Clinical Observation of Sodium Oligomannate Capsules in the Treatment of Cognitive Dysfunction in Parkinson's Disease

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To observe the effect of sodium oligomannate capsules on cognitive dysfunction in Parkinson's disease. 120 patients with cognitive dysfunction were randomly divided into, 60 in treatment and 60 in control group and given sodium oligomannate capsules dose of 5 mg/d, 450 mg/d respectively and compared cognitive function scores (mini-mental state examination, Montreal cognitive assessment). After treatment, serotonin, dopamine, norepinephrine levels and event-related potential are measured. Compared with pre-treatment, the Montreal cognitive assessment and mini-mental state examination scores were significantly different after treatment (both $p<0.05$), and Montreal cognitive assessment and mini-mental state examination scores were significantly higher after treatment (both $p<0.05$). Compared to the control group, Montreal cognitive assessment and mini-mental state examination scores before treatment (both $p>0.05$), and Montreal cognitive assessment and mini-mental state examination scores were significantly increased after treatment (both $p<0.01$). Before treatment, serum serotonin, dopamine and norepinephrine levels were compared ($p>0.05$), and serotonin, dopamine and norepinephrine were higher than the control group ($p<0.01$). The latency period of N2 and P3 was significantly prolonged, and the N2 and P3 incubation periods were significantly reduced, with significant differences ($p<0.01$). Sodium oligomannate capsules can improve the cognitive function of Parkinson's disease patients by regulating neurotransmitter levels, reducing N2 and P3 latency, improving short and delayed memory and directional force.

Key words: Sodium oligomannate capsules, parkinson's disease, cognitive function, dyskinesia, depression

Parkinson's Disease (PD) is a common neurological degenerative disease with a prevalence of about 17/100 million in elderly over 65 y old, and is clinically manifested by motor symptoms such as dykinesia, muscle tonic, static tremor and non-motor symptoms such as depression, sleep disorders and cognitive impairment. With deeper knowledge of the disease, it was found that Parkinson non-motor symptoms appeared earlier than motor symptoms, with cognitive impairment being the most common symptoms[1]. Patients with PD combined with cognitive impairment had an abnormal secretion, Norepinephrine (NE), Serotonin (5-HT), and other neurotransmitters[2]. Monoamine neurotransmitters are important neurotransmitters in the brain and are closely related to learning, memory and cognitive ability in the brain[3]. Event-Related Potential (ERP) is an emerging international brain electrophysiology technology, which refers to the potential recorded on the scalp during the advanced cognitive process of a certain stimulus, which can reflect the brain's memory and judgment of the stimulus. Currently, drugs targeted for PD cognitive impairment are still very limited[4]. In recent years, sodium oligomannate capsules have achieved better results in the treatment of mild to moderate cognitive impairment. This paper discusses the clinical effect of sodium oligomannate capsules on cognitive impairment in PD. 120 patients with PD and dementia admitted from February 2018 to May 2020 are selected. Inclusion criteria meets the diagnostic criteria for PD in China (2016 version)[5]; diagnostic criteria with varying degrees of cognitive impairment; Montreal Cognitive Assessment (MoCA) scale score of <26;

