



Case Report

Drug-Induced Gastrointestinal Dysfunction in Parkinson's Disease: Treatment with Korean Medicine



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ABSTRACT

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Parkinson's disease (PD) is a neurodegenerative disease, where treatment with medication may lead to gastrointestinal (GI) symptoms. The objective of this case study was to investigate the effectiveness of Korean medicine (KM) in treating PD with drug-induced GI dysfunction. A 70-year-old female participant was diagnosed with PD in 2010 and drug-induced gastritis in 2016. Her major symptoms were related to GI, PD, and overall feeling of weakness. She was treated with KM including pharmacopuncture, acupuncture, moxibustion, and herbal medicines, in combination with Western medicines during 46 days of in-patient care. This study showed an improvement in symptoms and scores on the GI symptom scale, Unified Parkinson's disease rating scale, Hoehn and Yahr staging, Berg balance scale, PD quality of life, and stress index at discharge. This case demonstrated that the symptoms of drug-induced GI dysfunctions in PD was improved by treatment with KM.

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Introduction

Parkinson's Disease (PD) is the second-most common neurodegenerative disease in adults, however, its exact cause is unknown. There is not a cure for PD and symptomatic treatment including drugs and surgery, are often used to balance dopamine and acetylcholine concentrations. Treatment with levodopa, a precursor of dopamine, is known to be the most effective, but the long-term use can cause bloating, dyskinesia, and other adverse effects. Surgery can also have risks like any other brain operation [1-3]. Therefore, research into complementary and alternative medicine (CAM), and the synergistic effects of combination treatment with Western medicine are increasingly being reported [2-5].

PD is characterized by motor dysfunction (rigidity, tremors, slowness of movement (bradykinesia) and postural instability), and non-motor dysfunction [neuropsychiatric features, dysautonomia, sleep disorders, sensory dysfunction, pain, fatigue,

and gastrointestinal (GI) symptoms]. Among these symptoms, GI symptoms are 1 of the most common, serious non-motor dysfunctions that contributes to the reduction of the PD patient's quality of life. This results in an increase in healthcare costs, and disease-related morbidity and mortality. GI symptoms can occur when either the central or the enteric nervous system are involved in the disease process, in addition to the side effects produced by drugs for PD [6]. Levodopa has been shown to cause drug-induced GI side effects, with acupuncture used for the treatment of these symptoms [7].

In this case report, a 70-year-old female patient diagnosed with PD in 2010 and with drug-induced gastritis in 2016, was studied. The symptoms related to PD and drug-induced GI dysfunction were treated with Korean medicine (KM) including pharmacopuncture, acupuncture, moxibustion, and herbal medicines and the results of the treatment examined.

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Case Report

Case description

In this case, a 70-year-old female participant was diagnosed with PD in the Department of Neurology in 2010. While taking PD-related medications, she was diagnosed with drug-induced gastritis by gastric endoscopy in 2016. She was taking digestion-related medications, several inpatient treatments, and received several emergency room consultations. Her major complaints were GI symptoms (low appetite, dyspepsia, and constipation), and general PD symptoms (tremor, postural instability with general weakness, headache, dizziness, lower back pain, and numbness in both legs). Her symptoms were treated by hospitalization in April, 2018. However, these symptoms progressed in May, 2018, resulting in East-West collaborative treatment on June 1, 2018 at a Gachon University KM hospital. Her medical history showed that she had urinary stones in 1988, 1993, 1998, and 2013, fractures due to falls that were operated on (left ankle in 2002, right ankle and wrist in 2017), lumbar stenosis and thyroiditis in 2010, and cataract surgery on both eyes in 2018. These entries did not appear in her social and family history. This case report involved retrospective chart reviews, for which the patient provided informed consent, and approved by the Institutional Review Board of Gachon University Korean Medical Hospital (IRB No.: GIRB-19-103).

Intervention

Western medications

Trilevo Tab (levodopa 125 mg, carbidopa 31.25 mg, entacapone 200 mg) 3T#3, Mirapex Er 2T#2, Sinemet Cr Tab 1T#1 hs, Rivotril Tab 1T#1 hs, ULCERLMIN 4po#4, and Motilitone Tab 3T#3.

