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Parkinson's Disease in Traditional Chinese and Western Medicine: A Review

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Abstract: ***Parkinson's disease (PD) is a neurodegenerative disease that seriously endangers the health of the middle-aged and elderly people. The main clinical manifestations include motor symptoms such as bradykinesia, static tremor, and myotonia and non-motor symptoms like constipation, mental disorders, sleep disorders, and autonomic nervous dysfunction. Its etiology and pathogenesis have not been fully understood, and the clinical efficacy is not satisfactory. By searching the relevant literature in China and abroad in recent years, this paper summarized the etiology, pathogenesis, and treatment of PD in both traditional Chinese medicine (TCM) and western medicine as well as the integrated TCM and Western medicine treatment.***

Keywords: Parkinson's disease, Traditional Chinese and western medicine, Progress, Review.

1. Introduction

Parkinson's disease is a slowly progressive degenerative disease of the substantia nigra striatum pathway disorder, which is more common in middle-aged and elderly people. The main clinical features are bradykinesia, resting tremor and myotonia. Parkinson's disease is still mainly treated with drugs, but there is no cure so far. Compound levodopa is still the most effective western medicine to control motor symptoms, but almost all cases require lifelong medication to control symptoms, and many patients are often forced to discontinue due to intolerance of drug side effects; deep brain stimulation can significantly improve symptoms, but it still can not cure, nor can it control the progression of the disease [1].

Traditional Chinese medicine has unique advantages in the treatment of Parkinson's disease. The combination of traditional Chinese and Western medicine can play a good synergistic effect, which can significantly improve the curative effect and reduce the side effects of Western medicine. Especially in the early stage of the disease and the improvement of non-motor symptoms of Parkinson's disease, traditional Chinese medicine and its characteristic therapy have obvious therapeutic advantages.

2. Understanding of Parkinson's Disease in Chinese and Western Medicine

2.1 TCM Etiology and Pathogenesis of Parkinson's Disease

The understanding and treatment of Parkinson's disease in traditional Chinese medicine has a long history. There is no name for Parkinson's disease in traditional Chinese medicine classics, but as early as the 'Huangdi Neijing', there have been symptoms such as tremor, rigidity, reduced movement, and panic gait. In the Ming Dynasty, Sun Yikui first proposed the disease name 'flutter' with tremor as the main clinical manifestation for the first time in 'Chishui Xuanzhu', and pointed out that ' flutter, the patient's hands and feet shake like quiver, the tendons can not be restrained, and can not be held, the image of the wind is also '. After the 1990 s, Parkinson's disease was established as a category of ' tremor syndrome ' in traditional Chinese medicine at the symposium on senile encephalopathy of the All-China Association of Traditional Chinese Medicine [2].

Traditional Chinese medicine believes that there are many causes and complex pathogenesis of this disease. Most Chinese medicine scholars believe that this disease is deficiency in origin and excess in superficiality, liver and kidney loss, qi and blood deficiency is its origin, wind, fire, phlegm, blood stasis as its standard. The wind, fire, phlegm and blood stasis are mixed with each other as the disease progresses, poisoning the brain collaterals, and the tendons and veins are dystrophic for a long time, resulting in this disease. In short, liver and kidney deficiency is the basic pathogenesis, phlegm and toxin are pathological factors, blood stasis is the pathological link.

2.2 The Modern Pathogenesis of Parkinson's Disease

2.2.1 Oxidative stress response

Studies have found that oxidative stress can lead to dopamine neuron damage, which is closely related to the pathogenesis of PD. The brain is the most active organ in the body's oxidative metabolism. Neurons consume a large amount of oxygen, but the antioxidant level is relatively low, so it is susceptible to oxidative stress. Under normal circumstances, the body's antioxidant substances (glutathione, superoxide dismutase, uric acid and reductase, etc.) can remove the excess free radicals produced by oxygen metabolism in brain tissue in time, thereby repairing cell oxidative damage and protecting neurons; under pathological conditions, a large amount of antioxidant substances in the substantia nigra of the brain are reduced, resulting in a large amount of free radicals, which in turn stimulates oxidative stress. Oxidative stress can lead to the accumulation of cytotoxic compounds, the failure of protein enzymes, the formation of lipid peroxides, etc., and ultimately lead to the death of substantia nigra cells, thereby triggering PD. Studies have shown that oxidative stress-induced DA neuron death may be related to the JNK signaling pathway; some scholars have found that the level of

oxidative stress in the substantia nigra of PD rats is very high; sEET RC et al. found that the measured values of lipid peroxidation products in PD patients were at a high level [3].

