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A randomized, controlled, and clinical trial to evaluate the efficacy of electrical vestibular stimulation, compared to a sham control for the management of sleep and autonomic parameters in patients with Parkinson's disease

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ABSTRACT

Background: Electrical vestibular nerve stimulation (VeNs) was simple, non-invasive, and can administer the stimulus in a controlled manner. The studies related to the application of electrical VeNs in the management of sleep and autonomic parameters were sparse in the Indian population. **Aims and Objectives:** The present study was undertaken to observe the effectiveness of electrical VeNs in the management of sleep and autonomic parameters in patients with Parkinson's disease (PD). **Materials and Methods:** Thirty cases of PD, both the genders, were recruited in the study by convenient sampling after obtaining written informed consent. After recording baseline parameters of Insomnia Severity Index (ISI), systolic and diastolic blood pressure (DBP), and pulse rate, electrical VeNs was administered to the intervention group and placebo stimulation was administered to the control group for 12 weeks. Post-intervention parameters were recorded after 6 weeks and after 12 weeks after the intervention in both control and intervention groups. **Results:** There was a significant decrease in the ISI scores, pulse rate, and systolic blood pressure after the intervention in the participants of the intervention group. DBP was decreased but was not statistically significant. There was no significant difference in the ISI scores, pulse rate, and systolic and DBP before and after the intervention in the participants of the control group. **Conclusion:** The present study results support the improvement of sleep followed by electrical VeNs. The study recommends detailed studies in this area to support the incorporation of electrical VeNs in the management strategy of PD.

Key words: Autonomic functions; Non-Motor symptoms; Parkinson's disease; Sleep; Vestibular stimulation

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INTRODUCTION

Parkinson's disease (PD) comprises of motor and non-motor symptoms. Sleep problems and autonomic disorders are the most common non-motor symptoms of PD.[1,2] Decline in sleep quality and failure of autonomic functions has a negative impact on a patient's quality of life.[3,4] About 64% of PD patients are affected by sleep disorders.[1] The sleep disorders in PD patients may be due to motor symptoms or autonomic symptoms like nocturia or disorders like REM sleep behavioral disorder or restless legs syndrome.[5] Due to the sleep disorders, the patients might

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be affected by excessive daytime sleepiness, sudden sleep attacks, and dysregulation of the sleep-wake cycle. Further, sleep disorders drastically decrease cognitive functions and affect daily life functioning. Hence, the management of sleep and autonomic disorders in PD patients has a pivotal role to improve the quality of life in these patients.

The sleep-inducing effect of vestibular stimulation was well explained in the literature and it is common to the experience getting sleep while rocking.[6] Stimulating the vestibular system is a well-known technique to manage several psychiatric and neuronal disorders including sleep disorders.[7] It was reported that vestibular stimulation promotes sleep by decreasing the latency of sleep transition from wakefulness to deep sleep.[8] Animal studies reported that peak acceleration is required to promote sleep whereas human studies reported optimal stimulation is essential to promote sleep.[9,10] Electrical vestibular nerve stimulation (VeNs) was simple, non-invasive, and can administer the stimulus in a controlled manner. The studies related to the application of electrical VeNs in the management of sleep and autonomic parameters were sparse in Indian population. Hence, the present study was undertaken to observe the effectiveness of electrical VeNs in the management of sleep and autonomic parameters in patients with PD.

Aims and objectives

The present study was undertaken to observe the effectiveness of electrical VeNs in the management of sleep and autonomic parameters in patients with PD.

MATERIALS AND METHODS

Study design and setting

This study was a randomized and controlled trial. (ClinicalTrials.gov Identifier: NCT04450550) conducted at the Department of General Medicine and Department of Physiology, R.D. Gardi Medical College. Participants were assessed thrice. After recording baseline parameters of insomnia severity index (ISI), systolic and diastolic blood pressure (DBP), and pulse rate, electrical VeNs was administered to the intervention group and placebo stimulation was administered to the control group for 12 weeks. Post-intervention parameters were recorded after 6 weeks and after 12 weeks after the intervention in both control and intervention groups.

Study participants and sampling

Thirty cases of PD, both the genders, were recruited in the study by convenient sampling after obtaining written informed consent. Patients were recruited from the outpatient ward of the General Medicine Department, R.D. Gardi Medical College. Patients were randomly assigned to control and intervention groups with 15 participants in each group. The following criteria were used to recruit the participants. There is one left-handedness individual in the control group and one in the intervention group. The rest of the participants were right-handed individuals. Willing male and female participants 18 years and older, who were in Stages 1 and 2 Hoehn and Yahr Classification of Disability 79,80, ambulate with or without an assistive device for at least 50 feet, and we are able to get up and down from the floor with minimal assistance or less and score of 24 or above on the Folstein Mini-Mental State Examination were included in the study. Participants with declined immune functions, progressive degenerative disease besides PD, spinal fusion, or other orthopedic surgery in the past 6 months, mental disease/psychosis such as dementia, greater than minimal assistance required for gait and transfers, and inability to make regular time commitments to the scheduled intervention sessions, experience with regular practice of any form of vestibular stimulation within the past year were excluded from the study.

After recruiting, the participants were randomly assigned into two groups.

- Group 1: Control group (n = 15): Placebo stimulation was administered for 12 weeks
- Group 2: Intervention group (n = 15): Electrical vestibular stimulation was administered for 12 weeks.

