Objective: To observe the effect of medicated thread moxibustion combined with electroacupuncture treatment on cognitive function of patients with vascular cognitive impairment of non-dementia and provide scientific clinical and practical basis for medicated thread moxibustion therapy.

Methods: 75 patients with vascular cognitive impairment of non-dementia who met the inclusion criteria were divided into medicated thread moxibustion combined with electroacupuncture group, electroacupuncture group and control group, each consisting of 25 cases. 75 patients herein were treated with the basic treatment of neurology. In addition, medicated thread moxibustion combined with electroacupuncture group received acupuncture and medicated thread moxibustion therapy. The treatment was conducted every other day, three times a week for a total of 8 weeks. Before treatment and at the end of 8 weeks, the impact on each patient's neuropsychology was evaluated with the Montreal Cognitive Function Assessment Scale (MoCA).

Results: After 8 weeks of treatment, MoCA scores of both the medicated thread moxibustion combined with electroacupuncture group and the electroacupuncture group were significantly higher compared with the control group (P<0.01). Also, compared with the electroacupuncture group, MoCA scores of the medicated thread moxibustion combined with electroacupuncture group were significantly increased (P<0.01).

Conclusion: The medicated thread moxibustion combined with electroacupuncture and electroacupuncture therapy can improve and enhance overall cognitive abilities of the patients with vascular cognitive impairment of non-dementia. The medicated thread moxibustion combined with electroacupuncture therapy was superior to the electroacupuncture therapy in improving patients’ attention. Similarly, both groups could reasonably improve visual space and executive function as well as abstract thinking ability. Both electroacupuncture as well as medicated thread moxibustion are effective in treating VCI, and should be widely applied clinically.

Keywords: Electroacupuncture, Vascular cognitive impairment of non-dementia, Clinical study, Medicated thread moxibustion.
improvement as it has a higher level of sensitivity and specificity for early stages of cognitive impairment as compared to MMSE (Mini Mental State Exam) [4]. The areas evaluated include visuospatial construction abilities, execution, language, memory, computing power, attention and concentration, abstraction and orientation. Normal people should attain a score of $\geq 26/30$. A score lower than 26 would indicate cognitive impairment. One complete evaluation would take about 10 minutes [5], therefore feasible in the clinical setting.

Research shows [6,7] that electroacupuncture can improve the cognitive function of patients with vascular cognitive impairment, promote the recovery of cognitive function, and improve quality of life. It can also improve the blood flow [8] of the main intracranial arteries.

According to theories of Traditional Chinese Medicine (TCM), clearing through warming has a good effect on blood stagnation syndromes like vascular cognitive impairment. Therefore we hypothesized that combining a unique type of moxibustion with electroacupuncture has a beneficial effect on patients. Medicated thread moxibustion is a type of direct moxibustion [9] in TCM methods of moxibustion. It is being widely used by the minority groups in China. There are 2 types of medicated thread moxibustion. One involves wrapping medicinal powder in cotton or any thin thread to form medicated thread for moxibustion; the other uses thin hemp thread soaked in medicine to form medicated thread for moxibustion. This study uses the second form of medicated thread, also known as Zhuang Medicine medicated moxibustion. This method uses thirty over fresh herbs found locally in the Zhuang minority group, for instance root of lineate supplejack, *Berchemia lineata*, *Fallopia japonica*, *Embelia parviflora*, *Herba sarcandrae*. These herbs are soaked in 95% alcohol to form medicinal liquid, and then this liquid is used to soak double strand hemp thread of diameter 2 mm. After soaking for 4 weeks, the medicated thread is harvested and used immediately. During the treatment, one end of the medicated thread is ignited and direct moxibustion is performed on a specific point or area of the patient’s skin. This method of moxibustion has a complete system of diagnosis and treatment, and is widely used in the Ling Nan area of China (Guang Xi, Guang Dong, Gui Zhou, Yun Nan etc.) to treat conditions related to internal medicine, dermatology and pain.

For the past two years, we have achieved good results of the medicated thread moxibustion combined with electroacupuncture on patients with VCND. The results are reported below.

