

## **Changes of BFGF and VEGF in patients with ischemic stroke treated by acupuncture-moxibustion with du channel-unblocking acupuncture method.**

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### **Abstract**

**Objective:** This research is aimed to explore the changes of Basic Fibroblast Growth Factor (BFGF) and Vascular Endothelial Growth Factor (VEGF) before and after treatment with acupuncture-moxibustion with Du channel-unblocking acupuncture in patients with ischemic stroke.

**Methods:** In our hospital from Jan 2014 to Sep 2016, 240 cases of ischemic stroke patients were randomly divided into acupuncture-moxibustion with Du channel-unblocking acupuncture group (Group A) and routine acupuncture group (Group B) and treatment group (Group C). Group A was treated by acupuncture-moxibustion with Du channel-unblocking acupuncture therapy, Group B was treated with acupuncture therapy, and Group C was treated with routine drugs. Before and after treatment, the levels of BFGF and VEGF were compared between the three groups before and after treatment. The NIHSS score, MESSS score and ADL score were compared before and after treatment.

**Results:** Before treatment, the three groups of patients with BFGF, VEGF levels and NIHSS score, MESSS score, ADL score no statistical difference ( $P>0.05$ ); After treatment, three groups of BFGF, VEGF levels and NIHSS score, MESSS score, ADL score than before treatment were improved ( $P<0.05$ ); After treatment, the levels of BFGF, VEGF and NIHSS score, MESSS score, ADL score of Group A were higher than that of Group B and Group C ( $P<0.05$ ).

**Conclusion:** The treatment of ischemic stroke patients with acupuncture-moxibustion with Du channel-unblocking acupuncture therapy can improve the expression level of VEGF and BFGF, and also has a good effect on improving the clinical symptoms of patients.

**Keywords:** Cerebral ischemic stroke, Acupuncture-moxibustion with Du channel-unblocking acupuncture, BFGF, VEGF.

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### **Introduction**

Ischemic cerebral stroke is common diseases and multiple diseases of cardiovascular diseases. In Traditional Chinese medicine (TCM), it belongs to “stroke”, which is similar to ischemic infarction in western medicine [1]. Statistical data show that incidence of ischemic cerebral stroke is about (116-219)/100 thousand people in our country, among which ischemic cerebral stroke occupies 70% of cerebral stroke patients. The age is mainly over 50 y old. But in recent years, incidence age tends to young age [2]. The onset mechanism of ischemic cerebral stroke is sudden decreased perfusion and blood interruption of normal blood supply of cerebral tissue. The normal metabolism of cerebral tissue is lost. Local cerebral tissue has edema, which cause necrosis of cerebral tissue in ischemic region [3]. During the treatment of ischemic cerebral stroke, reconstruction of cerebral blood circulation is

the most important part. Expression of VEGF and BFGF regulates upwards during the process of reconstruction [4]. Based on traditional Chinese medicine theory, the famous veteran practitioner of TCM, Professor Zhang Daozong, proposed a method of Du channel-unblocking acupuncture for the treatment of stroke. After many years of clinical research, he further proposed the theoretical thought of “Du channel-unblocking, Mind-regulating, Mind-regulating and Rehabilitation”, with proven effects to the benefits of nerves brain and dredging the meridian by plenty of subsequent researches and clinical applications. Therefore, this study aims at improving vascular reconstruction of ischemic cerebral stroke patients and symptoms by using new acupuncture connecting Du meridian.

## Material and Methods

### Clinical data

240 ischemic cerebral stroke patients from Jan 2014 to Sep 2016 in the first affiliated Hospital of Guang Xi Medical University were selected. They were randomly divided into acupuncture connecting Du meridian group (Group A), routine acupuncture group (Group B), drug treatment group (Group C). There were 32 female patients and 48 male patients in Group A. There were 38 female patients and 42 male patients. There were 35 female patients and 45 male patients. The data of age, sex, history in three groups were as Table 1. Contents of this study had informed patients and relatives and informed consent was signed.

**Table 1.** Statistical table of basic information in three groups.

General data		Group A	Group B	Group C
Sex (n)	Male	48	42	45
	Female	32	38	35
Age (y)	Age range	42~78	42~76	44~77
	Average age	58 ± 1.5	57 ± 2.0	58 ± 1.5
History (month)	History	0.5~6.5	0.5~6	1~6.5
	Average history	2.1 ± 0.5	2.5 ± 0.3	2.3 ± 0.3

Note: 1. There were no statistical differences in general data between Group A and Group B,  $P>0.05$ ; 2. There were no statistical differences in general data between Group B and Group C,  $P>0.05$ ; 3. Here were no statistical differences in general data between Group A and Group C,  $P>0.05$ .

