ORIGINAL

Single session osteopathic manipulative treatment in Parkinson's disease: a randomized clinical trial protocol

Tratamiento de manipulación osteopática en una sola sesión en la enfermedad de Parkinson: un protocolo de ensayo clínico aleatorizado

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Abstract

The aim of the study is to evaluate the influence of a single session of OMT in individuals with PD based on ICF domains. Randomized clinical trial protocol available at the link: https://ensaiosclinicos.gov.br/rg/RBR-7pkypg3, in which 60 individuals diagnosed with PD are randomly allocated to one of two groups (Control, n=30 and OMT, n=30). Participants will be evaluated in 2 moments (baseline and post-treatment). The control group will not undergo any intervention and remains lying for 30 minutes. Protocol will be applied to the OMT group. The following outcomes will be compared: TUG (G-Walk®), gait speed (G-Walk®), C7 measurement test for the wall of the flexed trunk posture, evaluation of the range of motion of ankle dorsiflexion and MiniBESTest. A descriptive analysis of sociodemographic variables will be carried out. The statistical analysis will consider data distribution for the statistical test selection. The dependent T-test will be used to compare baseline and post-measurements for variables with normal distribution. For variables with non-normal distribution, the Wilcoxon signed rank test will be adopted. The effect size will be evaluated through the Pearson coefficient in which 0 (no effect) and (perfect effect). A confidence interval of 95% will be adopted and statistical significance $p<0.05$ will be considered. We hypothesized that the use of OMT could bring positive effects in relation to the improvement of gait, posture, balance, dorsiflexion ROM and general mobility. OMT may be a therapeutic approach to consider for individuals with PD.

Key words: Parkinson's disease, osteopathic manipulative treatment, ICF, gait, balance.

Resumen

El objetivo del estudio es evaluar la influencia de una sola sesión del Tratamiento Manipulativo Osteopático (TMO) en personas con Enfermedad de Parkinson (EP), en función de los dominios de la CIF. El protocolo de ensayo clínico aleatorizado está disponible en el enlace: https://ensaiosclinicos.gov.br/rg/RBR-7pkypg3, en dicho estudio, participaron 60 personas diagnosticadas con EP y se asignaron aleatoriamente a uno de dos grupos (Control, n=30 y TMO, n=30). Los participantes serán evaluados en 2 momentos (línea base y postratamiento). El grupo control no se someterá a ninguna intervención y permanecerá tumbado durante 30 minutos. Se le aplicará el protocolo al grupo TMO. Se compararán los siguientes resultados: TUG (G-Walk®), la velocidad de la marcha (G-Walk®), la prueba de medición C7 para la pared de la postura del tronco flexionado, la evaluación del rango de movimiento de la dorsiflexión del tobillo y el MiniBESTest. También se llevará a cabo un análisis descriptivo de las variables sociodemográficas. El análisis estadístico, considerará la distribución de datos para la selección de la prueba estadística. La prueba T dependiente se utilizará para comparar las mediciones iniciales y posteriores de las variables con distribución normal. Para las variables con distribución anormal, se adoptará la prueba de los rangos con signo de Wilcoxon. El tamaño del efecto se evaluará a través de Pearson, el coeficiente en el que 0 (sin efecto) y (efecto perfecto). Se adoptará un intervalo de confianza del 95% y la significación estadística $p<0,05$ será considerada. Presumimos que el uso de TMO podría traer efectos positivos en la relación con la mejora de la marcha, la postura, el equilibrio, el rango de movimiento de dorsiflexión y la movilidad general. TMO puede ser un enfoque terapéutico a considerar para personas con EP.

Palabras clave: Enfermedad de Parkinson, tratamiento manipulativo osteopático, CIF, marcha, equilibrio

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease in the world[1]. It is a disease that affects the central nervous system. The most characteristic motor signs of the disease are rigidity, bradykinesia, resting tremor and postural instability, constituting the parkinsonian tetrad[2]. Due to motor signs and the evolution of PD, people affected by the disease may present a flexed posture, which worsens gait performance, balance, and mobility[3,4]. Other factors, such as degenerative disc disease, weakness of the extensor muscles of the spine, vertebral fractures and postural habits are associated with postural alteration[5].

Physical exercise is a type of non-pharmacological treatment indicated for patients with PD due to the motor impairments caused by the disease[6]. Among the possible approaches to physical exercise, there is scientific evidence indicating that osteopathic manipulative treatment (OMT) can positively influence both postural instability in elderly people with vertigo, and gait in PD[7,8]. OMT emphasizes the central role of the musculoskeletal system, which could be ideal for addressing somatic dysfunction associated with rigidity in people with PD[9]. In published studies, patients with PD improved gait parameters (increased step length and gait speed) after OMT, while healthy people did not show significant changes. These findings suggest a positive effect in patients with PD after OMT regarding gait and dynamic mobility of the lower limbs[7,8].

