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ORIGINAL ARTICLE

Electroacupuncture therapy on non-motor symptoms of patients with Parkinson's disease: results of a pilot study

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Abstract

Objective: *This study aims to assess the effect of electroacupuncture (EA) on non-motor symptoms in Parkinson's disease (PD) patients as a primary goal and motor symptomatology as a secondary outcome.* **Methods:** *Twenty-five patients were enrolled in a non-controlled pilot study that involved a 10-session EA intervention in 16 acupoints, applied 3 times a week for 4 weeks. Motor, non-motor, cognitive, and quality of life evaluation were conducted before intervention and 7 days after concluding the last EA session through MDS-Unified PD rating scale (MDS-UPDRS), Non-motor Symptom Scale (NMSS), montreal cognitive assessment (MoCA), and PD questionnaire (PDQ-8), respectively.* **Results:** *Patients showed significantly lower scores in the MDS-UPDRS Part II (7.0 ± 5.7 vs. 10.5 ± 7.6, p = 0.046) and Part III (14.0 ± 8.6 vs. 23.1 ± 13.9, p = 0.002), and NMSS total score (35.2 ± 26.6 vs. 54.6 ± 32.5, p = 0.004) in the post-intervention evaluation, with mood/cognition domain of the NMSS being the only significantly affected by treatment. MoCA total score increased after the intervention (24.2 ± 4.5 vs. 21.6 ± 4.3, p = 0.020), while PDQ-8 scores were not significantly affected by the intervention.* **Conclusions:** *Non-motor and motor symptomatology were significantly improved after concluding a 10-session EA therapy. Mood and cognitive disorders were the most positively affected by the intervention. Evaluation of the long-term effects of EA in PD is further needed.*

Keywords: *Acupuncture. Parkinson's disease. Complementary therapy. Integrative medicine. Non-motor symptoms. Quality of life.*

Efecto de la electroacupuntura en los síntomas no-motores de pacientes con Enfermedad de Parkinson: resultados de un estudio piloto

Resumen

Objetivos: *Evaluar el efecto de la electroacupuntura (EA) sobre los síntomas no motores en pacientes con Enfermedad de Parkinson como objetivo principal y la sintomatología motora como resultado secundario.* **Métodos:** *Se incluyeron 25 pacientes en un estudio piloto no controlado cuya intervención implicó 10 sesiones de EA en 16 acupuntos, aplicada 3 veces por semana durante 4 semanas. Se realizó una evaluación motora, no motora, cognitiva y de calidad de vida antes de la intervención y siete días después de concluir la última sesión de EA mediante la escala unificada de la enfermedad de Parkinson modificada por la Sociedad de Trastornos del Movimiento (MDS-UPDRS), la escala de síntomas no motores (NMSS), Test Cognitivo de Montreal (MoCA) y cuestionario sobre la enfermedad de Parkinson 8 (PDQ-8), respectivamente.* **Resultados:** *En la evaluación posterior a la intervención, los pacientes mostraron scores significativamente menores en la*

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Parte II (7.0 ± 5.7 vs. 10.5 ± 7.6, p = 0.046) y la Parte III (14.0 ± 8.6 vs. 23.1 ± 13.9, p = 0.002) de la MDS-UPDRS y en el score total del NMSS (35.2 ± 26.6 vs. 54.6 ± 32.5, p = 0.004), siendo el dominio del estado de ánimo/cognición del NMSS el único afectado significativamente. El score total del MoCA aumentó después de la intervención (24.2 ± 4.5 vs. 21.6 ± 4.3, p = 0.020), mientras que los scores del PDQ-8 no se vieron afectados significativamente. **Conclusiones:** *La sintomatología motora y no motora mejoró significativamente después de concluir una terapia de EA de 10 sesiones.*

Palabras clave: *Acupuntura. Enfermedad de Parkinson. Terapia complementaria. Medicina integrativa. Síntomas no motores. Calidad de vida.*

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease, with morbidity and mortality increasing in the last 25 years[1,2]. Regarding prognosis, it is expected that its incidence in the general population continues to grow[3], which has raised awareness toward an early and integrative diagnosis.