**Materials and Methods**

**The scale used in this research diagnostic criteria**

This research used both western medicine and TCM syndrome diagnostic criteria. The western medicine diagnostic criterion used was ‘2014 edition of “Vascular Cognitive Impairment (VCI) diagnostic criteria’ [10]:

1. Patients with decrease in acquired cognitive level; (2) Clinical manifestations suggest that vascular source pathogenesis is the remarkable cause of cognitive impairment, but it is not absolutely the only one. At the same time, the VCIND diagnostic criteria of 2007 edition of “Expert Consensus on Vascular Cognitive Impairment” [11] was also referred to:

1. Does not meet the criteria of dementia; (2) Cognitive impairment is considered to have a vascular source; There is sudden onset, with ladder-like course and patchy cognitive impairment; there is evidence of atherosclerosis, focal signs and radiographic evidence; with vascular risk factors, not including patients with only vascular risk factors but without infarction/ischemia signs.

With reference to the ‘Guidelines for clinical research of Chinese medicine treatment of senile dementia’ of 2002 edition ‘Chinese new drug clinical research guidelines (Trial)’ [12], TCM syndrome differentiation and diagnosis was performed.

**Inclusion criteria and exclusion criteria**

**Inclusion criteria:** (1) Satisfies the Western medicine diagnostic criteria of vascular cognitive impairment of non-dementia; (2) Satisfies TCM syndrome diagnostic criteria; (3) aged 45 to 85; (4) Montreal Cognitive Assessment (MoCA) score $<26$; Mini-Mental State Examination (MMSE) score: illiteracy $>17$, elementary school level $>21$ points, high school level or above $>23$; Hachinski Ischemic Scale (HIS) score $\geq 7$; (5) lucid, no language barriers, able to complete the relevant examinations (6) voluntarily accept treatment, and signed informed consent.

**Exclusion criteria:** (1) Decrease in cognitive function caused by systemic disease and drugs that influence cognitive function; (2) patients suffering from central nervous system infections, metabolic encephalopathy, multiple sclerosis, Parkinson's disease, Cushing's syndrome or with primary hypothalamic dysfunction; (3) imaging studies failed to detect significant cerebrovascular disease; (4) patients with severe cardiovascular diseases, liver and kidney dysfunction and those in the acute stage of cerebrovascular disease; (5) patients with geriatric depression or other mental illness, severe vision, hearing impairment, severe aphasia, or those with poor strength, not able to cooperate with related physical examination; (6) patients receiving other acupuncture therapy that may affect evaluation.

**General information**

All the 75 subjects, who met the diagnostic and inclusion criteria, were recruited from the department of acupuncture and moxibustion, as well as encephalopathy division Dongfang Hospital of Beijing University of Chinese Medicine from June 2014 till January 2016. This study fully considered the right to choose of patients and their families, recruiting them into groups according to their own wishes thus meeting ethical requirements. Eventually, 64 patients completed the study including 20 cases from the medicated thread moxibustion
The effect of medicated thread moxibustion combined with electroacupuncture treatment on Montreal Cognitive Assessment (MoCA) of patients with vascular cognitive impairment of none dementia

combined with electroacupuncture group, 21 cases from the electroacupuncture group and 23 cases from the control group. Amongst these 64 cases, 32 cases were male, 32 were females; the youngest was 49 years old, the oldest was 78 years; the shortest disease course was 3 months and the longest was 18 months; 26 cases had received high school level of education and below (including high school), 38 cases had high school education and above. In all three groups, there were no statistical difference in gender, age, course of disease, level of education, the Montreal Cognitive Assessment (MoCA) and other general information (P>0.05).

Therapeutic method

All the 75 patients in the groups underwent individualized treatment to control blood pressure, blood glucose, lipids, oral enteric-coated aspirin tablets 0.1 g, qd (imported drug registration No: H20090978, Bayer healthcare) and other symptomatic treatment. Complications were prevented, and patients were not allowed to take drugs that could improve intelligence. Acupoints: Baihui, Sishencong, Shenting, bilateral Fengchi, Neiguan, Zusanli and Sanyinjiao. Add Xuanzhong for kidney deficiency and marrow injury, add Taichong for yin deficiency of heart and liver; add Yinlingquan for deficiency of heart and spleen; add Fenglong for sputum turbid blocking aperture; add Xuehai for qi stagnation and blood stasis. Methods of operation: the skin around the selected points was routinely disinfected, then 0.25 × 25 mm acupuncture needles were used (scap acupuncture horizontally inserted, body needle obliquely inserted). When the local area achieved the desired sensation, the needle was retained. Baihui was connected to the negative electrode and Shenting to the positive electrode of the electroacupuncture apparatus. Continuous wave of 100 HZ was administered, intensity adjusted to the degree of patient tolerance, then the needles were retained for 20 minutes. The treatment was carried out every other day, three times weekly for total 8 weeks.