Acupuncture

The acupoints selected were the GV20, LR3, ST36, SP6, and GB34 acupoints which are commonly used in the treatment of PD [2] and in addition, ouch points (ashi points) were used according to the sites of symptoms. Moreover, on the days when essential bee venom (eBV) was not used for treatment, acupuncture was performed at Hyeopcheok (Huatuojiaji)-acupoints in the supine position. Acupuncture treatment was performed twice every weekday and once on weekend days, for 15 minutes. Acupuncture needles (0.25 mm in diameter and 40 mm in length, Dong Bang, Boryeong, Korea) were manually inserted to a depth of 15 mm to 20 mm, depending on the insertion site.

Pharmacopuncture

GI symptoms were treated using pharmacopuncture performed with Homince Placenta (HP) at CV4, CV12, and CV13 acupoints, and PD symptoms using pharmacopuncture with eBV at Hyeopcheok (Huatuojiaji)-acupoints. HP pharmacopuncture was performed once every 2 days in the prone position, and eBV pharmacopuncture was performed 2 times a week in the supine position. HP and eBV were provided by Jaseng Herbal Medicine Dispensary (Korean Good Manufacturing Practice compliant extramural facility). The total amount of 0.5-1.0 mL for HP, and 0.2-0.4 mL for eBV was injected into each site to a depth of 0.5-1.0 cm using a 30-gauge insulin syringe (Shinamed Co., Ansong, Korea).

Moxibustion

Moxibustion was first applied at the CV12 position (which is known to tonify the spleen qi), and at the CV4 position (which is known to improve resistance to disease and immunity) [8], twice

a day for 15 minutes to tonify qi and improve overall symptoms (including digestion function). From the 19th day of hospitalization, moxibustion was additionally applied at CV8, CV12, and CV15, twice a day for 30 minutes to help constipation.

Herbal medicine

During the first 5 weeks, the subject was prescribed modified Hyangsayukgunja-tang to treat spleen-deficiency and dyspepsia, and Kyungohkgo-pill was given upon request to treat urinary incontinence, 3 times a day (Table 1).

Clinical evaluation

To evaluate the patient's condition and the therapeutic effects of treatment, Hoehn and Yahr staging (H-Y stage), Unified PD rating scale (UPDRS), and Berg balance scale (BBS) were performed weekly to quantify PD symptoms, and the GI symptom scale (GSRS) was performed weekly to ascertain GI dysfunction. The degree of major symptoms was measured daily by numerical rating scales (NRS). The stress index was measured by uBioMacpa (Biosense, Seoul, Korea), and PD quality of life (PDQL) questionnaire was performed at admission to and discharge from hospital.

Results

Improvement on GI symptoms

At admission, the subject felt discomfort in the upper abdomen without appetite, so she had less than 1/6 of the normal amount of food each meal. She also had constipation and had only passed 1 hard stool in the last 2-3 days despite wanting to pass stool. The GSRS score was 19 and the NRS score was 7. After 1 week of treatment in hospital, she started to feel hungry with increased appetite. After 2 weeks of hospitalization, the portion of meals increased to 1/2 that of a normal portion, and she felt no discomfort. On the 19th day, the number of positions of moxibustion treatment was increased to treat the patient's constipation, which improved noticeably. From the 4th week of hospitalization, the meal portion size increased to 2/3 that of a normal portion, with the patient experiencing a little GI discomfort. Thereafter, the improvement in GI symptoms was sustained, and GSRS score was 1 and the NRS was 0-1, with improved bowel movement to once in 1-2 days with the stool appearing to be normal (compared with the previously hard stools), and there was no longer a constant feeling of constipation (Fig. 1A).

Improvement on the general symptoms on PD

At hospital admission, the patient stated that after taking her PD medication, she felt more hand tremors accompanied by a feeling of weakness in both legs until the medication disseminated. Tremor was increased at rest and reduced whilst walking, and her symptoms were evaluated as a score of 3 on the H-Y stage, 39 on the BBS, 30 on the UPDRS I, 29 on the UPDRS II, 89 on the UPDRS III, and 13 on the UPDRS IV. From the 12th day, the tremors started to improve and looked remarkably reduced. On the 3rd week, the general feeling of weakness and tremor suddenly worsened, but recovered within 3-4 days. After 4 weeks of hospitalization, her symptoms continued to improve. On the 5th week, there was heavy rain and the patient's condition suddenly deteriorated, but it recovered after 4-5 days. At discharge from hospital, the patient's symptoms showed improved scores in the H-Y stage, the BBS, and the UPDRS (Figs. 1B, 1C, 1D).