In the absence of a disease-modifying drug and the development of motor complications arising from standard pharmacological treatment with levodopa, patients with PD often seek complementary and alternative therapies. Acupuncture is the most commonly employed[4,5], with reports of up to 50% of patients using this modality.[6]

Several studies have been conducted assessing the effect of acupuncture in PD symptomatology, with a special focus on motor symptoms[7]. Two meta-analyses showed inconclusive results regarding acupuncture effectiveness in PD[7,8], with sample size being a major limitation in most included studies. Another limitation of these studies is their low quality, which limits the applicability of their results. A more recent meta-analysis demonstrated a positive effect of acupuncture in PD symptomatology, suggesting a potential role as a complementary therapy alongside symptomatic treatment[9]. Nonetheless, evaluation of PD symptomatology was focused on motor symptomatology, with no emphasis on acupuncture's effect on non-motor symptoms.

Scarce studies have evaluated electroacupuncture (EA) therapy on non-motor and motor symptoms in PD patients[10]. Specifically in Mexico, no studies were found that reported acupuncture or EA use in PD patients. We aimed to evaluate EA effect on non-motor symptomatology as a primary outcome and motor symptoms and quality of life as a secondary outcome in PD patients through a 10-session EA intervention.

Material and methods

Consecutive patients from the neurology outpatient clinic of our University with idiopathic PD diagnosis according to UK PD Society Brain Bank clinical criteria[11] were recruited between September 2019 and January 2020 for a 10-session EA therapy intervention.

This study was approved by the local Research Ethics Committee of our institution (NR 19-00004). All patients signed informed consent for inclusion in this study, all in compliance with the Declaration of Helsinki.

Inclusion and exclusion criteria

Inclusion criteria involved: patients > 18 years, any gender, and PD diagnosis according to UK PD Society Brain Bank clinical criteria. Exclusion criteria included: acupuncture exposure in the previous 4 months, receiving anticoagulant treatment or having blood dyscrasias, prolonged fasting (> 6 h), and having a cardiac pacemaker. Among the withdrawal criteria: patients who did not assist for ≥ 2 acupuncture sessions, without any clinical evaluation, or presented inflammatory reaction or infection in any acupunctural sites were withdrawn from the study.

Recruitment

During follow-up consultation, PD patients who fulfilled the inclusion criteria were invited to participate in the study, explaining EA therapy's objectives and possible side effects. Patients that accepted and signed informed consent were evaluated, where demographics and clinical assessments through Non-Motor Symptom Scale (NMSS), Movement Disorder Society-unified PD rating scale (MDS-UPRDS), Hoehn and Yahr (HY), Montreal Cognitive Assessment (MoCA), and PD questionnaire-8 (PDQ-8) were registered. After this, they were scheduled to attend their initial EA session.

Intervention

EA was conducted through 10 sessions, each lasting 30 min, three sessions per week. A total of 16 acupoints

were used for all patients according to Chinese Traditional Medicine[12,13] (see Supplementary Material for acupunctural sites used). Physicians with a master's degree in Chinese Traditional Medicine with at least 5 years of clinical experience performed the intervention.

With the patient in a prone position, asepsis was performed with alcohol 96% to later proceed with needle colocation. The sterile needles used (Natural E-M Medical Treatment and Electron (Suzhou) Co., Ltd., China) are made from surgical stainless steel with a silicon guide tube. Needle diameter and length were 0.22 mm and 40 mm, respectively. The depth and direction in which the needles were inserted varied based on the acupoint, the maximum depth was no > 25 mm. The effective depth of needling was determined when the DeQi response was obtained[14]. This is described by patients as aching or soreness, numbness, distention, or heaviness, and felt by acupuncturist as tense and tight needle grasp[14]. Electrical stimulation was applied with a KWD808-I electrostimulation device in a dense-dispersed mode in the EX-HN-1 Sishencong points, with a frequency of 2 Hz and intensity depending on the patient's tolerance. The needles remained inserted for 20 min and were later removed, ending the session. The study adhered to the revised standards for reporting interventions in clinical trials of acupuncture.

