Original Article

Behavioral therapy associated with neuromodulation in the treatment of bladder and bowel in individuals with Parkinson's: a pilot study

Terapia comportamental associada a neuromodulação no tratamento da bexiga e intestino em indivíduos com Parkinson: um estudo piloto

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ABSTRACT | AIMS: The study aims to evaluate the effects of behavioral therapy associated with neuromodulation at neurogenic bladder and bowel on Parkinson's disease. **METHODS:** It is a pilot study. After signing consent forms, the participants had an evaluation of elimination functions, quality of life, and Parkinson's staging through specific instruments. Subjects had sixteen sessions of parasacral neuromodulation and cognitive behavioral therapy attendance. **RESULTS:** Revaluation showed improvement of urinary and evacuatory symptoms and quality of life domain. There was also an increase in bladder capacity which, although not significant, expresses improvement in the clinical condition expressed by the patient. Improvements at evacuatory frequency, feces consistency, and evacuation strain were also found. **CONCLUSION:** The study results suggest that neuromodulation associated with behavioral therapy is a low-cost procedure that shows significant results to urinary symptoms and improvements to the quality of life measurements to domains of activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort.

KEYWORDS: Parkinson Disease. Transcutaneous Electric Nerve Stimulation. Urinary Incontinence. Constipation.

RESUMO | OBJETIVO: O objetivo deste estudo foi avaliar os efeitos da terapia comportamental associada à neuromodulação na bexiga e intestino neurogênicos na Doença de Parkinson. **MÉTODOS:** Trata-se de um estudo piloto. Os participantes, após assinarem o termo de consentimento, foram submetidos à avaliação das funções eliminatórias, qualidade de vida e estágio da doença por meio de instrumentos específicos. Os sujeitos realizaram dezesseis sessões de neuromodulação parassacral e acompanhamento da terapêutica comportamental. **RESULTADOS:** Na reavaliação apresentaram melhoras dos sintomas urinários, evacuatórios e dos domínios de qualidade de vida. Foi apresentado também aumento da capacidade vesical que embora não significativos já expressam melhora do quadro clínico expresso pelo paciente. Também observou-se melhora para frequência evacuatória, consistência das fezes e eliminação do esforço para evacuar. **CONCLUSÃO:** Sugere-se que a neuromodulação acrescida da terapêutica comportamental é uma técnica de baixo custo e com resultados significativos para os sintomas urinários e melhora dos valores de atividade de vida diária, bem-estar emocional, estigma, suporte social, cognição, comunicação e desconforto corporal medidos para qualidade de vida.

DESCRITORES: Doença de Parkinson. Estimulação Elétrica Nervosa Transcutânea. Incontinência urinária. Constipação.

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Introduction

Parkinson's Disease (PD) is considered a neurodegenerative disorder that is progressive, irreversible, and characterized by the loss of dopaminergic neurons located at the basal ganglia[1]. PD patients might present motor symptoms as resting tremor, muscular stiffness, and bradykinesia, which compose the classical motor triad[2]. However, the clinical course of the disease is not restricted to motor symptoms and includes sleep, neuropsychiatric, autonomic (urogenital, gastrointestinal, cardiovascular, and respiratory), sensory and pain dysfunctions[3]. Those non-motor symptoms may start before the motor ones at the pre-clinic phase of the disease which generally begins approximately 20 years before the PD diagnostic and tend to aggravate over time[4].

Despite its clinical meaning, those last symptoms are frequently neglected or confounded to aging natural symptoms[5] as the Low Urinary Tract Symptoms (LUTS) and Intestinal Constipation (IC). In PD patients, primary urinary complaints are commonly frequency improvement, Urinary Incontinence (IU), and bedwetting. These urinary storage symptoms are prevalent in 57-83% of this population[6].

The International Continence Society (ICS) defines overactive bladder as the group of storage symptoms. When it is associated with a relevant neurological disease is called neurogenic bladder, being investigated by the urodynamic observation[6]. In these cases, urodynamic studies present a reduction of bladder capacity and detrusor muscle hyperactivity in 43-93% of PD patients[7]. Concerning bowel complaints, constipation is the most prevalent symptom in PD, approximately 50%. Constipation is a subjective symptom, including hard feces, reduced bowel movements, swelling, abdominal pain, and the necessity to push during the defecation[8].

