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Original Article

The effectiveness of cross electro-nape-acupuncture in treating vascular dementia and the influence of homocysteine

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Abstract: Objective: To observe the effect of cross electro-nape-acupuncture combined with Duxil (almitrine 30 mg, raubasine 10 mg) in the treatment of vascular dementia. Methods: A total of 90 patients with vascular dementia were randomized into three groups: the acupuncture group, the cross electro-nape-acupuncture combined with Duxil group, and the medicine group, with 30 patients in each group. In the acupuncture group, we selected yifeng (SJ17), fengchi (GB20), sishencong (EX-HN1) and baihui (DU20) as the acupuncture points; the cross electro-nape-acupuncture combined with Duxil group used Duxil in addition to the treatment the acupuncture group received, with this electrode connection: the left-sided SJ17 was connected to the anode, and the right-sided GB20 was connected to the cathode. Similarly, the right-sided SJ17 was connected to the anode, and the left-sided GB20 was connected to the cathode. The left EX-HN1 was connected to the right EX-HN1. In the medicine group, we used only Duxil as the treatment. We treated the patients for six weeks in each group, and we administered the mini-mental state examination (MMSE) scale, the Hasegawa Dementia scale (HDS), and the Ability of Daily Living (ADL) scale before the treatment, and then after six weeks, when the treatment courses were completed, we administered the three examinations again. We also measured the homocysteine (HCY) levels before and after the treatment. Results: The efficiency of the acupuncture group was 73.33%, the efficiency of the medicine group was 63.33%, and the efficiency of the cross electro-nape-acupuncture combined with Duxil group was 90%. Conclusion: The cross electro-nape-acupuncture combined with Duxil group experienced a significant effect in the treatment of vascular dementia, for the treatment improved the patients' social, daily living, and personality (emotional personality) abilities, reduced their serum homocysteine levels, increased the excitability of their cerebral cortexes, and improved the patients' learning, memory and other recovery capabilities.

Keywords: Cross electro-nape-acupuncture, vascular dementia, Duxil, dementia scale, homocysteine

Introduction

Vascular dementia refers to dementia caused by brain damage, which is caused by cerebrovascular lesions such as ischemia or bleeding and acute or chronic hypoxia. Its clinical manifestations include impairments in memory, the ability to solve problems in daily life, and the ability to respond [1, 2]. The occurrence of the disease is positively related to age, and vascular dementia is increasing due to the aging of the population [3, 4]. Vascular dementia is one of the most common causes of dementia after Alzheimer's disease, but unlike Alzheimer's disease, there are no approved treatments for vascular dementia [2]. VD is a preventable dementia disease, and appropriate treatment should be given as soon as possible. Modern medicine has made great progress in diagnosing vascular dementia, but progress in its treatment has been slow. The treatment of vascular dementia has become a well-known and difficult problem

in the world today. Acupuncture, an ancient Chinese treatment method, has been used for both the prevention and treatment of diseases for over 3,000 years. Electroacupuncture is a therapeutic method combining acupuncture with electrical stimulation. Many clinical studies have confirmed the positive effects of electricity on patients with dementia [5-7], and this study aims to determine the efficacy of cross electro-nape-acupuncture treatment on vascular dementia.

Materials and methods

General information

The Second Affiliated Hospital of Heilongjiang University of Chinese Medicine provided the observed cases from January 2018 to December 2019. The study cohort came from the hospital's outpatient departments and the house of acupuncture and the severe wards. We divided the 90 cases of vascular dementia patients into three groups using the random digital meter method. The patients included 45 men and 45 women, ranging in age from 45 to 79 years old. Regarding the patients' stays in the hospital or its facilities, the longest duration was fifteen years, and the shortest duration was three months. The general situation of the three groups of patients is shown in **Table 1**. The general situation of the three groups of patients before the treatment and compared with each other, after we completed the chi-square tests and the analyses of variance, we found that the *p*-values were all more than 0.05 (P>0.05), so the differences were not statistically significant, and the three groups were comparable, as shown in **Table 1**.

Diagnostic criteria

The diagnostic criteria for vascular dementia from the international experts committee AIREN standards for NINDS.