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family members were informed of the study and signed consent. In exclusion criteria; combined with liver, cardiac and renal dysfunction; previous brain injury and craniotomy; involved drug allergy in this study. In the observation group, 36 men and 24 women; age 50 y-77 y, mean age (62.9±7.4) y; course (1-8) y, mean course (5.89±1.34) y; degree (H and Y):19 cases, 26 cases, V 15 cases. The control group had 35 men and 25 women; age 50 y-76 y, mean age (62.5±7.3) y; course 1-8 y, mean course (5.67±1.29) y; degree (H and Y) 23, 28 and 9 V. This study was approved by the hospital ethics committee. The basic conditions of the two groups were comparable ($p>0.05$). The control group was treated with donepezil (Jiangsu Hausen Pharmaceutical Group Co., Ltd., Sinopharm quasi word H20030472) at an initial dose of 5 mg per time, once a day, taken orally. Observation group of patients for sodium oligomannate capsules treatment drug manufacturer: Shanghai Green Valley Pharmaceutical Co., Ltd. Approval Document No. Sinopharm quasi H20190031.At 450 mg/times, 2 times/d. The MoCA evaluates patients' cognitive conditions, including concentration, executive function, memory, language ability, visual space and abstract thinking, with a full score of 30 points and 26 points as normal. Mini-Mental State Examination (MMSE) is the preferred scale for screening for dementia, including time orientation force, location orientation force, immediate memory, attention and computing force, delayed memory, language, visual space, the lower the score, the worse the symptoms of dementia. Serum 5-HT, Dopamine (DA), NE levels, 5 ml of fasting venous blood in the morning, continuous centrifugation at 3000 r/min for 10 min, isolated serum, and measured 5-HT, DA, NE levels before and after treatment with an High Performance Liquid Chromotagraphy (HPLC) (Shimazine, Japan, UFLCX-R). All objects were measured using a Nissan photoelectric four-channel evoked potentiometer. In a quiet shielding room, the subjects took the supine position, kept awake and mental concentration, and all the body muscles relaxed. According to the international Electroencephalography (EEG) 10/20 system placement method, the recording electrode is placed in the central midline (CZ), reference electrode is placed in the earlobe (A1 or A2), earhead (FPZ), inter-electrode impedance is less than 5 KΩ, The analysis time was 600 ms, the experiment used short-tone stimulation, non-raking stimulation (frequency of 1000 Hz) probability is 80 %; regular occurrence, the target stimulus (4000 Hz) is 20 %, random occurrence, interspersed in the non-target stimuli, subjects had to key press button responses to rake stimulation. The instrument automatically recorded the reaction time and hit rate, two test rounds per case and average. Abnormal criteria; P3 latency and (or) P3 amplitude decreased more than the control group. Statistical Package for the Social Sciences (SPSS) 22.0 software statistical data processing, measurement data in mean±standard deviation ($\bar{x}\pm s$), count data by rate, Chi-square (χ^2) test and t-test for paired sample t-test, and t-test for two independent samples. $p<0.05$ was considered as a statistically significant difference. Comparison of MMSE and MoCA scores before and after treatment in the 12 groups are shown in Table 1. Before treatment, the MMSE and MoCA scores were not statistically significant ($p>0.05$) and were comparable. The MMSE and MoCA scores before, 3 mo and 6 mo after treatment were all statistically significant ($p<0.01$). MMSE, MoCA scores after March and 6 mo were significantly higher than before treatment, with statistical significance ($p<0.01$); MMSE and MoCA scores after 3 mo of treatment were significantly higher than the control group, both significant ($p<0.01$). Before serum 5-HT, DA and NE levels, serum 5-HT, DA and NE levels were not significant ($p>0.05$). After treatment, serum 5-HT, DA and NE levels were higher than the control group ($p<0.05$) as shown in Table 2. ERP measurements comparing N1 and P2 wave latency (N1PL, P2PL) ($p>0.05$) between the two groups in Table 3; N2 and P3 wave latency (N2PL, P3PL) were significantly reduced in the treatment group compared with the control group, ($p<0.01$). The cognitive decline of PD occurs throughout the disease process, and about 80 % of the patients develop Parkinson's dementia[6]. These patients showed a decline in cognitive functions such as execution, attention, visual spatial capacity and memory, and a significant decline in daily quality of life. Patients with PD had late memory decline, and their work, social ability and living ability all decreased to varying degrees. Some patients were also accompanied by mental, behavioural and personality abnormalities. These disability manifestations can seriously affect the patient's daily life and bring a greater burden on the family. The mechanism of cognitive impairment in PD patients is unclear and may be caused by multiple factors leading to different cortical areas and their connectivity damage[7]. Early cognitive impairment

may be primarily related to the impairment of the dopaminergic system. As the disease progress, many factors are involved, and Lewy degeneration in cortical and limbic structures, and Alzheimer disease-like pathological alterations may play an important role. PD cognitive dysfunction is affected by many factors. Older onset has a higher incidence of cognitive impairment and dementia than younger age-onset PD patients and the longer the course, the heavier the degree of cognitive impairment[8,9]. The prevalence of dementia in PD, 12.4 % between 50 y–59 y, compared to 68.7 % after 80 y[10]. Monoamine neurotransmitters belong to the very important neurotransmitters in the human body, which directly affects the human endocrine regulation, emotion, cognitive functions and various behaviours. Once the monoamine neurotransmitters in the elderly are reduced, they will cause senile dementia, and the patients will have severe memory decline and cognitive dysfunction. Brain neurotransmitter expression level can directly reflect the brain tissue damage, is an important evaluation index of PD dementia efficacy, NE, DA, 5-HT widely exists in the cerebral cortex and nerve synapses, is an important brain neurotransmitter, modern medical research shows that monoamine neurotransmitters NE, DA, 5-HT involved in synaptic transmission, can directly or indirectly participate in brain function activities, consistent with the degree of dementia[11]. Among them, the NE is closely related to memory retention, and while the DA release acts on memory improvement, the 5-HT indirectly affects learning memory by regulating mood, appetite and motivation. The extensive projection to the brain central nervous system through axonal connections, regulating the excitatory state of the cerebral cortex, has broad effects on arousal, mood, cognitive function and movement[12]. DA has multiple biological effects, such as inhibition of lipid peroxidation, reducing oxidative stress damage, increase of blood flow supply in the brain, improving the utilization of glucose in brain neurons, to regulate the excitatory state with NE[13]. 5-HT is an important neurotransmitter for the maintenance of intelligence by regulating the release of Acetylcholine (ACh) in the brain tissue, thus regulating central cholinergic neural activity[14]. The results of this experimental study showed that the monoamine neurotransmitter NE, DA and 5-HT content were significantly increased compared with controls, suggesting that the mechanism of action of sodium oligomannate capsules to improve cognitive function in PD patients may be by improving the brain monoamine neurotransmitter NE, DA and 5-HT content. ERPs are a response to the brain in combination with cortical activity, where N2 and P3 are generated from the temporal, parietal and prefrontal regions.