### Inclusive criteria and exclusive criteria

Patients in this study should meet the standards as followed: First, all patients should meet the fourth national conference on the diagnosis of cerebrovascular disease academic standards [5]. Second, it met diagnostic standards of stroke in TCM. Third, vital signs of all patients were stable. They had no disturbance of consciousness. Fourth, the disease course of patients lasted more than three days. Patients needn't thrombolysis and anti-freezing treatment. Patients met one of the following items should be excluded: First, vascular malformation of brain, tumour disease, cerebral trauma. Second, patients had bleeding trends. Third, patients accompanied with other system disease, such as heart, liver and kidney. Fourth, women in gestation period and lactation period.

### Basic treatment

Before treatment, patients should be given health education and informed various conditions during treatment process. Patients should be given basic disease treatment according to their conditions. If patients had hypertension, diabetes, they should be given routine anti-blood glucose and anti-hypertension drug continuously during treatment.

### Acupuncture connecting Du meridian (Group A)

First, moxibustion on main point: DU 20. Acupuncture on main point: DU 14. Acupuncture on main point: GB20, LI11, LI4, ST36 and SP6. Adjunct point by syndrome differentiation: patients with excess wind-phlegm fire, the points should add ST40 and ST44. Patients with phlegm-dampness, the points should add RN4, SP9 and ST 40. Patients with di deficiency and blood stasis, points should add RN6 and SP 10. Patients with excess yang, points should add LR3 and KI3. Second, operation, needling part should be sterilized by 75% ethyl alcohol. Patients should select the best comfortable position. DU 20 was given suspending moxibustion. LI11 was given collateral puncture-bleeding method. Other points were given routine acupuncture. GB20 and LI11 were given reducing method. LI4 was given even reinforcing and reducing method. ST36 and SP6 were given reinforcing method. Treatment course: the time of needle retain was half hour each time. Once a treatment in one day. Two weeks were a complete treatment course. According to the effects after each course, whether gave next treatment or not was decided.

### Routine acupuncture group (Group B)

Main point: GB20, LI11, LI4, ST36 and SP6. Its adjunct points by syndrome differentiation, operation methods, and course were similar to acupuncture connecting DU group.

### Drug treatment group (Group C)

Tongxinluo capsule ( from Shijiazhuang Yilin Pharmaceutical Co. Ltd, Approved by state Z19980015), which were composed of ginseng, leech, scorpio, radix paeoniaerubra, cicada ecdysis, ground beetle, centipede, sandalwood, rosewood heart wood, frankincense (decoction), semen ziziphispinosae (fry). Oral administration. Two to four granules once a time. Three times one day.

### Evaluation index

Compared changes of BFGF and VEGF level before and after treatment in three groups. Venous blood was collected when patients were admitted into hospital. Venous blood was collected once time after treatment and sent to laboratory department in our hospital for detecting BFGF and VEGF level.

Compared NIHSS (The National Institutes of Health Stroke Scale) scores, MESSS (clinical neural function defect score scale) scores, ADL (daily life mobility) scores before and after treatment in three groups. The first two were score scale of stroke syndromes. The total score was 45. Type: slight 0 to 15. Moderate 16-30. Severe 31-45. The latter included stool, urine, eating, walking, wearing coat, which for evaluation. Full mark was 100. Score below 25, it was extreme severe function defect. 25 to 45, it was severe function defect. 46 to 74, it was moderate function defect. 75 to 95, it was slight function defect. Over 96, it was self-care completely.

**Statistical methods**

Data of this study were given SPSS19.0 software analysis. Measurement data were given t value test. Enumeration comparison used chi square test. Test standards were equal to 0.05. P<0.05, there were statistical differences.

**Results**

**The changes of BFGF and VEGF of patients before and after treatment in three groups**

BFGF and VEGF level of patients before and after treatment in three groups, seen as Table 2.

**Table 2.** Statistical table of changes of BFGF and VEGF of patients before and after treatment in three groups.

Before and after treatment	BFGF (pg/ml)			VEGF (pg/ml)		
	Group A	Group B	Group C	Group A	Group B	Group C
Before treatment	19.32 ± 5.371	19.83 ± 6.02	20.15 ± 5.73	387.71 ± 52.91	386.19 ± 56.18	385.24 ± 54.67
After treatment	37.94 ± 6.712	25.37 ± 7.16	24.96 ± 6.01	499.79 ± 76.15	436.81 ± 64.06	433.46 ± 61.95
χ <sup>2</sup> value	5.826	4.973	5.342	4.332	4.143	3.963
P value	0.013	0.035	0.021	0.033	0.037	0.042

Note: <sup>1</sup>Compared Group A with Group B and Group C, there were no statistical differences in BFGF and VEGF before treatment, P>0.05; <sup>2</sup>Compared Group A with Group B and Group C, there were statistical differences in BFGF and VEGF after treatment, P<0.05.

The above table shows that there is statistical difference between the values of BFGF and VEGF before and after treatment for the 3 groups. However, there is no statistical difference between the values of BFGF and VEGF for Group A, B and C before the treatment, P>0.05. <sup>2</sup>Shows that, there is statistical difference between the values of BFGF and VEGF for Group A, B and C after the treatment, P<0.05.