There is still a lack of studies that address the effects of a therapeutic program based on Osteopathy in individuals with PD, and there is a lack of knowledge on the subject. To date, the possible influence of OMT on the range of motion (ROM) of ankle dorsiflexion, balance, and spatiotemporal gait variables (stride length, swing phase, single stance phase and double stance phase of the lower limbs) has not been evaluated in patients with PD. In studies, it was not clear which protocols were used, and each study evaluated only one variable, that were balance or gait. Based on clinical reasoning, OMT can improve the biomechanical functions of joints and muscles. For this reason, allied health professionals who work to promote physical activity can consider OMT as a possibility to manage musculoskeletal symptoms of PD[10].

Our study aims to evaluate different variables based on the ICF and single-session application of a OMT protocol. Therefore, the problem question presented in this article is: Can OMT acutely influence lower limb mobility, balance, and gait in patients with PD?

Methods

Experimental design

This is a randomized controlled clinical trial approved by the Ethics Committee and registered in the Brazilian Registry of Clinical Trials under the number RBR-7pkypg3, available at the link: https://ensaiosclinicos.gov.br/rg/RBR-7pkypg3. The study will be carried out in a Physical therapy Service. All participants will sign a Free and Informed Consent Term (FIC), based on the Helsinki Resolution.

Population and sample size

The formula below was used to determine the sample size (n) based on the estimation of Brazilian population proportion:

$$n = \frac{(N \cdot p \cdot q \cdot (Z\,\alpha/(2))}{p \cdot q \cdot (Z\,\alpha/2)^2 + (N-1) \cdot E^2}$$

Where:

N = Brazilian population according to 2010 Census (190.755.799 people).
p = prevalence Parkinson's Disease – 2% average of the elderly population (0.02).
q = 1 - p (0.98)
Z α/2 = critical value associated with a confidence level of 95% (1.96).
E = 5% sample error (0.05).

From the formula above, the result obtained by the sample calculation is 30 participants. Sixty individuals of both sexes with a diagnosis of idiopathic PD will be allocated in the Control (n=30) and Osteopathic Manipulative Treatment (OMT) (n=30) groups. All assessments and treatment protocol will be performed in the "on" phase of medication (period of drug action, from 30 minutes to 2 hours after the last dose) where patients are able to move more freely when antiparkinsonian drugs are working well. Volunteers can only be included in the research after understanding and consenting to participate in the research by signing the FIC.

Inclusion criteria

Adults with idiopathic PD diagnosed by a neurologist, classified in stages 1 to 3 of disability on the Modified Hoehn & Yahr scale, being on stable antiparkinsonian medication; participants' ability to obey verbal commands analyzed by the Montreal Cognitive Assessment (MoCA).

Exclusion criteria

Presence of other associated neurological diseases; severe osteoporosis, significant change in the ability to understand and perform tasks according to MoCA, acute rheumatologic diseases, previous history of spinal surgery using osteosynthesis and arthrodesis-type procedure, individuals classified in stages 4 and 5 of the Modified Hoehn & Yahr.

This study will be carried out according to the phases of randomized trial of two groups (enrollment, intervention allocation and data analysis).

ICF-based clinical tools

The assessment based on the ICF domains comprises body function and structure, activities, participation and contextual factors (environmental and personal). These domains cover aspects of functionality and disability. In the domain "body function and structure" the following assessment instruments/tests will be adopted: the MoCA scale for cognition assess; the Modified H&Y staging scale to assess PD clinical staging; section I of the Unified Parkinson's Disease Rating Scale (UPDRS) for the assessment of mental activity, behavior and mood in PD; the C7 measurement test to verify the flexed posture; the evaluation of ankle dorsiflexion ROM and the MiniBESTest for the analysis of static and dynamic balance. In the "activities" domain, the following assessment instruments/tests will be adopted: freezing of gait questionnaire (FOGQ); Timed up and go (TUG) using G-Walk® to assess the dynamic mobility of the lower limbs; 7-meter walk test that will also use the G-Walk®; section II of the UPDRS to analyze activities of daily living and section III of the UPDRS to assess motor impairment stage. Contextual factors will be addressed through anamnesis and verification of the equivalent daily dose of patient's levodopa.

