# Chinese herbal formula comprehensively and significantly ameliorated a range of autonomic symptoms accompanying Parkinson's disease: a case report

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# Abstract

We reported a Parkinson's disease (PD) patient with a range of severe forms of autonomic dysfunction, who achieved notable and comprehensive improvements in autonomic dysfunction, including orthostatic hypotension, anorexia, constipation, sexual dysfunction, intolerance to cold and heat, and hyperhidrosis, after taking a Chinese herbal formula (CHF). Furthermore, this CHF significantly reduced the total dose of antiparkinsonian drugs taken by the patient. Furthermore, the case report provides some clues about the pathogenesis of PD-related autonomic symptoms; that is, hypothalamic–pituitary–adrenal (HPA) axis hypofunction or kidney-*yang* deficiency may be the key mechanism for autonomic dysfunction in PD patients.


# Case History

The patient, a 77-year-old male, was admitted to our department on October 15, 2021, due to recurrent syncope caused by neurogenic orthostatic hypotension for 6 months. He had been suffering from PD for 12 years and was taking levodopa and benserazide hydrochloride tablets (250 mg per time, 4 times a day), entacapone tablets (0.2 g each time, 4 times a day), and pramipexole dihydrochloride sustained-release tablets (1.5 mg, once a day). The motor fluctuations in the patient were not obvious. Dyskinesia appeared as mild, whole-body, dance-like movements that occurred 1 hour after each administration of levodopa and lasted for approximately 1 hour, and this did not affect the daily life of the patient. The patient suffered from restless legs syndrome and took clonazepam 4 mg every night before going to bed. Due to constipation, the patient used 60 ml glycerine to defecate, and this entire process lasted for more than 30 minutes each time. The patient had been taking lactulose and probiotics for constipation; however, these treatments were not helpful. The blood pressure of the patient was 100/55 mmHg in the supine position; however, it dropped to zero when he stood upright; therefore, he had to stay in bed. When the patient had to stand to engage in some daily activity, he took 200 mg droxidopa; however, the effects of this drug lasted for only 1 hour. The patient had diabetes and was taking sitagliptin tablets and acarbose tablets. Typically, he could not tolerate the cold, and he did not smoke or drink alcohol. In addition, he would perspire excessively during both day and night and had low appetite, nausea and lethargy for more than 12 hours a day. The H&Y stage score of the patient was 3 points. The Part I A, Part I B, Part II, Part III, and Part IV scores on the 'on-period' MDS-UPDRS were 2, 17, 14, 22, and 3, respectively. The Scales for Outcomes in PD-Autonomic (SCOPA-AUT) total score was 39 points. A traditional Chinese medicine (TCM) examination showed that the tongue of the patient was dark and swollen, there were some cracks in the middle of the tongue, and the tongue coating was white. The pulse of the radial artery was weak. The routine blood and liver function tests indicated that the patient was normal; nevertheless, his creatinine level was 127 μmol/l. According to TCM theory, the patient was diagnosed with kidney-*yang* deficiency and blood stasis syndrome and was prescribed Sini Decoction as the main formula (Table 1). The herbs were put into water, boiled and concentrated into a 400-ml mixture. The patient took 200 ml each time, twice a day. Administration of droxidopa was discontinued. After taking the CHF for 4 days, the patient walked by himself, and the blood pressure and heart rate of the patient were 106/55

mmHg and 64 beats/min in the supine position, 115/60 mmHg and 70 beats/min after 1 minute of standing, 123/69 mmHg and 70 beats/min after 2 minutes of standing upright, and 127/67 mmHg and 71 beats/min after 3 minutes of standing. At the same time, a small amount glycerine was used to defecate, and the defecation course does not exceed 5 minutes each time. He was discharged from the hospital on October 21, 2021, and it was recommended that he continue taking the CHF as described above. On November 4, 2021, during a follow-up visit, the patient had no syncope or dizziness in the standing position after taking the CHF. His constipation had almost disappeared: he occasionally used a small amount of glycerine, and the defection process took less than 5 minutes each time. The appetite of the patient had returned to normal, and the nausea had disappeared. His drowsiness had disappeared, and he slept only 5 hours a day. The dyskinesia of the patient was worse than before; therefore, it was suggested that he gradually reduce the dose of antiparkinsonian drugs (Table 2). The antiparkinsonian drugs of the patient have been stable since December 30, 2021, and the levodopa equivalent dose of the patient was reduced from 1214 mg to 741 mg since this PD patient began taking the CHF. The clonazepam dose was also decreased to 1 mg before bedtime each night. Until now, the patient had no obvious off-period symptoms every day, and mild dyskinesia lasted for 1 hour after taking levodopa. At each visit, the CHF was adjusted according to the changes in the patient's medical condition (Table 1). On November 4, 2021, the tongue of the patient returned from a dark color to light red, so *Leech* and *Ground Beetle* were removed from the herbal formula. On December 2, 2021, the defecation of the patient had returned to normal, so *Citrus Aurantium* was removed from the formula. After the third visit of the patient, the composition of the CHF remained unchanged. On March 2, 2022, the patient returned to my clinic and reported that he had discontinued CHF on his own from January 3, 2022, to January 10, 2022, at which point, the constipation, dizziness and bradykinesia of the patient slightly worsened. After this event, the patient resumed taking the CHF. In the clinic, the patient completed some scales and questionnaires. Part I A, Part I B, Part II, Part III, and Part IV of the ‘on-period’ MDS-UPDRS were separately scored as 1, 7, 13, 21, and 3. The total SCOPA-AUT score was 13 (Table 3). The patient had normal routine blood and liver function test results, and his creatinine was 132 mmol/l on March 1, 2022. The patient has had no new complaints since he began taking the CHF. The patient views himself as an almost normal old man and is very satisfied with the current treatment plan.

