J Acupunct Res 2020;37(4):247-253

Journal of Acupuncture Research

Journal homepage: http://www.e-jar.org

Original Article

Effects of Acupuncture & Qigong Meditation on Nonmotor Symptoms of Parkinson's Disease

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Article history:
Submitted: March 24, 2020
Revised: June 24, 2020
Accepted: July 10, 2020

Keywords:
acupuncture, Qigong, meditation, Parkinson's disease, olfactory bulb, olfactory dysfunction

ABSTRACT

Background: Parkinson's disease(PD) affects not only motor symptoms, but also nonmotor symptoms. This study is a clinical trial to determine whether Qigong and acupuncture affect nonmotor symptoms of PD.
Methods: A 2-arm parallel and randomized trial was performed with 21 participants who had received either Qigong meditation only [control group (CG)] or acupuncture and Qigong meditation [experimental group (EG)]. The participants' levels of the discomfort in nonmotor symptoms from Parkinson's disease were evaluated by using the Unified Parkinson's Disease Rating Scales (UPDRS 1) and Test of Smell Identification (TSI) before and after 12 treatments at baseline and 1 month after 12 treatments.
Results: The both CG and EG showed improvements in the UPDRS 1 score after treatment by 5.6 ± 5.15 (p= 0.003; 74%) and 4.8 ± 3.80 (p = 0.004; 79%), respectively. The both CG and the EG did improvements in the TSI after treatment by 10.3 ± 4.37 (p < 0.001; 84%) and 12.6 ± 1.77 (p = 0.022; 100%), respectively. However, statistical differences were not observed between the CG and the EG using the UPDRS 1 and the TSI scores.
Conclusion: The combination of Qigong and acupuncture and Qigong alone was shown to improve the nonmotor symptoms and olfactory function of PD. In the future, large-scale clinical studies on alternative treatment for PD and studies on mechanisms affecting nonmotor symptoms of acupuncture and Qigong are needed.

https://doi.org/10.13045/jar.2020.00066
pISSN 2586-288X eISSN 2586-2898

Introduction

Parkinson's disease (PD, in hereafter) is a common, chronic, neurodegenerative disorder with which 1 million people in the United States and 5 million people worldwide have suffered from this disease. In particular, its prevalence has been increasing with aging populations [1]. It is the second most common neurodegenerative disease after Alzheimer's disease [2]. The pathological stages of PD are based on the location of α-synuclein-immunopositive Lewy bodies [3] which indicates the presence of not only numerous motor symptoms, but also nonmotor symptoms [4,5] that include neuropsychiatric disturbances [6], abnormal sensations [7], sleep disorders [8], autonomic dysfunctions [9], dopamine uptake [10], and olfactory dysfunction [11,12].

Olfactory dysfunction is a symptom of PD that affects millions of people worldwide [13], in which it disrupts the quality of life of those who has been experienced it. Treatments such as drug therapy, surgery, deep brain stimulation, gene therapy and implants are being proposed for PD. However, side effects have been reported with long-term use of dopaminergic medication. And costs of surgery are expensive, or there are restrictive criteria.

Accordingly, acupuncture and Qigong are emerging as alternative treatments to PD. There are increasing evidences by illustrating that acupuncture is effective at reducing motor and nonmotor symptoms. Qigong is another alternative treatment which is an exercise by aiming to promote health and relaxation, by integrating balance, flexibility, and neuromuscular coordination by training with a number of cognitive components in which all treatments together may be effective to the PD patients by regulating and transferring of energy [14].

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The purpose of this research was to investigate whether acupuncture and Qigong meditation combination therapy could improve the nonmotor symptom of PD and recovering the sense of smell through pre-post comparison and comparison with Qigong meditation alone.

