Review

A Practical Consensus Guideline for the Integrative Treatment of Parkinson's Disease in Shanghai, China

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Key Words

Consensus guideline · Parkinson's disease · Integrative medicine · Traditional Chinese medicine · Complementary and alternative medicine · Acupuncture · Tai chi chuan · Yoga · Preventive treatment

Abstract

Integrative medicine, including traditional Chinese medicine (TCM), is a new concept in clinical practice for the treatment of neurodegenerative and most chronic diseases. However, integrative consensus or a guideline for the management of patients with Parkinson's disease (PD) is still lacking. The aim of this paper is to provide a review of experiences in clinical practice from Chinese neurologists and physicians (including TCM doctors) in Shanghai, China, and try to provide a clinical guideline for the treatment of the complex and progressive disease of PD with integrative medicine. We included the following treatments: common Western medication, surgery, TCM decoction and patent medicines, acupuncture and Tui na, Yoga, Tai chi chuan, hyperbaric oxygenation, rehabilitation, and other complementary and alternative

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medicines for the integrative management of the disease. Neurologists and physicians in Shanghai, China, and all over the world should pay attention to integrative medicine, which may be a good choice of treatment for PD.

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Background

Integrative treatment for Parkinson's disease (PD) such as dopaminergic therapy, neuro-protective therapy, and traditional Chinese medicine (TCM) might be the unmet medical needs to slow down or stop disease progress [1, 2]. The current therapies include Western medicine (oral medicine), surgery, physical therapy (kinesiotherapy), psychological counseling, and nursing care, whereas traditional medicines provide beneficial effects on symptoms that help to control the classic motor features of the disease (i.e., tremor, rigidity, and bradykinesia) as well as the non-motor symptoms, including autonomic disturbance, dementia, sleep disturbance, psychiatric disorders, and depression; however, eventually, intolerable disability and invalid clinical effects develop in most patients with PD [3]. Over the past 3 decades, significant progress has been achieved in the diagnosis and treatment of PD in China. Not only TCM but also other integrative medicine proved more and more important in treating the disease in Shanghai, China [4]. Movement disorder clinics and associated centers only exist in part of the tertiary hospitals, and the resources cannot satisfy the need of most patients with PD [5]. In many cases, both general neurologists and physicians are responsible for the diagnosis and treatment of PD patients and are sometimes treating them without adhering to the guidelines. For almost 5 years, the management of PD has been improving. A consensus was prepared according to the guideline from the Chinese Parkinson's Disease and Movement Disorders Society for the management of PD (third edition) [6] which summarized the integrative clinical research in China [4, 7–10]. It is important that neurologists and TCM doctors offer more effective and reasonable integrative treatment to their patients. However, the opinions of physicians, general neurologists, and movement disorder specialists in the clinical practice for the treatment of PD are diverse, which will have a significant influence on the actual benefits of patients suffering from the disease.

Principle of Treatment

Integrative Treatment

Most patients with PD have motor and/non-motor symptoms in the early or later stages of the disease. These symptoms not only influence the ability to work but also the activities of daily living (ADL). PD cases should be treated individually, including oral medicine, operations, exercise, psychotherapy, and health care as effective treatment options. Oral medicine is the main treatment choice, and surgery, such as deep brain stimulation (DBS), may be initiated as independent therapy or a complementary and alternative method to assist oral medicine [11, 12]. So far, all therapies have improved the symptoms of PD, but they could not stop disease progression. We should thus focus on the long-term management of PD in order to extend the treatment period, delay disease progression, and decrease the side effects of medical therapy.

Principle of Medication

Both motor and non-motor symptoms can influence the ADL of patients suffering from PD, and neurologists or physicians should aim to control the symptoms early, thus improving the ability to work and the ADL. Early diagnosis and early medication can improve symptoms,

delay progression, and prevent motor fluctuation and dyskinesia. The compound levodopa or dopamine receptor agonist used for the treatment of motor symptoms should be started at a small dosage and increased slowly according to the progression of the disease. Individual medication management may be more effective and lessen the side effects with regard to tremor (with/without), dementia (with/without), age at morbidity, occupation, combinative diseases, potential side effects, aspiration, and the economic situation of the patients. Dopaminergic treatment should not be stopped abruptly in order to avoid dopaminergic dysregulation syndrome [6].