Although the high LUTS and IC prevalence as well as its impact on the quality of life, there are limited treatment options, and many of them are not well tolerated or ineffective for PD patients. Moreover, behavioral and lifestyle modifications (investigation of patient life habits, orientations related to the position during defecation, respiratory techniques, adequate liquid ingestion, abdominal therapeutic massage, and physical exercise practice) may mitigate the symptoms as the sacral neuromodulation (SNM)[9].

Theories suggest that SNM can block stimuli originated in the pelvic floor and bladder, which causes detrusor hyperactivity, thus restoring the voiding normal balance. Blok et al. (apud Sacomani e Goldman) have shown that SNM changes the cortical response and modulates the cerebral activity of areas related to sensitive-motor control involved during the beginning of urination and the vesical filling feeling[10].

It is important to study the SNM effect associated with behavioral treatment due to its significant impact on the quality of life caused by neurogenic bladder and bowel, leading to activity limitation, embarrassment, depression, and social isolation[11]. Besides, with no treatment, NB may trigger sepsis and renal insufficiency, which would impose high costs on the health system[12].

Considering the caring relevance in the management of bladder and bowel neurogenic, this study aims to evaluate the effects of behavioral therapy associated with parasacral neuromodulation in subjects with Parkinson's Disease.

Methods

Study Design

This is a clinical trial pilot study where individuals diagnosed with stages 1 to 4, according to Hoehn & Yahr scale of PD were submitted to a therapeutic intervention to treat eliminatory dysfunctions.

Study local and period

The study was performed from June to November 2019 at Physiotherapy service of Centro de Educação e Pesquisa em Saúde Anita Garibaldi (CEPS) in the city of Macaíba, state of Rio Grande do Norte, Brazil.

Sample and eligibility

Participants selection were conducted through the following inclusion criteria: individuals of both genders diagnosed with PD idiopathic in accordance to UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria[13]; classified between stages 1 and 4 of Hoehn & Yahr incapacity scale; present urinary symptoms and neurogenic bladder diagnosed by the urodynamic study; present more than 2 symptoms of intestinal constipation and be currently using anti-Parkinsonian medication. As exclusion criteria we used: do not attend two consecutive appointments, do not complete the 16 therapy sessions, and voluntarily drop out of the protocol, and/or withdraw their consent.

Data collection procedures

All participants were submitted to a semistructured interview proposed by the researchers to collect identification and sociodemographic data in addition to an evaluation composed of validated questionaries and urodynamic study. The questionaries applied were: International Consultation Incontinence Questionnaire - Overactive Bladder (ICIQ-OAB), Parkinson s Disease Questionnaire (PDQ–39), the voiding diary, and Bristol Stool Scale.

The ICIQ-OAB questionnaire is composed of 6 specific questions regarding voiding symptoms – frequency during the daytime, bedwetting, urgency, and urine loss during urgency, as well as their correlations to quality of life. The Portuguese version of ICIQ-OAB was translated, culturally adapted, and has shown satisfactory reliability and construct validity[14]. In terms of results analysis, values of 3a, 4a, 5a, and 6a questions were added and resulting in a total of 0-16 points. The higher the value, the greater is the patient impairment.

Considering this, the use of the questionnaire is recommended during the clinical investigation of voiding symptoms related to overactive bladder. The O Parkinson´s Disease Questionnaire (PDQ–39) contains 39 items, evaluates the disease impact on the individual's quality of life when compared to the past month, and has its Brazilian version validated[15]. The questionnaire is divided into eight dimensions: (1) Mobility (10 items); (2) Day living activities (6 items); (3) Emotional well-being (6 items); (4) Stigma (4 items); Social support (3 items); (6) Cognition (4 items); Communication (3 items) and (8) Body discomfort (3 items).

Each item can be answered through five options, and its score varies from 0 (never) to 4 (always or impossible to me). The dimension score was calculated according to the following formula: 100 x (sum of scores / 4 x number of items); and the total score is the sum of each dimension result divided by 8 (total of dimensions). Both results are presented in percentage. The total points vary from 0 (no problems) to 100 (maximum level of problems), namely, a low score indicates a better quality of life perception.

