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Effect of Western medicine therapy assisted by *Ginkgo biloba* tablet on vascular cognitive impairment of none dementia

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ABSTRACT

Objective: To discuss the clinical effects of Western medicine therapy assisted by *Ginkgo biloba* tablet (GBT) on patients with vascular cognitive impairment of none dementia (VCIND). **Methods:** A total of 80 patients with VCIND were divided into two groups randomly: Conventional treatment group (control group) and combined treatment group. Conventional treatment group was given conventional treatment with anti-platelet aggregation. In this group, 75 mg aspirin was given three times a day for 3 months. While in combined treatment group, 19.2 mg GBT was given three times a day for 3 months together with conventional treatment (anti-platelet aggregation drugs). Montreal cognitive assessment (MoCA) and transcranial Doppler (TCD) were used to observe changes of cognitive ability and cerebral blood flow in VCIND patients before and after treatment in both groups. Then the clinical data were analyzed so as to compare the efficacy in two groups. **Results:** After 3 month-treatment in combined treatment group, the scores of executive ability, attention, abstract, delayed memory, orientation in the MoCA were significantly increased compared with those before treatment and those in control group after treatment. Besides, blood flow velocity of anterior cerebral artery increased significantly than that before treatment and that in control group after treatment. **Conclusions:** GBT tablet can improve the therapeutic efficacy as well improve cognitive ability and cerebral blood flow supply of patients with VCIND.

1. Introduction

As the approaching of aging society, senile dementia is gradually turning into a serious medical issue that affects both medical sector and society. Vascular cognitive impairment (VCI) is a large class of syndrome from mild cognitive impairment to dementia caused by risk factors of cerebrovascular disease, obvious or not obvious cerebrovascular disease[1]. Vascular cognitive impairment of none dementia (VCIND), not reaching the dementia stage, can be controlled and reversed with medicine[2]. It is proposed by oversea scholars that vascular dementia (VD) shall be replaced by VCI[3,4] and three types of VCI were proposed as well: VCIND, VD and Alzheimer's disease with vascular factors. The crypticity of VCI symptoms makes it a main reason for the high morbidity of VD.

Gingko leaf, dry leaf of *Ginkogo biloba*, with main composition being flavonoids and terpene, is effective in the treatment of ischemic cerebrovascular disease and VD[5,6].

There are two major problems in the evaluation of cognitive function at present: 1) neuropsychological scale used for cognitive appraisal could not determine the normal line easily; 2) the identification that whether cognitive impairment was caused by vessel factors or not is difficult[3]. In addition, the heterogeneity is also a reason. In this experiment, the intervention effect of Gingko leaf on VCIND patients was evaluated through the Montreal cognitive assessment (MoCA) rating scale and transcranial

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doppler (TCD) from the aspects of neural psychology and cerebral blood flow. It provided practical foundation and experimental basis for therapy of VCIND using traditional Chinese medicine as an adjunctive.

2. Materials and methods

2.1. Diagnosis and criteria

By referring to related literature and relevant criteria, a criteria was made as follows: 1) 60-75 years old; 2) cognitive disorder shown by revised mini mental state examination (MMSE); 3) Cognitive impairment shown by neuropsychological evaluations; 4) Memory relatively reserved or slightly impaired while cognitive function such as attention and executive ability impaired seriously; 5) Difficulty in identifying whether the cognitive function impairment was caused by vascular factors; 6) Hanchinski inchemic score >7; 7) Cognitive function impairment fluctuated.

2.2. Subject

Eighty cerebral infarction patients treated in our hospital from March 2009 to May 2011, including 46 males and 34 females were enrolled. They were 60-75 years old and the average age was 66.5±5.6, including 35 hypertension, 42 diabetes mellitus, and 33 cases of hyperlipemia. They were divided into two groups randomly: Conventional treatment group (n=40) and combined treatment group (n=40). There were no significant differences between the two groups in gender, age, cognitive rating scale score or TCD detection (P >0.05). All subjects should be examined by MoCA and TCD.

