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Therapeutic effect of piracetam with nimodipine on vascular dementia after cerebral infarction

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Abstract: This article investigated the clinical effects of piracetam with nimodipine in the treatment of vascular dementia (VD) after cerebral infarction. 98 patients with vascular dementia after cerebral infarction were selected and divided into the control group and the study group according to the treatment method. The control group was treated with nimodipine alone. The study group was treated with piracetam on the basis of this observation, and we test the ADL (life ability score), MoCA(montreal cognitive assessment scale), ADAS-Cog(alzheimer's scale-cognition), MMSE(mental status examination) scores and quality of life scores before and after treatment in the two groups. Before treatment, there were no significant differences in ADL, MoCA, and ADAS-Cog scores between the two groups (P>0.05). After treatment, the ADL, MoCA, and ADAS-Cog scores of the study group were superior to the control group. The difference was statistically significant (P<0.05). There was no significant difference in MMSE scores between the two groups before treatment and 1 month after treatment (P>0.05). The MMSE scores of the study group were better than the control group after 3 months of treatment and half a year after treatment. The difference was statistically significant (P <0.05). Before treatment, there was no significant difference in the quality of life scores between the two groups (P>0.05). After treatment, the quality of life scores was significantly higher than the control group, and the difference was statistically significant (P<0.05). For patients with vascular dementia after cerebral infarction, piracetam combined with nimodipine can improve the cognitive function, improve the quality of life, and have a significant clinical effect.

Keywords: Piracetam, nimodipine, cerebral infarction, vascular dementia.

INTRODUCTION

Vascular dementia VAD is a general term for a series of cerebrovascular factors that cause dementia caused by cerebral vascular damage(Cristina *et al.,*2018). It is the result of degeneration of the damage caused by stroke after the intelligence is fully developed (Bagatini *et al.,* 2011). It is a mental disorder with the main characteristics of misunderstanding and calculation of poor power, including multiple infarct dementia (MID), cerebral hemorrhage, and post-cerebral thrombosis. The incidence rate is increasing year by year(Bergmann *et al.,* 2016). Due to the different examination methods, population samples, age and dementia diagnostic criteria, the results are quite different (Carroll *et al.,* 2012). The European and American literature reports that the prevalence of dementia in people over 60 years old is as high as 16-29%, and VAD accounts for all. I2-37.2% of dementia: In Japan, VAD accounts for 60-70% of senile dementia. In China, the prevalence of dementia in the elderly over 60 years old (Beijing area) is 3.96%, VAD is 2/3, about in 30% of stroke patients, there may be a mental decline (Aparicio *et al.,* 2018).

In the past, the medical profession focused on the study of post-stroke consciousness, language and physical dysfunction, but did not pay enough attention to the study of mental disorders caused by stroke. In recent years, with the improvement of medical standards and the prolongation of human life, people realize that dementia can also cause patients to lose their daily living ability, and bring a heavy burden to society and families (Ceylan *et al.,* 2016). It has become one of the important diseases that threaten the lives of the elderly (Chtourou *et al.,* 2015). Therefore, exploring VAD early diagnosis methods and prevention measures has become an important issue in modern scientific research and clinical practice. At present, the clinical treatment of VAD lacks the ideal drug, the key is to prevent cerebrovascular disease and reduce the risk factors of the disease, so domestic and foreign scholars A lot of observations and analysis have been made on the risk factors of this disease, and more similar conclusions have been drawn (Carloto *et al.,* 2019). It is agreed that the occurrence and development of stroke is closely related to the production of VAD (Ajami *et al.,* 2016). Hypertension is the most dangerous single factor, about 66% of patients with VAD are associated with hypertension, followed by hyperlipidemia, accounting for 21%. Other factors such as diarrhea, coronary heart disease, etc., these factors are also the risk factors for stroke and multiple strokes are the direct factors of VAD.