Drug suture specifications: Double-stranded rope ramie of diameter 1 mm, origin of suture: Guangxi Zhuang Medicine Hospital. Operation: acupoints were the same as electroacupuncture acupoints, modifications were made based on syndrome differentiation. The corresponding acupoints each acupoint underwent moxibustion for 3 Zhuang. Moxibustion was conducted every other day, three times weekly for total 8 weeks. The medicated thread moxibustion combined with electroacupuncture therapy group: firstly acupuncture treatment; medicated thread moxibustion treatment after raising the needle. The electroacupuncture group: treated with electroacupuncture (specific methods as the above).The control group: only general treatment, observation for 8 weeks.

Observable indicator

General project: Before treatment, observation of head MRI or CT, gender, age, education level, underlying disease, duration of syndromes of the patients. Montreal Cognitive Scale (MoCA) score. The Montreal Cognitive Scale (MoCA) score was applied to determine the effectiveness, and the MoCA score was classified into four grades: Excellent (MoCA score elevated by 7 points or more); Effective (MoCA score elevated by 4 to 6 points); Improved (MoCA score elevated by 1 to 3 points); Invalid (MoCA rates unchanged or declined). The calculation formula of the total efficiency: (total (excellent +effective+improved) patients/total evaluable patients) × 100%. The above scale was applied in all patients before and after the treatment group, and the ratings were recorded for the statistics and analysis.

Statistical analysis

SPSS19.0 software was used for statistical analysis. When the measurement data follows a normal distribution, the overall comparison was analysed with single factor of variance analysis, and the comparison between the two groups was checked with LSD test. Results are expressed as mean ± standard deviation (x̄ ± s); when the data is not normally distributed, the two groups were compared using non-parametric H test. P<0.05 indicated a statistically significant difference.

Results

The comparison of MoCA total score

Based on variance analysis, after treatment the MoCA total scores of the three groups group were compared, there was significant difference between the groups with statistical significance (F=9.074, P=0.000<0.01); the difference values of the three groups before had significant differences with statistical significance (F=22.898, P=0.000<0.01) (Table 1).

LSD was used for pair wise comparison of the MoCA total scores after treatment. The medicated thread moxibustion combined with electroacupuncture therapy was significantly difference with the electroacupuncture therapy (▲P=0.026<0.05), also with the control group (▲P=0.000<0.01); and the electroacupuncture group is compared with the control group with statistical significance (P=0.048<0.05) (Table 1).

The differences before and after treatment between the two groups were compared with LSD. The medicated thread moxibustion combined with electroacupuncture therapy was significantly different with the electroacupuncture therapy (▲▲P=0.002<0.01), also with the control group (▲▲P=0.000<0.01); and the electroacupuncture group is compared with the control group with statistical significance (P=0.001<0.01) (Table 1).

The comparison of sub-items of MoCA

There was significant differences of "Visual space" between the three groups with statistical significance (P<0.01). In the pair wise comparison between the groups, the medicated thread moxibustion combined with electroacupuncture therapy had no statistical difference with the electroacupuncture therapy (P=0.832>0.017), but significant difference with the control.
The difference of "Memory" before and after the treatment compared between the three groups had significant differences with statistical significance (P<0.01). In the pairwise comparison between the groups, the medicated thread moxibustion combined with electroacupuncture therapy had no statistical difference with the electroacupuncture therapy (P=0.153>0.017), but significant difference with the control group (P=0.005<0.017); and the electroacupuncture group is compared with the control group with statistical significance (P=0.04>0.017, Table 2).

The difference of "attention" before and after the treatment compared between the three groups had significant differences with statistical significance (P<0.01). In the pairwise comparison between the groups, the medicated thread moxibustion combined with electroacupuncture therapy had statistical difference with the electroacupuncture therapy (P=0.002<0.017), also with the control group (P=0.010<0.017); and the electroacupuncture group is compared with the control group with statistical significance (P=0.741>0.017, Table 2).

The differences of "nomenclature" before and after the treatment compared between the three groups had no significant differences (P>0.05, Table 2).

The differences of "abstraction" before and after the treatment compared between the three groups had significant differences with statistical significance (P<0.01). In the pairwise comparison between the groups, the medicated thread moxibustion combined with electroacupuncture therapy had no statistical difference with the electroacupuncture therapy (P=0.578>0.017), but significant difference with the control group (P=0.012<0.017); and the electroacupuncture group is compared with the control group with statistical significance (P=0.008<0.017, Table 2).