At admission to hospital, the patient had felt pain at the

Table 1. Components of Herbal Medications.

Time Period	Name	Scientific name	Dose (g) per administration
2018.06.01 - 2018.07.05	Modified Hyangsayukgunja-tang	Cyperi Rhizoma	4
		Amomum villosum	4
		Magnolia officinalis	4
		Fraxini Cortex	4
		Ginseng Radix	4
		Atractylodis Macrocephalae Rhizoma	4
		Paeoniae Radix Alba	4
		Atractylodis Rhizoma	4
		Dioscoreae Rhizoma	4
		Glycyrrhiza uralensis	2
		Zingiber officinale	3
		Pinelliae Tuber	3
		Amomum kravanh	3
		Longanae Arillus	4
2018.7.6 - 2018.7.16	Kyungohkgo-pill	Cervi Cornu	4
		Rehmanniae Radix Recens	4
		Ginseng Radix	0.4
		Poria Sclerotium	0.8
		Honey	2.5

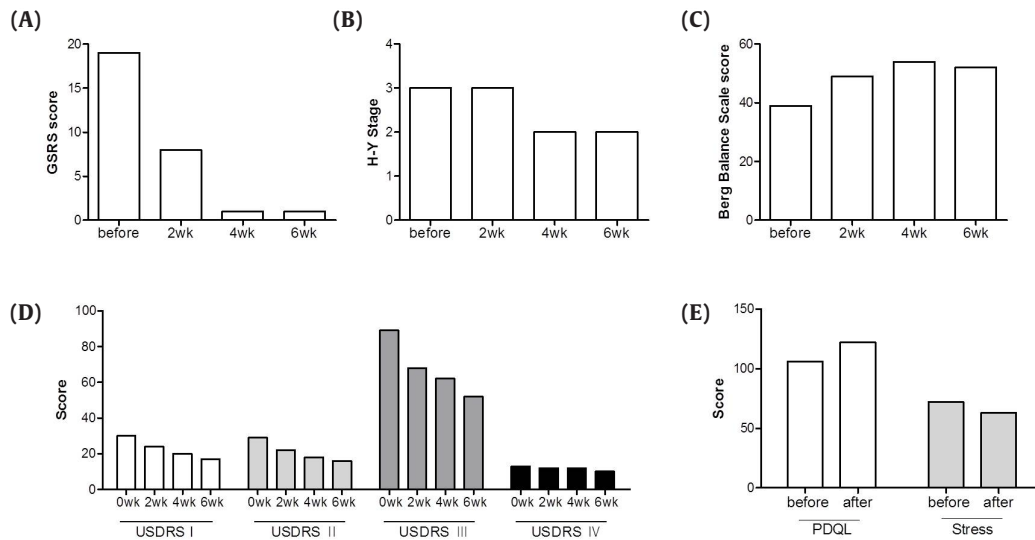


Fig. 1. Improvement on (A) GRS, (B) H-Y stage, (C) BBS, (D) UPDRS scores, (E) PDQL and Stress index. GRS, gastrointestinal symptom scale; H-Y stage, Hoehn and Yahr staging; BBS, Berg balance scale; UPDRS, unified PD rating scale; PDQL, Parkinson's disease quality of life questionnaire.

front and the left side of her head, as well as feeling dizziness, this was continuous and the NRS score was 7. After 1 week of hospitalization, the duration and intensity of symptoms decreased and the NRS score was 4. After 2 weeks, the symptoms occurred 1-2 times a day, lasting approximately 2 hours. At discharge from hospital, her headache and dizziness were mild, and the NRS score was 2 because her symptoms were occurring once a day with a 30 minute duration. Furthermore, at admission, she had lower back pain and numbness in both legs registering a score of 8 on the NRS. After 8 days, these symptoms showed a 50% improvement, and from the 4th week, there was a 50%-70% improvement. At discharge from hospital, the LBP and numbness in both legs was evaluated to be a score of 2 on the NRS.

Improvement on quality of life and stress index

The PDQL score at admission was 106, and the score improved to 126 at discharge from hospital. The stress index score was 72 at admission, which decreased to 63 at discharge (Fig. 1E).