2.2.2 Abnormal aggregation of α-synuclein

The α-synuclein gene encodes a presynaptic protein that is easily misfolded, and together with ubiquitin, vesicle structure, lysosomes, deformed mitochondria, and destroyed cytoskeleton structure, it constitutes a Lewy body. Studies have found that abnormal aggregation of α-synuclein is the main symbol and central link in the pathogenesis of PD, and it is the main target of PD genetic gene concentration. It can aggravate mitochondrial dysfunction, cause oxidative stress, activate neuroinflammation, cause or aggravate the dysfunction of ubiquitin-proteasome system, and induce axonal injury. Studies have shown that α-synuclein oligomers are the main toxic substances involved in the production of LBs amyloid. Injection of adeno-associated virus vector overexpressing α-synuclein into mice can replicate the neuropathological features of PD [4], indicating that overexpression of α-synuclein is an important cause of PD. Oxidative stress, PD gene mutation and overexpression can affect the conformational changes and aggregation of α-synuclein.

2.2.3 Inflammatory response

Some scholars have found that the activation of microglia in the brain of PD patients is significantly increased, and the level of inflammatory factors is significantly increased, indicating that the injury of substantia nigra in PD patients is closely related to the inflammatory response. Studies have shown that there is a vicious circle in the substantia nigra of PD patients, that is, microglia and astrocytes are activated under the catalysis of certain risk factors (such as endogenous chemicals, cytokines, disintegrated neurons, etc.), thereby initiating the immune response system, leading to the accelerated expression of pro-inflammatory factors and chemokines, and then irreversible damage to DA neurons. After neuronal damage, microglia are further activated, and so on. Repeatedly, it eventually leads to degenerative changes in the nervous system of PD patients.

2.2.4 Mitochondrial dysfunction

Mitochondrial dysfunction is critical to the susceptibility of PD dopaminergic neurons. PD-related clinical and basic studies have found that mitochondrial dynamics damage, bioenergy defects, complex I inhibition, electron transport chain and increased reactive oxygen species play an important role in the pathogenesis of PD [5]. Most PD-related genes play a role in mitochondrial homeostasis. Recently, the mechanisms of PD-related mitochondrial protein phosphatase and PTEN-induced PINK1 and Parkin function and induction of neurodegeneration have been identified. In addition, studies have found that PD-related proteins such as α-synuclein and LRRK2 may have great functional overlap with PD in mitochondrial dysfunction of PD genetic cases [6]. In substantia nigra DA neurons, the deletion of mitochondrial DNA fragments also increased significantly with age, and the mutation rate of mitochondrial DNA in DA neurons of PD patients was higher than that of normal people [7].

2.2.5 Other

In addition to the above mechanisms, environmental factors, genetic factors, excitatory neurotoxicity, calcium homeostasis imbalance and so on can also lead to PD. It has been reported [8] that xylenes, acetones, heavy metals and other chemicals may lead to PD. Under normal circumstances, glutamic acid and aminoamide can be transformed into each other under the action of related enzymes (glutamic acid synthase, glutamine synthetase); when the body is diseased, this circulation pathway is destroyed, resulting in abnormal Glu metabolism. Studies have confirmed that the increase of Glu content will lead to the degeneration of DA neurons in the substantia nigra. In addition, excessive Glu will also produce NO to cause neuronal damage and death; at the same time, the high level of Glu around neurons will lead to the excitation of N-methyl-D-aspartate receptor, which will cause more calcium influx, produce calcium overload, and destroy the normal function of mitochondria. Neuronal cells die due to lack of normal energy supply. The above mechanisms are involved in the development of PD.

3. Progress in Treatment

There are many types of tremor syndrome in traditional Chinese medicine. The disease can be roughly divided into eight types of treatment, liver qi stagnation type, phlegm turbidity stagnation type, phlegm heat wind type, qi stagnation and blood stasis type, liver and kidney yin deficiency type, heart and spleen deficiency type, qi and blood deficiency type, marrow sea empty type. Some scholars have summarized three types of TCM syndrome differentiation, one is the rigidity type of liver and kidney yin deficiency, the second is the tremor type of qi stagnation and blood stasis, and the third is the mixed type of qi and blood deficiency. However, most of the Parkinson's patients seen in clinical practice have a long course of disease, and often change their syndromes during the treatment process. Various symptom factors are mixed with each other and cannot be generalized. This requires physicians to flexibly differentiate syndromes in clinical practice. This is also the theoretical core of traditional Chinese medicine, the essence of disease prevention, and the secret of traditional Chinese medicine to exert its unique curative effect.