Internal Medicine (Oral Medication)

According to its severity, PD has been divided into two stages – the early stage (Hoehn-Yahr 1–2.5), and the middle and severe stages (Hoehn-Yahr 3–5).

PD Patients in the Early Stage

As evidence indicates that the development of PD in the early stage is faster than in the middle and severe stages [13, 14], it is necessary to treat PD patients with oral medication in the early stage, which includes Western medicine and/or TCM and/or other complementary and alternative medicine (CAM). Dopaminergic medicine and/or monoamine oxidase B inhibitors, vitamin E, herbs, complementary nutrition, and even physical therapy (kinesiotherapy), psychological counseling, and nursing care can be used. The aim of the treatment is to improve the mild movement disorders, such as rigidity, tremor, and some non-motor symptoms, and delay disease progression.

In the case of early-onset PD without dementia, we suggest that neurologists or physicians use a non-ergot dopamine receptor agonist, such as pramipexole, piribedil, and ropinirole, monoamine oxidase B inhibitors, such as selegiline and rasagiline, adamantanamine, or compound levodopa, such as Madopar or Sinemet combined with or without entacapone [6]. If the symptom of tremor cannot be controlled, benzhexol is also a good choice. Most tonifying TCM components or patent medicines can be used in treating this stage of PD, such as 'Liu-Wei-Di-Huang-Wan' (六味地黃丸), 'Zhen-Gan-Xi-Feng-Tang' (鎮肝熄風湯), 'Tian-Ma-Gou-Teng-Yin' (天麻勾藤飲), 'Ma-Ren-Zi-Pi-Wan' (麻仁滋脾丸), 'Cong-Rong-Tong-Bian-Kou-Fu-Ye' (從蓉通便口服液), and others [4, 12].

In the case of later-onset PD, cognitive impairment, or dementia, the compound levodopa is the first-choice treatment. With progression of the disease, dopamine receptor agonist, monoamine oxidase B inhibition, or compound levodopa combined with entacapone are beneficial choices. Cholinergic resistance should be avoided, especially for elderly, later-onset PD patients with cognitive impairment [6].

PD Patients in the Middle and Severe Stages

Symptoms will become more complex for patients in the middle and severe stages, due to the development of the disease, the side effects of medication, and motor complications such as motor fluctuation and dyskinesia. The scope of treatment in these stages is to improve the movement disorders, motor complications, and non-motor symptoms.

Motor fluctuations such as end-of-dose deterioration, on-off phenomenon, and dyskinesia (abnormal involuntary movements) are common motor complications in the severe stages of PD. Changing the kind of medication as well as modifying the dose and dosing time may help to improve the complex symptoms. Insect TCM drugs such as stiff silkworm (僵蠶), earthworm (地龍), scorpio (全蝎), and centipede (蜈蚣), as well as tonifying 'Gan' (liver) and 'Shen' (kidney) TCM herbs are helpful in modifying the doses and dosing times of Western medicine adminis-

tered to these patients. TCM doctors not only use oral TCM decoction or patent medicine, but they also individually use TCM as external application to improve complex complications. Sometimes, DBS, Tai chi chuan, and acupuncture can be used as additional non-drug treatments.