Table 1
Chinese herbal formulae used by the patient from Oct 15, 2021, to Dec 2, 2021

| Chinese herbal formula (dose, g) | 10/15/2021 | 11/4/2021 | 12/2/2021 |
|---|---|---|---|
| *Aconite* | 15 | 15 | 15 |
| *Dried Ginger* | 10 | 10 | 10 |
| *Licorice* | 10 | 10 | 10 |
| *Antler Cream* | 10 | 10 | 10 |
| *Cistanche* | 20 | 20 | 20 |
| *Hemp Seed* | 20 | 20 | 20 |
| *Bupleurum* | 25 | 20 | 20 |
| *Citrus Aurantium* | 15 | 15 | |
| *Ophipogon Japonicus* | 30 | 30 | 30 |
| *Chinese Yam* | 30 | 30 | 30 |
| *Astragalus* | 60 | 60 | 60 |
| *Angelica* | 20 | 20 | 20 |
| *Codonopsis* | 15 | 15 | 15 |
| *Jujube* | 20 | 20 | 20 |
| *Leech* | 10 | | |
| *Ground Beetle* | 10 | | |

Table 2
Changes in antiparkinsonian drugs used by the patient from Oct 15, 2021, to Dec 30, 2021.

| Antiparkinsonian drugs | 10/15/2021 | 11/4/2021 | 12/2/2021 | 12/30/2021 |
|---|---|---|---|---|
| Levodopa and benserazide hydrochloride, mg | 250, q6h | 250, q6h | 250, q6h | 187.5, q6h |
| Entacapone, g | 0.2, q6h | 0.2, q6h | 0.1, bid | 0.1, bid |
| Pramipexole dihydrochloride sustained release, mg | 1.5, qd | 0.75, qn | 0.75, qn | 0.75, qn |

Table 3
Scales for Outcomes in Parkinson's Disease (SCOPA) autonomic (SCOPA-AUT) results for the patient before and after CHF.

| | 10/15/2021 | 12/30/2021 |
|---|---|---|
| 1. In the past month have you had difficulty swallowing or have you choked? | 2 | 1 |
| 2. In the past month, has saliva dribbled out of your mouth? | 1 | 0 |
| 3. In the past month, has food ever become stuck in your throat? | 1 | 1 |
| 4. In the past month, did you ever have the feeling during a meal that you were full very quickly? | 3 | 0 |
| 5. *Constipation is a blockage of the bowel, a condition in which someone has a bowel movement twice a week or less.* In the past month, have you had problems with constipation? | 4 | 0 |
| 6. In the past month, did you have to strain hard to pass stools | 4 | 0 |
| 7. In the past month, have you had involuntary loss of stools? | 0 | 0 |
| 8. In the past month, have you had difficulty retaining urine? *(Extra: use catheter)* | 1 | 1 |
| 9. In the past month, have you had involuntary loss of urine? *(Extra: use catheter)* | 1 | 1 |
| 10. In the past month, have you had the feeling that after passing urine your bladder was not completely empty? *(Extra: use catheter)* | 1 | 1 |
| 11. In the past month, has the stream of urine been weak? *(Extra: use catheter)* | 1 | 0 |
| 12. In the past month, have you had to pass urine again within 2 hours of the previous time? (Extra: use catheter) | 1 | 1 |
| 13. In the past month, have you had to pass urine at night? (Extra: use catheter) | 3 | 2 |
| 14. In the past month, when standing up have you had the feeling of becoming either light-headed, or no longer being able to see properly or no longer being able to think clearly? | 3 | 0 |
| 15. In the past month, did you become light-headed after standing for some time? | 2 | 0 |
| 16. Have you fainted in the past 6 months? | 2 | 0 |
| 17. In the past month, have you ever perspired excessively during the day? | 2 | 0 |
| 18. In the past month, have you ever perspired excessively during the night? | 2 | 0 |

| | 10/15/2021 | 12/30/2021 |
|---|---|---|
| 19. In the past month, have your eyes ever been oversensitive to bright light? | 2 | 1 |
| 20. In the past month, how often have you had trouble tolerating cold? | 2 | 0 |
| 21. In the past month, how often have you had trouble tolerating the heat? | 2 | 0 |
| 22. In the past month, have you been impotent (unable to have or maintain an erection)? *(Extra: not applicable)* | 4 | 2 |
| 23. In the past month, how often have you been unable to ejaculate? *(Extra: not applicable)* | 4 | 2 |
| 23a. In the past month, have you taken medication for an erection disorder? (If so, which medicine?) *(no or yes)* | no | no |
| 24. In the past month, have you used medication for: | | |
| a. constipation? *(no or yes)* | yes | no |
| b. urinary problems? *(no or yes)* | no | no |
| c. blood pressure? *(no or yes)* | no | no |
| d. other symptoms *(no or yes)* | no | no |