3.1 Deficiency Syndrome

3.1.1 Liver and kidney deficiency

Parkinson's disease often occurs in the elderly, but rarely in the middle-aged. The elderly have liver and kidney deficiency, tendon loss, and tendon and pulse contracture; the liver also loses nourishment, and the world is too, then the virtual wind moves inside, and sees the tremor disease. Sun Qiaojie [9] 56 patients with Parkinson's disease were randomly divided into 2 groups, 28 cases in the control group were treated with conventional western medicine cocktail therapy; 28 cases in the treatment group were treated with self-made Ziyang Shujin Decoction (drug composition: Radix Rehmanniae Preparata, Cornus officinalis, Uncaria, Cassia, Radix Paeoniae Alba, Cortex Eucommiae, Radix Achyranthis Bidentatae, Herba Taxilli, Semen Cuscutae, Rhizoma Dioscoreae, Radix Rehmanniae, Radix Glehniae, Radix

Angelicae Sinensis, Fructus Lycii, Radix Ophiopogonis, Pericarpium Citri Reticulatae) on the basis of the treatment of the control group. Both groups were treated for 6 months. Results: The total effective rate was 92.9% in the treatment group and 71.4 % in the control group. The curative effect of the treatment group was better than that of the control group ($P < 0.05$). After that, 88 patients with Parkinson's disease were randomly divided into two groups. 44 patients in the control group were treated with levodopa and benserazide tablets. 44 cases in the observation group were treated with Guishao Roujin Decoction (drug composition: Puerariae Lobatae Radix, Chuanxiong Rhizoma, Paeoniae Radix Alba, Spatholobi Caulis, Gastrodiae Rhizoma, Trachelospermi Caulis, Angelicae Sinensis Radix, Bombyx Batryticatus) on the basis of the control group. Both groups were treated for 4 weeks. Results: The total effective rate was 95.45% in the observation group and 75.00% in the control group. The curative effect of the treatment group was better than that of the control group ($P < 0.05$). After treatment, the score of Parkinson's disease comprehensive score scale in the observation group was significantly lower than that in the control group ($P < 0.05$). Xiao Gaiqin et al. [10] believed that the main pathogenesis of Parkinson's disease is liver and kidney deficiency, so the treatment should be based on tonifying liver and kidney, combined with tonifying qi and activating blood. Methods: 96 patients with Parkinson's disease were randomly divided into 2 groups. 48 patients in the control group were treated with levodopa and benserazide tablets. 48 patients in the observation group were treated with Huangqi Bushen Decoction (drug composition: Astragalus, ginseng, Poria, fried Atractylodes, roasted licorice, Notopterygium, papaya, cicada) combined with electroacupuncture (acupoints: Tianzhu, Wangu, Yamen, Fengchi, Hegu). Both groups were treated for 2 months. Results: After treatment, the scores of mini-mental state examination scale and activity of daily living scale in the two groups were increased ($P<0.05$), and those in the observation group were better than the control group ($P<0.05$).

3.1.2 Qi and blood deficiency

The main pathogenesis of Parkinson's disease is the long-term disease of the elderly, the deficiency of qi and blood, and the loss of nourishment of tendons and veins. Professor Li Rukui believes that deficiency of both qi and blood is the root cause of Parkinson's disease. He created Zhichan Decoction (drug composition: Zhihuangqi, Danshen, Zhimu, Baishao, Gouteng, Zhidahuang, Shengma) to supplement qi and blood, and to nourish kidney yin, calm liver wind, reduce turbidity fire, resolve phlegm and blood stasis, and raise Qingyang. It is effective in treating Parkinson's disease with anxiety and depression. It can improve the symptoms of Parkinson's disease, reduce anxiety and depression, and improve the quality of life of patients [11]. He randomly divided 60 patients with Parkinson's disease with deficiency of both qi and blood into two groups. 30 patients in the control group were treated with levodopa and benserazide tablets alone, and 30 patients in the treatment group were treated with Shiquan Dabu Pills on the basis of the treatment in the control group. Both groups were treated for 12 weeks. Results: The total effective rate was 56.7% in the treatment group and 10 % in the control group. The curative effect of the treatment group was better than that of the control group ($P < 0.01$). The improvement of TCM syndromes in the treatment group was better than that in the control group ($P < 0.01$), and its improvement effect was enhanced with the prolongation of treatment course.