Post-intervention assessment

The patients were scheduled to attend the neurology outpatient clinic 7 days after concluding the last EA session (session 10). A neurologist expert in movement disorders evaluated non-motor, motor, cognitive function, and quality of life through the NMSS, MDS-UPDRS, MoCA, and PDQ-8, respectively. The estimated time for outcome evaluation was approximately 60 min, depending on the severity of the disease. Moreover, any changes in pharmacological treatment that occurred during sessions were documented.

Sample size calculation

We used a formula for estimating the mean in a population. No other studies have evaluated acupuncture's effect on non-motor symptoms through NMSS; however, two studies have shown a decrease of 21-50% in the UPDRS Part I score, which assesses non-motor symptoms, after acupuncture therapy[15,16]. Using the mean NMSS score (52.6 ± 47.0) of our registry of treated PD patients from the neurology outpatient clinic of our University Hospital (total n = 105), we set a 38% decrease in the baseline value of NMSS with EA therapy as effective, with a precision of ±13.3 points. Thus, a sample of 40 patients should provide approximately 80% test power at a confidence level of 95% and considering a dropout rate of 10%.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences computer program (SPSS version 22.0, SPSS Inc., Chicago, Illinois, USA). Data were tested for normality using the Shapiro–Wilk test, and continuous variables were thus expressed as mean ± standard deviation (SD) or as median (range), and categorical variables as percentages. A paired t-test was conducted to evaluate differences between parametric measures in the pre-and post-intervention evaluations, whereas the Wilcoxon test was conducted for non-parametric variables. A $p < 0.05$ was considered significant.

Results

Baseline characteristics

Forty patients were initially invited to participate in the study protocol, with only 30 accepting and 25 initiating the EA sessions. Three of these 25 patients were withdrawn from the protocol as they discontinued the therapy, stating lack of time. The rest (22 patients) concluded the therapy sessions and clinical evaluation. No more patients could be recruited due to COVID-19 pandemic contingency.

Regarding baseline characteristics, 11 (50%) patients were male; the mean age of the whole sample was 60.7 ± 11.7 years, with a mean age at diagnosis of 53.6 ± 12.2 years. Most patients corresponded to a tremor motor subtype at onset. Mean H and Y were 2.2 ± 0.8, the mean MDS-UPDRS score was 32.3 ± 11.7, the mean NMSS score was 54.6 ± 32.5, and the mean MoCA score was 21.6 ± 4.3. During the intervention period, no modifications to the pharmacological treatment were reported among patients. The rest of the baseline characteristics are shown in table 1.

Acupuncture effect on non-motor symptomatology

When comparing NMSS and MDS-UPDRS Part I scores between pre-and post-intervention evaluations,

Table 1. Baseline characteristics of the total population

Variable	n = 22
Gender (%)	
Male	11 (50.0)
Female	11 (50.0)
Age, mean ± SD (years)	60.7 ± 11.7
Comorbidities (%)	
Arterial hypertension	5 (22.7)
Dyslipidemia	9 (40.9)
Type 2 diabetes mellitus	6 (27.2)
Cardiovascular disease	10 (45.5)
Familiar history of PD (%)	17 (77.2)
Parkinson's disease features	
Years of evolution, mean ± SD	7.1 ± 5.1
Age at onset, mean ± SD	53.6 ± 12.2
Motor subtype at onset	
Tremor (%)	14 (63.6)
Rigidity-bradykinesia (%)	5 (22.7)
Levodopa equivalent daily dose, mean ± SD (mg)	781.7 ± 399.9
Hoehn and Yahr, mean ± SD	2.2 ± 0.8
MoCA, mean ± SD	21.6 ± 4.3
MDS-UPDRS total score, mean ± SD	32.3 ± 11.7
NMSS, mean ± SD	54.6 ± 32.5
PDQ-8, mean ± SD	8.0 ± 7.1

SD: standard deviation; PD: Parkinson's disease; MoCA: Montreal Cognitive Assessment; MDS-UPDRS: Movement Disorders Society-unified Parkinson's disease Rating Scale; NMSS: Non-motor Symptom Scale; PDQ-8: Parkinson's disease questionnaire-8.

a significant decrease in NMSS total score (p = 0.011) and MDS-UPDRS Part I (p = 0.004) was observed. When evaluating each domain from NMSS, only the mood/cognition domain showed a significant decrease in scores (p = 0.013). Other domains, except for the gastrointestinal tract domain, showed a reduction in scores that were, however, non-significant (Table 2).