# Discussion

From this case report, we can see that the SCOPA-AUT total scores of the patient sharply decreased from 39 at first admission to 13 three months after taking CHF, especially in gastrointestinal functioning and cardiovascular functioning. Even when the patient discontinued the CHF, these beneficial effects did not immediately disappear. At the same time, the CHF also significantly reduced the levodopa equivalent dose from 1214 mg to 741 mg. Therefore, the CHF was a very successful treatment for this PD patient. To date, there is no treatment that comprehensively and significantly improves autonomic dysfunction related to PD and decreases the levodopa equivalent dose in PD patients. From before to after treatment, the patient's routine blood, liver and kidney function did not significantly change, and he had no new complaints, which confirmed the safety of CHF.

Almost all PD patients experience autonomic dysfunction, and with the prolongation of the disease course, these autonomic symptoms significantly contribute to a deterioration of quality of life in PD patients [1–2]. Therefore, the guidelines for the treatment of nonmotor symptoms in PD patients were updated again in 2019 [3]. However, in general, these treatments are symptomatic treatments, the level of evidence for these treatments is not high, and the efficacy of the treatments is indefinite. For example, the patient in this report had been treated according to the guidelines; however, the effects on orthostatic hypotension and constipation were not adequate. At the same time, most PD patients experience a

variety of autonomic symptoms, which leads to patients taking all kinds of drugs. Therefore, thus far, such treatments for autonomic dysfunction have not been successful and satisfactory. Palma et al. suggested that pathophysiology-based drug therapy was key to effective management for autonomic dysfunction [4]. We think that the key reason that this patient achieved marked and comprehensive improvements in the autonomic symptoms experienced by PD patients is that the CHF is a pathophysiology-based therapy. According to TCM theory, the autonomic symptoms associated with PD are manifestations of kidney-*yang* deficiency, which can be induced in animal models by glucocorticoid administration [5]. The manifestations of kidney-*yang* deficiency mainly consist of weakness, dizziness, chills, constipation, low sexual function, lethargy, low appetite and so on, which is very similar to the clinical symptoms of hypothalamic–pituitary–adrenal (HPA) axis hypofunction. TCM believes that kidney-*yang* deficiency is a term for a certain pathological state that reflects systemic hypofunction and that kidney-*yang* deficiency can appear in certain stages during the pathogenesis of different diseases [6], which is basically consistent with modern medicine's understanding of HPA axis hypofunction. Therefore, some scholars think the essence of kidney-*yang* deficiency in TCM is equivalent to HPA axis hypofunction described in modern medicine [5–7]. At the same time, we found that the manifestations of HPA axis hypofunction were similar to the autonomic symptoms associated with PD. A number of animal experiments have shown that administration of drugs that strengthen kidney-*yang* can significantly improve clinical manifestations of hypofunction of the glucocorticoid-induced HPA axis and increase cortisone and 17-hydroxycorticosteroid levels [5, 8–9]. Xu et al. found that strengthening kidney-*yang* was effective in improving the quality of life and reducing drug dosage in PD patients with kidney-*yang* deficiency by protecting dopaminergic neurons [10]. Therefore, we think the pathophysiology of the autonomic symptoms related to PD are probably related to HPA axis hypofunction or kidney-*yang* deficiency, which, of course, requires more clinical trials to study the associations between autonomic symptoms accompanied by PD and HPA axis activity to support our hypothesis.

To date, there has been no treatment enhancing the function of the HPA axis for clinical use in modern medicine. However, many Chinese medicinal herbs can ameliorate HPA axis hypofunction [5, 8–10] or kidney-y*ang* deficiency, such as *Aconite, Dried Ginger, Deer Antler Cream, Cistanche*, and *Astragalus Membranaceus*, which had been taken by this patient. Therefore, we can consider treating autonomic symptoms accompanied by PD by using a CHF.

The strength of our work lies in the detailed description of the condition, diagnosis and treatment of autonomic impairment in PD patients and the analysis of the possible mechanisms for the successful TCM treatment of autonomic dysfunction. However, the major limitations consist of the lack of ability to generalize and limited support within the scientific literature.

In conclusion, a CHF may be an alternative therapy for PD patients with autonomic dysfunction, which may comprehensively and significantly ameliorate a range of autonomic symptoms and reduce the total dose of antiparkinsonian drugs. Furthermore, the case report provides some clues about the pathogenesis of PD-related autonomic symptoms; that is, HPA axis hypofunction may be the key mechanism for autonomic dysfunction in PD patients.

# Declarations

**Author contributions** Yong Zhang conceived of the case report and wrote the manuscript. All authors read, edited, reviewed, and approved the final manuscript.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflicts of interest.

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