Discussion

The exact cause of PD is unknown but it is thought that both genetic and environmental factors are involved. There is no cure for PD. Symptomatic treatment (including drugs and surgery), of PD usually aims to balance dopamine and acetylcholine levels [1] but there are side effects. CAM treatment of PD is increasing. More than 40% of PD patients in the United States and Europe have been reported to use CAM, and in another study an even higher percentage has been recorded in Europe and Asia [9,10]. In CAM, there are various treatment methods available, such as herbal medicines, acupuncture, pharmacopuncture, electroacupuncture, moxibustion, and cupping.

In this study, a 70-year-old female patient with PD and drug-induced GI symptoms was treated using KM methods, which involved pharmacopuncture, acupuncture, moxibustion, and herbal medicines in combination with Western medication during 46 days of inpatient treatment. Improvement in symptoms were observed and scores in the GSRs, UPDRS, BBS, H-Y stage, PDQL, and the stress index improved.

Acupuncture is 1 of the most popular CAM treatments for PD, and is reported to have the greatest benefit without adverse effects and without detrimentally affecting the PD Western medicine drug response. Acupuncture treatment of PD was reported to improve every aspect of functional daily life, including motor and neurological skills [2,11]. This current study employed acupuncture twice a day during the total treatment period. GV20, LR3, ST36, SP6 and GB34 acupoints were selected because they have been reported to be used in the treatment of PD [2]. Additionally, 4-6 touch points, were selected to perform acupuncture on (as determined by tenderness or other pathological responses for some symptoms such as headache, dizziness, lower back pain, and leg numbness).

Pharmacopuncture is a form of acupuncture that involves stimulating acupoints with injection of herbal medicine [12]. In CAM, HP which is a tonifying and replenishing medicine, has been reported to have anti-oxidant, anti-viral, anti-inflammatory, analgesic, anti-coagulant, and anti-osteoporotic effects, and it is reported to have neuroprotective effects on dopaminergic neurons in vitro and in vivo models of PD [13]. In addition, previous studies [14-16] have reported that HP pharmacopuncture had a therapeutic effect on pain and discomfort of severe dyspepsia. In this study, HP pharmacopuncture was used at CV4, CV12, and CV13 once every 2 days for the total treatment period in hospital, to help movement in the GI tract, and replenish qi and blood.

BV is a type of toxin extracted from honeybees that has been reported to have neuroprotection, anti-inflammatory, anti-apoptotic, anti-nociceptive, anti-fibrotic, and anti-atherosclerotic effects. It has been used therapeutically for various diseases including PD [5,17]. This current study also performed treatment with BV to treat PD. The type used was eBV, which was developed to reduce allergic reactions (by removing phospholipase A2 and histamine) [14] and was safely used to treat the patient's low energy and weakness of qi and blood, in spite of the previous experiences with BV. She was treated twice a week during the total treatment period, with no side effects. Hyeopcheok (Huatuojiaji)-acupoints was selected for eBV pharmacopuncture. Hyeopcheok (Huatuojiaji)-acupoints (located between the Governor Vessel and the Bladder meridian), can usually be selected by the distribution of meridians, nerve roots spinal cord, or by the presence or absence of tenderness in the acupoints, and has been reported to have effects on blood circulation, act as an analgesic, and have neuromodulatory effects [12,18]. At each treatment, the appropriate segment was chosen depending on the symptoms of the patient.

Moxibustion applies warm stimulation at acupoints and reportedly promotes blood circulation through enzyme activation, to stabilize the mental state through autonomic regulation, and restores intestinal motility, and relaxes muscle contraction [12]. These mechanisms may be in effect in the treatment of GI symptoms in the patient in this current study.

Hyangsayukgunja-tang was prescribed to decrease dyspepsia and increase appetite, and Kyungohkgo-pills were prescribed to address fatigue and offer replenishment for the source qi. However, neither treatment led to an improvement in the patient's symptoms compared with the immediate improvement pharmacopuncture offered.

Through the combined use of KM methods and Western medication, improvement of symptoms (including loss of appetite, dyspepsia, constipation, tremor, headache and dizziness, LBP, numbness in both legs, stress index, and scores of GSRs, UPDRS, BBS, H-Y stage, and PDQL) was observed.

In summary, this case study reported on 1 patient and observed that combined treatment of PD using Western medicine and KM, can help relieve PD symptoms and drug-induced GI dysfunctions. In further studies, a large sample size will be necessary to evaluate the therapeutic effects of each treatment.

Conflicts of Interest

The authors have no conflicts of interest to declare.