Pathophysiological studies have shown that cerebral blood flow decline is one of the important pathological

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causes of WAD. BaHistin et al used positron emission tomography (PET) to study 15 patients with multiple infarct dementia (Ayinuer *et al.,* 2019). Most of the cortical areas showed a significant decrease in blood perfusion, and the parietal lobe was the most prominent (Dindo *et al.,* 2004). There were two main reasons for the decrease of blood flow in the brain. First, due to multi-focal microinfarction in the brain, or repeated episodes of cerebral hemorrhage and cerebral artery stenosis or occlusion after extensive infarction, resulting in global cerebral ischemia, decreased brain tissue perfusion, circulatory disturbance, and decreased function. Studies have shown that only destructive enough brain tissue (60-80ml) can damage brain function and dementia; second, due to decreased excitability of brain tissue function, leading to a decrease in brain metabolic rate and blood flow (Dabash *et al.,* 2015). More information indicates that VAD is not only related to the volume of damage, but also to the location of brain damage and changes in subcortical white matter. MRI study of 24 patients with VAD showed that the average volume of cerebral infarction was significantly greater than that of non-dementia (Forero *et al.,* 2018). The infarct site was mainly located in the left parietal cortex, which was 8 times that of non-dementia patients. Event-related potential (EPR) can reflect brain potential changes related to human brain cognitive activity. It has been widely used in the detection of dementia patients in recent years. Various studies have shown that the P300 latency of various dementia EPRs is significantly prolonged.

In the past 20 years, many developed countries have studied the causes of VAD from the aspects of neurotransmitters and neurobiochemistry. Acetylcholine (ACH) is a neurotransmitter for performing and maintaining advanced neurological functions (Goldstone *et al.,* 2017). Mainly related to memory, thinking and intelligence. The metabolic enzymes of the biliary system, choline acetylated strontium (CAT) and cholestasis (CHE), reflect the state of cholinergic energy (Henkel *et al.,* 2018). Researchers in the United States, Britain, Finland, and Japan have successively proposed that the activity of acetylcholinesterase CACHE in brain tissue and cerebrospinal fluid in patients with senile dementia (SDAT) is reduced, and attempts to reduce ACHE activity as a reference for the diagnosis of SDAT First, SDAT and VAD are two types of diseases that differ from clinical and biochemical mechanisms to pathological aspects. There is also a decrease in ACHE in the cerebrospinal fluid of patients with VAD (Isabel *et al.,* 2019). Domestic Ding Qiang and other small patients who were diagnosed with MID were found to have a significant reduction in activity. In addition, Li *et al* found that the levels of growth inhibition (SS) and arginine vasopressin (AVP) in cerebrospinal fluid of patients with VAD were significantly lower than those of the control group, and these two substances were memory-related neuropeptides.

The diagnosis of VAD must have three important conditions: one is the basis of clinical dementia syndrome; the other is that there must be sufficient evidence of cerebrovascular disease at the same time, confirmed by neuropathology or neuroradiology and other auxiliary examinations: Three is before, both must be related to each other (Danir *et al.,* 2017). The National Institutes of Health (NIH) clearly stated in 1993 that the symptoms of dementia must occur within 3 months of the onset of cerebrovascular disease to be diagnosed as VAD. The diagnosis of dementia is based on the internationally recognized DSM-R standard, which performed. The "ischemic score table" developed by Hnchm is used to distinguish VAD from SDAT. The severity of dementia is determined by a series of scale tests to objectively characterize subjective symptoms (Ji *et al.,* 2015). The Wechsler Adult Intelligence Scale (WMS-RC) is a reliable and effective method for measuring intelligence. It has been widely used in clinical practice (Fardeau *et al.,* 2014). The scale reported in the country is also the Hasegawa Dementia Scale (HDS) and the Simple Semen Condition Examination Dementia. Scale (MMSE), Social Activity Function Questionnaire (FAQ), and Cognitive Function Questionnaire (CCSE).

The average age of our population is getting higher and higher, and the incidence of various senile diseases is increasing year by year (Goldberg *et al.,* 2015). Especially the cerebrovascular diseases such as hypertension and coronary heart disease have been widely concerned. Cerebral infarction is also known as ischemic cerebrovascular disease in the clinic, mainly due to insufficient blood supply to the brain due to thrombosis formed in the cerebral blood vessels and other causes (Gatter *et al.,* 2015). Vascular dementia is a common syndrome of cerebrovascular disease, with a good clinical incidence and many predisposing factors, mainly manifested as cognitive and memory defects. Patients will be accompanied by emotional and language abnormalities, which will pose a certain threat to patients' life and health (Gao *et al.,* 2010). At present, most of the clinical treatments include antihypertensive, calcium antagonists and cholesterol lowering. This study focused on the clinical efficacy of piracetam combined with nimodipine in the treatment of vascular dementia after cerebral infarction.

