

# Exploration on the Comprehensive Advantages of Integrative Chinese and Western Medicine in the Treatment of Parkinson's Disease

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**Abstract:** *Parkinson's disease is a chronic neurodegenerative disease, which is prone to occur in the middle-aged and elderly. With the progression of the disease, multiple systems can be affected, and eventually the patient becomes disabled. This not only seriously affects the patient's work and life, but also brings a heavy burden to society and family. Although Parkinson's disease is characterized by incurability and high disability, it has a long course and slow progression with strong clinical intervention. Based on this, the reasonable, effective and long-term diagnosis and treatment of Parkinson's disease are put forward higher requirements. We cannot deny that western medicine plays a pivotal role in the treatment of Parkinson's disease. However, with the aggravation of motor symptoms and non-motor symptoms as well as the emergence of adverse drug reactions and motor complications, the limitations of western medicine in the diagnosis and treatment of Parkinson's disease have become increasingly prominent. A large number of clinical studies have shown that traditional Chinese medicine has significant advantages in the treatment of Parkinson's disease, especially in the early stage of Parkinson's disease and the improvement of non-motor symptoms of Parkinson's disease. Therefore, the treatment of Parkinson's disease with traditional Chinese medicine should not only become a beneficial attempt in its clinical research and diagnosis, but also become a routine process in the diagnosis and treatment of Parkinson's disease. Integrative Chinese and Western medicine can complement each other, improve the curative effect, reduce the side effects of western medicine, and effectively control the motor and non-motor symptoms of Parkinson's disease.*

**Keywords:** Parkinson's disease, Treatment with traditional Chinese medicine, Integration of traditional Chinese medicine and western medicine, Comprehensive advantage.

## 1. Introduction

Parkinson's disease (PD) is the second largest neurodegenerative disease after Alzheimer's disease [1]. A report based on the prevalence of Parkinson's disease pointed out that with the increase in global life expectancy, the number of Parkinson's disease patients over 50 years old will more than double to 9.3 million by 2030 compared with 2005, and the number of people suffering from Parkinson's disease is becoming younger and younger [2]. It is reported that the total number of Parkinson's disease patients in China may be as high as 3.62 million. By 2030, 50% of the global Parkinson's disease patients will be from China [3]. And the average life expectancy of PD patients can be up to 17 years since the diagnosis. Based on this, it is very important to establish long-term, effective standardized treatment strategy [4]. Parkinson's disease is mainly manifested as motor symptoms and non-motor symptoms. Motor symptoms include resting tremor, bradykinesia, myotonia, and postural balance disorders; Non-motor symptoms are complex and diverse, mainly manifested as sensory disorders, sleep disorders, autonomic nervous dysfunction and mental and cognitive disorders. Although Parkinson's disease is an ancient disease, the etiology and pathogenesis of Parkinson's disease are not fully understood at present, which may be the main reason why Parkinson's disease cannot be cured. It is currently recognized that the degeneration and loss of large numbers of dopaminergic neurons in the substantia nigra and the appearance of eosinophilic inclusion bodies—Louis bodies in the residual neurons are related, which finally lead to the imbalance of two major neurotransmitters dopamine and acetylcholine in the striatum, causing the dysfunction of

the "cortex-basal ganglia-thalamus-cortex" circuit and a series of motor symptoms [5]. However, the mechanism study of non-motor symptoms of PD is still unclear and there is no unified consensus. Although many of the non-motor symptoms in PD precede motor dysfunction and span preclinical stages of 20 years or more, few animal models reproduce the non-motor symptoms in PD, which leaves no clear direction for its mechanism research [6], clinical treatment to symptomatic drugs, relieve symptoms.

## 2. The Western Medicine Treatment of Parkinson's Disease and Its Limitations

### 2.1 Western Medicine Treatment of Parkinson's Disease

Due to the unique pathogenic characteristics of Parkinson's disease, its treatment advocates an individualized, multidisciplinary and comprehensive treatment mode, aiming to develop an individualized plan through multi-disciplinary cooperation, effectively control the symptoms of multiple systems of patients, improve the ability of daily life and the quality of life [7]. Up to now, drug therapy is still the first choice for the treatment of Parkinson's disease and the main treatment during the whole treatment process. Surgical treatment is an effective complement to drug therapy. Other treatments include rehabilitation and psychological treatment, as well as promising stem cell therapy which is still in the exploratory stage [8].