The voiding and evacuation diaries were used to evaluate elimination functions. During the diaries filling, the subjects were oriented to note their urinary frequency (during day and nighttime), ingested liquid volume, the volume that was urinated or removed by intermittent catheterization, number of urine loss episodes as well as the number of diapers used per day during 3 days[16]. In addition, the filling of the evacuation diary was instructed during 7 days (frequency, needing of pushing, and feces consistency according to the Bristol scale). The feces consistency Bristol Scale is translated and validated to Portuguese and Brazilian use and presented high reliability, which means that it can be used in clinical practice[17]. This scale is both descriptive and visual, presenting 7 types of feces (types 1 and 2 are dried, 3 and 4 normal, and 5 to 7 are liquids), each of them contains images and their respective definitions and meets the propose of its elaboration.

After filling and analyzing the questionaries, if there is any complaint, patients were referred to the CEPS Anita Garibaldi urologist, and explanations regarding the urodynamic study, the reason to indicate as well as instructions to perform the exam were given.

Through the test, it is possible to identify the cause of urinary symptoms and quantify the pathophysiological process. It also allows the dysfunction diagnostic to orientate the choice of correct treatment, and verify its response according to the storing and voiding phases of the bladder[18].

In our study, these phases were evaluated by the urodynamic study, lasting 30 to 40 minutes. Emphasis was given mainly to vesical capacity values and presence or absence of overactivity as outcomes. After the test, all included patients were submitted to our intervention protocol composed of neuromodulation and behavioral therapy.

Intervention

Appointments were conducted twice a week for 8 weeks, totalizing 16 sessions with 40 minutes each. In the first meeting, the participants received orientations about behavioral therapy and neuromodulation followed by the beginning of the treatment. According to Benevento and Sipski, 2002[19], behavioral therapy comprises the analyses of the relationship between a patient's symptoms and their environment to change harmful voiding and evacuation habits. For this study, the behavioral therapy comprised patient education regarding voiding habits, vesical re-education, strategies to control voiding desire, positioning, and evacuation training (patient should be stimulated to sit on the toilet, rest their feet on support appropriated to each one's height during 5 to 10 minutes after the main meals, when occurs the gastro-colic reflex), orientations regarding their diet and liquid ingestion. The orientations were given according to the voiding and evacuation diaries as well as urodynamic study results.

After that, the noninvasive parasacral neuromodulation application was explained and performed. Patients used a transcutaneous electric stimulator (Neurodyn portable of Ibramed brand) with two superficial self-adhesive sizing 5cmx5cm on the parasacral region (S2-S4). The stimulation was conducted following the parameters: pulse width of 450 μs and a frequency of 5 Hz. The intensity was adapted to each participant immediately below the threshold which determines muscle contraction. The neuromodulation was performed at CEPS by the physiotherapist in charge for 30 minutes. The last 10 minutes were used to reinforce behavioral therapy and perform any modification needed. After the intervention phase, the reevaluation was conducted by applying the evaluation form, previous questionnaires, and urodynamic study.

Statistical analysis

Descriptive analysis of studied data was used as frequency, mean, median, and standard deviation. To assess if the intervention would cause an improvement of vesical capacity and recovery from urinary symptoms, the difference between before and after the therapy was analyzed through the non-parametrical test of Wilcoxon. As the statistical significance level, we considered $p \leq 0,05$. Also, we used the statistical program SPSS version 20.0 to perform the analyses.

Ethical aspects

The Project was approved by the ethics and research committee of Universidade Federal do Rio Grande do Norte-UFRN in June 2019, register number: CAAE:09905119.7.0000.5537. All patients have signed the consent term in order to participate in the study.

Results

The 19 patients with idiopathic PD who presented urinary and intestinal symptoms were evaluated, however, 15 of them have received the neurogenic bladder diagnostic according to the urodynamic study, and during the study, 9 patients were excluded or lose (Figure 1). Finally, the sample was composed of 6 patients of both genders but mainly men, (66,67%) varying on stage and duration of the disease (Table

1). After 16 sessions, recovery was observed on urinary symptoms, according to the ICIQ-OAB, among all patients, with a mean ranging from 9,33 (±3,5) to 4,66 (±3,07) with a significant increase of values (P=.027).