2.3. Methods

75 mg aspirin enteric-coated tablets (Shijiazhuang Pharmaceutical Goup Ou Yi Pharmaceutical Industry Limited Company) was given to conventional treatment group 3 times a day for 3 months, while 40 mg oral *Ginkgo biloba* tablet (Tanakan EGb761, Tianjinbofu- Yi pu sheng Pharmaceuticals Co., Ltd., The registered number of the imported drugs: X19990156) was given to combined treatment group 3 times a day for 3 months on the basis of conventional treatment with anti-platelet aggregation drug.

2.4. Monitoring indexes

2.4.1. MoCA

Seven of the 30 indexes in MoCA such as executive ability, name, memory, attention, language, abstract, deferred memories and orientation force were chosen as analysis indexes. According to the severity of symptoms, patients were graded as 3, 2, 1 or 0 (for absence of symptoms). The decrease of clinical score ≥2/3 will be considered significant improvement while it ≥1/3 will be considered as partial improvement and the treatment is considered ineffective if the score remains the same.

2.4.2. TCD evaluation

Before and after the treatment, TCD meter probe from Germany Doppler-Box (2 MHz electromagnetic pulse) was applied through the temporal window and pillow window to detect the middle cerebral artery (MCA), anterior cerebral artery (ACA), posterior cerebral artery (PCA), vertebral artery (VA) and basilar artery (BA). Online state can real-time display peak systolic velocity, end-diastolic velocity, average flow velocity, PI index, RI index and S/D ratio of blood flow frequency spectrum in two directions.

2.5. Statistical method

All the data were processed by using SPSS software (Version 13.0) and results were expressed as Mean±standard deviation ($\bar{\chi}$ ±sd). t test was used to test measurement data and χ^2 was used for enumeration data. P<0.05 means that the tested difference had statistical significance.

3. Result

3.1. Comparison of MoCA score indexes before and after treatment

In conventional treatment group and combined treatment group, there were no obvious differences in the seven scores and the total score of MoCA before and after treatment (P >0.05). After treatment, the scores of five indexes (except naming and language) and the total score in combined treatment group were significantly different compared with those before treatment (P<0.05, P<0.01). Besides, the executive ability, attention, abstract, deferred memories, orientation force and the total score of MoCA in combined treatment group were also significantly different compared with those of the control group after treatment (P<0.05, Table 1).

3.2. Changes of blood flow monitored by TCD before and after treatment

There was no significant difference between conventional treatment group and combined treatment group in vascular velocity before treatment (P>0.05), blood flow velocity of MCA and ACA in combined treatment group increased remarkably after treatment, and there was significant difference compared with that before treatment (P<0.05) as well as compared with the control group (P <0.05) (Table 2).

Table 1
Scores of all indexes of MoCA before and after treatment.

Index	Conventional treatment group		Combined treatment group	
	Before treatment	After treatment	Before treatment	After treatment
Executive ability	2.25±1.21	1.97±1.22	2.49±0.77	4.02±0.49$^{\triangle *}$
Name	0.97±0.56	0.98±0.45	1.15±0.93	1.40±0.56
Attention	2.14±1.05	2.29±0.73	2.31±0.41	4.61±0.42$^{\triangle\triangle *}$
Language	1.51±0.33	2.02±0.31	1.42±0.45	2.22±0.38
Abstract	0.82±0.70	0.86±0.52	0.78±0.59	1.67±0.35$^{\triangle *}$
Deferred memories	1.01±0.84	0.89±0.71	1.11±0.56	3.03±0.37$^{\triangle *}$
Orientation force	4.02±0.46	3.95±0.89	3.43±0.39	5.34±0.91$^{\triangle *}$
Total score	11.46±2.98	12.99±2.81	12.42±2.66	19.10±2.94$^{\triangle *}$

Note: $^{*}P<0.05$, compared with that before treatment; $^{\triangle\triangle}P<0.01$, $^{\triangle}P<0.05$, compared with control group.

Table 2
Result of TCD spectrum blood flow velocity (Vm) before and after treatment (cm/s).

