

A Prospective Open-Label Study of Combined Treatment for Idiopathic Parkinson's Disease Using Acupuncture and Bee Venom Acupuncture as an Adjunctive Treatment

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Abstract

Objectives: The purpose of this study was to examine the effectiveness and safety of combined treatment using acupuncture and bee venom acupuncture (BVA) as an adjunctive treatment for idiopathic Parkinson's disease (PD).

Methods: Eleven patients (7 men and 4 women) with idiopathic PD who had been receiving a stable dose of anti-parkinsonian medication for at least 4 weeks. Participants received conventional treatment for 12 weeks. Subsequently, they received additional treatment with acupuncture and BVA twice weekly for 12 weeks while still maintaining conventional treatment. All participants were assessed at baseline, 12 weeks, and 24 weeks by using the Unified Parkinson's Disease Rating Scale (UPDRS), the Parkinson's Disease Quality of Life Questionnaire (PDQL), the speed and number of steps required to walk 20 m, and the Beck Depression Inventory (BDI). Maximum excursion and directional control, measured by computerized dynamic posturography (Balance Master[®] System, NeuroCom, San Carlos, CA), were used to assess postural stability.

Results: Patients who underwent 12 weeks of twice-weekly combined treatment with acupuncture and BVA showed significant improvements in gait speed, PDQL score, activities of daily living (UPDRS part II), motor symptoms (UPDRS part III), and combined UPDRS part II+III scores compared with assessments after conventional treatment.

Conclusions: Combined treatment with acupuncture and BVA showed promising results as a safe adjunctive therapy for PD.

Introduction

PARKINSON'S DISEASE (PD) is a neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra, which leads to progressive dopamine depletion in the striatum. This disrupts the balance of the basal ganglia circuit and subsequently leads to motor function disorders, rigidity, tremor, and akinesia.¹

Administration of the dopamine precursor levodopa (L-dopa) is one of the gold standards for PD treatment. Despite its widespread use, more than 50% of patients with PD undergoing long-term treatment with L-dopa experience adverse effects within 5 years, such as hallucination, insomnia, nausea, and dyskinesia.^{2,3} Thus, the best treatment seeks to use the lowest dosage of L-dopa that is effective in

controlling symptoms.⁴ Furthermore, with respect to the motor aspects of the disease, dopaminergic therapies are effective, but most nonmotor symptoms of PD do not respond to these therapies.⁵

Because of these limitations, interest is increasing in potentially beneficial complementary and alternative therapies, such as acupuncture, for treating PD.^{6–9} Studies conducted in the United States reported that 40% of patients with PD used at least one complementary and alternative medicine treatment for PD, with acupuncture being the most used among all such modalities.^{10,11}

Acupuncture has been used to relieve PD-like symptoms in Asian countries for centuries. Several studies have reported that acupuncture treatment leads to substantial neuroprotective effects in PD animal models.^{12–14} In addition, research using

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neuroimaging demonstrated that acupuncture stimulations can activate neural responses in brain regions, including the substantia nigra, caudate, thalamus, and putamen, that are impaired in PD.¹⁵ Recently, bee venom acupuncture (BVA) has become a treatment for neurodegenerative diseases such as PD. Several studies have demonstrated that BVA has neuroprotective, anti-apoptotic, and anti-inflammatory effects that can reduce damage to dopaminergic neurons.^{16–19}

In a previous clinical trial we conducted,²⁰ acupuncture and BVA each showed promising results as adjunctive therapies for idiopathic PD. In a clinical setting, BVA is usually combined with manual acupuncture. However, no clinical studies have assessed the effectiveness of combined treatment with acupuncture and BVA for PD. The current prospective, open-label, self-controlled study was conducted to investigate the effectiveness and safety of the combined treatment as an adjunctive treatment.

Materials and Methods

Ethics approval

The study was done in accordance with the ethical standards of the Helsinki Declaration. The institutional review board of the university hospital approved the protocol (KHNMC-OH-IRB-2012-01-013). After being given a full description of the study, all participants provided written informed consent.