About the quality-of-life scores specific to PD (PDQ-39), there was a decrease in the total score of 66,67%. Considering the dimension score, there was an improvement in 6 of 8 assessed dimensions, which can be seen in Table 2.

Regarding the urodynamic study through cystometry, there was an improvement in vesical capacity values which, despite not significant, has occurred in 83,3% of the participants. Concerning bladder overactivity, it was possible to observe an improvement in 5 to 6 patients, which 2 of them did not present any overactivity during the cystometry test (Table 3).

Considering the evacuatory aspects assessed by the evacuation diary, 5 patients presented a recovery in terms of frequency, and one has maintained its daily evacuation. In relation to the aspect necessity of pushing, 100% of the participants referred to recovery and stopped needing to performing an effort to beginning the evacuation.

With respect of feces aspects evaluated by the Bristol Scale, before the intervention, 33,33% of the sample presented feces type 1, 16,66% type 2, 33,33% type 3 and 16,66% type 5. After the intervention, 16,66% presented feces type 2, 66,66% feces type 3 and 16,66% type 4 (Table 4).

Figure 1. Study sample's flowchart

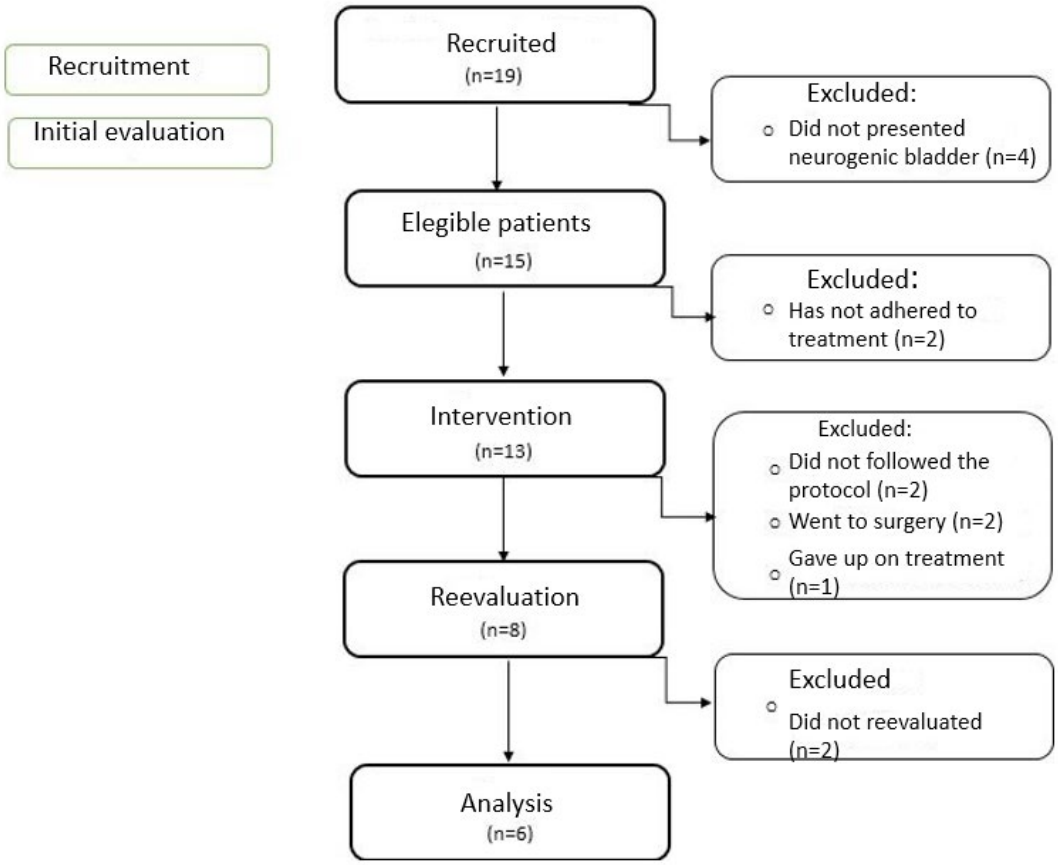

Table 1. Sample Charactherization

Gender (n=6)	N (%)
Male	2 (33,3%)
Female	4 (66,6%)
Hoehn &Yahr	
1	2 (33,6%)
2	1 (16,6%)
3	2 (33,6%)
4	1 (16,6%)
Time of the disease (years)	
4	2 (33,6)
5	1 (16,6%)
8	2 (33,6%)
10	1 (16,6%)