Materials and Methods

Study design

This study compares of combination of acupuncture and Qigong meditation before and after 12 treatments at baseline (Fig. 1). And it is compared the effect of acupuncture and Qigong meditation [experimental group (EG)] versus Qigong meditation alone[control group (CG)] on the symptom of idiopathic PD patients. Outcomes were measured using the Unified Parkinson's Disease Rating Scales (UPDRS 1) and Test of Smell Identification (TSI) before and after 12 treatments at baseline and 1 month after 12 treatments.

Participants

Subjects were recruited through advertisements of the Institute of Integrative Medicine at South Baylo University. All participants were diagnosed as having idiopathic PD (based on UK Parkinson's Disease Society Brain Bank criteria), who were taking an anti-Parkinson medication, were asked not to change their anti-Parkinsonian medications during the study period, were included in the study. Demographic characteristics, including sex, age, race, disease duration, and daily dose of anti- Parkinsonian drugs were recorded for all participants.

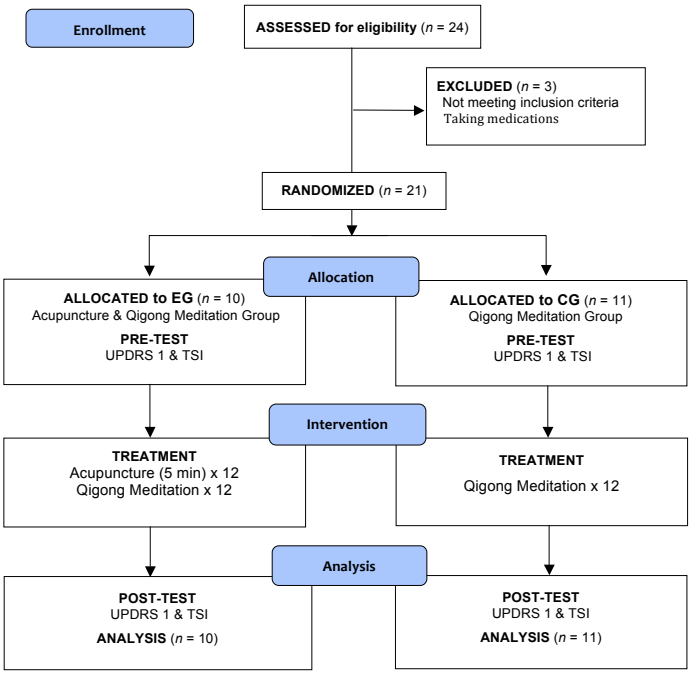

Fig. 1. Flow Chart of the design scheme of the study.
CG, control group; EG, experimental group; TSI, test of smell identification; UPDRS, Unified Parkinson's Disease Rating Scales.

Randomization

Participants were randomized for the study according to Vickers stratified randomization method [15]. Participants were stratified into EG or CG. For the EG and the CG, a Random Number Generator was used [16] and a concealed envelope method was used to allocate participants into the EG, where participants were treated with Qigong Meditation and acupuncture for 5 minutes, and the CG were treated with Qigong Meditation alone. Practitioners had over 5 years clinical experienced and were licensed by the California Acupuncture Board.

Treatment

Acupuncture treatment

The EG received treatments twice a week up to 12 times, 6 acupuncture points including bilateral GB20 (Fengchi) and LI4 (Hegu) and central Du14 (Dazhui) and Du16 (Fengfu) were selected as primary acupuncture points (Table 1). Sterile, stainless steel acupuncture needles (Dongbang Inc, Boryeong, Korea) with a diameter of 0.25 mm and a length of 40 mm were inserted obliquely to a depth of 2.0-2.5 cm, for 5 minutes until De qi was achieved.

Qigong & Meditation

The time required for one time was 50 minutes, and Healing breathing, Kwanjeong Meditation, and Qigong healing were repeated 12 times. This Kwanjeong Meditation and Qigong was special designed by So-jung An for relieve their stress and trauma furthermore the olfactory dysfunction.