Patient recruitment and selection

This study took place between November 2012 and May 2014 at Kyung Hee University Hospital at Gangdong, Korea. Participants were recruited through the university's website and bulletin boards. Interested patients contacted the study coordinator for further information. Potential participants were then offered a formal in-person assessment.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) diagnosis of with idiopathic PD according to the UK Parkinson's Disease Society Brain Bank criteria;²¹ (2) receipt of a stable dose of anti-parkinsonian medication for at least 4 weeks before the trial; (3) stage 1–4 PD according to the Hoehn and Yahr scale;²² (4) score of greater than 1 point in 2 or more categories on the Unified Parkinson's Disease Rating Scale (UPDRS) part III, including tremor, rigidity, postural instability, and bradykinesia; and (5) a Mini-Mental State Examination–Korean version score greater than 24.

Exclusion criteria were as follows: (1) having epilepsy, dementia, alcohol or drug addiction and having received psychiatric medication; (2) secondary parkinsonism caused by cerebrovascular disease, neoplasm, and infection; (3) Parkinson-plus syndromes; (4) pregnancy; and (5) a positive result on a bee venom skin allergy test.

Dropout criteria were the following: (1) skipping of more than 8 of the 24 total treatment sessions, (2) serious abnormal reactions, and (3) withdrawal of agreement to participate in the study.

Study protocol

This study was a prospective, open-label, self-controlled trial. All participants were assessed by using UPDRS parts II and III, the Parkinson's Disease Quality of Life Questionnaire (PDQL), the Beck Depression Inventory (BDI), postural stability, and the time and number of steps required to walk 20 m. Patients maintained their anti-parkinsonian medication without any additional treatment for 12 weeks (conventional treatment). After this, patients were treated with acupuncture and BVA (combined treatment) twice a week while still maintaining conventional treatment. All patients had to keep using their anti-parkinsonian medications, but the method of delivery or dosage could be changed during the study period.

Study participants underwent stimulation of 10 acupuncture points using acupuncture and BVA twice a week for 12 weeks. The initial assessment was repeated after conventional treatment (12 weeks) and after the combined treatment (24 weeks) (Fig. 1). At the conclusion of the study, the patients were interviewed by using open-ended questions to explore subjective changes in their symptoms after the combined treatment.

Interventions

All interventions were performed by one doctor of Korean medicine with more than 10 years of experience. Patients received treatments with BVA and acupuncture at 10 acupuncture points (bilateral GB20, LI4, GB34, ST36, and LR3) twice a week for 12 weeks (total of 24 sessions). Bee venom, 0.1 ml diluted to 0.005% in normal saline (Yumil Farm, Hwasun, Jeonnam, Korea), was injected into each point; sterile, disposable, stainless steel acupuncture needles (diameter, 0.25 mm; length, 30 mm [Dongbang, Boryeong, Chungnam, Korea]) were inserted into the points listed above to a depth of 1.0–1.5 cm and rotated at 2 Hz for 10 seconds to achieve *de qi*, the sensation felt by the patient when the acupuncture needle is

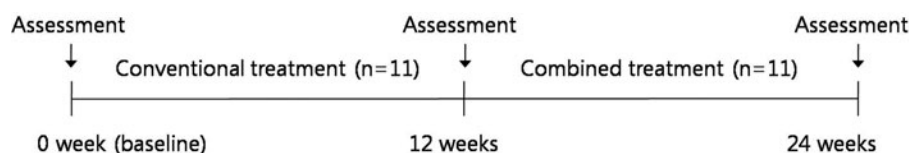


FIG. 1. Research procedure. Conventional treatment: Patients maintained their anti-parkinsonian medication without any additional treatment for 12 weeks; combined treatment: Patients were treated with acupuncture and bee venom acupuncture twice a week while maintaining the conventional treatment; assessment: All patients were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS), the Parkinson's Disease Quality of Life Questionnaire (PDQL), the speed and number of steps required to walk 20 m, the Beck Depression Inventory (BDI), and postural stability measured by computerized dynamic posturography.

at the appropriate position for clinical efficacy. This needle position was then maintained for 15 minutes.