**Intention to treat analysis**

The trial included 75 patients; finally 64 cases completed the test. The test results analysis was by "worst-case scenario analysis" of intention to treat analysis, namely exited and deciduous cases of the medicated thread moxibustion combined with electroacupuncture therapy group and the electroacupuncture group were considered as ineffective cases, while the deciduous cases of the control group as effective cases. As a result, the total effective rate of the medicated thread moxibustion combined with electroacupuncture therapy group was 68%, the electroacupuncture group of 56%, and the control group of 32%. According to test standard of α=0.05, the total efficiencies of the three groups were compared with the χ² test, and there were significant differences between the three groups with statistically significance (P=0.035<0.05, Table 3).

The results showed that there was significant difference in the total efficiency between the control group and the medicated thread moxibustion combined with electroacupuncture therapy group or the electroacupuncture group with statistical significance (χ²=6.731, P=0.035<0.05). Tests demonstrated that medicated thread moxibustion combined with electroacupuncture therapy and electroacupuncture therapy had potential clinical efficacy on intervening patients with vascular cognitive impairment of non-dementia.

### Table 1. The MoCA scale score change comparison between the three groups before and after treatment (scores, x̄ ± s).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Total scores before treatment (scores)</th>
<th>Total scores after treatment (scores)</th>
<th>Scores of the difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>The medicated thread moxibustion combined with electroacupuncture therapy group</td>
<td>20</td>
<td>21.50 ± 3.19</td>
<td>24.25 ± 3.39</td>
<td>2.75 ± 2.29</td>
</tr>
<tr>
<td>The electroacupuncture group</td>
<td>21</td>
<td>21.38 ± 2.44</td>
<td>22.19 ± 3.01</td>
<td>0.81 ± 1.44</td>
</tr>
<tr>
<td>The control group</td>
<td>23</td>
<td>21.65 ± 2.64</td>
<td>20.20 ± 2.21</td>
<td>-1.22 ± 1.95</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td>0.057</td>
<td>9.374</td>
<td>22.898</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.945</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Note:** indicates the comparison of the medicated thread moxibustion combined with electroacupuncture therapy group and the electroacupuncture group, P<0.05, : P<0.01; indicates the comparison of the medicated thread moxibustion combined with electroacupuncture therapy group and the control group, P<0.05, "": P<0.01; indicates the comparison of the electroacupuncture group and the control group, P<0.05, : P<0.01.

### Table 2. The comparison of difference of MoCA scale scores before and after treatment (scores, x̄ ± s).

<table>
<thead>
<tr>
<th>Item</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The medicated thread moxibustion combined with electroacupuncture therapy group (n=20)</td>
</tr>
<tr>
<td></td>
<td>The electroacupuncture group (n=21)</td>
</tr>
<tr>
<td></td>
<td>The control group (n=23)</td>
</tr>
<tr>
<td></td>
<td>Chi-square P</td>
</tr>
</tbody>
</table>

P
The effect of medicated thread moxibustion combined with electro acupuncture treatment on Montreal Cognitive Assessment (MoCA) of patients with vascular cognitive impairment of none dementia

<table>
<thead>
<tr>
<th>Group</th>
<th>Excellent</th>
<th>Effective</th>
<th>Improved</th>
<th>Invalid</th>
<th>The total effective rate</th>
<th>χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>The medicated thread moxibustion combined with electroacupuncture therapy group</td>
<td>2</td>
<td>4</td>
<td>11</td>
<td>3+5</td>
<td>68%</td>
<td>6.731</td>
<td>0.035</td>
</tr>
<tr>
<td>The electroacupuncture group</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>7+4</td>
<td>56%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The control group</td>
<td>0</td>
<td>0</td>
<td>6+2</td>
<td>17</td>
<td>32%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Chinese scholars generally believe that disease location of vascular dementia is in the brain, deficient root and excessive superficial, intermingled deficiency and excess, which is closely related to internal organs. Toxicity and deficiency pathogenic theory [13] is an important part of basic theoretical system of the Zhuang Medicine, considering toxicity and deficiency as two major necessary factors for the disease occurrence. Patients were suffering from foreign toxin invasion or endogenous disturbance, "deficiency" is the internal cause of disease. Thus poison the virtual phase of the disease. The mediated thread moxibustion combined with electroacupuncture therapy mainly stimulated acupuncture points on the body surface in three-road or two-way through warm and pharmacodynamic point moxibustion and the meridians to remove toxin directly, unimped "three-road two-way", adjust the body qi and blood for balance. The flow of three-road two-way makes the body functions return to normal, three qi reset in synchronization, up right rehabilitation, so as to achieve the purpose of disease defence.