Healing breathing method

In this study, 3 types of 'An's 4444 breathing' specially designed by So-Jung An to improve olfactory function including Heart and Lung Healing Breathing, Energy Supply Breathing, and Brain Healing Breathing, including 1 minute of training time step by step. Each was carried out for 10 minutes .

Step 1: Heart and Lung Healing Breathing
1. Exhale by making a hahaha hahaha sound through your mouth
2. Hold your breath for 4 seconds
3. Inhale for 4 seconds through the nose
4. Hold your breath for 4 seconds
5. Repeat 4 times in the order of 1,2,3,4

Step 2: Energy-Supplying Breathing
1. Place both hands lightly on your knees, close your eyes and close your mouth
2. Inhale through the nose continuously for 4 seconds
3. When you relax your nose, excess inhalation is released by itself.

Table 1. Acupoints to Treat Parkinson's Disease.

Location	Acupoints
Bilateral	GB-20 (Fengchi) and LI-14 (Hegu)
Central	DU-14 (Dazhui) and Du-16 (Fengfu)

4. Repeat 4 times in the order of 2, 3

Step 3: Brain Healing Breathing.
1. Place both hands lightly on your knees, close your eyes and close your mouth
2. Exhale for 4 seconds through the nose and pause for 4 seconds
3. Inhale for 4 seconds through the nose while drawing an image of breathing through the brain
4. Hold your breath for 4 seconds
5. Exhale through the nose for 4 seconds
6. Repeat 4 times in the order of 2, 3, 4, 5

This breathing method is designed to help relieve poor olfactory function such as mental and physical stability and energy recovery by discharging the cloudy energy in the body and recharging vitality, which is good energy.

Kwanjeong Meditation method

1. The practitioner designed the observation-centered Kwanjeong Meditation different from general meditation so that the participant could use the unconscious mind to heal the mind and body and maintain homeostasis.
2. Kwanjeong Meditation method was performed to relieve PD symptoms such as olfactory disorder, constipation, haste, depression, anxiety disorder, and tension obsessive-compulsive disorders.
3. Kwanjeong Meditation method where participants reminisced about the peaceful and wide sea by concentrating their mind, in silence to repeat the phrase "peace of mind and body." to induce healing of the trauma by own healing through Kwanjeong Meditation. It did 10 minutes

Qigong treatment method

This Qigong treatment method was used to maximize energy transfer to the olfactory tract area by means of Qigong treatment to comfort the spirit, mind, and body of the PD patients (Table 2). This was performed following the Qigong treatment when participants were feeling relaxed.

1. The participants' breaths were matched and the researcher concentrated on both hands to merge his/her magnetic field. The Qigong treatment began by utilizing the resonance action. The researcher transmitted energy that pulling from the cosmic(without touching and was non-invasive).
2. Energy transfer treatment was performed for 30 minutes with focus on 11 areas including the sinuses, olfactory bulb, thalamus, pituitary gland, amygdala, hippocampus, hypothalamus, temporal lobes, frontal lobes, prefrontal lobes, the olfactory tract in the mesolimbic pathway and the mesocortical pathway.

Outcome measurement

Subjects with PD were assessed by a series of specialized scales before treatment, including nonmotor symptoms and olfactory disorder. Nonmotor symptoms and quality of life were measured using the UPDRS 1 and the TSI was used to measure the participants' olfactory function. Participants were assessed before and after 12 treatments and after 1 month.

UPDRS 1

The UPDRS 1 is a rating tool used to gauge nonmotor symptoms of PD patients behavior, mood, and effects of the disease on daily life quality, as well as clinical complications, which is a popular, useful and precise evaluating method for the symptoms of nonmotor PD.

Olfactory evaluation by TSI

The TSI is an assessment tool to test the capacity of a patient to smell. All participants underwent an evaluation of their olfactory dysfunction by using the TSI where 5 odorants were presented for identification (alcohol, vanilla, coffee, tobacco, and cinnamon). Each odorant was presented once for approximately 3 seconds, with a time interval of at least 30 second between odorants. One point was given for each correct answer (maximum score of 5 points).