Skin testing for venom allergy

A skin test was performed to determine whether the patient was allergic to bee venom. Bee venom, 0.1 ml diluted to 0.005% in normal saline, was injected at LI4. Development of a wheal larger than 5 mm, a rash bigger than 11 mm in diameter, or severe itching at the site within 15–20 min were considered to indicate a bee venom allergy; patients developing any of these reactions were excluded from this study.

Outcome measures

The primary outcome measure was the combined UPDRS parts II and III score. The secondary outcome measures were UPDRS parts II and III individually, PDQL, BDI, postural stability, and the speed and number of steps required to walk 20 m.

Postural stability, maximum excursion (MXE) and directional control (DCL) were assessed by computerized dynamic posturography (Balance Master[®] System, NeuroCom, San Carlos, CA). MXE is the maximum distance that the patient can achieve without falling during performance of shifting and reaching in each of eight target directions. Scores range from 0% to 100%, with higher percentages indicating better balance. DCL is a measure of center-of-gravity movement in the right direction and is defined as the ratio of the amount of intended movement minus the amount of extraneous movement, divided by the amount of intended movement. Scores range from 0% to 100%, with higher percentages indicating increased movement control.²³

Responders—participants who showed a greater than 1-point improvement in score for each item on UPDRS part II and part III after combined treatment—were counted. In addition, changes in each motor symptom were evaluated by item analysis.

Statistical analysis

Data were expressed as mean \pm standard deviation or medians along with the lower and upper quartiles. The Wilcoxon signed-rank test was used to examine statistical significance using SPSS software, version 18.0 (SPSS Inc., Chicago, IL). A *p*-value less than 0.05 was considered to represent a statistically significant difference.

Results

Baseline characteristics

A total of 11 patients were included. All received conventional treatment and combined treatment, each for a total of 12 weeks. Participants consisted of 7 men and 4 women, with a mean age of 64.6 ± 6.2 years. The mean scores on the Hoehn and Yahr scale and UPDRS parts II and III were 1.9 ± 0.7 and 31 ± 4.8 , respectively (Table 1).

Changes in the UPDRS scores

The UPDRS scores (the sum score of part II and part III, as well as parts II and III individually) did not significantly change after conventional treatment. However, after combined treatment for 12 weeks, significant improvement was found in

TABLE 1. BASELINE PATIENT CHARACTERISTICS

Characteristic	Patients (n = 11)
Men/women (n/n)	7/4
Age (y)	64.6 \pm 6.2
MMSE-K score	27.2 \pm 2.0
Hoehn and Yahr stage	1.9 \pm 0.7
UPDRS II score	14.1 \pm 3.6
UPDRS III score	16.9 \pm 4.3
UPDRS II + III score	31 \pm 4.8
20-m gait speed (s)	21.6 \pm 3.9
20-m gait number	41.2 \pm 9.3
PDQL score	119.6 \pm 17.9
BDI score	14.2 \pm 6.8
MXE (%) ^a	59.6 \pm 16.5
DCL (%) ^b	75.8 \pm 17.9

Values are mean \pm standard deviation.

^aMeasured by computerized dynamic posturography (Balance Master[®], NeuroCom) was assessed as the farthest distance displaced by a participant's center of gravity during performance of shifting and reaching in each of eight target directions. Scores range from 0% to 100%, with higher percentages indicating better balance.

^bDirectional control measured by computerized dynamic posturography (Balance Master) was assessed as the amount of movement toward a target, as compared with movement away from the target. Scores range from 0% to 100%, with higher percentages indicating better movement control.