ICF - Body function and structure domain
Cognitive Assessment - Montreal Cognitive Assessment (MoCA)

The MoCA is a brief global cognitive scale useful in detecting mild cognitive impairment in patients with PD. In MoCA, different cognitive domains are evaluated, such as visuospatial and executive functions as memory, attention, language, abstraction, delayed recall, concentration and calculation, repetition and orientation[11].

Modified Hoehn & Yahr Staging Scale (H&Y)

The modified Hoehn and Yahr scale assesses disease staging in individuals with PD[12,13], including postural instability. To assess postural stability, the patient is pulled back abruptly from the shoulders[12]. In addition to sample characterization, H&Y will be used as an important tool included in exclusion criteria of the study, excluding individuals with stages 4 and 5.

Measurement of C7 trunk flexion to wall distance

The flexed posture of the trunk in individuals with PD is associated with a general worsening of the disease. It can have, in particular, a negative effect when it comes to mobility and balance, becoming a compensatory mechanism that increases risk of falls[14]. To perform the test, patients will be instructed to stand up against the wall in their usual posture. Their feet should be shoulder-width apart and slightly away from the wall. Then, the evaluator measures the distance, in centimeters, between the seventh cervical vertebra and the wall, in a horizontal direction[14].

Assessment of ankle dorsiflexion range of motion

The assessment of ankle dorsiflexion ROM in closed kinetic chain (CKC) is used to assess joint mobility. The test consists of placing the foot to be evaluated on a measuring tape on the floor in a straight line from a wall. Patients in an orthostatic position keep the hallux on the tape. Then, patients are instructed to perform the dorsiflexion movement in CKC, placing the foot as far as possible, keeping the knee in contact with the wall. Patients' heels must also maintain contact with the ground. When the patients reach the maximum amplitude, the evaluator performs the measurement of the distance between the wall and the hallux[15].

Subjective assessment of postural balance – Mini BESTest

The Mini BESTest assesses dynamic balance in individuals with PD. Anticipatory postural adjustments; reactive postural control; sensory orientation, and gait stability are covered in this test[16].

ICF - Body function and structure /Activities domains
Clinical assessment of PD - Unified Parkinson's Disease Rating Scale (UPDRS)

The UPDRS determines, through self-report and clinical observation, the disease progression and the effectiveness of the treatment evaluating signs, symptoms and certain activities of the patients[17,18,19]. Composed of 42 items, the scale is divided in 4 parts, namely: 1) mental activity, behavior and mood, 2) activities of daily living, 3) motor exploration and 4) complications of drug therapy. The maximum value indicates more severe impairment, while the minimum value indicates mild impairment from PD[19].

ICF - Activities domain
Assessment of dynamic mobility of lower limbs, using the Timed up and go test (TUG) through G-WALK®

The Timed Up and Go test consists of measuring, in seconds, the time in which the individual stands up from a chair, walks a 3 meters distance in a safe and comfortable way, turns 180 degrees, walks towards the chair again and sits down[20]. The longer the time, the greater the association with fall risk. During the test, participants can use, if necessary, walking aids, but without any physical assistance from the evaluator. Subjects are instructed to perform the test once to become familiar with the movements[20,21]. The test will be performed with the triaxial G-WALK® sensor positioned in the lumbosacral region. The sensor transmits the information, via bluetooth, to a computer with GStudio software for data storage[22]. G-WALK® sensor makes it possible to determine the time in the test 5 phases, namely: transition from sitting

to standing, forward walking, pivoting, back walking and transition from standing to sitting.

Evaluation of freezing of gait phenomenon – Freezing of Gait Questionnaire (FOGQ)

The freezing of gait (FOG) is described as a sudden inability to start or continue walking and usually lasts less than 10 seconds, reaching 30 seconds as the disease progresses, increasing the risk of falls[23]. Individuals with PD report having their feet glued to the ground sensation, especially when starting to walk, changing direction, passing through narrow places, immediately before reaching a destination and when trying to avoid objects[24]. The Freezing of Gait Questionnaire (FOGQ) has 6 items, 4 of which are used to assess the severity of FOG, and the other 2 items are used to assess gait. The application of the questionnaire is indicated during the ON phase of medication. All questions, with the exception of question 3, are based on events of the last week or general presence of the phenomenon. Question 3, "Do you feel like your feet are glued to the floor as you walk, turn around, or when you try to start walking (freezing)?" it is extremely important since the answer "no" considers the individual to be non-freezing, and the assessment is completed. The evaluator must demonstrate what an episode of FOG would be like to the individual[24]. FOGQ will be used for sample characterization.