Although there are various medications clinically available that can effectively improve the motor symptoms of Parkinson's disease, their general mechanism of action

involves restoring the balance between dopamine and acetylcholine neurotransmitters. These medications can be divided into cholinergic drugs (anticholinergics) and drugs that improve dopamine neurotransmitter function, including amantadine, levodopa preparations, dopamine agonists (DAs), monoamine oxidase type B inhibitors (MAO-BI), and catechol-O-methyltransferase (COMT) inhibitors. While MAO-BI and DAs are thought to potentially have disease-modifying effects, sufficient evidence-based medical evidence has not yet emerged to confirm that any specific drug can delay the progression of Parkinson's disease. In other words, regardless of the medication chosen, it can only improve symptoms and delay the course of the disease, but cannot stop the progression of the condition nor cure it [9].

Catechol-O-methyltransferase (COMT) inhibitors are a class of medications used in the treatment of Parkinson's disease. While monoamine oxidase type B inhibitors (MAO-BI) and dopamine agonists (DAs) are believed to potentially possess disease-modifying effects, sufficient evidence-based medical evidence has not yet emerged to confirm that any specific drug can delay the progression of Parkinson's disease. In other words, regardless of the medication chosen, it can only improve symptoms and delay the course of the disease, but cannot stop the progression of the condition, nor can it cure it. Therefore, current therapeutic strategies primarily focus on managing symptoms and maintaining the patient's quality of life.

## 2.2 Early Diagnosis and Staging of Parkinson's Disease

Parkinson's disease has an insidious onset and atypical early symptoms, and its clinical features may overlap with those of other neurodegenerative diseases. In addition, so far, no biomarker or imaging detection method with high sensitivity and specificity has been identified for the diagnosis of parkinson's disease, so not only its early recognition is difficult, but its accurate diagnosis is also a challenge [10].

In clinic, the modified Hoehn-Yahr classification is usually used to record the severity of Parkinson's disease. The general principles of treatment for PD in different stages are different. Among them, Hoehn-Yahr grades 1.0-2.5 were the early stages of Parkinson's disease. The patients only had slight involvement of unilateral or bilateral limbs, and they could take care of themselves completely in daily life. The course of disease in this stage progressed faster than that in the later stages, and the clinical treatment effect was significant. Early diagnosis and early treatment were advocated. Drug intervention and non-drug intervention can be carried out with the basic purpose of meeting the needs of daily life of patients. According to the individual needs, we strive to achieve the goal of optimal efficacy, longer maintenance time and the lowest incidence of sports complications. Hoehn-Yahr grade 3 was the middle stage of Parkinson's disease, in which the bilateral limbs and balance were involved, the motor function was moderately damaged, and others' assistance was often needed in daily life. The clinical treatment effect was acceptable. In this stage, drug therapy was mainly used, and surgical treatment could be used as an effective supplement. Grade 4-5 is the advanced stage of Parkinson's disease, in which the patients have severe bilateral limb involvement and are unable to take care of themselves in daily life. The clinical

manifestations at this stage are extremely complex and involve many factors, including not only the progression of the disease itself, but also adverse drug reactions or exercise complications. Although there are various treatment methods, the clinical treatment effect is often unsatisfactory, and palliative treatment can be selected at this stage [11].

Based on the whole course progression of parkinson's disease, the concept of prodromal stage was proposed. Although the diagnosis of Parkinson's disease is still based on the diagnosis of clinical symptoms as the gold standard, the concept of only understanding Parkinson's disease as a motor syndrome is outdated. Patients may have a longer prodromal period before the onset of motor symptoms. However, due to the significant heterogeneity of Parkinson's patients in occupation, education level, and personal preference, the impact and importance of their prodromal symptoms on individuals are also quite different. Therefore, Parkinson's disease is rarely diagnosed due to prodromal symptoms [11]. However, whether effective intervention in the prodromal stage of Parkinson's disease can delay or alleviate the motor symptoms of Parkinson's disease remains to be further explored. But one thing is certain, the non-motor symptoms in the prodromal stage of Parkinson's disease do have a serious impact on the quality of life of patients, and the impact is even more prominent than the motor symptoms [12].

## 2.3 Non-motor Symptoms of Parkinson's Disease

Non-motor symptoms can occur in all stages of Parkinson's disease, which may occur in the prodromal stage of the disease. Along with the disease, it fluctuates with the fluctuation of motor symptoms or gradually aggravates with the progression of the disease [13].

Sleep disorders are the most common of the non-motor symptoms and include insomnia, sleep behavioral abnormalities during rapid eye movement (RBD), excessive daytime sleepiness (EDS), restless legs syndrome (RLS), and sleep-related breathing disorders (SDB). At present, there is no consensus on the management recommendations for PD patients with sleep disorders, which leads to the lack of uniform standards for the diagnosis and treatment of sleep disorders in PD patients. The clinical treatment relies on the doctors' diagnosis and treatment experience, and the treatment effects are different [14].