MMSE-K, Mini-Mental State Examination-Korean version; UPDRS, Unified Parkinson's Disease Rating Scale; UPDRS part II, activities of daily living; UPDRS part III, motor examination; 20-m gait speed, the time required to walk 20 m; 20-m gait number: the number of steps required to walk 20 m; PDQL, Parkinson's Disease Quality of Life Questionnaire; BDI, Beck Depression Inventory; MXE, maximum excursion; DCL, directional control.

the sum score of UPDRS part II and part III, as well as on UPDRS part II and UPDRS part III individually (Table 2).

There were more than three responders in categories such as "falling," "tremor," and "sensory complaints related to parkinsonism" in the UPDRS part II and "tremor at rest," "action or postural tremor of hands," "finger taps," "hand movements," "rapid alternating movements of hands," and "postural stability" in the UPDRS part III (Table 3). Furthermore, according to the item analysis, tremor, bradykinesia and postural instability and gait disorder (PIGD) were significantly improved after the combined treatment (Table 4).

Changes in Gait, PDQL, BDI, and postural stability

The 20-m gait speed changed significantly after combined treatment. The PDQL score was significantly changed after both conventional treatment and combined treatment. The BDI score and postural stability (MXE, DCL) were not changed significantly after conventional treatment or combined treatment (Table 5).

Subjective changes in symptoms

To explore and understand how the patients experience acupuncture and BVA, subjective changes in their symptoms after the combined treatment were collected using open-ended questions. The patients reported the following variety of changes in their symptoms.

Speech. "My voice and slow speech speed improved"; "I was told that my voice was improved while speaking on

TABLE 2. CHANGES IN UPDRS SCORE AT 24 WEEKS

Variable	Baseline (n=11)	Post-conventional treatment (12 wk) (n=11)	Post-combined treatment (24 wk) (n=11)
UPDRS II+III	32 (29, 36)	32 (29, 35)	27 (22, 31) ^a
UPDRS II	14 (11, 17)	13 (11, 16)	12 (10, 14) ^a
UPDRS III	17 (13, 20)	17 (13, 21)	15 (12, 16) ^a

Values are the median (lower quartile, upper quartile). There were no significant changes in UPDRS parts II+III, UPDRS part II, and UPDRS part III scores after conventional treatment, as determined by Wilcoxon signed-rank test.

^aSignificant changes compared with 12 weeks, as determined by Wilcoxon signed-rank test ($p < 0.05$).

the phone"; and "I became more articulate and was less often speechless."

Tremor. "A month and half after treatment started, my tremors when walking decreased by greater than 50%"; "Tremors of temporomandibular joint gradually improved and eventually disappeared"; and "Tremor was improved by 40~50%."

Sense. "The strange shooting sensations in my face disappeared entirely, while the shooting sensations in my arms and legs decreased by about 50%."; "The numbness that extended from my legs to feet decreased by 70~80%"; and "I had symptoms in which my legs stiffened and seized

with a cramp when sleeping every day before treatment, but after treatment these symptoms disappeared."

Motor. "One to 2 months after treatment I drag my feet less when walking"; "I gained strength and the feeling that I might fall down decreased, therefore my discomfort when walking decreased"; "My ability to take short and quick steps improved significantly"; "Before treatment, I only felt comfortable after walking for at least 200~300 m. But now, I feel comfortable soon after I start walking"; "My movement is nearly the same as in the past"; "My movements quickened"; and "I don't drop food when eating."

Others. "People tell me that my face looks better"; "After four treatments, my general condition improved by nearly 80% and this improvement has been maintained"; "Before treatment, I needed to rest several times during exercise. But 3 months after treatment, I don't need to take a break anymore"; "After treatment, I felt that my body and steps were lighter, and I felt good"; "My sleep quality was improved by 30~50%"; "My sleep habits of dreaming a lot, talking and shouting, and biting my tongue disappeared."; and "My handwriting improved."