Assessment of gait speed through the 7-meter walk test using the G-WALK

The 7-meter walk test with the G-WALK® consists of analyzing the gait phases, speed (m/sec), cadence (steps/min), stride length (m), step length and number of steps. Moreover, propulsion and symmetry are analyzed. Propulsion describes the ability to adapt total load in relation to body weight in one of the lower limbs after the deceleration phase, and to push the center of mass forward in the opposite lower limb. Symmetry provides information about the patient's ability to similarly maintain the acceleration of the center of mass during right and left step cycles. All analyses will be performed for both sides. Patients will be instructed to walk 7 meters comfortably. If assistance is needed, it should be provided as little as possible, just so patients can perform the test. This assistance must be documented to reflect the highest level of assistance offered[25].

ICF Contextual factors
Identification form - anamnesis

Patients will fill in the identification forms with socio-demographic and clinical data that include: patient's name, date of birth, age, gender, height, body mass, education level, profession, address, contact phone, Parkinson's disease diagnosis time.

Calculation of the Levodopa equivalent daily dose

The levodopa equivalent daily dose (LEDD) will be calculated to verify the amount of the study patients' ingestion of equivalent daily dose of Levodopa. The literature suggests that high doses of levodopa can influence directly the functional status of patients with PD[26,27].

For this purpose, the formula used to calculate the LEDD is as follows: 100 mg of levodopa = 130 mg of controlled-release levodopa = 70 mg of levodopa + catechol-O-methyl-transferase inhibitor = 1 mg of pergolide = 1 mg pramipexole = 5 mg ropinirole[28,29].

Description of OMT protocol

Patients randomly allocated to the OMT group will receive a protocol containing 13 specific osteopathic techniques lasting approximately 30 minutes. Specific techniques are described below.

1. Suboccipital muscles inhibition technique with the patient in supine position[30]
A: The technique starts with the patient relaxed in the supine position.
B: Progression to therapist's fingers tension increase towards ceiling. Source: Own authorship.
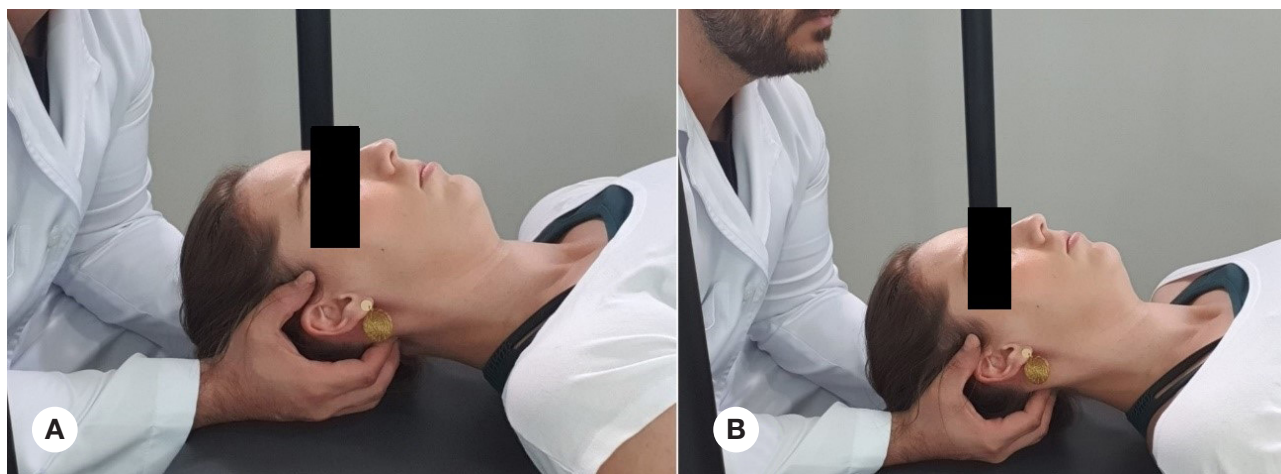
2. Cervical vertebrae articulation technique in dorsal decubitus[31]
A: The technique starts with the patient in the supine position, head in flexion and resting on the therapist's abdomen. Therapist contacts the articular facets of the atlas and axis region.
B: Therapist articulates the region in 8.
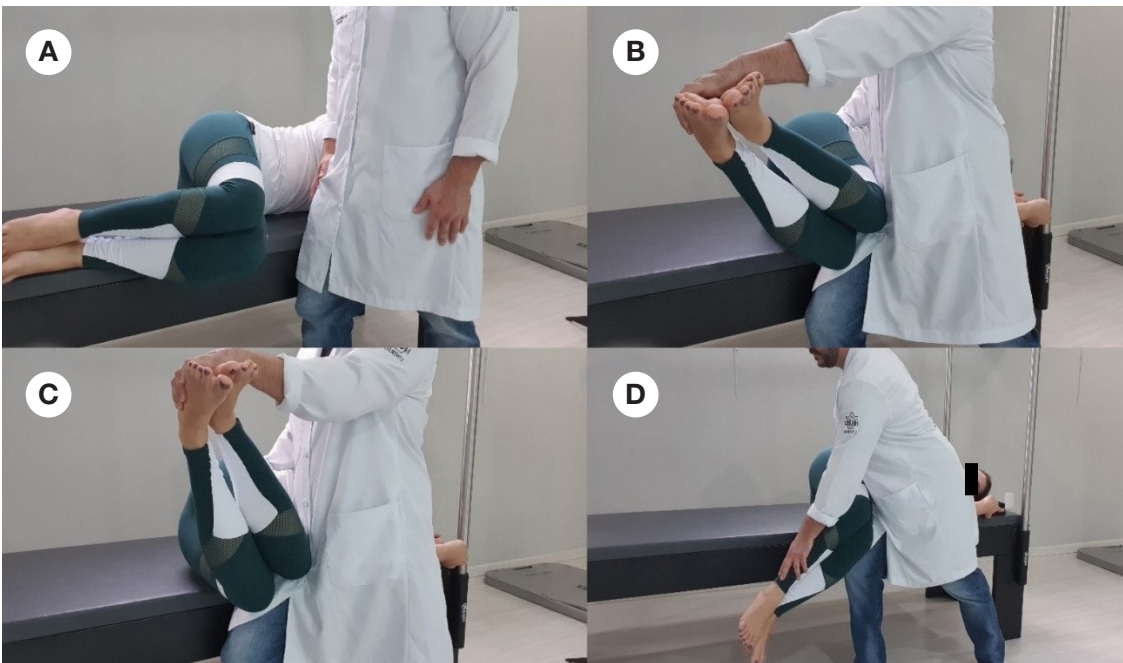**C:** Technique continues the for the opposite side.

