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Effect of Shenzhi Capsules on Oxidative Stress and Neurological Function in Parkinson's Disease

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Keywords

Shenzhi capsules, Donepezil hydrochloride tablets, Parkinson's disease, Oxidative stress, Neurological function

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Abstract

Objective To analyze the effect of Shenzhi capsule adjuvant therapy on oxidative stress and neurological function in patients with Parkinson's disease (PD). **Methods** 108 patients with PD in our hospital from January 2018 to August 2020 were selected and randomly divided into the control group (n=54) and the observation group (n=54). The control group was treated with donepezil hydrochloride tablets, and the observation group was treated with Shenzhi capsules on the basis of the control group. The severity of dementia, cognitive impairment and PD, activities of daily living, neurological function and oxidative stress were compared between the two groups. **Results** After treatment, the score of simple scale mental state examination (MMSE), montreal cognitive assessment scale (MoCA), activity of daily living (ADL) in the two groups were apparently higher than those before treatment (P<0.05). The score of Parkinson's assessment subscales (UPDR) in the two groups were apparently lower than that before treatment (P<0.05), and the score of MMSE, MoCA, ADL in the observation group were apparently higher than those in the control group (P<0.05). The score of UPDR in the observation group was apparently lower than that in the control group (P<0.05). After treatment, the levels of brain derived neurotrophic factor (BDNF), superoxide dismutase (SOD) in the two groups were apparently higher than those before treatment (P<0.05), and the levels of acid calcium binding protein (S-100β), neuron-specific enolase (NSE), malonic dialdehyde (MDA) were apparently lower than those before treatment (P<0.05). The levels of BDNF, SOD in the observation group were apparently higher than those in the control group (P<0.05), and the levels of S-100β, NSE, MDA in the observation group were apparently lower than those in the control group (P<0.05). **Conclusion** On the basis of donepezil hydrochloride tablets treatment, Shenzhi capsules adjuvant treatment has a good effect on patients with PD, which could effectively reduce oxidative stress level, improve neurological function, cognitive function, and mental state, and improve their activities of daily living.

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder that tends to affect the middle-aged and elderly. Its main clinical manifestations include resting tremor, muscle rigidity, cognitive impairment, akinesia and mental disorder, which seriously affect the quality of life and physical and mental health of patients [1]. Pathological studies have found that PD seems to mainly result from abnormal acetylcholine levels and neuron injury. As a second-generation acetylcholinesterase inhibitor, donepezill hydrochloride can specifically inhibit the degradation of acetylcholine in the brain, and has become a common drug for PD treatment, but long-term use of which is prone to drug resistance, resulting in some unsatisfactory therapeutic effect and prognosis [2]. Traditional Chinese medicine (TCM) treatment is characterized by fewer side effects and significant efficacy, having certain advantages in the treatment of PD. Besides, studies have shown that complementing Western medicine treatment with TCM treatment for patients with PD cloud improve the effectiveness of treatment [3]. Shenzhi capsule is a preparation of Chinese materia medica made from dozens of Chinese medical herbs including Panax Ginseng, Radix Polygalae, Rhizoma Acori Tatarinowii, Radix Scutellariae, Radix Angelicae Sinensis and Radix Paeoniae Alba, and is used to treat brain diseases such as PD, cerebral palsy and dementia. However, the efficacy of Shenzhi capsule in combination with donepezill hydrochloride in the treatment of patients with PD remains to be studied. Therefore, this study was expected to investigate the clinical efficacy of Shenzhi capsule combined with donepezill hydrochloride in the treatment of patients with PD, which is reported below.

Information and materials

Clinical information

Basic information

A total of 108 cases patients diagnosed with PD in our hospital were selected as study objects. All participates were randomly divided into the control group (n=54) and the observation group (n=54). There was no difference in the basic information between the two groups (P>0.05), and the data were clinically comparable, as detailed in Table 1. The study was approved by the Ethics Committee of the hospital, with informed consent form all patients.