Electrical VeNs

Bilateral electrical VeNs was administered using a battery-powered vestibular nerve stimulator (ML 1000, Neurovalens, UK). The total duration of the intervention is 12 weeks with 5 sessions per week. Each session duration is 1 h.[11]

Ethical considerations

The study protocol was approved by the Institutional Human Ethical Committee of R.D. Gardi Medical College. (IEC Ref. N0- 124 / 2019).

Data collection tool and technique

Data were collected using a standard questionnaire to assess insomnia which is the ISI.[11] Blood pressure and pulse rate were recorded using the OMRON HEM 7120 automated BP monitor.

Data analysis

Data were analyzed using SPSS 20.0. One-way ANOVA followed by the *post hoc* Tukey HSD test was applied to observe the significance of differences between the groups. A probability value <0.05 was considered significant.

RESULTS

Results were presented in Tables 1 and 2. Table 1 presents the ISI scores, blood pressure, and pulse rate of the participants of the intervention group before and after the intervention. Table 2 presents the ISI scores, blood

Table 1: ISI scores, blood pressure, and pulse rate of the participants of the intervention group before and after intervention

Parameter	Baseline	After 6 weeks	After 12 weeks	F value	P-value
ISI score	22.8±2.3	19.9±1.9	16.4±1.8	35.45029	<0.00001***
Pulse rate (beats/min)	83.4±10.6	76.8±5.8	76.1±4.5	4.41628	0.018166*
SBP (mmHg)	143.5±25.7	126.2±19.2	123.4±15.6	3.8465	0.029244*
DBP (mmHg)	80.5±11.1	77.4±6.7	78.5±4.5	0.57335	0.567986

*P<0.05 is significant, ***P<0.001 is significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ISI: Insomnia severity index

Table 2: ISI scores, blood pressure, and pulse rate of the participants of the control group before and after intervention

Parameter	Baseline	After 6 weeks	After 12 weeks	F-value	P-value
ISI score	22.6±2.1	22.6±2.1	22±1.7	0.3511	0.705962
Pulse rate (beats/min)	84.8±11.1	84±8.2	83.6±8.5	0.06306	0.938979
SBP (mmHg)	142.4±20.8	135.4±20	128.6±22.2	1.60728	0.212515
DBP (mmHg)	80.4±13.2	79.3±7.5	80.1±6.6	0.05536	0.946214

*P<0.05 is significant; ***P<0.001 is significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ISI: Insomnia severity index

pressure, and pulse rate of the participants of the control group before and after the intervention. There was a significant decrease in the ISI scores, pulse rate, and systolic blood pressure after the intervention in the participants of the intervention group (Table 1). DBP was decreased but was not statistically significant (Table 1). There was no significant difference in the ISI scores, pulse rate, and systolic and DBP before and after the intervention in the participants of the control group (Table 2).

DISCUSSION

PD is a neurodegenerative disease effecting especially in the elderly people. There will be degeneration of basal ganglia. The common features seen are rigidity, akinesia, tremors, and palilalia. Palilalia means repetitive pronunciation of same words. It was seen in few patients with PD. Some patients also develop symptoms such as emotional disturbances, loss of cognitive functions, loss of will power, and diminished or degraded hand writing. Sleep disturbances are one of the most important non-motor parameters that need to be addressed in patients with PD. Autonomic dysfunction or dysregulation was reported as one of the prominent causes of sleep disturbances. Pharmacological therapies can manage sleep problems effectively but cannot be followed on a long-term basis as they are associated with side effects. Hence, there is a need for alternative therapies that can improve sleep and also regulate autonomic imbalance with minimum or no side effects. Rocking is soothing as it offers a monotonous stimulus as well as offers relaxation effect. However, studies related to the implementation of vestibular stimulation in the management of PD are sparse. Hence, the present study was undertaken to observe the effectiveness of electrical VeNs in the management of sleep and autonomic parameters in patients with PD. Sleep is essential for homeostasis and the restoration of body energy. Vestibular stimulation was reported to decrease sleep latency and induce sleep.[12] Earlier studies reported that administration of electrical VeNs was reported to reduce ISI scores.[13] Vestibular stimulation may induce sleep by influencing the suprachiasmatic nucleus of the hypothalamus.[14,15] Vestibular stimulation stimulates the dorsal raphe nucleus and releases serotonin which further converts to melatonin and induces sleep.[16,17] Inhibition of locus coeruleus which is the sympathetic nucleus and stimulation of the dorsal motor nucleus were observed followed by the vestibular stimulation.[18,19] The effect of vestibular stimulation on autonomic regulation was well reported.[20] The present study results support the results of earlier studies as there was a significant decrease in the ISI scores and significant decrease in the pulse rate and systolic blood pressure followed by the electrical VeNs.

Limitations of the study

The study was conducted at one center, hence results may not be generalized.

CONCLUSION

The present study results support the improvement of sleep followed by electrical VeNs. The study recommends detailed studies in this area to support the incorporation of electrical VeNs in the management strategy of PD.

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SSKG- Concept and design of the study, data acquisition, interpreted the results, reviewed the literature and manuscript, and prepared first draft of manuscript; **GS, AC, and PGG**- Statistical analysis and interpretation; **MP, AP, and RSC**- Data acquisition, preparation, and editing of manuscript; and **MVK**- Reviewed the literature and manuscript.

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