Statistical analysis

Statistical analysis was performed using R Version 3.5.1 (2018-07-02) "Feather Spray" [17]. A generalized linear repeated mixed model was employed to analyze the missing data (mostly due to noncompliance). The difference rate of each outcome measurement was calculated as (before treatment-after treatment)/before treatement*100. After applying the Kolmogorov-Smirnov test and the Shapiro-Wilk test to check for normality, either a paired samples t test and independent samples t test or Wilcoxon signed rank test and Mann-Whitney U test were performed to evaluate the statistical significance. Cohen's distance was used to compare effect sizes of the CG treatment with the EG treatment to determine the meaning of differences. The level set for statistical significance was $p < 0.05$.

Table 2. Qigong Meditation Process.

Process	Details
4-second Breathing	1st: Heart & Lung Healing Breathing 2nd: Energy-Supplying Healing Breathing 3rd: Brain Healing Breathing Breathing for 10 minutes
KwanJeong Meditation	Participants reach delta, theta, and alpha state of mind while performing the breathing techniques. Meditation in 10 minutes
Healing Qigong	11 treatments of energy transfer to olfactory tract area: sinuses, olfactory bulb mainly together with mesocortex pathway and mesolimbic pathway. Healing Qigong in 30 minutes

Ethics

The study was conducted in accordance with the Helsinki Declaration of 1975. The study started after receiving approval from the Institutional Review Board of South Baylo University (Approval no.: SBAIRLA0208).

Results

Demographic characteristics

24 participants were recruited. Three patients whose prescriptions changed during the study period were excluded from the study. 10 participants were assigned to the EG group and 11 to the CG group. To examine whether the trial was performed without bias, p values using Fisher's Exact test were determined for gender (p = 0.183), age (p = 0.330), onset (p = 0.670), constipation (p = 0.659), depression (p = 1.000), insomnia (p = 1.000), and anosmia (p = 1.000). At baseline, there was no significant difference in baseline characteristics between groups.

Effect of UPDRS 1 between CG and EG

The change in the UPDRS 1 before and after treatment are shown in Table 3. UPDRS 1 value in the CG decreased from 8.1 ± 6.49 to 2.5 ± 2.95 after treatment, showing a difference of 5.6 ± 5.15 (p = 0.003). UPDRS 1 value in the EG decreased from 6.1 ± 4.60 to 1.3 ± 1.51 after treatment, showing a difference of 4.8 ± 3.80 (p = 0.004). The differences were statistically significant after treatment in both groups. The UPDRS 1 value in the CG changed from 2.5 ± 2.95 following 12 sessions, to 2.6 ± 3.01 following 1 month after the 12th treatment, showing a difference of -0.05 ± 1.54 (p = 1.000). The UPDRS 1 value in the EG changed from 1.3 ± 1.51 following 12 treatments to 1.4 ±1.63 1 month after the 12th treatment, showing a difference of -0.1 ± 0.70 (p = 0.924). Fig. 2 shows the bar graph of UPDRS 1 before and after 12 treatments.

The difference of UPDRS 1 score after treatment was 5.6 ± 5.15 for the CG and 4.8 ± 3.80 for the EG. Note that the results showed the CG and EG not to be statistically significantly different (p = 0.751).

$$= \frac{UPDRS\ Before\ Tx - UPDRS\ After\ Tx}{UPDRS\ Before\ Tx} \times 100$$

The UPDRS difference rate of the CG and the EG after 12 treatments was 73.8 ± 26.86% and 79.3 ± 19.44%, respectively, and the result showed them not to be statistically significantly different (p = 0.603).