3.2 Empirical

Internal wind is the pathological basis of Parkinson's disease, so stopping endogenous wind often runs through its treatment, but the influence of phlegm and blood stasis cannot be ignored. Clinically, the medicine of promoting blood circulation and removing phlegm is added at the same time of extinguishing wind, and the curative effect is remarkable. Phlegm and blood stasis is an important pathological factor of Parkinson's disease. Phlegm and blood stasis run through all stages of the occurrence and development of Parkinson's disease. Phlegm and blood stasis is the pathological product of deficiency of zang-fu organs. Phlegm and blood stasis form obstruction in meridians and collaterals, resulting in internal movement of liver wind, malnutrition of brain marrow and tendons, movement disorders, limb tremor and other diseases. Because of the deficiency of blood stasis, because of the deficiency of blood stasis, blood stasis turbidity does not go, then the deficiency is difficult to make up. Therefore, the method of removing blood stasis and resolving phlegm plays an important role in the treatment of Parkinson's disease. At the same time of tonifying deficiency, paying attention to the use of removing blood stasis and resolving phlegm can achieve better clinical efficacy.

4. Western Medicine Treatment

4.1 Drug Therapy

At present, the most effective method for the treatment of PD is still drug therapy. Therapeutic drugs can be divided into anticholinergics, levodopas, dopamine receptor agonists, dopamine degradation enzyme inhibitors, neuroprotective agents, etc. Anticholinergic drugs are effective in the treatment of rigidity and tremor, but poor in the treatment of bradykinesia. They are often used as adjuvant drugs, and there are many adverse reactions, mainly manifested as dry mouth, constipation, memory loss and interference with the central nervous system to cause hallucinations in patients. At present, compound levodopa is considered to be the best therapeutic drug to supplement exogenous dopamine and control PD. However, the efficacy of long-term use of levodopa drugs will gradually decrease, and central and peripheral adverse reactions will occur. Dopamine receptor agonists are important drugs for clinical treatment of PD. The symptoms of PD can be improved by stimulating dopamine receptors. Although the clinical effect is not as obvious as levodopa, early application of dopamine receptor agonists may delay the application of levodopa preparations, thereby reducing the occurrence of motor fluctuations [12]. Common adverse reactions include dizziness, nausea, drowsiness, sleep disorders, cognitive dysfunction, lower extremity edema and orthostatic hypotension, as well as mental symptoms such as hallucinations and delusions. Dopamine degrading enzyme inhibitors include catechol-oxygen-methyltransferase inhibitors and monoamine oxidase-B inhibitors. The main adverse reaction of dopamine degrading enzyme inhibitors is liver damage. Although modern medicine has recognized the

importance of neuroprotective therapy, and there are many treatments for nerve repair and neuroprotection in clinical trials, a drug for protecting nerves has not yet been found. Other drugs, such as N-methyl-D-aspartate receptor antagonists, adenosine receptor antagonists, iron chelators, antioxidants, botulinum toxin and selective serotonin receptor antagonists, also have certain therapeutic effects on PD, but have obvious adverse reactions.

4.2 Surgical Treatment

The lesion of substantia nigra and substantia nigra striatum pathway in PD is caused by the loss of dopaminergic neurons in the substantia nigra pars compacta. The surgical treatment of PD has a long history. From the accidental discovery in 1939 that the destruction of the caudate nucleus can relieve tremor, to the beginning of the 1950 s, the anterior dorsal globus pallidus lesion was not effective, and then to the treatment of the ventral posterior globus pallidus lesion in the 1960 s, until the emergence of levodopa. However, in the 10 years of the 1980 s, the efficacy of levodopa was not good, and there were adverse reactions. At present, surgical treatment mainly includes nerve nucleus lesion and deep brain electrical stimulation. However, surgery can only improve the clinical symptoms of PD, and the effect is not good. Clinically, there have been successful cases of transplantation of autologous adrenal medulla and allogeneic embryonic substantia nigra cells into the striatum. Although the system balance of dopamine and acetylcholine transmitters in the striatum has been improved, only 50 % of patients have improved motor symptoms, and there are problems such as limited donor sources, immune rejection, and uncertain long-term efficacy [13]. In addition, treatment methods such as tyrosine hydroxylase, human retinal pigment epithelium, neurotrophic factor gene transfection and stem cells are still being explored. At present, they are still in the stage of animal experiments, and there is still a long way to go from the formal entry into the clinical treatment stage.