This is the first study that combined medicated thread moxibustion with electroacupuncture as a form of intervention to vascular cognitive impairment. The results showed that all 3 groups showed statistical difference in MoCA scores before and after treatment. Of the 3 groups, the greatest increase in scores was in the combined treatment group, followed by the electroacupuncture group. There was a slight decrease in the scores for the control group. This shows that both electroacupuncture and medicated thread Moxibustion combined with electroacupuncture can improve and increase the overall cognitive abilities of vascular cognitive impairment of none dementia. The mechanism behind electroacupuncture increasing the overall cognitive function could be due to it stimulating the regeneration and repair of cranial nerves [14], improving intracranial blood flow [15] and intravascular activity factors, improve the metabolism of oxygen free radicals [16], inhibiting excessive cell apoptosis, promote proliferation of neural stem cells post infarction [17], therefore protecting neural nerves. When electroacupuncture was combined with medicated thread Moxibustion, there was an additional warming mechanism, thus causing the improvement in overall cognitive function to be more significant. Its detailed mechanism should be researched further. In the control group that only received baseline treatment, the MoCA score reduced slightly after 8 weeks, indicating that some patients might have a decline in cognitive function if they do not undergo specific treatment.

The group receiving combined treatment had statistically significant differences in memory and attention as compared to the control group. The group receiving combined treatment had statistically significant differences in attention as compared to the electroacupuncture group. This shows that electroacupuncture combined with medicated thread moxibustion can increase patients’ memory and attention. Its ability to improve attention is superior to that of electroacupuncture. We know that learning, memory and attention is due to the regulation of brain neurotransmitters and neuropeptides [18]. Neurotransmitters combined with their receptors, through a series of signalling pathways, produce corresponding responses in brain function. Electroacupuncture with medicated thread moxibustion, due to the addition of warming effects, could influence the release of some neurotransmitters from the brain, hence enhancing the effects of electroacupuncture, so the improvement in attention was
more pronounced. This is the first time that electroacupuncture was used together with medicated thread moxibustion; therefore the mechanism needs to be further explored.

In terms of improving visual space, executive function and abstract thinking ability, there was no statistical significance between the combined therapy and electroacupuncture, but there was a statistical difference when compared with the control group. This shows that both groups could improve the visual space, executive function and abstract thinking ability, but adding the warming effect of medicated thread moxibustion to electroacupuncture, it does not improve patients’ visual space and executive function and abstract thinking ability significantly.

The naming ability of the 3 groups did not have any statistical difference. This shows that 8 weeks of intervention did not pose benefit to the naming ability of patients. The naming process has 4 steps: brain cortex receives information-analyse-extract corresponding word-express. Usually cognitive impairment presents as difficulty in analysing and remembering words. 8 weeks of observation may be too short for the groups to show any significant improvement in naming ability.

Intention to treat analysis shows medicated thread moxibustion combined with electroacupuncture and electro-acupuncture alone can improve and enhance overall cognitive abilities of the patients with vascular cognitive impairment of non-dementia. There is a certain level of clinical efficacy, so this method of treatment is worthy of promotion. The medicated thread moxibustion combined with electroacupuncture was superior to the electroacupuncture therapy in improving the patient’s memory.

The subjects in this study are patients with vascular cognitive impairment of non-dementia. This condition has an insidious onset, and seldom would patients seek medical help proactively. It is common for doctors to discover it through routine examination due to other cerebrovascular diseases. The uniqueness of this condition resulted in difficulty in recruiting patients. While considering the issue on ethics, this study respects the wishes of the patients to allow them to choose the treatment they would like to receive. This eliminates the randomized aspect of subjects, but increases compliance and reduces dropout rate. This study is not randomized, and had a small sample size, so the results might have some limitations. Future studies should increase the sample size so as to reflect the masses more objectively. This study verified the results of the combined effect of electroacupuncture and medicated thread moxibustion. Due to the limitations of workers, time and funds, this study only assessed patients with vascular cognitive impairment of non-dementia, which might not be comprehensive enough. Future studies could increase related laboratory tests, to evaluate the combined effect of these 2 therapies more objectively.

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References


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