**Table 3.** Changes of NIHSS scores, MESSS scores, ADL scores before and after treatment in three groups.

Items	Group	Before treatment*	After treatment#	χ <sup>2</sup> value	P value
NIHSS	Group A	22.15 ± 4.73	9.35 ± 2.78	4.742	0.032
	Group B	21.78 ± 4.77	15.61 ± 3.91	4.143	0.037
	Group C	22.55 ± 4.82	16.23 ± 3.57	4.596	0.028
MESS	Group A	25.79 ± 6.13	5.27 ± 2.57	4.332	0.033
	Group B	26.07 ± 5.90	16.72 ± 4.83	4.224	0.035
	Group C	26.23 ± 6.37	14.82 ± 4.27	3.963	0.042
ADL	Group A	28.19 ± 4.04	64.86 ± 7.28	5.194	0.026
	Group B	25.29 ± 4.52	43.71 ± 6.09	4.124	0.036
	Group C	25.18 ± 4.81	41.16 ± 6.28	4.392	0.031

Note: \*shows, compared with before treatment, there were no statistical differences in ANIHSS scores, MESSS scores, ADL scores in three groups, P>0.05; #shows, compared with after treatment, there were statistical differences in ANIHSS scores, MESSS scores, ADL scores in Group A, B and C, P<0.05.

The above table shows that, compared with that before treatment, there is no statistical difference between the values of ANIHSS scores, MESSS scores, ADL scores in three groups, P>0.05; #shows that, compared with that after treatment, there is statistical difference between the values of ANIHSS scores, MESSS scores, ADL scores in Group A, B and C; Furthermore, there is statistical difference between the values of ANIHSS scores and MESSS scores in three groups before and after treatment (Table 3).

**Discussion**

Ischemic cerebral stroke (ICS), it also can be called cerebral infarction. Its incidence is high. With the progress of treatment in this disease, death rate of this disease decreases. But its disability rate reaches to 80% [6]. ICS mainly cause central nervous function injury of patients, motion function disorder further, and language function disorder, psychological and emotional disorder [7]. The onset mechanism of ICS is vascular stenosis and blocking of brain, which cause local ischemia of cerebral tissue, release of inflammatory factors, finally cause malacia of cerebral tissue. At present, the molecular onset mechanism of ICS is not very clear. Most scholars think that cellular apoptosis of cerebral nerve cells are the central part. After apoptosis of cells, structure of cytomembrane is destroyed. There is anti-oxygen substance in membrane, such as cholesterol, which can protect cells from free radical. But after destruction of cytomembrane structure, normal metabolism pathway of cerebral cells is affected. Clear and metabolism of free radical in brain are affected. It gathers in cells, then cause edema and necrosis of cells [8].

In TCM, ICS belongs to stroke. The records about stroke, it had been seen in Neijing first in the early time. Spiritual Pivot. Heat disease came up with acupuncture for treating stroke. The principle is “tonifying deficiency and reducing excess”. In other words, excess should be given reducing method; deficiency should be given tonifying method [9]. Before Tang dynasty, the simple point is selected for treating stroke. In A-B classic of acupuncture and moxibustion, it comes up with “patients cannot walk with paralysis, wind invades furtively. Point should use LI6”. “Paralysis, paralysis of limbs, easily to fright, point should use ST27”. “Patients can not drink. Point should use DU26”. “Dryness of mouth cannot open. Point should use SI6”. “Paralysis of arms and waist which caused by yang phlegm. Mouth cannot close. Point should use LI4” [10]. Compendium of Medicine in Tang and Song dynasty came up with stroke should add points of Faji, LI4, GB20, GB2, ST6, ST4, DU20, LI15, GB31, ST36 and GB39. The effects will be better [11]. Acupuncture of connecting DU meridian is advocated by Zhang Daozong professor of TCM, who thinks main points of ischemic cerebral diseases are LI11 and DU20. Traditional medicine thinks that various yang gathers in DU20.

Moxibustion on DU 20 can regulate qi of meridians in whole body, which can smooth qi and blood, also can refresh spirit and brain. Various yang gathers in LI11. LI 11 is given bleeding, which can reduce various yang. On the basis of DU20 moxibustion and LI4 bleeding, combing with traditional needling method, which has significant effects on ICS [12].

Repair of cerebral ischemia accompanies with recanalization of vessels. BFGF and VEGF are important neural nutrient factors and vascular active peptide substance. Its main function is induction angiogenesis, which can improve local microcirculation, reduce edema of ischemic cerebral tissue [13].

In this study, patients with ICS were treated by using acupuncture of connecting DU meridians, which compare with traditional acupuncture therapy and drug therapy. This study shows the patients who use acupuncture of connecting DU meridians. The effects of BFGF and VEGF are better than traditional therapy and drug therapy ( $P<0.05$ ). In comparison of symptom improvement and self-care recovery, acupuncture of connecting DU meridians have more advantages ( $P<0.05$ ) [13].

In conclusion, patients with ICS can be given acupuncture of connecting DU meridians, which can improve expression level of BFGF and VEGF, improve clinical symptoms of patients.

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