Traditional Chinese Medicine

The Theory of TCM in PD Treatment

TCM has gained increasing attention in the treatment of PD. Although it is not curative, it may play a significant role in delaying disease progression and reducing the side effects of Western medicine, as well as improving the patients' ability to perform their ADL [7, 8]. TCM ameliorates various symptoms, particularly the age-related symptoms that are called 'Shen xu' (kidney deficiency) in Chinese. 'Shen' (the kidney) denotes a functional visceral system ('Zang') that plays a central role in the regulation of growth, maturation, and aging and is subdivided into 'Shen yang' (kidney 'yang') and 'Shen yin' (kidney 'yin'). Kidney 'yang' can be described as the driving force of all metabolic processes that improve the movements of the body. The production of kidney 'yin' is considered to be effective in increasing nutrition to the muscles and improving the smoothness of body movements by constituting the constructive potential for the production of kidney 'yang'. Based on this concept, TCM aims to potentiate the diminishing vitality of this transformative cycle caused by a decline in the essence ('Jing'), which is stored in the kidneys and underpins the functions of both kidney 'yin' and 'yang' [7]. In TCM theory, most PD patients (about two thirds) belong to 'deficiency in "yin" or "Jing" and "yang" or "Qi" in "Gan" (liver) and "Shen" (kidney)' by TCM 'Zheng' classification, whereas the other 'Zheng' such as blood stasis, deficiency in 'Qi' with blood, and phlegm are much less than the first 'Zheng' [15].

TCM Treatment in PD

Our consensus guideline suggests that decoction with medicinal ingredients or Chinese patent medicine tonifying the 'yin' and 'yang' of 'Gan' (liver) and 'Shen' (kidney) may be useful to treat or improve rigidity, tremor, bradykinesia, sleep disorders, constipation, depression, anorexia, and automatic symptoms using 'Di-Huang-Yin-Z' (地黃飲子), 'Da-Ding-Feng-Zhu' (大定風珠), 'Zhen-Gan-Xi-Feng-Tang' (鎮肝熄風湯), 'Tian-Ma-Gou-Teng-Yin' (天麻勾藤飲), 'Da-Bu-Yin-Wan' (大補陰丸), 'Ren-Shen-Yang-Rong-Tang' (人參養榮湯), and others, according to the 'Zheng' classification of PD [15]. Other TCM decoctions or patent medicines such as 'Dao-Tan-Tang' (導痰湯), 'Tian-Wang-Bu-Xin-Dan' (天王補心丹), 'Gui-Pi-Tang' (歸脾湯), 'Bu-Yang-Huan-Wu-Tang' (補陽還五湯), 'Qi-Ju-Di-Huang-Tang' (杞菊地黃丸), 'Ma-Ren-Wan' (麻仁丸), 'Yang-Xue-Qing-Nao-Ke-Li' (養血清腦顆粒), and others may improve some of the other non-motor symptoms of the other 'Zheng' classification patients with PD. If the TCM doctor or neurologist is an expert in TCM, he may make an individual prescription choosing ingredients according to the individual manifestation of 'Zheng' and the 'pulse' properties of the patient. All of the TCM therapies can be used for all stages and periods of PD [7, 15–18]; if the patient suffers from dysphagia, TCM medication can be taken via a nasogastric tube.

Acupuncture and 'Tui na' (推拿, TCM massage) are often used as complementary treatment for PD patients with motor and non-motor symptoms; sometimes, the two therapies are used in early-onset PD as initial management to delay disease progression [19]. Acupuncturists and massagers may choose acupoints according to TCM theory which may tonify the 'yin' and 'yang' of 'Gan' and 'Shen' or which may prompt the blood circulation of the body and/or remove blood stasis. The acupoints normally used are 'Chen Shan' (承山, BL57), 'Tai Xi' (太溪, KI3), 'Tai Chong' (太衝, LR3), 'Shen Shu' (腎腧, BL23), 'Zu San Li' (足三里, ST36), 'San Yin Jiao' (三陰交, SP6), 'Xue Hai' (血海, SP10), 'Yang Lin Quan' (陽陵泉, GB34), 'He Gu' (合谷, LI4), 'Qu Chi' (曲池, LI11), 'Du Bi' (犢鼻, ST35), 'Shou San Li' (手三里, LI10), 'Pi Shu'

(脾腧, BL20), 'Gan Shu' (肝腧, BL18), 'Wei Zhong' (委中, BL40), 'Yin Lin Quan' (陰陵泉, SP9), 'Yao Yang Guan' (腰陽關, DU3), 'Ming Men' (命門, DU4), 'Qi Hai' (氣海, RN6), and 'Guan Yuan' (關元, RN4) [20–26].