Adverse events

Patients were encouraged to report all adverse events. During the study period, no serious adverse events occurred. Some patients reported mild pain or slight bleeding after

TABLE 3. NUMBER OF RESPONDERS ON UPDRS PART II AND UPDRS PART III

Variable	Responders (n)
UPDRS II	
Speech	1
Salivation	1
Swallowing	1
Handwriting	1
Cutting food and handling utensils	0
Dressing	1
Hygiene	1
Turning in bed and adjusting bed clothes	2
Falling	4
Freezing when walking	2
Walking	1
Tremor	3
Sensory symptoms related to parkinsonism	3
UPDRS III	
Speech	1
Facial expression	2
Tremor at rest	3
Action or postural tremor of hands	4
Rigidity	0
Finger taps	7
Hand movements	3
Rapid alternating movements of hands	4
Leg agility	0
Arising from chair	0
Posture	1
Gait	2
Postural stability	3
Body bradykinesia and hypokinesia	2

Responders were participants whose scores improved by more than 1 point for each item after 12 weeks of combined treatment. The total number of patients was 11.

TABLE 4. ITEM ANALYSIS OF UPDRS SUBSCORES

Variable	Baseline (n=11)	Post-conventional treatment (12 wk) (n=11)	Post-combined treatment (24 wk) (n=11)
Tremor	3 (0, 6)	2 (1, 5)	2 (0, 2) ^a
Bradykinesia	5 (4, 5)	5 (4, 7)	4 (3, 5) ^a
PIGD	5 (4, 7)	4 (4, 7)	4 (3, 5) ^a
Rigidity	0 (0, 0)	0 (0, 0)	0 (0, 0)

Values are the median (lower quartile, upper quartile). Subscores of the UPDRS were analyzed as follows: tremor=arm and leg rest and action tremor (scores no. 20+21); bradykinesia=finger taps, hand movements, rapid alternating movements of the hands, and leg agility (scores no. 23+24+25+26); rigidity=arm and leg rigidity (score no. 22); and PIGD=walking, freezing, and falling from UPDRS II scores+gait and postural stability (scores no.13+14+15+29+30).

^aSignificant changes between before and after combined treatment, as determined by Wilcoxon signed-rank test ($p < 0.05$).

PIGD, postural instability and gait disorder.

TABLE 5. CHANGES IN 20-M GAIT SPEED/NUMBER, PDQL, BDI, MXE, AND DCL AT 24 WEEKS

Variable	Baseline (n=11)	Post-conventional treatment (12 wk) (n=11)	Post-combined treatment (24 wk) (n=11)
20-m gait speed (s)	21 (19, 25)	21 (18, 25)	19 (17, 23) ^a
20-m gait number	40 (33, 46)	38 (34, 46)	34 (30, 48)
PDQL score	122 (105, 132)	138 (126, 151) ^b	147 (144, 160) ^a
BDI score	14 (10, 19)	8 (5, 15)	11 (3, 16)
MXE (%) ^c	59.6 (41, 76.4)	66.9 (46.9, 73.6)	70.1 (61.4, 78.6)
DCL (%) ^d	82.8 (52.4, 88.5)	83.9 (64.5, 85.6)	84.1 (72.9, 88.5)

Values are the median (lower quartile, upper quartile).

^aSignificant changes compared with 12-week outcome, as determined by Wilcoxon signed-rank test ($p < 0.05$).

^bSignificant changes compared with baseline, as determined by Wilcoxon signed-rank test ($p < 0.05$).

^cSignificant changes measured by computerized dynamic posturography (Balance Master[®] System, NeuroCom), which was assessed as the farthest distance displaced by a participant's center of gravity during performance of shifting and reaching in each of eight target directions. Scores range from 0% to 100%, with higher percentages indicating better balance.

^dDirectional control, measured by computerized dynamic posturography (Balance Master[®] System, NeuroCom), was assessed as the amount of movement toward a target, as compared with movement away from the target. Scores range from 0% to 100%, with higher percentages indicating better movement control.

acupuncture treatments and mild redness or mild itchiness after BVA.