Table 2. PDQ-39 scores and validation according to dimension

Dimensions	Mobility		Daily activities		Emotional well-being		Stigma		Social support		Cognition		Comunication		Body discomfort	
Patient	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	7,75	8,25	70,83	75	70,83	62,5	70,83	31,25	70,83	41,66	70,83	31,25	70,83	50	70,83	50
2	1,5	1,25	25	25	41,66	45,83	6,25	6,25	16,66	25	18,75	31,25	33,33	33,33	66,66	58,33
3	2,75	1,5	37,5	58,33	16,66	25	0	25	0	0	25	12,5	16,66	16,66	50	50
4	42,5	15	50	37,5	79,16	83,33	18,75	6,25	25	33,33	75	37,5	0	8,33	41,66	50
5	7,75	7	70,83	70,83	54,16	54,16	62,5	62,5	16,66	16,66	50	50	83,33	83,33	66,66	66,66
6	0	0	0	0	4,16	0	6,25	6,25	0	0	12,5	0	0	0	0	0
Total (mean)	10,37	5,5	42,36	44,44	44,43	45,13	27,43	22,91	21,52	19,44	42,01	27,08	34,02	31,94	49,3	45,83

Table 3. Results of Maximal Cystometric Capacity before and after the intervention

Maximal Cystometric Capacity		
Patient	**Before**	**After**
1	448	484
2	196	296
3	266	162
4	95	470
5	132	142
6	115	190

Discussion

Neurogenic bladder and bowel are common conditions among PD patients. About the treatment, despite many interventions are available, there is little evidence proving recovery in this population. Moreover, conservative approaches are suggested to be applied at first[6].

Among these approaches are pharmacological interventions, especially anticholinergic drugs, which are the first option for this treatment[6]. In our study, the drug intervention was not the first choice due to the polypharmacy history in our patients, as well as the possibility of presenting side effects as constipation exacerbation and drug interaction, which may cause therapeutic choose assessment bias. In addition, Palleschi G et al. Study evaluated and treated neurogenic bladder with antimuscarinic drugs in 39 participants, 7 of them are PD patients. 20% of the sample have left the treatment due to constipation, dizziness, headache, and no clinical improvement[20].

In our study, the behavioral therapy and neuromodulation treatment effects were assessed, which also are conservative options to neurogenic bladder and bowel. Two pilot studies were conducted considering behavioral therapy. However, they used pelvic floor muscle exercises associated with biofeedback as behavioral treatment, as result, they had high bias risk and low clarity[6]. In this study, behavioral therapy comprised orientations regarding evacuation position, diaphragmatic breathing technique, adequate hydric ingestion, abdominal therapeutic massage, and physical exercises regular practice, once all participants were included in a physiotherapy program.

Behavioral therapy was associated with neuromodulation twice a week for 30 minutes. This technique usage is becoming more popular as a therapeutic option. In a prospective study with 10 PD patients, the anterior tibial nerve was stimulated, and slight improvements were observed despite being statistically insignificant, with incontinence and urgency episodes[6].

In our study, parasacral electrostimulation was used, because it tends to directly stimulate spinal reflexes, and achieves supraspinal centers with an intensity more effective than posterior tibial nerve stimulation, which is more peripherical[21]. The sacral nerve stimulation performed through electrodes placed on the sacral foramen (S3) has shown to be able to modulate important cortical and subcortical structures which are involved in the conscience an alert process, bladder full-filling sensation, and urination, leading to an inhibition in the voiding reflex among adult patients with urinary incontinence. This benefic effect originates from the brain's supraspinal areas, which are activated or inhibited by the spine's caudal portion during the stimulation, as stated by Blok et al. (apud Sacomani e Goldman)[10].