Table1. Comparison of basic information

groups	cases	gender (case)		age (year)	duration of disease (year)	Hoehn-Yahr grade (year)		
		male	female			I	II	III
observation group	54	31	23	64.53±6.74	3.95±1.24	14	22	18
control group	54	28	26	65.23±7.05	3.77±1.16	12	20	22
$\chi^2/t/Z$		0.336		-0.527	0.779		-0.761	
P		0.562		0.599	0.438		0.446	

Inclusion and exclusion criteria

Inclusion criteria: (i) patients with PD met the diagnostic standards in *Chinese Guidelines for the Treatment of Parkinson's Disease* [4]; (ii) patients aged 55 to 75 years. Exclusion criteria: (i) patients with severe cardiac, hepatic, pulmonary and renal insufficiency; (ii) patients who were allergic to the drugs used in this study; (iii) patients with severe mental or conscious dysfunction caused by other reasons.

Treatment methods

The control group was given administration (2.5 mg/time, 1 time/day) of donepezill hydrochloride

tablets (Jiangsu Hansoh Pharmaceutical Co., Ltd, certificate number of SFDA: H20030472). On the basis of treatment in the control group, patients in the observation group were additionally given administration (1.5 g/time, 3 times/day) of Shenzhi capsules (Sichuan Nuodi Kangwei Pharmaceutical Co., Ltd, certificate number of SFDA: B20020339). Both groups were treated for total 3 months.

Observational indicators

The severity of dementia

Before and after treatment, the severity of dementia in both groups was assessed using mini-mental state examination (MMSE), with the lower the score, the more severe the dementia, with scores >20 being mild dementia, 10-20 being moderate dementia and <10 being severe dementia [5].

The assessment of cognitive impairment

Before and after treatment, the cognitive impairment in both groups was measured by montreal cognitive assessment (MoCA), with the lower the score, the more severe the dementia, with scores <20 being significant cognitive impairment, 20-24 being mild cognitive impairment and >24 being normal cognitive function [5].

The severity of PD

Before and after treatment, the severity of PD in both groups was estimated using Parkinson's assessment subscale (UPDR), with the higher the score, the more severe the PD [6].

The assessment of activity of daily living (ADL)

Before and after treatment, ADL scale was applied for assessment in both groups, with a full score of 100, the higher the score, the better the patient was able to take care of himself/herself [6].

The assessment of neurological function

Before and after treatment, 5 ml of venous blood was taken from each fasting patient in both groups, and was centrifuged for obtaining serum. Enzyme linked immunoserbent assay (ELIA) was conducted to measure acid calcium binding protein (S-100β), brain-derived neurotrophic factor (BDNF) and neuron-specific enolase (NSE) levels. All ELIA-related kits were purchased from Roche Diagnostics (USA), and were operated in strict accordance with the protocols.

The assessment of oxidative stress

Before and after treatment, 5 ml of venous blood was taken from each fasting patient in both groups, and was centrifuged for obtaining serum. Then, ELIA was performed to detect superoxide dismutase (SOD) and malonic dialdehyde (MDA) levels. All ELIA-related kits were purchased from Roche Diagnostics (USA), and were operated in strict accordance with the protocols.

Statistically analysis

SPSS software (version 20.0, IBM, USA) was used for statistical analysis. Count data were compared using χ^2 test. Rank sum test was used to the comparison of ranked data. Quantitative data was demonstrated as the mean ± standard, with comparison using the *t*-test. There was statistical significance if $P<0.05$.

Results

Comparison of the scores between the two groups

Before treatment, there was no significant difference between the MMSE, MoCA, ADL and UPDR scores in the two groups ($P>0.05$). After treatment, the MMSE, MoCA and ADL scores in both groups were significantly higher than before treatment ($P<0.05$), and the UPDR scores were significantly lower than before treatment ($P<0.05$). Besides, the MMSE, MoCA and ADL scores in the observation group were significantly higher than those in the control group ($P<0.05$), and the UPDR score in the observation group was significantly lower than that in the control group ($P<0.05$), as shown in Table 2.

Table 2. Comparison of the scores between the two groups

groups	cases	MMSE		MoCA		ADL		UPDRS	
		pre-treatment	post-treatment	pre-treatment	post-treatment	pre-treatment	post-treatment	pre-treatment	post-treatment
observation group	54	16.55±4.26	25.34±3.27*	19.56±4.38	25.74±3.12*	58.74±7.45	76.77±7.22*	56.37±8.76	34.62±6.77*
control group	54	15.79±4.57	22.76±4.15*	20.23±4.72	23.12±2.85*	60.26±8.38	70.38±9.15*	57.52±7.96	41.38±7.81*
t		0.894	3.588	-0.765	4.556	-0.996	4.029	-0.714	-4.806
P		0.373	0.001	0.446	0.000	0.321	0.000	0.477	0.000