Sensory disturbances include decreased sense of smell, visual disturbances, somatosensory disturbances and pain. Of these, hyposmia, pain and numbness are common [9]. Olfactory decline is commonly seen as a prodromal symptom, but effective measures for improving olfactory dysfunction are still lacking. The pain and numbness in the treatment of non-motor symptoms of Parkinson's disease is more difficult, generally related to a variety of factors, can fluctuate with the symptoms of Parkinson's disease.

Autonomic dysfunction includes constipation, postural hypotension (OH), and urinary dysfunction. A deficiency of dopamine neurotransmitter in the brain of patients with parkinson's disease leads to slow gastrointestinal movement. At the same time, intestinal dysfunction leads to an increase in the synthesis of misfolded  $\alpha$ -synuclein that gradually spreads

from the enteric nervous system (ENS) to the central nervous system (CNS) through the "enteric-cerebral axis". This creates a vicious circle that causes symptoms of constipation to worsen as Parkinson's disease progresses [15]. OH is not only a symptom of the disease itself, but also an adverse reaction of drugs for treating Parkinson's disease.

Although motor symptoms are the core of the diagnosis of Parkinson's disease, in many cases the mental symptoms and signs are considered to be highly correlated with the diagnosis of Parkinson's disease. Therefore, in a sense, Parkinson's disease can be considered as a complex neuropsychiatric disorder. These neurological symptoms and signs are categorized into emotions (i.e., depression and anxiety), perceptions and thinking (i.e., psychosis), and motivations (i.e., impulse control disorder and apathy) [16]. Mental disorders in patients with Parkinson's disease may affect patients as much as motor symptoms, but clinical research on its treatment and related guidelines are far behind motor symptoms.

Cognitive function declines with the progression of Parkinson's disease. In the early stage of Parkinson's disease, it may only show a mild decline in the perception of things, memory, speech communication ability, and abstract thinking ability. With the development of Parkinson's disease, the cognitive impairment will gradually worsen, and in the late stage, it may progress to dementia. The cumulative probability of dementia after 10 years in patients with parkinson's disease is 46% [17], 83% of parkinson's disease patients survived for 20 years with dementia [18]. The treatment of dementia is more accumulated in the control of the primary disease of Parkinson's disease clinically. That is, the progression and deterioration of his disease is an irrevocable outcome.

#### **2.4 Limitations of Western Medicine Treatment of Parkinson's Disease**

Based on the above description, we recognize that no matter which drug is chosen to treat the motor symptoms of PD, the outcome of PD cannot be changed, and surgical treatment differs greatly from individual to individual, and can only be used as a supplementary means of drug treatment. As for the treatment of non-motor symptoms, there is no unified consensus in clinical practice, and the main purpose of treatment is to effectively improve the symptoms. The treatment plan often relies on the personal experience of the physician, resulting in little clinical treatment effect. In the middle and late stage, exercise complications and adverse drug reactions make the treatment of PD a more difficult problem.

We use levodopa, a "specific drug" for Parkinson's disease, as an example to illustrate the limitations of drugs for Parkinson's disease. Although levodopa can effectively improve the motor symptoms of PD, and levodopa is basically the necessary drug for patients regardless of any period of Parkinson's disease, how and when to start levodopa therapy has always been a controversial issue based on the comprehensive consideration of levodopa saving strategy and neurotoxicity of levodopa. It may be because levodopa has no disease modification effect, and the sports complications and

clinical efficacy caused by long-term taking levodopa are so heterogeneous that there is no evidence that early starting levodopa can slow the progression of disease [19]. That is to say, the treatment of levodopa is very limited based on the consideration of the whole course of PD. Other treatments for Parkinson's disease also have certain limitations and individual differences. That is to say, although there are many drugs available, there are few drugs that can provide sustained and stable dopaminergic stimulation and benefit the general population, which makes our patient need to constantly adjust the drug type and dose throughout the course of the disease. Even so, the worsening of motor symptoms cannot be avoided. Not to mention in the treatment for non-motor symptoms, there is currently no effective drug and universal program that can universally benefit patients.