Discussion

In this study, patients who underwent 12 weeks of twice-weekly combined treatment with acupuncture and BVA showed significant improvement in gait speed, PDQL score, activities of daily living (UPDRS part II), motor symptoms (UPDRS part III), and combined UPDRS part II and III scores compared with their post-conventional treatment assessments. According to the item analysis, among the four main symptoms of PD, tremor, bradykinesia, and PIGD were all significantly improved after the treatment.

In addition to the quantitative evaluation, open-ended questions were used to explore changes that occurred after the treatment. The patients described various subjective changes in their symptoms and feelings. Most of them reported improvement in their speech, sense, tremor, and motor impairment. These qualitative comments provide basic information about PD patients' response to acupuncture and BVA.

This study included patients who had been receiving a stable dose of anti-parkinsonian medication for at least 4 weeks before the trial and allowed the patients to change the administration method or dosage of their medications on the basis of the opinion of their neurologists. During the conventional treatment period, three patients increased their medication dosage. On the other hand, no patients increased their dosage during the combined treatment. Furthermore, one patient who had improved for the time period decreased the dosage according to the opinion of his neurologist.

How acupuncture improves the symptoms of patients with PD who are receiving medication is not yet clear. Recently, an experimental study reported that acupuncture may improve the motor function of patients with PD by increasing the dopamine efflux and turnover ratio of dopamine, suggesting that acupuncture-induced enhancement of synaptic dopamine availability may play a critical role in motor function improvement.²⁴ An additional study showed that acupuncture and L-dopa in combination can enhance the benefits of L-dopa and alleviate the adverse effects, thereby suggesting a synergistic effect between acupuncture and L-dopa.¹

BVA (bee venom acupuncture point injection) is a subcutaneous injection with diluted bee venom into an acupuncture point. Acupuncture point injection is the injection of a small amount of a substance, such as bee venom, vitamins, saline, or plant extract, at a point of acupuncture. The goal is to enhance and prolong the effects of stimulation of acupuncture points. Consequently, the mechanisms of action of BVA might be similar to those of acupuncture. There could also be another effect due to the bee venom itself. At present, this remains unclear.

In the authors' previous study, after 8 weeks of BVA, the Berg Balance Scale scores of participants improved significantly.²⁰ In the current study, PIGD was also significantly improved after 12 weeks of combined treatment. However, postural stability measured by the Balance Master[®] system did not change significantly. To participate in this study, patients had to visit the hospital twice a week for 12 weeks. For this reason, most patients were in the mild stages of disease, corresponding to a staging of 1.9 ± 0.7 on the Hoehn and Yahr scale. MXE and DCL scores were nearly normal at the baseline assessment. This is believed to be the reason postural stability, measured by the Balance Master[®] system, did not change during our study.

No serious adverse events were observed and no patients dropped out because of adverse effects. Consequently, the combined treatment with acupuncture and BVA is thought to be safe.

This pilot study has several limitations. It was not a double-blind controlled trial. The sample size of 11 patients was small, but the study could be important because the conventional treatment and the combined treatment were provided to the same group for a total of 24 weeks. Additionally, through the use of open-ended questions, the study could describe patients' responses to the treatment; these findings cannot be evaluated by using quantitative tools, such as UPDRS, PDQL, and BDI.

In conclusion, combined treatment with acupuncture and BVA showed promising results as a safe adjunctive therapy for PD. On the basis of this study, a larger and long-term follow-up trial is needed to more definitively determine the safety and efficacy of combined treatment and to elucidate how long the effect lasts.

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Author Disclosure Statement

No competing financial interests exist.