Inclusion criteria

1. NINDS-IREN vascular dementia with diagnostic criteria; Dementia onset over 3 months earlier. 2. MMSE score: higher than 17, persistent primary Illiteracy 1%, more than 20 points, more than 24 points, high school or above. 3. Hachinski ischemia rating scale 7 points: Hamilton depression rating scale (HAMD) score eight points. 4. According to the vascular dementia classification table (CDR), dementia degree for mild (CDR = 1.0) and moderate (CDR = 2.0).

Exclusion criteria

1. Patients who do not meet the above inclusion criteria. 2. Patients diagnosed with dementia using the DSM-IV standard from other causes of dementia. 3. Patients with other mental illnesses or mental disorders. 4. Patients with hearing, speech, or visual impairment. 5. Patients who received systematic treatment related to the disease in the previous one month.

Treatment

(1) The acupuncture group: Acupoints selection: SJ17 (bilateral), GB20 (bilateral), EX-HN1, DU 20. SJ17 (bilateral), perpendicularly 0.8-1.2 inches. GB20 (bilateral), towards the opposite nose tip, penetrate 1.0 inches. EX-HN1, toward DU20, penetrate 0.5-0.8 inches. DU20, penetrate flatly 0.5-0.8 inches. Needle every 30 minutes, twice a day for six weeks.

(2) The medicine group: Drug name: mesylate. Prescription common name: Duxil. Manufacturer: France Servier Pharmaceutical Factory. Preparation: tablets, containing dimethyl sulfonic acid, almitrine 30 mg, raubasine 10 mg. Usage: take orally, one tablet each time, 2 times a day, and with meals. Six weeks for one period of treatment.

(3) The cross electro-nape-acupuncture combined with Duxil group: Based on the acupoint selections of the acupuncture group and treated using crisscross electroacupuncture combined with Duxil.

A Changzhou INTI KWD_808 pulse acupuncture instrument (YING DI KWD-808 multi-purpose health device) was applied through continuous wave every 30 minutes, twice a day for six weeks. Crisscross electroacupuncture in the nape points namely: the left-sided SJ17 was connected to the anode, the right-sided GB20 to the cathode. Similarly, the right-sided SJ17 was connected to the anode, the left-sided GB20 to the cathode.

Statistical analysis

The statistical analyses was performed using GraphPad Prism for Windows statistical soft-

Table 1. The general situation of the three groups of patients ($\bar{x}\pm s$)

Group	n	Sex		Age Year	Cultural degree			Course Mouth	Illness degree	
		Man	Woman		Primary	Middle	University		Light	Middle
Acupuncture	30	15	15	58.67±7.52	12	12	6	60.00±7.59	14	16
Electro-nape-acupuncture combined with medicine	30	14	16	59.03±6.84	14	9	7	60.17±6.64	16	14
Medicine	30	16	14	60.27±7.36	13	12	5	59.67±7.12	17	13
P		0.875		0.677		0.905		0.962	0.732	

Table 2. Comparison of clinical curative effects of the three groups of patients before and after the treatment

Group	n	Marked effect	Powerfully	Effective	Invalid	Total effectiveness	X^2	P
Acupuncture	30	8	6	8	8	73.33%	8.152	0.227
Electro-nape-acupuncture combined with medicine	30	11	8	8	3	90.00%		
Medicine	30	4	6	9	11	63.33%		

Table 3. Comparison of the MMSE scale scores before and after the treatment among the three groups ($\bar{x}\pm s$)

Group	n	Before treatment	After treatment	t	P
Acupuncture	30	17.50±2.52	23.60±2.27	-27.71	0.000
Electro-nape-acupuncture combined with medicine	30	17.47±2.57	27.50±1.20	-26.69	0.000
Medicine	30	17.77±2.40	20.30±3.11	-5.16	0.000