3. Stretching technique for iliolumbar ligaments, in lateral decubitus
A: The technique starts with the patient in lateral decubitus.
B: Support of the patient's lower limbs on the therapist's knee and abdomen.
C: Tension increase towards the ceiling.
D: Tension increase towards the ground.

Contact in the iliolumbar ligaments' region.

4. Articulatory technique with crossed pisiforms for the thoracic spine
A: Contact with crossed pisiforms in the upper thoracic spine, inner hand with finger in cephalic direction and external hand with fingers in caudal direction.
B: Contact with the mid thoracic spine.
**C:** Contact with the lower thoracic spine.

5. Articulation technique for the lumbar spine in prone position
A. Contact with crossed pisiforms in the patient's lumbar region.
B. Start of rotation movement associated with light pressure towards the ground.
C. Increased rotation and compression.

6. Articulation technique in ventral decubitus for sacroiliac[32]
A: The technique starts with the patient in prone position, contact of the cephalic hand with the contralateral sacroiliac, stabilizing the region. Caudal hand in contact with the patient's ankle.
B: Internal rotation of the coxofemoral.
C: In a rhythmic and continuous way, the tension is increased.
D: Return to the starting position.
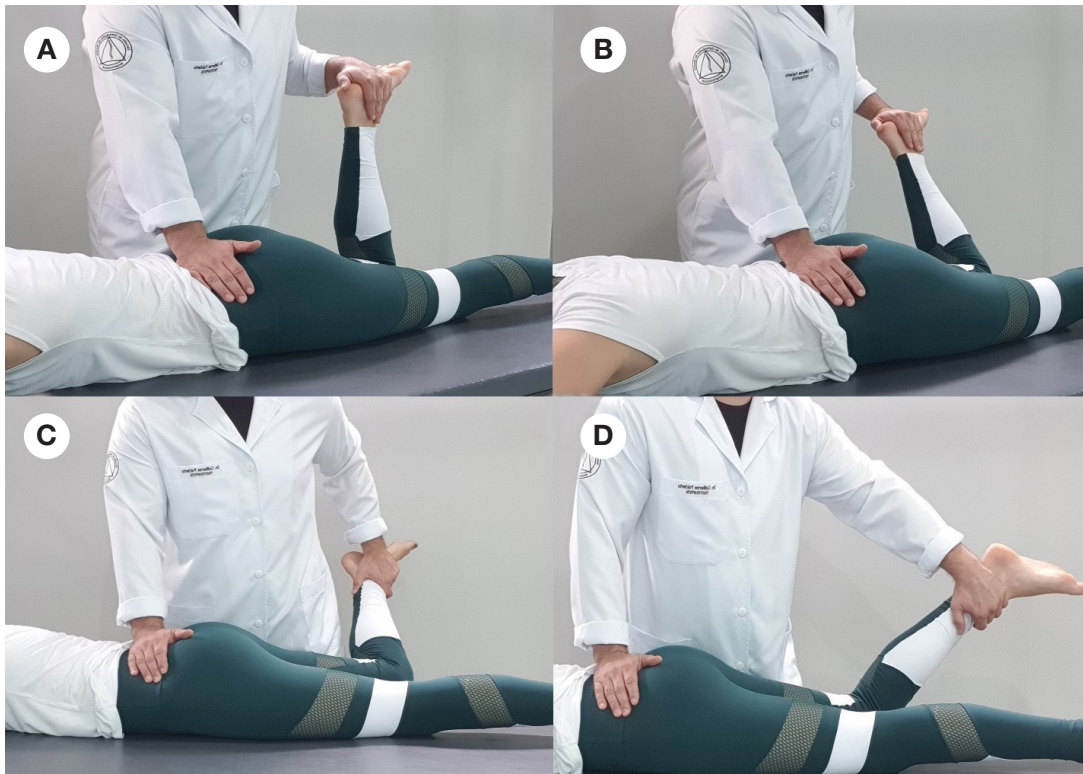
7. Muscle energy technique for psoas[33]
A: The technique starts with the patient on the edge of the stretcher, in dorsal decubitus and lower limb out.
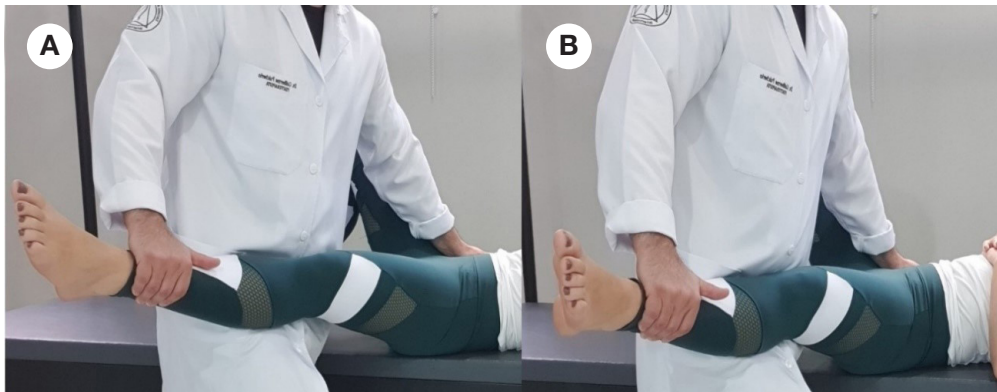**B:** Isometric contractions begin.
C: Passive return to the starting position.

8. Muscle energy technique for adductor muscles
A: The technique starts with the patient in dorsal decubitus, with the first lower limb motor barrier in abduction. Isometric contractions starts.
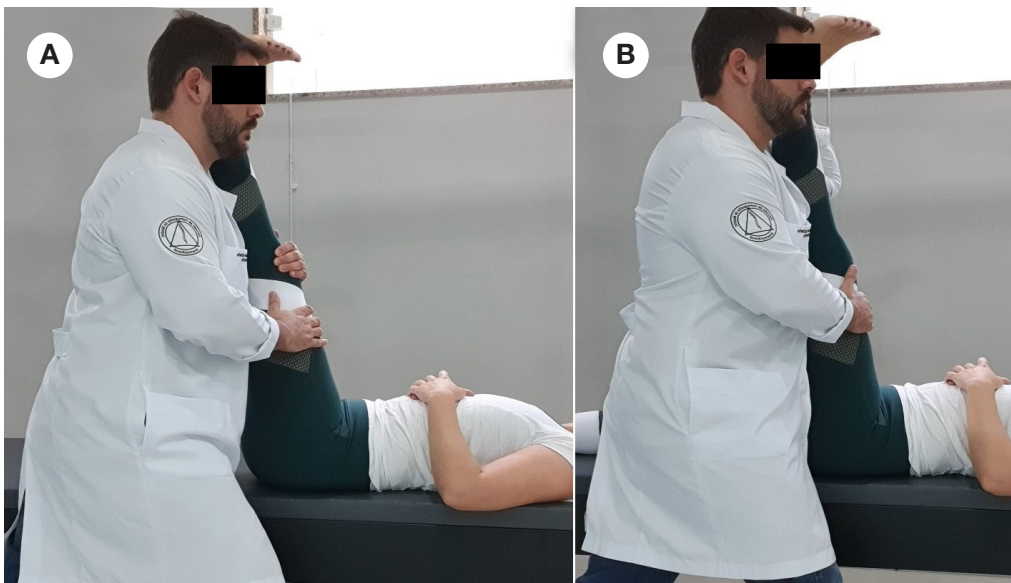**B:** Take the new motor barrier so that in the end of the technique, passively return to the starting position.