MATERIALS AND METHODS

General information

98 patients with post-infarction vascular dementia admitted to our hospital from May 2018 to May 2019 were selected. According to the different treatment methods, there were 49 cases divided into two groups. There were 26 males and 23 females in the control group; the age ranged from 54-76 (63.69±4.52) years; the course of disease was 1-9 (5.25±1.58) years. There were 27

males and 22 females in the study group; the age ranged from 54-76 (63.34±4.34) years; the course of disease was 1-9 (5.32±1.53) years. There were no significant differences in the general data of age and gender between the two groups (P>0.05).

Inclusion and Exclusion Criteria

Inclusion criteria: (1) All patients were diagnosed by routine examination and diagnosis; (2) the level of education above primary school, with simple living ability; (3) no other serious medical diseases; (4) the family members of the patients are aware of this study and are willing to participate. Exclusion criteria: (1) combined with neurological diseases; (2) taking drugs that affect cognitive function; (3) cognitive decline caused by other factors; (4) weakened limbs or severe aphasia.

Methods: In the control group, only nimodipine (manufacturer: Yabao Pharmaceutical Group Co., Ltd., approval number: National Drug Standard H14022821) was used for treatment, orally, 3 times/d. The research group gave patients with piracetam tablets (manufacturer: Jiangsu Pengyi Pharmaceutical Co., Ltd., approval number: Guoyao Zhunzi H32021019).

Clinical Observation Indicators

Observing and comparing the two groups: (1) Life ability score (ADL): Observing the patient's ability of daily living activities, divided into 10 evaluation items such as eating, entering and leaving the toilet, dressing, and stool control, with a score of 100 points and a score of more than 60 points. Can be done, <20 is completely in need of help (3). (2) Montreal Cognitive Assessment Scale (MoCA): Includes 8 tests in the cognitive field. The total score is 30 points, out of 30 points, divided into 26 points, and M26 is classified as normal. (3) Alzheimer's Scale-Cognition (ADAS-Cog): Observational items include structural exercises, naming, instruction, orientation, and oral ability. The score range is 0-75. The higher the score, the more cognitive impairment. serious. (4) The patient's cognitive impairment was scored by the Simple Intelligence Mental Status Examination Scale (MMSE), which was divided into 7 scoring dimensions. The score ranged from 0 to 30, both before treatment, 1 week, and treatment 3. The scores were evaluated in months and treatments, including 27-30 points for normal, 21-26 points for mild cognitive impairment, 10-20 points for moderate cognitive impairment, and 0-9 points for severe cognitive impairment. (5) Using the Quality of Life Scale (GQOL-74) to investigate the quality of life of the two groups of patients, including psychological function, material life, physical function, and social function. Each item has a score of 100, and the score is proportional to the quality of life.

Ethical approval

All patients were approved by Ethics Committee of our hospital and signed on the informed consent. Ethical approval number as 17TCPHTD2.

STATISTICAL ANALYSIS

All the data were processed by SPSS 21.0 statistical software. The measurement data is represented by $x \pm s$ and t test. P<0.05 showed statistically significant differences. Chi square test is applicable to the significance test of the rate or percentage difference between two groups and independent sample t-test was used for comparison between groups. P<0.05 showed significant difference.

RESULTS

Comparison of Scores before and after Treatment in Both Groups

Before treatment, there were no significant differences in ADL, MoCA, and ADAS-Cog scores between the two groups (P>0.05). After treatment, the scores of the study group were better than the control group, and the difference was statistically significant (P<0.05). See table 1.

Comparison of MMSE Scores before and after Treatment in Both Groups

There was no significant difference in MMSE scores between the two groups before treatment and 1 month after treatment (P>0.05). The MMSE scores of the study group were better than those of the control group after 3 months of treatment and half a year after treatment. The difference was statistically significant (P<0.05) (table 2).

Comparison of GQOL-74 Scores before and after Treatment in Both Groups

Before treatment, there was no significant difference in the quality of life scores between the two groups (P>0.05). After treatment, the GQOL-74 scores of the study group were higher than the control group, the difference was statistically significant (P<0.05) (table 3).

Comparison of MMSE and ADL Scores between MMSE Scores before Treatment

The difference was not statistically significant (P>0.05). The MMSE and ADL scores of the observation group were higher than those of the control group after 6 months of treatment (P<0.05) (table 4).