### **3. TCM Reatment of Parkinson's Disease and the Treatment of Integrated Traditional Chinese and Western Medicine**

#### **3.1 TCM Understanding of PD**

In recent years, the understanding of Parkinson's disease (PD) in traditional Chinese medicine (TCM) has continuously deepened. Based on the two common clinical subtypes of PD, TCM categorizes it into "Trembling Disease" ("Chan Bing"), "Rigidity Disease" ("Ju Bing"), and "Trembling-Rigidity Disease" ("Chan-Ju Bing"). Specifically, PD with resting tremor as the main symptom is diagnosed as "Trembling Disease", while PD with rigidity and hypokinesia as the main symptoms is diagnosed as "Rigidity Disease". If both symptoms are present, it is diagnosed as "Trembling-Rigidity Disease". As the disease progresses, most patients with PD often develop both symptoms [20]. For the non-motor symptoms of PD, TCM often considers them as "combined diseases", such as PD with depression being seen as a combination of "Trembling Disease" and "Depression Syndrome", and PD with constipation as a combination of "Trembling Disease" and "Constipation".

The etiology of the tremor-dominant PD, or "Trembling Disease", can be traced back to the "Huangdi Neijing". "Suwen·Zhizhenyaodalun" states, "All winds, tremors, and dizziness belong to the liver.", "Suwen·Maiyaojingweilun" says, "Bones are the mansion of the marrow. If one cannot stand for long and shakes when walking, the bones are weary", "Suwen·Wuchangzhengdalun" mentions "tremors, dizziness, and falling illnesses", "the disease causes shaking", and "trembling, vibrating, and shivering", elucidating that limb tremors are related to the "wind element" and closely associated with the functions of the "liver" and "kidneys" [21]. For the rigidity-dominant PD, or "Rigidity Disease", ancient texts also provide explanations. Rigidity Disease manifests as stiffness and loss of flexibility in the muscles and bones. "Suwen·Wuzangshengchengpian" points out, "The feet receive blood to walk, the palms receive blood to grasp, and the fingers receive blood to pick up." It also states, "The liver is associated with the tendons, and its manifestation is in the nails.", "Leijing" further explains, "The spirit's agility and transformation are due to the clarity of Yang Qi; the tendons' movement and flexibility are due to the gentleness of Yang Qi... When Yang Qi departs, the spirit becomes disordered, and the muscles and bones waste away". This elucidates that

the flexibility of the tendons and the dexterity of the feet, palms, and fingers are closely related to the nourishment of liver blood and the warming of Yang Qi. Wang Kentang, in "Zhengzhi Zhunsheng", mentions that "this disease is rare in youth, more common in middle age, and even more prevalent in old age. In old age, Yin Xue is deficient, and Shao shui cannot control the Zhuang huo, making it extremely difficult to treat". This indicates that the incidence of the disease is mostly in middle-aged and elderly individuals, which aligns with the pathogenesis of Trembling-Rigidity Disease. Most PD patients are elderly and their physical strength declines, leading to a gradual decline in the essence of the kidneys. This results in the impairment of the kidney essence's ability to transform into kidney Qi, and subsequently, the functions of kidney Qi to differentiate into Yin and Yang are also weakened. On one hand, "the Yin Qi of the five organs cannot be nourished without it," leading to an excess of Yang Qi rising upwards, which is the fundamental cause of the "wind element" in PD. On the other hand, "the Yang Qi of the five organs cannot be manifested without it," causing the organs and the limbs to lose their source of warmth, which is the fundamental cause of the "rigidity symptom" in PD. Furthermore, "the liver and kidneys share a common source," with the liver storing blood and the kidneys storing essence. The essence of the kidneys and the blood of the liver are interdependent, thriving or declining together. Therefore, the decline of the liver and kidneys often occurs successively. The deficiency of liver blood can lead to various pathological changes, such as malnutrition of the tendons, resulting in limb numbness, hand and foot tremors, and muscle twitching; deficiency of liver blood can also cause the tendons to lose their support, leading to wind movements due to blood deficiency. In the pathogenesis of PD, the impairment of the spleen and stomach is also a key factor. Firstly, the spleen's function to produce Qi and blood is reduced, leading to malnutrition of the tendons and vessels. Secondly, the essence and blood of the liver and kidneys rely on the nourishment of the water and grain essences transformed by the spleen. With the onset and progression of the disease, as well as the influence of the seven emotions, the metabolism of body fluids is disrupted, and the circulation of Qi and blood is obstructed, leading to the accumulation of wind, fire, phlegm, blood stasis, and toxins. These substances are both pathological products and pathogenic factors, which interact with the "underlying deficiency" to exacerbate the disease. This makes the pathogenesis of PD complex, involving multiple organs.

### 3.2 Integrated Chinese and Western Medicine Treatment of PD

In view of the characteristics of the course of PD, the treatment of PD with the integration of traditional Chinese and Western medicine is currently a hot topic and a breakthrough in this field, and it has been widely used in clinical practice and has been unanimously recognized by patients. Staging treatment is the only breakthrough point of TCM-WM treatment, and the importance of its research significance is particularly prominent. The invention not only solve various adverse reactions which are puzzle people to use western medicine anti-PD drugs early for a long time, but also improves that effective rate of clinical treatment to a great extent [22].