Effect of TSI Between CG and EG

The change of the TSI before and after treatment is shown in Table 4. The TSI value in the CG decreased from 12.6 ± 2.20 to 2.4 ± 5.21 after treatment, showing a difference of 10.3 ± 4.37 (p < 0.001). The TSI value in the EG decreased from 12.6 ± 1.77 to 0.0 ± 0.00 after treatment, showing a difference of 12.6 ± 1.77 (p = 0.022). The TSI value of the CG has changed from 2.4 ± 5.21 after 12 treatments to 0.5 ± 1.07 1 month after the 12th treatment, showing a difference of 1.9 ± 5.39 (p = 1.000). The TSI value of the EG did not change 0.0 ± 0.00 to 0.0 ± 0.00 (p = 1.000). This data was represented in a bar graph of the TSI before and after 12 treatments (Fig. 3).

The difference in the TSI score before and after treatment was 10.3 ± 4.37 for the CG and 12.6 ± 1.77 for the EG. Note that the results showed no statistically significant difference (p = 0.201).

$$= \frac{TSI\ Before\ Tx - TSI\ After\ Tx}{TSI\ Before\ Tx} \times 100$$

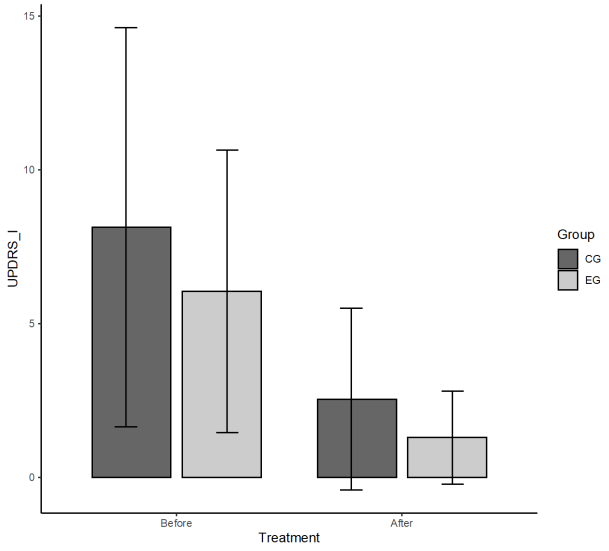

Fig. 2. Bar graph of UPDRS 1 before and after 12 treatments.
CG, control group; EG, experimental group; UPDRS, Unified Parkinson's Disease Rating Scales.

Table 3. Difference of UPDRS 1 Before and After Treatment.

Group	Before	After	Before - After (%)	p^*	$p^\dagger$
CG	8.1 ± 6.49	2.5 ± 2.95	5.6 ± 5.15 (73.8 ± 26.86)	0.003	0.751 (0.603)
EG	6.1 ± 4.60	1.3 ± 1.51	4.8 ± 3.80 (79.3 ± 19.44)	0.004	

* Paired samples t test / Wilcoxon signed rank test.
† Mann-Whitney U test (between groups).
CG, control group; EG, experimental group; UPDRS 1, Unified Parkinson's Disease Rating Scales.

Table 4. Difference of TSI Before and After Treatment.

Group	Before	After	Before - After (%)	p^*	p^{**}
CG	12.6 ± 2.20	2.4 ± 5.21	10.3 ± 4.37 (84.2 ± 34.72)	< 0.001	0.201 (0.076)
EG	12.6 ± 1.77	0.0 ± 0.00	12.6 ± 1.77 (100.0 ± 0.00)	0.022	

* Paired sample t test / Wilcoxon signed rank test.
** Mann-Whitney U test (between groups).
CG, control group; EG, experimental group; TSI, test of smell identification.

