and the Global Rate of Change Scale (GRC) after wearing the mouthpiece for one month.

Protocol

A phone screen will be used to screen for preliminary study suitability. If the potential participant passes the phone screen and would like to enroll in the study, we will then schedule them for their in-person visit.

The first visit will be in-person on the ground floor of the Movement Science Research Center at 4444 Forest Park Ave, St. Louis, MO, 63110. The study visit will follow the following schedule:

Informed consent, MMSE, nFOG (15 minutes): A trained researcher will review the informed consent document with the participant, outlining the study objectives and ensuring the participants have the opportunity to ask the researcher any questions they may have regarding the study and procedures. If the participant wants to continue, they will sign the consent form. The MMSE will be performed to screen for cognitive impairments which would affect study participation. The nFOG will provide us with information about freezing of gait if applicable.

Motor Assessment #1 without mouthpiece (45 minutes): MDS-UPDRS-III, GAITRite, Mini-Bestest (order will be randomized)

Dental Measurements (15 minutes): Dr. Moeller will take dental measurements for the purpose of creating a custom-fitted mouthpiece as outlined in the Methods section.

Questionnaires, Medical History, Medications (30 minutes): The participants will complete demographic, medical history/medications forms, sleep and quality of life questionnaires while their mouthpiece is being fabricated.

Mouthpiece in (25 minutes): After their mouthpiece has been fabricated and adjusted (smoothed as needed), participants will sit with the mouthpiece in for 25 minutes.

Motor Assessment #2 with mouthpiece (45 minutes): MDS-UPDRS-III, GAITRite, Mini-Bestest, (order will be randomized)

Participants who take medication for Parkinson symptoms, will be asked to take their medication 30 minutes before arrival to ensure participants are in the “on” phase for the motor tasks.

At completion of the in-person visit, participants will be instructed to use the mouthpiece as much as possible for the next month. Participants will be informed they can take the mouthpiece out while eating and will be instructed to keep track of how long they wear the mouthpiece each day by journal entry.

Follow-up will occur one month later.

Questionnaires, Medical History, Medications (30 minutes): The participants will complete sleep and quality of life questionnaires, record any changes in their medical history or medications, and complete an open-ended questionnaire regarding their thoughts on the mouthpiece and the GRC.

Randomization Method

The order in which the motor assessments are given in regards to wearing the mouthpiece or not will be randomized for each participant. The motor tasks (disease severity, gait, balance) will be randomized within each participant.

Safety and Adverse Events

The research team will do everything possible to ensure safety of all participants over the course of this study. The adverse event most likely to occur in this study is risk of falling while walking. Participants will be fitted with a gait belt. Members of the research team are trained in fall prevention and will closely monitor all participants throughout all aspects of the study in case of a need to assist with balance to prevent a fall. In the case of an adverse event, emergency medical care will be sought immediately if needed. Any serious adverse events will be reported to the local IRB immediately. Occurrence of an adverse event will be noted in a participant's file.

Potential risks will be addressed in the following ways:

a) Discomfort in answering questionnaires: Participants may refuse to answer any questions they prefer not to answer.

b) Loss of confidentiality: Loss of confidentiality is highly unlikely. To safeguard against this, we will comply with all HIPAA regulations. Data will not be identified by participant name. All data will be coded, and code sheets will be stored in locked files.

c) Stumbling during locomotion: Participants will be closely attended by a trained research staff member during walking and fitted with a gait belt. Walking will be performed in a large, open space and the staff member will be prepared to assist participants who may stumble.

d) Falling: Participants will be closely attended by a trained assistant who will ensure the safest of conditions. It is unlikely that participants will experience falls during testing or will be injured as the result of a fall. If a participant appears unsteady, breaks will be encouraged or testing will be terminated.

e) Fatigue from walking: Rest breaks will be provided as needed.

f) Discomfort or irritation while being fitted for the mouthpiece or while wearing the mouthpiece: the participants may remove the mouthpiece at any time.

Benefits

We do not yet know the full extent to which the mouthpiece may improve symptoms associated with Parkinson disease. This study may help inform future treatment techniques to improve motor and non-motor function in people with PD.

Interim Monitoring and Early Stopping

Data will be monitored throughout the study and, should any issues arise, we will adjust our protocol and submit any changes to the IRB project for review. We will not conduct interim data analyses.

Statistical Analyses Plan

We will use paired t-tests to determine if there are differences between conditions (with mouthpiece vs without mouthpiece). We will also use paired t-tests to compare sleep and quality of life questionnaires from baseline (prior to study) to follow up (after one month of mouthpiece use).

R will be used for data analysis across all aims.

Power

Because of the exploratory nature of this pilot study and relative lack of information in the literature, no formal power analysis was conducted.

References:

1. Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease (2009). Neurology 2009;72:S1-136.

2. Shulman LM. Understanding disability in Parkinson's disease. Mov Disord 2010;25 Suppl 1:S131-5.

3. Ellis T, Cavanaugh JT, Earhart GM, Ford MP, Foreman KB, Dibble LE. Which measures of physical function and motor impairment best predict quality of life in Parkinson's disease? Parkinsonism Relat Disord. 2011;17(9):693-697

4. Ellis TD C, JT, Earhart GM, Ford MP, Foreman KB, Thackeray A, Thiese MS, Dibble LE. Identifying clinical measures that most accurately reflect the progression of disability in Parkinson disease. Parkinsonism Relat Disord 2016;25:65-71.

5. Nomoto S, Nakamura M, Sato T, Hisanaga R. Occlusal treatment with bite splint improves dyskinesia in Parkinson's disease patient: a case report. Bull Tokyo Dent Coll. 2013;54(3):157-161.

6. Durham TM, Hodges ED, Henry MJ, Geasland J, Straub P. Management of orofacial manifestations of Parkinson's disease with splint therapy: a case report. Spec Care dentist. 1993;13(4):155-158.

7. Lane, H, Rose, L, Woodbrey, M, Arghavani, D, Lawrence, M and Cavanaugh, J. Exploring the effects of using an oral appliance to reduce movement dysfunction in an individual with Parkinson disease. Journal of Neurologic Physical Therapy. 2017; 41(1): 52-58.

8. Torvik, A. Afferent connections to the sensory trigeminal nuclei, the nucleus of the solitary tract and adjacent structures. An experimental study in the rat. Journal of Comparative Neurology. 1956; 106(1): 51-141.

9. Stack, B, Sims, A. The Relationship Between Posture and Equilibrium and the Auriculotemporal Nerve in Patients with Disturbed Gait and Balance. The Journal of Craniomandibular & Sleep Practice. 2009; 27(4): 248-260.

10. Moeller, DR. Evaluation of a removable intraoral soft stabilization splint for the reduction of headaches and nightmares in military PTSD patients: a large case series. Journal of Special Operations Medicine. 2013; 13(1): 49-54.

11. Moeller, DR, Duffey, JM, Goolsby, AM, Gallimore, JT. Use of a removable mandibular neuroprosthesis for the reduction of posttraumatic stress disorder (PTSD) and mild traumatic brain injury/PTSD-associated nightmares, headaches, and sleep disturbances. Journal of Special Operations Medicine. 2014; 14(3): 64-73.