According to the Hoehn-Yahr classification, PD can be divided into early, middle and late stages. The motor symptoms in patients with early PD can be symptomatic treated with western anti-PD drugs, which, although with good efficacy, are not required to be started in all patients at the time of diagnosis because none of these drugs has been proved to have a disease-modifying effect and in view of the "dopamine" saving strategy. With the development of the disease and the emergence of motor symptoms, western medicine anti-PD drugs can be slowly added under the principle of "dose titration" at this time, so as to achieve a satisfactory clinical treatment effect with the minimum dose [23].

Patients in the intermediate and advanced stages often suffer from motor fluctuation and dyskinesia due to disease progression or adverse reactions caused by long-term administration of anti-PD drugs in western medicine. In this stage, three or four drugs are usually combined for treatment, or multi-channel comprehensive treatment is selected. Motor fluctuation mainly included "end-dose deterioration", "switching phenomenon", "frozen gait". Dyskinesia mainly includes "peak dyskinesia", "bipolar dyskinesia" and "dystonia in the off phase" [24].

The expert consensus on clinical diagnosis and treatment of Parkinson's disease (PD) in traditional Chinese medicine (TCM) has identified five basic syndromes: deficiency of Yin and Blood, malnutrition of tendons; deficiency of Yin and Blood, internal stirring of liver wind; Qi stagnation in the shao Yang meridian, internal disturbance of phlegm-fire; deficiency of middle Qi, internal stirring of liver wind; and Yin deficiency affecting Yang, leading to deficiency of both Yin and Yang. It is believed that early treatment should primarily focus on nourishing Yin and Blood or nourishing Yin, nourishing blood, and calming liver wind. For the syndrome of deficiency of Yin and Blood with malnutrition of tendons, the strongly recommended treatment is the modified Lianmei Siwu Decoction (Grade Ib). For the syndrome of deficiency of Yin and Blood with internal stirring of liver wind, the strongly recommended treatment is the modified Ziyin Xifeng Decoction (Grade Ib). In the middle stage, the focus shifts to replenishing Qi and Blood, promoting blood circulation, and calming liver wind. For the syndrome of deficiency of middle Qi with internal stirring of liver wind, the recommended treatment is the modified Buchong Yiqi Decoction (Grade V). In the advanced stage, it is necessary to replenish both Yin and Yang, promote blood circulation, and calm liver wind, with the strongly recommended treatment being the modified Dihuang Yinzi Decoction (Grade Ia). The consensus also suggests using TCM alone in the early stages and adopting an integrated approach combining TCM with Western medicine in the middle and advanced stages of the disease [20].

A large number of clinical studies have proved the advantages of integrated Chinese and Western medicine treatment. Studies have shown that in PD patients of qi and blood deficiency type in the early and middle stages, the treatment was performed with Dosimethalin Tablets in combination with Bazhen Decoction. Three months later, the observation showed that the UPDRS (II, III) scores and Parkinson's disease quality of life scale (PDO-39) scores in the

combination group were significantly lower than those in the simple western medicine group. Moreover, the total effective rate of treatment was significantly higher than that in the western medicine group (90.00% v66.67%). It can not only obviously improve the motor symptoms and non-motor symptoms of PD patients and improve the quality of life of patients, but also reduce the dosage of dopa silk hydrazine tablets, thereby minimizing the toxic and side effects [25]. Studies have shown that in the treatment of advanced 70 PD patients of liver and kidney yin deficiency type dyskinesia, the use of dopa silk hydrazine tablets, piribedil combined with Xifeng Dingchan Decoction treatment, the integration of Chinese and Western medicine treatment in the daily activity scores, dyskinesia scores, motor function scores are better than the simple western medicine group [26]. Lan Siyang et al. treated 17 PD patients who met the inclusive criteria with the golden needle Wang Leting empirical formula and fire needle. Before continuing to take western medicine combined with acupuncture for 12 weeks, they observed the UPDRS score and PDO-39 score and found that the patients who cooperated with acupuncture were significantly lower than those who only received western medicine, and the total effective rate was 94.1% [27].

#### 4. Summary

TCM can not only reduce the dosage and toxicity of western anti-PD drugs, but also assist western anti-PD drugs in controlling the locomotor and non-motor symptoms and improving the quality of life of patients. A large number of studies have confirmed that the treatment of PD with the integration of traditional Chinese and Western medicine does have advantages over the simple western anti-PD drugs.

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