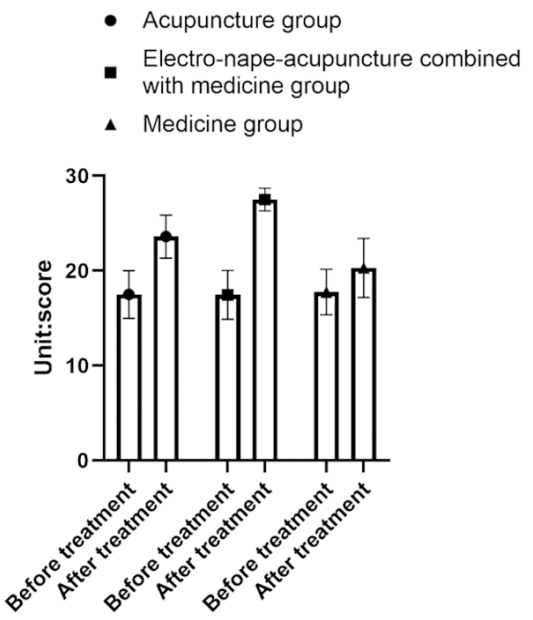

Figure 1. Comparison of the MMSE scale scores before and after the treatment among the three groups. After doing the paired-samples T tests, our comparison of the MMSE scale scores before and after the treatment in the acupuncture group, there was a very significant difference (P=0.000, P<0.01). Our comparison of the MMSE scale scores before and after the treatment in the electro-nape-acupuncture combined with medicine group, found that there was a very significant difference (P=0.000, P<0.01). Our comparison of the MMSE scale scores before and after the treatment in medicine group, found that there was a very significant difference (P=0.000, P<0.01).

ware (version 8.0). The measurement data were expressed as the mean ± standard deviation ($\bar{x} \pm s$); when the data were normally distributed, the same group of data before and after treatment using paired-samples T tests and between groups were compared using two independent sample T tests. Analysis of variance (ANOVA) was used to analyze the differences among group means and their associated procedures. P<0.05 indicated that a difference was statistically significant.

Results

Comparison of the clinical curative effect of the three groups of patients before and after treatment

After performing a chi-square test comparing the acupuncture group with the medicine group, there was no significant difference (P=0.601, P>0.05), but the electro-nape-acupuncture group combined with the medicine group compared with the medicine group had a significant difference (P=0.042, P<0.05). The electro-nape-acupuncture group combined with the medicine group compared with the acupuncture group showed no significant difference (P=0.387, P>0.05). Total effectiveness = the number of (marked + effective + powerfully effective)/30. The total effectiveness of the acupuncture group was 73.33%, the total effectiveness of the electro-nape-acupuncture group combined with the medicine group was 90.00%, and the medicine group's total effectiveness was 63.33%. After making the comparisons, we determined that the electro-nape-acupuncture group combined with the medicine group was the most effective. As shown in **Table 2**.

Comparison of the MMSE scale scores before and after the treatment among the three groups

After performing the paired-samples T tests, comparing the MMSE scale scores before and after the treatment in the acupuncture group, there was a very significant difference (P= 0.000, P<0.01). After comparing the MMSE scale scores before and after the treatment in the electro-nape-acupuncture combined with medicine group, there was a very significant difference (P=0.000, P<0.01). After comparing the MMSE scale scores before and after the treatment in the medicine group, there was a very significant difference (P=0.000, P<0.01). Our analysis of variance of the MMSE scores of the three groups of patients before the treatment indicated that there was no statistically significant difference (F=0.13, P=0.878, P> 0.05) and that the groups were comparable. Our analysis of variance of the MMSE scores of the three groups of patients after the treatment indicated there was a very significant difference (F=71.98, P=0.000, P<0.01), as shown in **Table 3** and **Figure 1**.

Comparison of the HDS scale scores before and after the treatment among the three groups

After performing the paired-samples T tests, our comparison of the HDS scale scores before and after the treatment in the acupuncture group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HDS scale scores before and

Table 4. Comparison of the HDS scale scores before and after the treatment among the three groups ($\bar{x}\pm s$)

Group	n	Before treatment	After treatment	t	P
Acupuncture	30	5.17±1.58	8.13±0.94	-11.40	0.000
Electro-nape-acupuncture combined with medicine	30	4.97±1.69	10.17±2.21	-20.35	0.000
Medicine	30	5.17±1.82	7.63±1.27	-11.58	0.000

