# Effect of Yiqi Huoxue Huatan Tongluo Method on Intestinal Flora Expression in Patients with Acute Cerebral Infarction

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Objective: To evaluate the clinical effect of Yiqi Huoxue Huatan Recipe (recipient for invigorating qi, activating blood and resolving phlegm) on ischemic stroke patients and its effect on intestinal flora expression through clinical study of Yiqi Huoxue Huatan Recipe, and to explore its possible mechanism and provide clinical basis for its further application. Methods: 60 patients with acute cerebral infarction were divided into treatment group (30 cases, combined Chinese traditional and Western medicine) and control group (30 cases, pure Western medicine). Fecal samples were collected at 24 hours and 14 days after the onset of the disease, and 16SrDNA high-throughput sequencing was used to observe the status of the faecal samples and the changes of intestinal flora abundance. To compare whether there was a difference between the two groups at 24 hours and 14 days after the onset of the disease. To compare whether there is a difference in microbiological status between the two groups during the same time period. To compare the difference of TCM syndrome integral between the two groups. Results: Before and after treatment of the patients with cerebral infarction in the two groups, those ranked the top six at the level of intestinal flora are: Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, Tenericutes and Cyanophyta. After treatment, the abundance of Bacteroides was up-regulated, while the abundance of Firmicutes and Proteobacteria was down-regulated. However, the adjustment range of treatment group with combined Chinese medicine and western medicine was larger and there was significant difference between the two groups (P<0.05). The improvement of TCM syndrome in the treatment group was more significant than that in the control group (P<0.05). Conclusion: Intestinal flora disturbance may be a potential causative factor of cerebral ischemic diseases. Yiqi Huoxue Huatan Recipe has a certain effect on the abundance of intestinal flora, and the symptom of the patients in the treatment group is improved more obviously. By regulating the intestinal flora, the patients' internal environment is improved and the constitution is improved, which may be one of the effective mechanisms of Yiqi Huoxue Huatan Recipe.

Ischemic stroke (CIS) is a common disease that seriously endangers the health of middle-aged and elderly people. The morbidity, recurrence rate, disability rate and mortality rate of CIS are all very high. According to the latest statistics, stroke has surpassed tumor as the top cause of death in China. At present, there are 2 million new cases of stroke and up to 6.5 million cases of disease each year in China, among which, ischemic stroke accounts

for 80% of all strokes, 80% of survivors have different degrees of labor loss, and severe disability accounts for more than 40%. With the increase of age and the improvement of people's living standard, China spends nearly RMB 20 billion a year on this disease, which brings heavy economic burden to the country and many families. In China, acute ischemic stroke is the most common type of stroke, accounting for about 60%-80% of all strokes, and is

the first disabling and first fatal cause in China [1].

In the treatment of ischemic stroke, traditional Chinese medicine (TCM) has a long history in treating ischemic stroke. With the development of current research, its clinical efficacy is improving. The pathogenesis of ischemic stroke cannot be separated from six aspects of wind, fire, qi, blood, phlegm, deficiency, qi deficiency and blood stasis is one of the main pathogenesis, and phlegm and blood stasis blocking collaterals are the important pathogenesis of ischemic stroke. Therefore, replenishing qi and activating blood circulation is one of the basic treatment methods for ischemic stroke, and the combination of phlegm and blood stasis is an important treatment method for ischemic stroke. In our department, the self-made Yiqi Huoxue Huatan Recipe has a satisfactory clinical effect in the treatment of ischemic stroke, and it has been established that the Yiqi Huoxue Huatan Recipe is safe and effective in the treatment of ischemic stroke, and its possible mechanism is related to the protective effect of neuronal endothelial cells [2].

In recent years, there have been many studies showings that intestinal flora is associated with stroke, Parkinson's disease, hyperlipidaemia, atherosclerosis and other diseases. Is this adjustment of intestinal flora also one of the ways in which it works? The purpose of this study was to investigate the relationship between intestinal flora and the action pathway of traditional Chinese medicine (TCM) by investigating the changes of intestinal flora abundance before and after treatment in patients with acute cerebral infarction.

## Clinical data
### Source of cases

All cases were from outpatient and inpatient patients of Taizhou Central Hospital from March 2018 to June 2020.