DISCUSSION

With the progress of our society and the improvement of the economic level, people's requirements for quality of life are getting higher and higher (Joanna *et al.,* 2019). They not only need to reduce the pain of the body, but also hope to maintain high-level cognitive and emotional needs and maintain their status as a social person. As a direct threat to human health, cerebral infarction has a

Table 1: Comparison of scores before and after treatment in both groups (x ± s, Fraction)

Group	ADL		MoCA		ADAS-Cog	
	Before treatment	End of treatment	Before treatment	End of treatment	Before treatment	End of treatment
Control group	35.85±5.52	51.25±4.58	20.30±3.61	23.62±2.58	65.52±4.25	58.63±4.02
Research group	36.52±5.26	60.58±4.25	20.58±3.25	27.52±2.02	65.33±4.02	48.63±3.69
t	-0.615	-10.453	-0.404	-8.331	0.227	12.828
P	0.540	0.000	0.687	0.000	0.821	0.000

Table 2: Comparison of MMSE scores before and after treatment in both groups (x ± s, Fraction)

Group	Before treatment	Treatment for 1 month	Treatment for 3 months	Half a year of treatment
Control group	10.34±4.43	12.23±3.53	14.26±3.11	17.69±3.32
Research group	10.23±4.12	12.41±2.32	17.34±2.69	22.04±2.36
t	0.127	-3.281	-5.243	-7.475
P	0.899	0.001	0.000	0.000

Table 3: Comparison of Quality of Life Scores before and after Treatment in Both Groups (x ± s, Fraction)

Group	Physical energy		Sleep quality		Joint movement function		Social life	
	Before treatment	End of treatment	Before treatment	End of treatment	Before treatment	End of treatment	Before treatment	End of treatment
Control group	51.76±6.25	63.23±6.36	55.47±6.20	66.30±6.34	53.36±7.22	65.54±7.54	60.54±7.54	70.54±7.34
Research group	51.56±6.36	72.65±5.47	55.30±6.14	75.34±5.12	53.46±7.43	74.43±6.54	60.42±7.43	80.34±6.51
t	0.181	-7.861	0.136	-7.765	-0.068	-5.533	0.079	-6.992
P	0.857	0.000	0.892	0.000	0.946	0.000	0.937	0.000

Table 4: Comparison of MMSE scores between the two groups

Group	n	MMSE score		ADL score	
		Before treatment	After 6 months of treatment	Before treatment	After 6 months of treatment
Control group	49	15.10±8.39	26.86±5, 36	35.69±5.71	54.38±4.52
Research group	49	15.08±&35	20.57±4.91	35.73±4.86	45.46±5.43
P		0.127	0.001	0.048	0.000

high disability rate and mortality rate, which will directly affect the patient's life safety (Kanninen *et al.,* 2018). The disease has the characteristics of rapid onset and rapid progress, so the early diagnosis of patients is of great significance for clinical diagnosis and treatment (Karen *et al.,* 2017). Vascular dementia after cerebral infarction occurs in the elderly, dementia caused by brain insufficiency caused by one or more cerebral infarctions. Studies have shown that cerebral arterial occlusion leads to decreased brain tissue perfusion and decreased brain function excitability (Kohlrausch *et al.,* 2018). It is related to the decrease of metabolism, which is related to the decrease of choline transmitter concentration in the relevant region of the brain and the direct damage to the cholinergic nerve conduction system (Kellermann *et al.,* 2011).

At present, symptomatic treatment is the main, including improving cerebral circulation drugs such as nimodipine, neurotransmitter replacement therapy, traditional Chinese medicine extract ingredient treatment and traditional Chinese medicine acupuncture treatment (Latino *et al.,* 2012). The first two types are the most widely used and the effect is better. The amount is significantly higher than normal tissue. In addition, nimodipine can also affect the electrical properties of neurons and the balance of neurotransmitters (Maria *et al.,* 2019). Piracetam is a cyclized derivative of a-amino-acid that selectively acts on the central nervous system, increases the brain's utilization of ATP/ADP, and promotes the synthesis of polyribosomes (Meydani *et al.,* 1998). It can improve the regional cerebral blood flow of ischemic tissue, counteract the brain function damage caused by physical factors and chemical factors, affect the excitatory transmission of cholinergic neurons, promote the synthesis of acetylcholine, increase the release of dopamine, and improve the hypoxia. Retrograde forgetfulness, enhance memory and improve learning ability (Martins *et al.,* 2018).