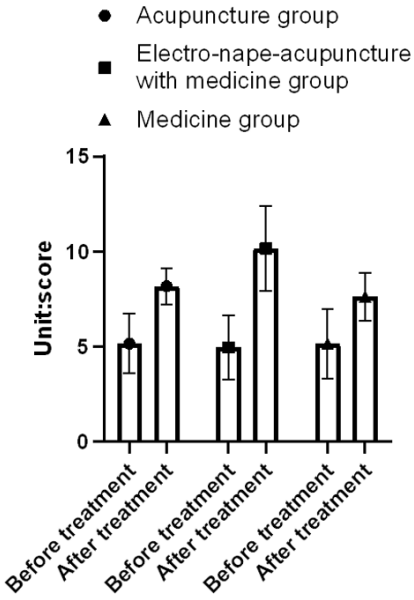

Figure 2. Comparison of HDS scale scores before and after the treatment among the three groups. After doing paired-samples T tests, our comparison of the HDS scale scores before and after treatment in the acupuncture group found that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HDS scale scores before and after the treatment in the electro-nape-acupuncture combined with medicine group found that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HDS scale scores before and after the treatment in the medicine group found that there was a very significant difference (P=0.000, P<0.01).

after the treatment in the electro-nape-acupuncture combined with medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HDS scale scores before and after the treatment in the medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our analysis of variance of the HDS scores of the three groups of patients before the treatment indicated that there was no statistically significant difference (F=0.14, P=0.871, P>0.05) and the groups were comparable. Our analysis of variance of the HDS scores of the three groups of patients after the treatment indicated that there was a very significant difference (F=21.9, P=0.000, P<0.01), as shown in **Table 4** and **Figure 2**.

Comparison of the ADL scale scores before and after the treatment among the three groups

After we performed the paired-samples T tests, our comparison of the ADL scale scores before and after the treatment in the acupuncture group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the ADL scale scores before and after the treatment in the electro-nape-acupuncture combined with medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the ADL scale scores before and after the treatment in the medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our analyses of variance of the ADL scores of the three groups of patients before the treatment indicated there was no statistically significant difference (F=0.48, P=0, P>0.05) and that the groups were comparable. Our analysis of variance of the MMSE scores of three groups of patients after the treatment indicated that there was a very significant difference (F=4.98, P=0.009, P<0.01), as shown in **Table 5** and **Figure 3**.

Comparison of the HCY levels before and after the treatment among the three groups

After doing paired-samples T tests, our comparisons of the HCY levels before and after the treatment in the acupuncture group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HCY levels before and after the treatment in the electro-nape-acupuncture combined with medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HCY levels before and after the treatment in the medicine group indicated

Table 5. Comparison of the ADL scale scores before and after the treatment among the three groups ($\bar{x}\pm s$)

Group	n	Before treatment	After treatment	t	P
Acupuncture	30	40.07±3.21	50.67±5.37	-9.35	0.000
Electro-nape-acupuncture combined with medicine	30	39.20±4.86	54.73±4.65	-12.54	0.000
Medicine	30	40.17±4.33	51.60±5.62	-8.71	0.000

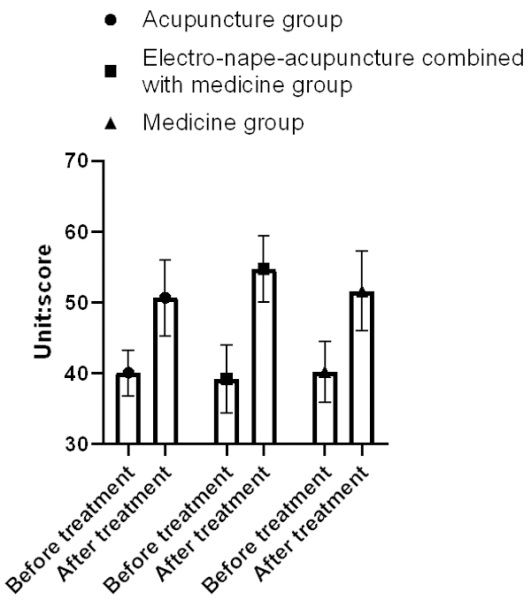

Figure 3. Comparison of the ADL scale scores before and after the treatment among the three groups. After we completed paired-samples T tests, our comparison of the ADL scale scores before and after the treatment in the acupuncture group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the ADL scale scores before and after the treatment in the electro-nape-acupuncture combined with medicine group found that there was a very significant difference (P=0.000, P<0.01). Our comparison of the ADL scale scores before and after treatment in the medicine group found that there was a very significant difference (P=0.000, P<0.01).

that there was no significant difference (P= 0.17, P>0.01). The HCY levels in the acupuncture group and in the electro-nape-acupuncture combined with medicine group were decreased, but the levels in the medicine group did not decrease significantly. Our analysis of variance of the HCY levels in the three groups of patients before the treatment indicated that there was no statistically significant difference (F=0.15, P=0.858, P>0.05) and that the groups were comparable. Our analysis of variance of the HCY levels in the three groups of patients after the treatment indicated that there was a very significant difference (F=924.09, P= 0.000, P<0.01), as shown in **Table 6** and **Figure 4**.