References

- Kim SN, Doo AR, Park JY, et al. Combined treatment with acupuncture reduces effective dose and alleviates adverse effect of L-dopa by normalizing Parkinson's disease-induced neurochemical imbalance. *Brain Res* 2014;1544:33–44.
- Fahn S, Oakes D, Shoulson I, et al. Levodopa and the progression of Parkinson's disease. *N Engl J Med* 2004;351:2498–2508.
- Rascol O, Brooks DJ, Korczyn AD, et al. A five-year study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with ropinirole or levodopa. 056 Study Group. *N Engl J Med* 2000;342:1484–1491.
- Kurlan R. "Levodopa phobia": a new iatrogenic cause of disability in Parkinson disease. *Neurology* 2005;64:923–924.
- Zesiewicz TA, Sullivan KL, Arnulf I, et al. Practice Parameter: treatment of nonmotor symptoms of Parkinson disease: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010;74:924–931.
- Wang X, Liang XB, Li FQ, et al. Therapeutic strategies for Parkinson's disease: the ancient meets the future—traditional Chinese herbal medicine, electroacupuncture, gene treatment and stem cells. *Neurochem Res* 2008;33:1956–1963.
- Eng ML, Lyons KE, Greene MS, et al. Open-label trial regarding the use of acupuncture and yin tuina in Parkinson's disease outpatients: a pilot study on efficacy, tolerability, and quality of life. *J Altern Complement Med* 2006;12:395–399.
- Tan LC, Lau PN, Jamora RD, et al. Use of complementary therapies in patients with Parkinson's disease in Singapore. *Mov Disord* 2006;21:86–89.
- Ferry P, Johnson M, Wallis P. Use of complementary therapies and non-prescribed medication in patients with Parkinson's disease. *Neurology* 2002;78:612–614.
- Rajendran PR, Thompson RE, Reich SG. Reich. The use of alternative therapies by patients with Parkinson's disease. *Neurology* 2001;57:790–794.
- Ferry P, Johnson M, Wallis P. Use of complementary therapies and non-prescribed medication in patients with Parkinson's disease. *Postgrad Med J* 2002;78:612–614.
- Park HJ, Lim S, Joo WS, et al. Acupuncture prevents 6-hydroxydopamine-induced neuronal death in the nigrostriatal dopaminergic system in the rat Parkinson's disease model. *Exp Neurol* 2003;180:93–98.
- Jeon S, Kim YJ, Kim ST, et al. Proteomic analysis of the neuroprotective mechanisms of acupuncture treatment in a Parkinson's disease mouse model. *Proteomics* 2008;8:4822–4832.
- Kang JM, Park HJ, Choi YG, et al. Acupuncture inhibits microglial activation and inflammatory events in the MPTP induced mouse model. *Brain Res* 2007;1131:211–219.
- Yeo S, Lim S, Choe IH, et al. Acupuncture stimulation on GB34 activates neural responses associated with Parkinson's disease. *CNS Neurosci Ther* 2012;18:781–790.
- Doo AR, Kim ST, Kim SN, et al. Neuroprotective effects of bee venom pharmaceutical acupuncture in acute 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced mouse model of Parkinson's disease. *Neurol Res* 2010;32:88–91.
- Kim CY, Lee JD, Lee SH, et al. Anti-inflammatory effect of bee venom acupuncture at Sinsu(BL23) in a MPTP mouse model of Parkinson's disease. *J Kor Acu Mox Soc* 2009;26:49–58.
- Jun HJ, Kim YS. Dose-dependent effects of Bee venom acupuncture on MPTP-induced mouse model of Parkinson's disease. *J Kor Acu Mox Soc* 2010;27:59–68.
- Chung ES, Kim H, Lee G, et al. Neuro-protective effects of bee venom by suppression of neuroinflammatory responses in a mouse model of Parkinson's disease: role of regulatory T cells. *Brain Behav Immun* 2012;26:1322–1330.
- Cho SY, Shim SR, Rhee HY, et al. Effectiveness of acupuncture and bee venom acupuncture in idiopathic Parkinson's disease. *Parkinsonism Relat Disord* 2012;18:948–952.
- Rajput DR. Accuracy of clinical diagnosis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1993;56:938–939.
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology* 1967;17:427–442.
- Li F, Harmer P, Fitzgerald K, et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012;366:511–519.
- Kim SN, Doo AR, Park JY, et al. Acupuncture enhances the synaptic dopamine availability to improve motor function in a mouse model of Parkinson's disease. *PLoS One* 2011;6:e27566.

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