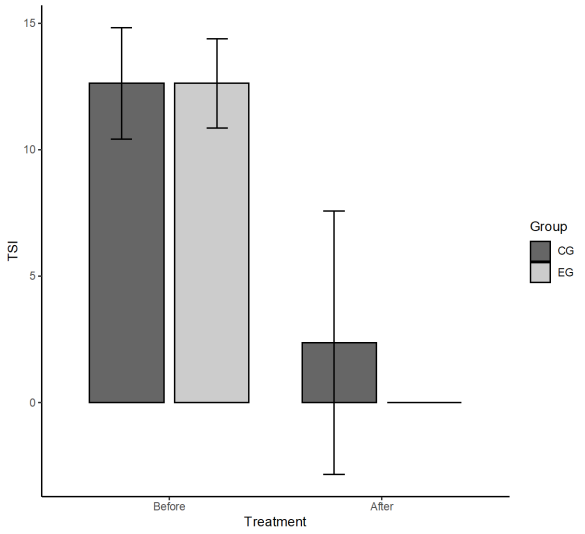

Fig. 3. Bar graph of TSI before and after 12 treatments.
CG, control group; EG, experimental group; TSI, test of smell identification.

The difference rate after the treatment was 84.2% ± 34.72% for the CG and 100.0 ± 0.00% for the EG, respectively. Note that the difference rate of the TSI after 12 treatments for the EG and the CG after 12 treatments was not statistically significant (p = 0.076). The TSI value of the CG has changed from 2.4 ± 5.21 after 12 treatments to 0.5 ± 1.07 1 month after the 12th treatment, showing a difference of 1.9 ± 5.39 (p = 1.000). The TSI value of the EG did not change 0.0 ± 0.00 to 0.0 ± 0.00 (p = 1.000). The differences 1 month after treatment were not statistically significantly different in both groups, which implied that the treatment effects would continue at least 1 month after treatment. The difference between the TSI score after 12 treatments and 1 month after the 12th treatment was 1.9 ± 5.30 for the CG and 0.0 ± 0.00 for the EG (p = 0.382). The differences of two groups in TSI value of that was 0,201(p =0.076) but there was no significant difference.

Cohen's distance of UPDRS 1 and TSI

Cohen's distance was used to compare the effect sizes of the CG treatment with the EG treatment to determine the meaning of differences. Cohen's distance of UPDRS 1 was 0.37 before treatment, and 0.52 after treatment. Cohen's distance TSI was 0.00 before treatment, and 0.64 after treatment.

Discussion

PD is a neurodegenerative disease with its causes not yet fully known. However, recent research is focused on α-synuclein mutations as a genetic cause, such as LRRK2, PARK2, PINK1, and Gva caused by the chemical environment with the increased amounts of methamphetamine, and MPTP. At the same time, research has focused on mitochondrial oxidative stress which is responsible for mitochondrial dysfunction.

These PD's cause not only changes in motor symptoms, but also changes in nonmotor symptoms such as behavior and mood, and olfactory dysfunction. In the process of olfactory function, olfactory bulbs send signals to various areas of the brain, one of which is the mesolimbic pathway. It is also known as the dopaminergic pathway [18] and the decline of the dopaminergic pathway causing PD, which have been resulted in olfactory dysfunction [19]. An impaired olfactory system negatively affects the social abilities and the interpersonal relationships of the individual. Further, it affects the brains capacity to form positive and negative emotional memories that are related to the smell. Losing the sense of smell has been reported to be similar to disability which has been resulted in a decreased quality of life [20] that is frequently leading to depression [21,22].

The olfactory dysfunction has been widely recognized as an early clinical sign of PD [23,24]. The olfactory bulb is involved in the regulation of microglial cells which appear to show deterioration [25]. Thereby, post-mortem studies implicate oxidative stress [26]. Deterioration of dopamine signaling pathways such as the nigrostriatal, mesocortical and mesolimbic ones caused by oxidative stress have been resulted in the damage to the surrounding neurons and cause cell death [27]. In these cases, the increased levels of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) that are related to the damage caused by oxidative stress in the nigrostriatal pathway in particular have been shown to be a major toxin that causes neuronal damage [28,29]. Under these conditions of deterioration, there is a consequent lowering of the threshold for managing oxidative stress [30], that can amplify the damage caused by the deterioration of the nigrostriatal and mesolimbic systems. The increased oxidative stress, dopamine pathways, and the olfactory system can be strongly associated in PD [31]. The focused treatment of the oxidative stress may reduce other nonmotor symptoms [32], in which, it consequently reduces the severity of PD symptoms [33].