9. Muscle energy technique for hamstring muscles
A: The technique starts with the patient in dorsal decubitus, hip flexion and knee extension.
B: Begin isometric contraction cycles and at the end of the technique, passively return to the starting position.

10. Popliteal release technique

The technique starts with the patient in the supine position. Therapist contacts the lower hand on the distal part of the tibia on the side to be treated. Upper hand in contact with the popliteus muscle region. The technique is performed dynamically, in lateral rotation of the tibia and extension.

11. Cuneiform articulation technique in 8

A: The technique starts with the patient in dorsal decubitus, therapist in abdominal contact at the metatarsals base and hands under the plantar surface, with thumbs in the cuneiform region.
B: Articulatory movement starts in "8".
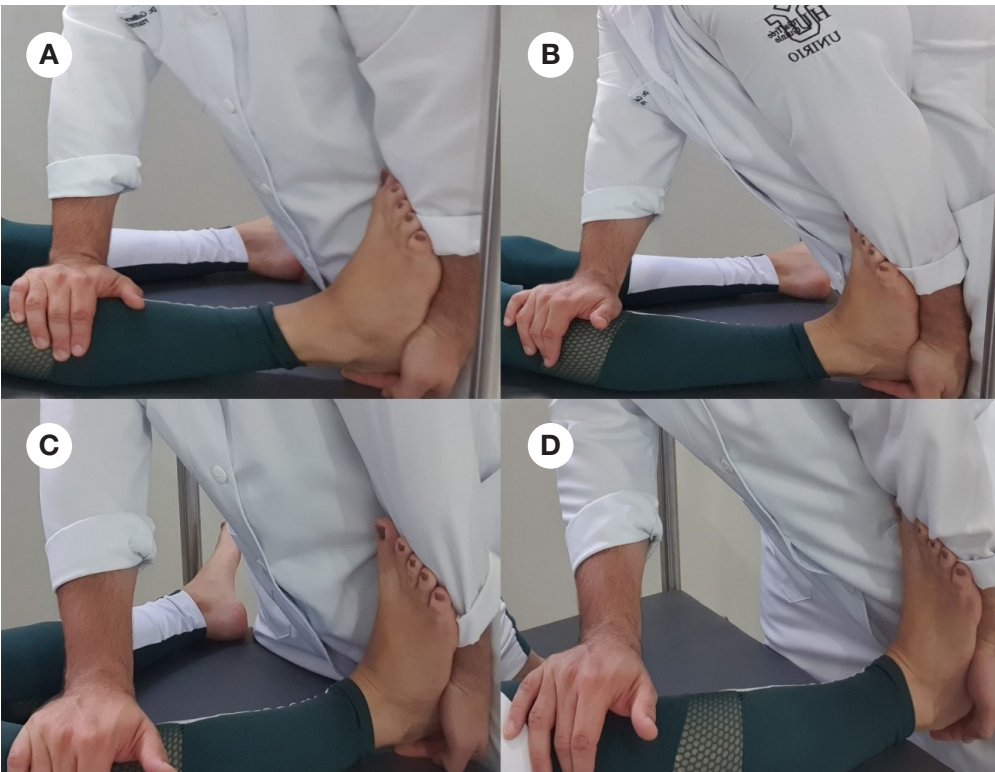**C:** Movement development.

12. Muscle energy technique for ankle plantarflexion muscles

A: Patient in dorsal decubitus, therapist in contact with the caudal hand on the calcaneus and forearm on the patient's plantar surface.
B: Isometric contraction cycle begins.
C: Gain of new motor barrier.
D: End of technique passively returning to starting position.

13. Diaphragm release with seated patient associated with trunk extension[34]
A. Knee supported on the patient's side, stabilizing the trunk.
B. Therapist's hands on the costal margin with posterior glide.
C. Trunk and cervical flexion in the expiratory phase and increase of diaphragm contact.
D. Trunk and neck extension in inspiratory phase.
E. Relaxation of therapist's hands.
F. Cycle repetition.

Source figures: Own authorship

Control group procedures

After performing the initial assessments, patients of control group will be directed to a room where the evaluator will ask them to lie down in a comfortable position, being able to change decubitus, lasting as the OMT group protocol, 30 minutes. After this period, patients will be reassessed.