TABLE 1: COMPARISON OF MMSE AND MoCA SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT ($\bar{x}$±s)

Group	Time	Cases	MMSE	MoCA	p value
Control	Pre-treatment	60	21.05±2.32	20.76±1.78	
	3 mo	60	22.47±2.12	22.62±2.16	p<0.05
	6 mo	60	24.97±1.01	23.75±3.55	p<0.05
Treatment	Pre-treatment	60	21.14±2.08	20.62±1.59	
	3 mo	60	25.16±2.26	24.94±1.87	p<0.01
	6 mo	60	29.06±3.45	28.36±2.25	p<0.01

TABLE 2: COMPARISON OF SERUM 5-HT, DA AND NE LEVELS BEFORE AND AFTER TREATMENT BETWEEN THE TWO GROUPS ($\bar{x}$±s, gL^{-1})

Group	Time	Cases	5-HT	DA	NE	p value
Control	Pre-treatment	60	8.28±1.62	9.73±1.47	7.77±1.43	
	3 mo	60	10.63±1.92	11.58±2.94	13.47±2.14	p<0.05
	6 mo	60	13.65±1.73	15.46±2.68	17.56±2.65	p<0.05
Treatment	Pre-treatment	60	8.35±1.69	9.82±1.59	7.82±1.49	
	3 mo	60	12.67±2.27	14.22±3.21	17.16±2.88	p<0.01
	6 mo	60	15.54±3.12	17.35±2.89	22.34±3.01	p<0.01

TABLE 3: ERP MEASUREMENTS COMPARING N1 AND P2 WAVE LATENCY (N1PL, P2PL) BETWEEN THE TWO GROUPS ($\bar{x}$±s)

Group	Time	Cases	N1PL	P2PL	N2PL	P3PL	P3AMP	p value
Control	Pre-treatment	60	96.5±12.6	17.6±15.3	256.3±12.4	335.8±13.2	8.6±3.1	
	3 mo	60	92.3±11.8	15.6±12.5	245.3±11.3	330.6±10.5	7.8±3.3	p<0.05
	6 mo	60	90.5±12.6	14.3±11.4	232.3±12.6	325.8±13.2	6.5±3.5	p<0.05
Treatment	Pre-treatment	60	98.5±13.2	18.5±12.6	252.3±11.6	338.2±12.2	8.8±3.2	
	3 mo	60	90.2±12.6	15.2±11.2	230.4±12.3	321.5±12.5	6.3±3.3	p<0.01
	6 mo	60	86.5±10.9	12.3±10.8	223.7±13.2	300.2±11.3	5.4±3.5	p<0.01

N2 reflects the short-term memory function and the pre-attention storage that occurs in the sensory cortex, and the P3 latency represents the process from receiving stimulation to making a response. Therefore, indicators of ERPs can objectively evaluate cognitive function. P3 as a component of ERP is currently an important electrophysiological indicator for the study of cognitive function. The close correlation of the endogenous components of ERP to cognitive processes can objectively reflect advanced thinking activities such as brain cognition and judgment[15]. P300 latency reflects that the human brain-stimulus evaluation time represents the judgment process of memory background updating and closure[16]. Our results showed significant differences in P300 latency in PD patients as compared with controls. Studies have found abnormal ERPs in patients with PDD. The study reported that P3 and N2 latencies in patients with dementia were significantly longer than normal controls, while patients with PD without dementia had only an extended P3 latency[17]. The study found that PD with dementia was significantly longer in P3 latency compared with control groups. The study found that the N2 and P3 latencies in non-dementia PD patients were longer than in normal controls, and were more pronounced in dementia patients than in non-dementia patients[18]. The study also found that the N2 and P3 latencies of PD patients were correlated with the total MMSE score, directional force and delayed memory, and the longer the latency of N2 and P3, the more serious the cognitive impairment[19]. This study showed that the latency of N2 and P3 was significantly prolonged, and that of N2 and P3 in the control group, which confirmed that sodium oligomannate capsules may improve patient cognitive impairment by improving short-term and delayed memory. In conclusion, the treatment of patients with cognitive dysfunction can effectively improve the learning, memory function and orientation, and the brain monoamine neurotransmitters NE, DA, 5-HT content and N2 and P3 latency are more obvious, which is more conducive to promoting the improvement of cognitive function in patients.

Conflict of interests:

The authors declared no conflict of interests.

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