Tai chi chuan is an effective treatment improving the stability of PD patients [27–29] and can be used to control some of the non-motor symptoms such as automatic impairment, sleep disorders, and depression. Any type of Tai chi chuan can be used for the improvement of the disease. Those PD patients who cannot keep a standing posture for the exercise of Tai chi chuan may remain seated until they are gradually able to stand up for the training [28–30]. The core of Tai chi chuan is to move the body by mind direction slowly, which differs substantially from aerobic and strength exercises [28].

Other Integrative Treatment or Exercises

Surgery

Most patients in the mild stage or with early-onset PD react well to anti-parkinsonism treatment and/or TCM and/or CAM. Surgery may be used in two situations. Firstly, with the progression of PD, motor fluctuation, dyskinesia, and even on-off phenomenon will occur, and DBS will be used to improve the movement disorders of the patients [11]. Secondly, if the patients suffer from very heavy motor symptoms such as tremor or rigidity, or the medication used shows a lack of efficacy, they may start treatment with DBS. We emphasize that DBS is most effective against tremor and rigidity and is not the first choice for posture and balance disorders. Age and the course of the disease are the selective factors for treatment with DBS [11, 12].

Aerobic Exercise, Strength Exercise, Yoga, Hyperbaric Oxygen, Rehabilitation, Psychological Guidance, and Health Care

These integrative therapies or exercises are helpful in improving rigidity, balance disorder, and parts of the non-motor symptoms, and some patients have self-initiated these activities or treatments during all periods or stages of anti-parkinsonism treatment [31–33]. Psychological guidance is useful to reduce depression, and health care is important to prevent inflammation, nutrition impairment, falls, and fractures. These exercises or therapies are not the main treatment for improving the symptoms of PD [34–40].

Supplementary Treatment

Ginkgo supplementary, Ginseng supplementary, *Rhodiola rosea* supplementary, melatonin, deep sea fish oil, and American ginseng are often used to improve fatigue, memory impairment, weakness, automatic impairment, and sleep disorders of PD patients, suggested by family members or patients themselves [41, 42]. These CAM are not harmful, but there is still no evidence-based research supporting their intake except for melatonin [43–45].

Preventive Treatment

PD is a progressive neurodegenerative disease; previous to morbidity, most patients have various preclinical symptoms such as sleep disorders, restless leg syndrome, olfactory dysfunction, and cognitive impairment. With the progression of these symptoms, patients tend to suffer from PD; our consensus guideline suggests that these patients should be treated in the preclinical stage to slow down or stop disease progression. Preventive treatment has two implications [44, 45]: firstly, to reduce or stop suffering from the disease, and secondly, to slow down the progression of PD. The TCM compound cream formula (膏方), herbs which

may tonify the 'yin' and 'yang' functions of 'Gan' and 'Shen', vitamin E, Ginkgo supplementary, Ginseng supplementary, *R. rosea* supplementary, melatonin, deep sea fish oil, and American ginseng may partly present alternative preventive therapies [2, 46, 47], but there is still a lack of evidence-based research.

Conclusion

There are no absolute fixed models for the management or treatment of PD, and thus, patients should be treated individually according to their condition, which may have its own individual sensitivity and specificity for each patient. Even the same patient may be treated by different medication in different stages of the disease. The choice of diagnostic methods and therapeutic strategies for PD varies among physicians, general neurologists, and movement disorders specialists. Further consensus programs on the diagnosis and management of PD patients are warranted, especially for physicians and general neurologists caring for PD patients in China. The aim and scope of this consensus guideline was to emphasize that neurologists and physicians (including TCM doctors) should pay attention to integrative therapy in the treatment of PD patients.

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