Note: compared to pre-intervention, [a]*P*<0.05

Comparison of neurological function indicators between the two groups

Before treatment, there was no significant difference in the comparison of S-100β, BDNF and NSE levels between the two groups (*P*>0.05). After treatment, S-100β and NSE levels in both groups were significantly lower than before treatment (*P*<0.05), and BDNF levels were significantly higher than before treatment (*P*<0.05). The levels of S-100β and NSE in the observation group were significantly lower than those in the control group (*P*<0.05), and the levels of BDNF in the observation group were significantly higher than those in the control group (*P*<0.05), as shown in Table 3.

Comparison of oxidative stress indicators between the two groups

Before treatment, there was no significant difference in SOD and MDA levels between the two groups (*P*>0.05). After treatment, SOD levels in both groups were significantly higher than before treatment (*P*<0.05), and MDA levels were significantly lower than before treatment (*P*<0.05). Moreover, the SOD level in the observation group was significantly higher than that of the control group (*P*<0.05), but the MDA level was the opposite (*P*<0.05), as shown in Table 4.

Table 3. Comparison of neurological function indicators between the two groups

groups	cases	S-100β (ng/L)		BDNF (ng/ML)		NSE (ng/mL)	
		pre-treatment	post-treatment	pre-treatment	post-treatment	pre-treatment	post-treatment
observation group	54	84.64±8.84	68.74±7.33*	11.85±3.14	19.26±4.27*	22.43±4.78	12.76±3.72*
control group	54	85.57±9.25	74.56±8.11*	12.38±2.96	16.34±3.88*	21.56±5.43	15.58±4.13*
t		-0.534	-3.912	-0.903	3.719	0.884	-3.728
P		0.594	0.000	0.369	0.000	0.379	0.000

Note: compared to pre-intervention, [a]*P*<0.05

Table 4. Comparison of oxidative stress indicators between the two groups

groups	cases	SOD (U/mL）		MDA (μmol/ML)	
		pre-treatment	post-treatment	pre-treatment	post-treatment

observation group	54	86.65±16.74	118.34±17.54*	10.64±2.77	6.74±1.85*
control group	54	88.26±15.82	106.47±18.25*	10.12±2.65	7.92±2.12*
t		-0.514	3.446	0.997	-3.082
P		0.609	0.001	0.321	0.002

Note: compared to pre-intervention, [a]$P<0.05$

Discussion

PD is a category of "tremor diseases" in TCM, stemming from liver-kidney deficiency and qi-blood deficiency that result in lack of nourishing of tendon and vessel, overstrain, generation of phlegm and static blood, internal stirring of deficient wind and blockade of brain collateral. Hence, the treatment of PD should focus on promoting blood circulation for removing obstruction in collaterals and benefiting qi and resolving phlegm. Yuan Chen applied Shaogan Dingchan decoction combined with acupuncture therapy of seven points in skull base to treat patients with PD, which showed a significant clinical efficacy [7]. Similarly, Lu Shen et al used the combined medication with Zhengan Xifeng decoction and levodopa and benserazide hydrochloride tablets to treat patients with PD, which achieved the definite therapeutic effects on PD [8]. These findings demonstrate that Chinese medicine has certain advantages in the treatment of PD.