Discussion

The results of this study showed that the clinical efficacy of the cross electro-nape-acupuncture combined with medicine group was significantly better than the efficacy of the other two groups. The MMSE and HDS scores and the HCY levels were significantly reduced, and the ADL score was increased. This result may be related to the fact that acupuncture at the head of the brain directly stimulates the cortical areas which can then act directly on the cerebral cortex, recovering various innervation functions of the brain [8, 9], promoting the release of dopamine, and activating the long-term strengthening effect of the D1/D5 receptors [10]. We used the method of cross electro-nape-acupuncture (CENA) in order to increase the amount of stimulation of the acupuncture and to increase the speed of functional recovery. Our ultimate goal was to improve the cognitive impairment caused by vascular dementia.

Chinese medicine believes that VD belongs to the categories of “dementia”, “forgetfulness”, and “foolishness”. The brain is the lesion’s location, which is connected to the kidney where the ‘gods’ are, and the kidney is where the essence is [11]. CENA administered through the acupuncture points of the electric needle head complement the qi deficiency to adjust the Yuanshen Palace. The governor meridian acupoints act on the kidney reservoir [12] with sufficient kidney essence to fill the emptiness of the marrow sea. This acupuncture method can reduce the neurological impairment of patients in various ways and can and improve the effectiveness of the VD treatment. The acupuncture method can improve the cognitive ability of patients with vascular dementia, and it performs well in treating the condition [13-15]. Adding current increases the amount of

Table 6. Comparison of the HCY levels before and after the treatment among the three groups ($\overline{x}\pm s$)

Group	n	Before treatment	After treatment	t	p
Acupuncture	30	15.72±0.69	9.50±0.57	37.93	0.000
Electro-nape-acupuncture combined with medicine	30	15.63±1.07	9.09±0.75	25.94	0.000
Medicine	30	15.74±0.73	15.51±0.60	1.40	0.17

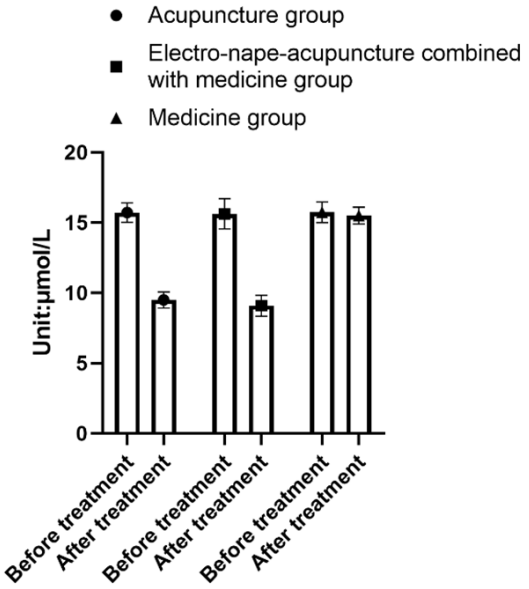

Figure 4. Comparison the HCY levels before and after the treatment among the three groups. After we completed the paired-samples T tests, our comparison of the HCY levels before and after the treatment in acupuncture group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HCY levels before and after the treatment in the electro-nape-acupuncture combined with medicine group indicated that there was a very significant difference (P=0.000, P<0.01). Our comparison of the HCY levels before and after the treatment in the medicine group indicated that there was no significant difference (P=0.17, P>0.01). The HCY levels in the acupuncture and electro-nape-acupuncture combined with medicine groups were decreased, but the levels in the medicine group did not decrease significantly.

stimulation and improves the efficacy. The results of the study have shown that CENA is effective in the later-stage treatment of cerebrovascular disease, but its mechanism is still very unclear. We found that CENA can also ameliorate neurological functions in rat models of CH. Moreover, the upregulation of RIPK1-mediated, necroptosis-related molecules in the brains of rats with CH were inhibited by CENA. Further investigation revealed that CENA partially blocked the interaction between RIPK1 and RIPK3 [16]. Clinical research shows that CENA can also effectively improve the recovery of the cough reflex and lung infections in patients with cerebral hemorrhages [8, 9].