Cognitive function by MoCA showed significantly higher scores in the post-intervention evaluation compared to the pre-intervention (p = 0.020) (Table 3). Among cognitive domains, only delayed recall showed a significant increase in score after the intervention (p = 0.038).

Acupuncture effect on motor-symptomatology and quality of life

Significant lower scores were observed in MDS-UPDRS Part II (p = 0.046), MDS-UPDRS Part III (p = 0.002), and total MDS-UPDRS score (p = 0.044) in the post-intervention evaluation. Regarding quality-of-life evaluation through PDQ-8, no differences were observed between both evaluations (Table 3).

Safety evaluation

Regarding potential side effects associated with EA therapy (nausea and vomiting, bleeding, infection at the puncture site, dizziness), no patient reported any of the previously mentioned.

Discussion

In the present study, a 10-session EA intervention improved non-motor symptomatology through NMSS. Mood/apathy domain of NMSS was the only that significantly decreased after concluding treatment. To the best of our knowledge, scarce literature has evaluated EA effect on non-motor symptoms[10], and no other study has conducted an overall evaluation of EA on non-motor symptoms through NMSS. Various studies have assessed acupuncture's effect on specific non-motor symptoms. For example, a recent study showed a greater improvement in depressive and sleep disorders after concluding an intervention that involved 18 weeks of twice-weekly acupuncture plus symptomatic treatment compared to symptomatic treatment alone[16]. Another study showed similar results regarding depressive symptoms[17], a finding shared by our study. Comparing methodological issues between studies, the former involved a small sample as ours (20 vs. 22 patients) but a longer treatment duration (36 vs. 10 sessions), whereas the latter was a multi-center randomized study with a higher sample size (76 patients) and longer treatment duration (32 sessions). Nonetheless, depressive symptoms improved in the latter from week 4 of treatment initiation, comparable to our study. Other symptoms ameliorated by acupuncture shown in other studies are constipation[18,19] and autonomic disorders such as bladder dysfunction[20], results not supported by our report.

In our study, cognitive function was improved after concluding the EA intervention. This finding has been observed in another study in a PD population[21], whereas evidence from patients with Alzheimer's disease shows upregulation of cognitive functions after acupuncture treatment[22]. This mechanism may be explained by the regulatory effect of neural activity within cognitive brain regions after acupuncture therapy in PD patients[23].

Regarding motor symptoms, EA treatment improved MDS-UPDRS Part II and Part III total scores, supporting other studies' findings[9]. In contrast, our study found no significant effect on the quality of life assessed by PDQ-8. This contrasts with other studies that have

Table 2. Electroacupuncture intervention effect on non-motor symptoms through MDS-UPDRS Part I and NMSS

Scale	Pre-intervention evaluation (n = 22)	Post-intervention evaluation (n = 22)	p
MDS-UPDRS Part I	7.7 ± 5.3	5.3 ± 4.5	0.004
NMSS total score	54.6 ± 32.5	35.2 ± 26.6	0.011
Cardiovascular domain	1.4 ± 3.4	1.1 ± 2.7	0.414
Sleep/fatigue domain	12.3 ± 10,1	7.1 ± 8.5	0.414
Mood/cognition domain	14.4 ± 14.9	4.0 ± 4.2	0.013
Perceptual problems/ hallucinations domain	1.3 ± 2.1	0.5 ± 1.0	0.109
Attention/memory domain	5.5 ± 5.1	4.2 ± 5.4	0.283
Gastrointestinal tract domain	4.7 ± 5.2	7.1 ± 11.4	0.899
Urinary domain	5.2 ± 6.5	5.1 ± 5.6	0.622
Sexual function domain	1.8 ± 5.8	0.1 ± 0.5	0.180
Miscellaneous domain	8.1 ± 8.7	6.0 ± 4.7	0.173

MDS-UPDRS: Movement Disorders Society-unified Parkinson's disease rating scale; NMSS: Non-Motor Symptom Scale. The value of bold numbers is p < 5.