In this study, the control group was treated with donepezill hydrochloride tablets and the observation group was treated with Shenzhi capsules on the basis of the treatment used in the control group. After treatment, the results showed that the MMSE, MoCA and ADL scores in both groups were significantly increased and the UPDR score was notably decreased. Besides, the MMSE, MoCA and ADL scores in the observation group were significantly higher than those in the control group, and the UPDR score in the observation group was significantly lower than that in the control group. Taken together, it indicates that the application of Shenzhi capsules as an adjunct to the treatment with donepezil hydrochloride tablets could exert a good efficacy by effectively improving the mental state of patients, alleviating cognitive impairment and improving their activity of daily living. After entering the body, donepezil hydrochloride tablets could play a role in postsynaptic membranes by inhibiting the catalytic action of acetylcholinesterase on the hydrolysis of acetylcholine, increasing the levels of acetylcholine in the brain and improving nerve conduction in the encephalic region. Therefore, this drug is effective in reducing neuron injury, improving cognitive function and mental state, and enhancing the activity of daily living when applied to the treatment of PD. Shenzhi capsule is a preparation of Chinese materia medica in which Panax Ginseng has the effect of invigorating qi for relieving desertion and tranquilizing the mind for benefiting intellectual development; Radix Polygalae and Rhizoma Acori Tatarinowii have effects on mentality improvement, tranquillization and phlegm removal; Radix et Rhizoma Rhei helps to eliminate indigestion and remove blood stasis; Rhizoma Coptidis and Radix Scutellariae have effects of purging fire and detoxifying as well as clearing away heat and eliminating dampness; Radix Paeoniae Alba is good for nourishing blood for softening liver; Radix Angelicae Sinensis, Radix Salviae Miltiorrhizae and Rhizoma Chuanxiong are effective in activating qi flow and blood circulation to dissipate blood. Taken together, the preparation plays a role in benefiting qi for activating blood circulation, removing obstruction in collaterals and dissipating phlegm [9]. Therefore, the application of Shenzhi capsule as an adjunctive treatment could further alleviate the condition of patients with PD, reduce the severity of dementia and improve their cognitive function and activity of daily living.

Enhanced oxidative stress and deficiencies in the oxyradical scavenging capacity play an important role in the development of PD. Hence, the key point in the treatment of PD is to decrease oxidative stress in order

to reduce nerve cell damage and improve neurological function in the patients. SOD and MDA are commonly used indicators to reflect the level of oxidative stress as SOD is the primary substance for scavenging free radicals in organisms, and its level can indirectly reflect the body's scavenging ability, and MDA is a common marker of oxidative stress, and the higher its level, the more intense the oxidative stress response. NSE, S-100β and BDNF are commonly used in the assessment of neurological function. As a metabolic enzyme of the glycolysis reaction, the expression level of NSE is significantly increased when brain tissue is damaged. S-100β is a group of acidic calcium-binding proteins in gliocytes, and will high express in the blood when brain nerves are impaired. BDNF acts a key role in the repair of neurons, and its elevated levels can promote the repair of damaged neurons. Results of this study demonstrated that BDNF and SOD levels were significantly increased in both groups after treatment, while S-100β, NSE and MDA levels were significantly decreased, compared with those before treatment. Moreover, the levels of BDNF and SOD in the observation group were significantly higher than those in the control group, and the levels of S-100β, NSE and MDA in the observation group were the opposite, suggesting that adjunctive treatment of Shenzhi capsule could improve the therapeutic effects of donepezill hydrochloride tablets on patients with PD by effectively reducing oxidative stress level and improving neurological function. It has been found that donepezill hydrochloride tablets could reduce the production of reactive oxygen species and inhibit oxidative stress response in the body, thereby alleviating oxidative stress-caused nerve cells injury and facilitating neurological function [10]. Modern pharmacological studies have shown that in Shenzhi Capsule, the main components in Radix Polygalae and Rhizoma Acori Tatarinowii could significantly inhibit neuronal fibrous degenerative lesions; the main component of baicalin in Radix Scutellariae reduce neuronal damage caused by mitochondrial dysfunction and exert neuroprotective effects through its multiple physiological and pharmacological mechanisms, including anti-inflammatory, antioxidant and mitochondrial protective functions; Radix Paeoniae Alba contains paeoniflorin which has good neuroprotective and regulatory effects by inhibiting glutamate-induced apoptosis of nerve cells; the main component of tetramethylpyrazine in Rhizoma Chuanxiong could dissolve fibrinogen, dilute blood viscosity and improve microcirculation, thereby reducing the inflammatory response and oxidative stress response, and reducing nerve cell damage; the main component of tanshinone in Radix Salviae Miltiorrhizae could alleviate neurological function damage caused by oxidative stress through inhibiting the inflammatory reaction. Therefore, Shenzhi capsules combined with donepezill hydrochloride tablets in the treatment of PD have a dually facilitating effect on the neurological function by effectively relieving oxidative stress level in the patient's body.

In conclusion, on the basis of donepezil hydrochloride tablets treatment, Shenzhi capsules adjuvant treatment has a good effect on patients with PD, which could effectively reduce oxidative stress level, improve neurological function, cognitive function, and mental state, and improve their activities of daily living.

Acknowledgement

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, Data curation and Writing-Original draft, X.Y.C; Writing-review and editing, C.F.H; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable.

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