Statistical analysis

The SPSS 23.0 statistical program will be adopted as a tool for statistical analysis. Descriptive analysis of socio-demographic variables will be performed. Numerical variables will be presented as mean and standard deviation. Nominal variables will be presented in frequency and percentage. Levene's test will be adopted to analyze the homogeneity of variances. The Shapiro-Wilk test will verify the distribution of variables regarding normality. T-test for independent samples will be adopted to compare measurements between groups at baseline and post-treatment, in normal distribution. For non-normal distribution, the non-parametric Mann-Whitney test will be adopted. Dependent T test will be used to compare baseline and post measurements for normally distributed variables. For variables with non-normal distribution, the Wilcoxon signed rank test will be adopted. The effect size will be evaluated through the Pearson coefficient where 0 (no effect) and 1 (a perfect effect). R = 0.10 (small effect), r = 0.30 (medium effect); r = 0.50 (large effect). A confidence interval of 95% will be adopted, considering statistical significance through $p<0.05$. Intention-to-treat analysis will also be considered for individuals who for some reason do not complete integrally the study[35]

Discussion

The present article is a randomized clinical trial protocol study with the objective of knowing the effects of an OMT session through studied outcomes based on ICF domains. The OMT intends to provide greater mobility in structures such as joints and muscles to improve the individual's functionality[7,8]. This protocol study used as a basis a previous study on OMT in patients with PD and healthy subjects that demonstrated an improvement in length, step cadence, and lower limb speed after performing OMT session in patients with PD, which did not occur in the control group participants[7]. The WELLS study[7] was also used as a basis for another study[8] that discussed the effects of a protocol on motor function, balance and gait stability. The results demonstrated a significant improvement in motor function, in addition to a significant clinical improvement in gait, balance and motor function.

In the present protocol study, some techniques were included in order to address different structures that influence the outcomes to be studied (cervical mobility, ankle mobility, balance, temporo-spatial gait variables). The diaphragm release technique aims to improve its function. The diaphragm is an extremely important muscle for breathing, and it also contributes to the maintenance of posture and postural changes[35]. Therefore, the technique for its release in the sitting position was included. The iliofemoral ligaments are important for the union between the lumbar spine and the pelvis, and their function is to limit the movements of lateral inclination, flexion (superior fasciculus) and extension (inferior fasciculus)[36]. Patients with PD have a decrease in ankle ROM, which can impair the activity of climbing a ladder[37,38] and, therefore, impair quality of life. Thus, a therapeutic approach emphasizing the ankles was included in the protocol, specifically, muscle energy for the plantarflexor muscles and articulatory mobilization for the cuneiform muscles. Postural disorders are also common, which also increases the risk of falling, immobility, and loss of independence[39]. Therefore, articulatory and muscle energy mobilizations will be carried out in order to optimize the structures functions related to posture.

The ICF domains will be considered in the participants evaluation in order to favor the integral view of each individual. The domain "body function and structure" will be evaluated using the following parameters: MoCA, Modified H&Y staging scale, UPDRS I, the C7 measurement test, the assessment of ankle dorsiflexion ROM and the MiniBESTest. In the "activities" domain, the following will be used: The Freezing of Gait Questionnaire (FOGQ), the G-Walk® in the Timed up and go (TUG) and in the 7-meter walk test. Furthermore, UPDRS II and III will also be used in ICF domain. Contextual factors will also be addressed through anamnesis and verification of Levodopa daily dose. The choice of ICF aims to identify how the same health condition (in this case, PD) can influence and be influenced by the domains of ICF and, consequently, the functioning in different ways in PD patients.

PD courses with motor signs and symptoms such as: bradykinesia, muscle rigidity and postural instability[2], leading to changes in gait and general mobility, including dynamic mobility of the lower limbs[7,40], which can impair activities of daily living performance. There is a knowledge gap in the acute effects of OMT in patients with PD based on the outcomes presented here. The studies found in the literature do not have a statistical importance, since presented a small number of patients[7,8]. In this work will be used the formula based on the population where the study will be carried out and on the prevalence of PD to set the number of patients in each group (OMT =30, Control =30). To date, there are no studies that use the ICF domains to study the functioning of people with PD after OMT. Most studies were not detailed in describing the osteopathic techniques used in people with PD, which make dificult their reproducibility. From a scientific point of view, it is important to detail the techniques/interventions adopted in scientific reports to confirm that the studied clinical outcomes are potentially influenced by the available treatment of experimental groups. The

hypothesis of the present study is that positive effects are found in the OMT group regarding improvement of dorsiflexion ROM, posture, balance, as well as general mobility compared to participants in the control group. Thus, further studies are needed to evaluate OMT as a complementary therapy in PD.

Conflict of interest

The authors declare that they have no conflict of interest.

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