A large number of studies have confirmed that there are many complications in patients with cerebral infarction. Among them, vascular dementia is a relatively common symptom, which has a certain impact on the quality of life

of patients (Norgren *et al.,* 2007). Because cognitive dysfunction is a common complication in cerebral infarction, most patients are caused by vascular or neurological factors, and vascular cognitive impairment is mainly due to cerebrovascular risk factors, and patients may even cause cardiovascular and cerebrovascular risk in later stages (Tooze *et al.,* 2006). In recent years, cerebral infarction has been paid more attention in clinical practice. The clinical focus is also on reducing the mortality rate of patients, promoting the recovery of physical function and paying attention to patients' cognitive dysfunction and restoring the recovery of patients (Ohannessian, 2016). With the continuous improvement of China's economic level, the clinical requirements for quality of life are also constantly improving, and more committed to maintaining patient cognitive and communication (Otify *et al.,* 2019). Regarding the current clinical treatment, there is no specific drug for vascular dementia, but early intervention can delay the impairment of cognitive function. This article included the treatment of piracetam and nimodipine, and the results showed that the two groups before treatment There was no significant difference between the scores of ADL, MoCA and ADAS-Cog. There was no significant difference in MMSE score between the two groups before and 1 month after treatment. There was no significant difference in the quality of life score between the two groups before treatment ($P>0.05$). The scores of ADL, MoCA and ADAS-Cog in the study group were better than those in the control group. The MMSE scores of the study group were better than those of the control group at 3 months of treatment and half a year after treatment. In the control group, the difference was significant ($P<0.05$). Among them, nimodipine has a better curative effect on improving cerebral circulation (Negron *et al.,* 2019). It is a calcium ion antagonist, which can improve the blood circulation of patients' brains in time. It has remarkable curative effect in treating vascular cognitive dysfunction, and its clinical safety is high (Patel, 2016). The patient has a certain dependence; through selective action and cerebral vascular smooth muscle, the blood vessels of the brain are dilated, the cerebral blood flow is increased, and the intelligence is protected and restored, and the recurrent stroke is actively prevented. It is the preferred drug (Pereira *et al.,* 2018). And piracetam can directly act on the cerebral cortex, play a good role in the protection and repair of nerve cells, promote the absorption of amino acids, stimulate the secretion of dopamine, improve the cognitive impairment of patients; drugs can selectively act on the hippocampus and The cerebral cortex promotes nerve excitation and increases brain metabolism; it can increase cerebral blood flow, activate nerve cells, reduce patient metabolism, repair brain nerves, and improve ischemic conditions in patients (Subar *et al.,* 2006). Because of cerebral infarction in patients with vascular dementia, the treatment is mainly symptomatic treatment, and improve the blood flow and metabolism of the patient's brain, to avoid the deterioration of the patient's condition and promote the recovery of brain function (Touvier *et al.,* 2005). As a clinically recognized cerebrovascular drug, nimodipine actually acts on cerebral vascular smooth muscle, promotes cerebral blood flow, promotes mental recovery and reduces the risk of brain damage (Santeliz *et al.,* 2019). Therefore, after treatment, the patients' daily living ability and cognitive function are significantly improved, and the adverse reactions during treatment are less, indicating that the combined treatment effect is significant, which can promote the patient's early recovery (Pilar *et al.,* 2018).

The CDT, ADL and CDR scores were mainly used to evaluate the improvement of VD cognitive function between virazacetam and nimodipine, although there was no significant difference in CDT and CDR results between the two groups at 3 months, but from the data point of view There have been signs of improvement, and there is a statistically significant difference in CDT and CDR scores between the two groups at 6 months after treatment (Selvin, 2004). Patients in the study group were significantly better than the control group in cognitive improvement, and the CDT score was consistent with MMSE in cognitive function evaluation (Verdot *et al.,* 2017). As the treatment time prolonged, the disease did not progress or progressed slowly. The combination of the two drugs can greatly improve the recovery rate and recovery of patients, improve the reduction of choline transmitter concentration in related areas caused by ischemic brain injury, improve blood flow perfusion and energy utilization of brain tissue, and stimulate brain Organize and improve cognitive function.

CONCLUSION

The total effective rate of the study group was significantly higher than that of the control group after treatment, suggesting that the MMSE scores of memory, computational power, comprehension and language function were significantly higher in the study group than in the control group. Two groups of patients with transient dizziness, anorexia, mild insomnia and other adverse reactions were relieved after symptomatic treatment, did not affect the normal treatment process, and the adverse reaction rate of the study group was significantly lower than the control group. In summary, patients with vascular dementia after cerebral infarction can be treated with piracetam and nimodipine. The blood flow in the brain is significantly increased, the cognitive function is significantly improved, and the quality of life is improved.

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