This study showed that associating these therapies is statistically significant to the severity of voiding symptoms of overactive bladder according to the ICIQ-OAB. In 2016, Kabay et al. has studied the effect of percutaneous stimulation of posterior tibial nerve among 47 DP patients during 12 weeks of intervention which also presented significant improvements[22].

Considering the quality-of-life aspects specific to DP, there was a recovery in 6 of 8 dimensions evaluated. Bolaños, in 2019, has investigated the importance of non-motor symptoms regarding fall frequency for DP patients, which highlights the mobility dimension. A possible explanation for the association between urinary symptoms and falls frequency is bedwetting, which is commonly the major cause of falls during nighttime. These findings suggest the need for an intensive approach in identifying and treating urinary symptoms among PD patients[23].

Regarding the urodynamic study, Vurture et al.[24]has studied urodynamic findings in PD patients with overactive bladder symptoms. Were included 42 patients with overactive bladder symptoms starting at, on average, 6,6 years past the PD diagnostic. Among all participants, was found some degree of detrusor overactivity and the mean of the maximal cystometric capacity of 274,8 mL (±174,3)[24]. These results corroborate those found in the initial evaluation of our study, where all patients presented detrusor overactivity and low maximal cystometric capacity.

Ohannessian et al. (2013) assessed the anterior tibial nerve neuromodulation effects and proposed a therapy lasting 6 weeks, 20 minutes per daily session with 6 PD patients with neurogenic bladder. There was no significant difference regarding urodynamic parameters despite presenting a recovering tendency in maximal cystometric capacity[25], which reinforces our findings.

On the other hand, considering evacuation aspects, our initial findings were low evacuation frequency, the necessity of pushing, and hard feces consistency. It is known that constipation is not only a problem involving the bowel but also may lead to bladder control dysfunction. When the rectum is full of feces, as an example, it can lead to a bladder disturbance and provoke urgency and frequency sensation[26], thus reinforcing the need of treating these patients.

In a systematic review, Knudsen et al observed, despite the great variation among individual studies, in the most homogeneous PD study's findings a constipation prevalence of 40% to 50% considering constipation as less than 3 evacuations per week or necessity of pushing during the evacuation. In addition to that, a clear increase in constipation prevalence related to disease clinical stage advance was observed[27].

Mukherjee, Biswas, and Das (2016) affirmed that constipation treatment starts with a diet high in fibers, correct liquid ingestion, and physiotherapy exercises. However, this condition management may be complicated since does not only includes symptomatic treatment but also antiparkinsonian drug optimization, mainly the anticholinergic and dopaminergic ones. To conclude, studies considering new therapeutic agents and pharmacological interventions would be useful[28].

Using the intervention proposed in our study, an evacuation frequency improvement was perceived with no need to pushing, which shows to be a positive alternative to this treatment.

Considering that this is a pilot study, some limitations are inherent to its non-randomized design as well as relatively small sample size and lack of statistic power. These factors impeded an evaluation with higher inferential power of the predictive factors to a successful intervention.

Despite the encouraging results, more studies are needed to assess the neuromodulation effects regarding PD symptoms attenuation. More amplified studies, better projected, randomized, and focused on the treatment require relevant investigation and correct management of voiding and evacuation dysfunctions to improve the quality of life and protect the superior urinary tract of PD patients.

Conclusion

According to our study is possible to conclude that the association between behavioral therapy and parasacral neuromodulation improves the urinary symptoms and the evacuation condition. The study also suggests its continuation to evidence positive changes on the quality-of-life values (mobility, stigma, social support, cognition, communication, and body discomfort dimensions) as well as cystometric capacity and overactivity after the protocol application.

Author contributions

Azevedo MAR participated in the conception, design, research, statistical analysis, result in interpretation, and article writing. Medeiros CEB participated in data collection and interpretation. Gonçalves RP participated in data collection and evaluation. Almeida VA participated in the data collection. Lisboa LL participated in the phases of study design, statistical analysis, result interpretation, and writing.

Competing interests

No financial, legal, political, or involving third-part (government, companies, privative institutions, etc.) conflict was declared in any aspect of the submitted study (including but not limiting to grants, funding, participating in the advisory board, study design, manuscript preparation, statistical analysis, etc.).

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