Table 3. Electroacupuncture intervention effect on motor and cognitive symptoms through MDS-UPDRS and MoCA

Scale	Pre-intervention evaluation (n = 22)	Post-intervention evaluation (n = 22)	p
MDS-UPDRS Part II	10.5 ± 7.6	7.0 ± 5.7	0.046
MDS-UPDRS Part III	23.1 ± 13.9	14.0 ± 8.6	0.002
MDS-UPDRS total score	32.3 ± 11.7	25.9 ± 16.2	0.044
MoCA total score	21.6 ± 4.3	24.2 ± 4.5	0.020
Visuospatial ability	3.4 ± 1.2	3.5 ± 1.0	0.796
Identification	2.9 ± 0.2	3.0 ± 0.0	0.317
Attention	4.9 ± 1.4	4.9 ± 1.3	0.764
Language	2.3 ± 1.0	2.2 ± 1.1	0.776
Abstraction	1.8 ± 0.5	1.8 ± 0.6	0.998
Delayed recall	2.2 ± 1.9	3.1 ± 1.4	0.038
Orientation	5.7 ± 0.7	5.7 ± 0.8	0.705
PDQ-8 total score	8.0 ± 7.1	5.9 ± 5.5	0.751

MoCA: Montreal Cognitive Assessment; MDS-UPDRS: Movement Disorders Society-unified Parkinson's Disease Rating Scale; PDQ-8: Parkinson's disease questionnaire-8. The value of bold numbers is p < 5.

found a significant improvement in quality-of-life measures[24,25], with more (> 12) acupuncture sessions than the present study. The latter may be a reason explaining the non-significant change in our results, in addition to a lack of long-term evaluation.

The therapeutic mechanisms behind acupuncture's effect are still not completely elucidated, with studies arguing for a placebo effect, while others showing biological changes due to acupuncture treatment[26]. Animal models of PD using 6-hydroxydopamine have reported a reduction in the loss of dopaminergic neurons after 14 sessions of stimulation in an acupoint and an improvement in behavior patterns caused by the induced lesion[27,28]. Other studies in animal models have shown

antioxidant and anti-inflammatory effects, regulation of neurotransmitters in the striatum, and neurochemical modulation in the basal ganglia, which could explain acupuncture's therapeutic effect[29]. Despite not producing the De qi sensation of real acupuncture, sham acupuncture may have other elements that contribute to its efficacy in alleviating some PD symptoms shared by real acupuncture and placebo[30].

On the other side, as the outcome evaluation time lasted approximately 60 min, it is reasonable to consider its influence on the accuracy of patients' responses. Nonetheless, an expert in movement disorders and with clinical experience in applying the MDS-UPDRS, NMSS, MoCA, and PDQ-8 guided the interview, which could diminish the bias of an extended evaluation time. For instance, this helped shorten the interview in mild PD cases. However, the lack of blinding of the intervention could contribute to a bias in data recording, a limitation of this preliminary study.

This study has some limitations. Among the most important, the lack of a control group limits the interpretation and generalization of results, considering the placebo effect that has been attributed to sham acupuncture. In addition, among other related potential biases, the constant interaction with eager researchers might influence patients' responses to the clinical scales evaluated in favor of the intervention, a point that needs consideration. Another important limitation is its preliminary characteristic, as the small sample size limits the further generalization of results. Finally, another potential limitation is the lack of evaluation of any long-term effect attributed to EA intervention. However, we believe the results justify implementing a randomized controlled study with sham acupuncture as a placebo control group. Among the strengths of this study, an overall formal evaluation of non-motor symptoms through NMSS allowed identifying those that could benefit the most from EA therapy. Thus, a new randomized, placebo-controlled trial with increased sample size and assessment of long-term outcomes lies in future research plans.

Conclusion

A 10-session EA intervention has a protective and ameliorating effect on non-motor and motor symptomatology of PD patients with no treatment-related side effects presented. Among non-motor symptoms, mood, and cognitive function appear to be improved by acupuncture, which might thus represent a complementary therapy for PD patients with any mood or cognitive disorders. A future placebo-controlled randomized study with a comprehensive assessment of mood and cognitive function would better characterize the potential role of EA in these non-motor symptoms.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

Supplementary data

Supplementary data are available at DOI: 10.24875/RMN.24000035. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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