References

- [1] Korean neurological association. Neurology. Seoul (Korea): Koonja; 2007. [in Korean].
- [2] Kim DH, Sin DC, Song HS. Current Status of Intervention Studies on Acupuncture for Parkinson's Disease. *Acupunct* 2017;34:13-21.
- [3] Zhang G, Xiong N, Zhang Z, Liu L, Huang J, Yang J et al. Effectiveness of traditional Chinese medicine as an adjunct therapy for Parkinson's disease: a systematic review and meta-analysis. *PLoS One* 2015;10:e0118498.
- [4] Lee SH, Lim S. Clinical effectiveness of acupuncture on Parkinson disease: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)* 2017;96:e5836.
- [5] Cho SY, Shim SR, Rhee HY, Park HJ, Jung WS, Moon SK et al. Effectiveness of acupuncture and bee venom acupuncture in idiopathic Parkinson's disease. *Parkinsonism Relat Disord* 2012;18: 948-952.
- [6] Kim JS, Sung HY. Gastrointestinal Dysfunctions in Parkinson's Disease. *J Korean Neurol Assoc* 2015;33:247-251. [in Korean].
- [7] Yang DH, Lee KY, Shin HS, Jo SH, Lim CS, Lim JH et al. Clinical Study of Acupuncture Therapy of Gastrointestinal Side Effect of Levodopa: Focused

- on Idiopathic Parkinson's Disease Patients. *J Korean Acupunct Moxib Soc* 2010;27:11-21. [in Korean].
- [8] Jang SG, Kang JH, Im YG, Lee H, Lee BL. Influence on the Anti-cancer and Immune response improvement of Herbal-acupuncture with *Asparagus cochinchinensis* infusion solution put into Chung-wan (CV12) and Kwanwon (CV4). *J Korean Acupunct Moxib Soc* 2003;20:159-171. [in Korean].
- [9] Shulman LM, Wen X, Weiner WJ, Bateman D, Minagar A, Duncan R et al. Acupuncture therapy for the symptoms of Parkinson's disease. *Mov Disord* 2002;17:799-802.
- [10] Lökk J, Nilsson M. Frequency, type and factor associated with the use of complementary and alternative medicine in patients with Parkinson's disease at a neurological outpatient clinic. *Parkinsonism Relat Disord* 2010;16:540-544.
- [11] Lee MS, Shin BC, Kong JC, Ernst E. Effectiveness of acupuncture for Parkinson's disease: a systematic review. *Mov Disord* 2008;23:1505-1515.
- [12] Korean Acupuncture & Moxibution Soc. *Acupuncture Medicine*. Paju (Korea): Hanmi medical publishing co; 2016. [in Korean].
- [13] Jun HJ, Nam SS, Kim YS. Neuroprotection of Dopaminergic Neurons by Hominis Placenta Herbal Acupuncture in in vitro and in vivo Models of Parkinson's Disease Induced by MPP+/MPTP Toxicity. *Acupunct* 2015;32:23-36.
- [14] Lee AR, Kim WI. The Retrospective Comparative Study of General Acupuncture Therapy and Hominis placenta Pharmacopuncture Therapy on Severe Dyspepsia. *Korean J Acupunct* 2013;30:319-328. [in Korean].
- [15] Korean Pharmacopuncture Institute. *Pharmacopuncturology*. Seoul (Korea): Elsevier Korea LLC; 2011.
- [16] Nam SC. *Immuno Pharmacopuncture*. Seoul (Korea): Meridian and Collateral Med Book; 2009. [in Korean].
- [17] Hartmann A, Müllner J, Meier N, Hesekamp H, Van Meerbeeck P, Habert MO et al. Bee venom for the treatment of Parkinson disease-A randomized controlled clinical trial. *PLoS One* 2016;11:e0158235.
- [18] Chung HJ, Lee J, Shin JS, Kim MR, Koh W, Kim MJ et al. In Vitro and In Vivo Anti-Allergic and Anti-Inflammatory Effects of eBV, a Newly Developed Derivative of Bee Venom, through Modulation of IRF3 Signaling Pathway in a Carrageenan-Induced Edema Model. *PLoS One* 2016;11:e0168120.
- [19] Jung YP, Jung HK, Chiang SY, Wi J, Yoon YC, Chae WS et al. The clinical study of electroacupuncture treatment at Hua-Tuo-Jia-Ji-Xue on spondylolisthesis. *J Korean Acupunct Moxib Soc* 2008;25:221-232. [in Korean].