As a current therapeutic treatment for PD, drug therapy can alleviate the symptoms, nonetheless, it fails to slow down or halt disease progression, and the long-term use of dopaminergic

medication inevitably induces motor complications [34,35]. Surgery can partially relieve symptoms, although it is expensive, and its long-term efficacy has not yet been determined. Deep brain stimulation, a common surgical intervention for PD revealed restrictive criteria if patients consent for the procedure [36,37]. Other therapeutic strategies such as gene therapy and implants have been reported to give neuroprotection in a laboratory study [38], clinical trials have not been conducted, yet [39].

As an alternative to the conventional treatment methods, acupuncture has acquired therapy recognitions for alleviating symptoms of neurodegenerative diseases [40]. The therapeutic effect of acupuncture in PD comes in under debate. However, there are increasing evidences by illustrating that acupuncture is effective at reducing motor and nonmotor symptoms, such as pain, olfactory dysfunction, sleep disorders [8], mood disturbances [41], and improving the quality of life of PD patients [42]. In animal models of PD, acupuncture is effective at reducing oxidative stress [43,44], decreasing neuroinflammation through controlled microglial activation, stimulating the release of neurotrophic factors [45], and regulating the network between cortex and striatum [46].

Qigong is also another alternative treatment for PD. Qigong consists of treatment Qigong and martial art action one. Treatment Qigong consists meditation techniques, whereas martial art action Qigong involves the movements of the body as a tool to direct practitioners' attention to reach a meditative state [47]. Combining the two techniques may manifest to the improved sleep quality and gait performance in the PD [48], thereafter, it improved the PD patients' quality of life [48,49].

Based on the above research results, this study was to investigate whether acupuncture and Qigong meditation combination therapy could improve the nonmotor symptom of PD and recovering the sense of smell through pre-post comparison and comparison with Qigong meditation alone in clinical trial. As a result of the study, both Qigong and acupuncture combination treatment and Qigong alone treatment improved nonmotor symptoms and olfactory function after treatment compared to before treatment. In addition, this treatment effect was found to persist in both groups even after 1 month after 12th treatment.

However, there was no significant difference between the acupuncture and Qigong combination treatment group and the Qigong single treatment group immediately after 12 treatments and after one month. This may be interpreted as the fact that the effect of Qigong performed in both groups was large enough to offset the effect of acupuncture, or that the effect mechanisms of acupuncture and Qigong were similar and combined with each other and added or increased effect was insufficient.

The limitation of this study is that it was conducted with a small number of 21 people. In addition, compared to PD as a disease with a long course, it is administered 12 times for a short period of 6 weeks, and its follow-up is also limited to 1 month later. Another limitation is that it does not have a more objective evaluation scale because it is conducted mainly on questionnaires such as UPDRS and TSI. However, it is significant as a clinical study using acupuncture and Qigong for PD, which is rapidly increasing in the future and has a great influence on the quality of life in old age.

Large-scale clinical studies on alternative treatments for PD in the future are needed. In addition, several studies on the mechanisms affecting the nonmotor symptoms and sense of smell of acupuncture and Qigong are considered necessary.

Acknowledgments

The author would like to express my deep appreciations to the chairman of the school board, Dr. David Park, President Dr. Edwin Follic, Vice-president Dr. Jennifer, faculty and staff members, and others (Ji-sun Kim, Sae-rom Choi, the DAOM students).

Conflicts of Interest

The authors have no conflict of interest to report.

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