Index	Conventional treatment group		Combined treatment group	
	Before treatment	After treatment	Before treatment	After treatment
MCA	52.1±9.7	56.2±8.9	51.5±9.4	79.6±11.2$^{\triangle *}$
ACA	43.5±12.2	48.3±11.1	47.6±12.8	72.1±10.3$^{\triangle *}$
PCA	37.6±5.9	42.3±7.5	40.2±6.4	49.8±9.1
VA	42.8±10.1	45.7±10.2	42.1±8.2	52.3±10.1
BA	40.9±5.8	31.1±7.7	42.7±8.8	49.9±6.5

Note: $^{*}P<0.05$, compared with that before treatment; $^{\triangle}P<0.05$, compared with the control group.

4. Discussion

VCI is a large class of syndrome from mild cognitive impairment to dementia caused by disease risk factors of cerebrovascular disease, obvious or not obvious cerebrovascular diseases[7-9]. VCIND is the earliest clinical stage of VCI and is also likely to be the most common VCI type. VCIND is insidious and its cognitive impairment degree does not reach dementia diagnosis standard[10].

Neuropsychological testing is not only an important tool for VCIND diagnosis but also an important method for curative judgment and defection of curative vest. There is no internationally recognized VCIND neuropsychological testing method at present. MoCA is the firstly recommended VCI neuropsychology screening scale with international specialists' consensus[3,11-14]. MoCA has become an internationally used screening scale that was verified by many evidence-based medicine for screening MCA and VCI. This screening scale is improved and established from Nasreddine on the basis of cognitive item setting and scoring criteria in MMSE. MoCA emphasized more on the evaluation of executive function and attention. MoCA is the most important clinical checking tool for cognitive function, which has good sensitivity compared with MMSE. But its results will be influenced by gender, age and educational level. There were no statistical differences in gender, age and educational level of the patients in this research, which make the result avoid being affected by the above factors effectively.

Abnormal cerebral blood flow is a significant reason for the incidence of VCIND. TCD is a non-invasive cerebrovascular detection means, which directly reflects haemodynamic changes of intracranial vascular through determining blood flow velocity and vascular resistance index[15-17]. TCD is mainly used to detect blood flow states and vascular function. It is reported that[18] the incidence of abnormal hemodynamics studied with TCD in VCI patients was higher than those of control group and cerebral stoke group. There was a positive correlation between MoCA score and TCD results in this group, indicating that MoCA and TCD can be jointly used for evaluating mild VCI. The outpatient visit rate and diagnostic rate among people with cognitive disorder and dementia in China is relative low. Survey shows that the outpatient visit rate among dementia population is around 23.3%, which is less than half of that in developed country. By using neuropsychological tests, even slight degree of cognitive disorder can be detected, which enables patients to receive early treatment so as to prevent and postpone the occurrence and development of dementia symptoms.

Flavonoids are main and effective components of *Ginkgo biloba* leaf. Pharmacological study shows that aqueous extracts of *Ginkgo biloba* leaf have pharmacological effects such as antioxidant activity and antiradical activity. It can reduce myocardial oxygen consumption, protect for injuries from reperfusion for myocardial ischemia, protect smooth muscle cell of cerebral microvessels, improve neural plasticity and neurodegenerative disease[6,19-21], and can

be used in early intervening treatment of VCIND patients. This research observed the clinical intervention effects of joint treatment of GBT and anti-platelet aggregation drug on VCIND patients. It shows that the score of patients' executive ability, attention, deferred memory, abstract, orientation force all increased significantly after 3 month-treatment, which indicated that GBT can improve the cognitive function of VCIND patients. And the blood flow velocity of MCA, ACA increased obviously after taking GBT, indicating that the regional cerebral blood flow in the area where frontal lobe and temporal lobe have a close relation with cognitive function increased significantly. This experiment verified that GBT can improve the cognitive ability of VCIND and the supply of their cerebral blood flow.

Conflict of interest statement

We declare that we have no conflict of interest.

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