The DU 20 point has the effect of awakening the brain. Acupuncture point DU 20 was beneficial to Sun Microsystems, using pulp gas to fill the brain. Modern research shows that DU 20 significantly enhances memory [14, 15]. DU 20 is located in the brain's frontal lobe hole, at the head of the surface in the brain's frontal lobe cortex, and it can adjust emotional intelligence, and where it has a special sensory (visual and auditory) and overall feeling of the general senses with attention and perception, function, dynamic, intelligence, planning, continuous behavior, time integration, memory, language, mood and personality are involved. There are four acupoints of EX-HN1, EX-HN1 by the strange acupuncture point of aristocracy, they work as the name suggests, and needling them can make a person be clever and adjust the yin and yang. There are four acupoints in EX-HN1, which treats insomnia and forgetfulness and other mental illnesses, and it can have the magical effect of refreshing the mind and nourishing the blood and benefiting the brain [6, 17].

Modern research shows that the acupuncture points on the brain neck foramen magnum and the medulla oblongata central body surface can improve brainstem reflex function, and using needle foramen magnum, the medulla oblongata central and the castor intracranial directly play a role in improving brain function [18-20]. In addition, GB 20 and SJ17 on both sides of the vertebral artery are deep at the site, and acupuncture using GB 20 and SJ17 can significantly improve the blood supply of the vertebral-basal artery [21], increase cerebral blood flow, and increase the cerebral perfusion pressure. Acupuncturing the two points and applying the electric current will increase the amount of stimulation and improve the efficacy.

Modern medical science thinks that people's advanced thinking, memory and spiritual activity functions are mainly related to the cerebral

hemisphere. Acupuncturing the points of the brain can act directly on the cerebral cortex, and keen perception in the cerebral cortex projection area is big, and the cortex area has a high quantity of neurons [12, 15, 22]. The brain, after the acupuncture point of the nerve impulses of the cerebral cortex, has a great influence, high neuronal excitability, and its neural reflex regulation or nerve humoral regulate the various functional activities which are active and widespread, it can also promote the release of dopamine and activate the long-term strengthening effect of the D1/D5 receptors, thus promoting and strengthening the compensatory function of the brain. In addition, after CENA treatment by the peripheral nerve endings of the acupoint near the exiting, the zang-fu organs and meridians and the subordinate ones, improve the local and state, the function of the relevant viscera promotes local blood circulation and metabolism. These factors work together to promote some nerve cell and brain functions, thus making sure the metabolism of the VD patients' intelligence, memory, and self-care ability has been improved.

Duxil can increase the blood oxygen content (PaO2) and increase the PaO2 in brain tissue, thus meeting the demand for oxygen and improving brain and nerve damage cognitive dysfunction. It is mainly used for older intelligence clinical disorders, mental and behavioral disorders, and other causes of cognitive and memory dysfunction in the present, so it is not yet destined for the treatment of specific DVD cases. Duxil is a relatively ideal adjuvant, it is small amount of medicine, safe to use, simple to take, and it has no significant side effects, but as with any other medicine, it is an efficacious, reliable, economic, and safe clinical medicine.

The results suggest that the treatment used in the observation and control groups can all improve VD patients' intelligence and daily living skills significantly. Modern medicine shows that the amount of stimulation of the electroacupuncture is far more than that of the ordinary acupuncture method, and the treatment method of the CENA is significant for the treatment of patients with vascular dementia. Compared with the control group, there was a statistically significant difference. The results of the study show that the CENA has a good clinical effect on patients with vascular dementia, but it does not reveal the mechanism of action of the CENA. In the future, more experimental studies are needed to prove the effectiveness of our action. This study has a small sample size and lacks a multi-center, large-sample randomized controlled trial. It is expected that it will be further improved in future clinical work.

Conclusion

1. Cross electro-nape-acupuncture can treatment improve intelligence and VD patients' self-care recovery ability. 2. Cross electro-nape-acupuncture treatment can reduce the content of HCY.

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Disclosure of conflict of interest

None.

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