5. Summary

Modern medical treatment of PD is highly targeted. Whether it is Chinese and Western medicine therapy, or deep brain stimulation, acupuncture, moxibustion, etc., can significantly improve the clinical symptoms of PD. However, the current treatment of PD is still targeted symptom control, and there is no way to control the development of the disease. Long-term use of western medicine is easy to produce drug resistance, adverse reactions, and with the prolongation of medication time, the efficacy gradually decreased. In the process of surgical treatment of PD, complications and recurrence will occur, and the disease cannot be cured fundamentally. Traditional Chinese medicine has achieved good clinical results in the treatment of PD, which can control the symptoms of non-motor disorders; at the same time, it also delays the use of dopamine preparations and the progression of the disease, which has certain development potential. However, in the long run, there are still many problems in the treatment of PD with traditional Chinese medicine. For example, the syndrome differentiation of PD has not yet been unified, and the standardization of syndromes also needs further exploration to reach a broad consensus.

References

[1] Luo Xiaodong, Li Zhe, Zhu Meiling, etc. Expert Consensus on Clinical Diagnosis and Treatment of Parkinson's Disease [J]. Journal of Traditional Chinese Medicine, 2021, 62 (23): 2109-2116.

[2] Huang Zhilan, Zhao Yang. The present situation and prospect of traditional Chinese medicine in the treatment of Parkinson's disease [J]. Integrated Chinese and Western Medicine Journal of Cardiovascular and Cerebrovascular Diseases, 2013, v. 11 (01): 81-83.

[3] Niu Liyun, He Jiani, Zhang Ding, Feng Weixing. Pathogenesis of Parkinson's disease and acupuncture treatment progress [J]. Journal of Liaoning University of Traditional Chinese Medicine, 2022, 24 (04): 217-220.

[4] Wang Jiabin, Shen Xiaoming, Ma Yunzhi, Su Chaoyang, Bian Songbo. Advances in Chinese and Western Medicine Research of Parkinson's Disease [J]. Chinese Journal of Experimental Prescriptions, 2022, v. 28 (01): 241-250.

[5] ROCHA E M, DE MIRANDA B, SANDERS L H. Alpha-synuclein: Pathology, mitochondrial dysfunction and neuroinflammation in Parkinson's disease[J]. Neurobiol Dis, 2018, 109(Pt B):249-257.

[6] RYAN B J, HOEK S, FON E A, et al. Mitochondrial dysfunction and mitophagy in Parkinson's: from familial to sporadic disease[J]. Trends Biochem Sci, 2015, 40(4):200-210.

[7] ZHU Z, YANG C B, IYASWAMY A, et al. Balancing mTOR signaling and autophagy in the treatment of Parkinson's disease[J]. Int J Mol Sci, 2019, 20(3):728.

[8] SHEIKH A, SHEIKH K. The expression change of glial fibrillary acidic protein and tyrosine hydroxylase in substantia nigra of the Wistar rats exposed to chlorpyrifos: a novel environmental risk factor for Parkinson's disease[J]. Experimental Brain Research, 2020, 238(9):2041-2051.

[9] Sun Qiaojie. Western medicine combined with Ziyang Shujin Decoction in the treatment of 28 cases of Parkinson's movement disorder [J]. Chinese folk medicine, 2017, 26 (18): 121-122.

[10] Xiao Gaiqin, Zhang Kexun. The clinical effect of Huangqi Bushen Decoction combined with acupuncture in the treatment of Parkinson's disease [J]. Clinical medical research and practice, 2018, 3 (25): 122-123.

[11] Wang Wei, Li Wentao, Li Rukui. Clinical study of Zhichan Decoction in the treatment of Parkinson's disease with anxiety and depression [J]. Integrated Chinese and Western Medicine Cardiovascular and Cerebrovascular Journal, 2018, 16 (17): 2556-2558.

[12] Dong Lihua, Hu Guohua, Wang Yushan, et al. A clinical study of dopamine receptor agonists in the treatment of early Parkinson's disease [J]. Clinical meta-analysis, 2006, 21 (13): 959-960.

[13] Zis P, Martinez-Martin P, Sauerbier A, et al. Non-motor symptoms burden in treated and untreated early Parkinson's disease patients: Argument for non-motor subtypes[J]. Eur J Neurol, 2015, 22(8):1145-1150.