## Criteria for case diagnosis

The diagnostic criteria of TCM refer to the item of "Study on the TCM Syndrome and Clinical Diagnosis" developed by the National Science and Technology Commission, and the "Criteria for the Diagnosis and Efficacy Evaluation of TCM" developed by the Scientific Research Group of Encephalopathy Emergency Diseases of China Food and Drug Administration [3] (1) The primary symptoms: hemiplegia, disillusionment, slurring of speech, paresthesia of hemiparesthesia, skew of tongue; (2) The secondary symptoms: headache, vertigo, change of mydriasis, cough when drinking water, misalignment of eyes, ataxia; 3) Tongue moss pulse: Tongue is pale and lichen-white or yellow, pulse is thin, string is slippery or string is thin; (4) Acute onset, there are many inducements before onset, often there are foreboding symptoms; (5) The age of onset is more than 40 years old.

Having two or more primary symptoms, or one primary symptom with two secondary symptoms, combined with onset, cause, aura, age, can be confirmed.

The diagnostic criteria of Western medicine refer to the diagnostic criteria of "Key Points in Diagnosis of Cerebrovascular Diseases" revised by the 4th National Academic Conference on Cerebrovascular Diseases in 1995 [4]. (1) It usually occurs in a quiet state; (2) Most of them have no obvious headache and vomiting; (3) The onset is slow and usually progresses gradually or is staged; most of them are related to atherosclerosis and can also be seen in arteritis and blood diseases; (4) It generally develops clear consciousness or mild disorder within 1-2 days after onset; (5) It has symptoms and signs of internal carotid artery system and/ or vertebrobasilar system; (6) Cerebral infarction was found by CT or MRI.

## Case selection criteria
## Case inclusion criteria

(1) According to the diagnosis of TCM, it was apoplexy (middle meridian), qi deficiency, blood stasis, phlegm stagnation and collaterals. (2) Patients diagnosed with cerebral infarction by Western medicine; (3) Patients over 18 years of age and under 65 years of age; (4) Patients within 2 weeks of onset; (5) Patients who have not recently taken antibiotics or probiotic preparations.

## Case exclusion criteria

Transient ischemic attack; (2) Visceral organs or associated disturbance of consciousness in patients with stroke; (3) Suspected hemorrhagic infarction on lumbar puncture or imaging examination; (4) Patients with cerebral embolism confirmed by brain tumor, brain trauma, cerebral parasitism, metabolic

disorder, rheumatic heart disease, coronary heart disease and other heart diseases complicated with atrial fibrillation; (5) Patients with primary diseases such as heart, kidney, hematopoietic system and endocrine system; (6) Patients with mental retardation; (7) Complicated with gastrointestinal bleeding; (8) Unstable vital signs; (9) Recent administration of antibiotics or probiotic preparations; (10) Excessive storage of stool samples or the presence of red blood cells or white blood cells on routine stool examination.

## Case grouping

62 patients with cerebral infarction were diagnosed by CT or MRI. There was incomplete data for elimination, among which 1 case was not suitable to continue the trial due to complications, 2 cases in total, and 60 cases in total meeting the requirements. According to the order of admission, the random number table method, and the parallel and control principle, the study objects were randomly divided into two groups, with 30 cases in each group. The study objects were aged 39-75 years, with an average one of 60.8 years. The gender and age were comparable between the two groups (P<0.05). Fecal samples were collected 24h after onset and 14 days after onset in both groups.

## TREATMENT

The control group was given anti-hypertension, lipid-lowering, blood glucose-lowering, anti-platelet aggregation and other conventional treatment from the day of admission; besides the above conventional treatment, the treatment group was given oral Yiqi Huoxue Huatan Recipe (formula: Radix Astragali 30g, Salvia Miltiorrhiza 20g, Ligusticum Wallichii 15g, Carthamus Tinctorius 10g, Angelica Sinensis 15g, Lumbricus 10g, Rhizoma Pinellinae Praeparata 15g, Rhizoma Acori Graminei 15g, Arisaema Cum Bile 15g, Hirudo 6g, Achyranthes Bidentata 15g) every day, all the drugs were decocted by Huadong Pharmaceutical Co., Ltd. Two packs in 1 dose, each pack of 200 ml, taken twice in the morning and in the evening for every day, for 14 days as one course of treatment.

Commonly used add and subtract: for those with dry stools, add 15g of Fructus Cannabis and 15g of Cistanche deserticola Ma; for those with abdominal distension, add 10g of Aurantii Fructus Immaturus and 10g of Mangnolia Officinalis; for those with thin stools, subtract Angelica Sinensis, add 15g of fried Rhizoma Atractylodis and 15g of fried Rhizoma Atractylodis Macrocephalae; for those with dizziness and headache, add 9g of Gastrodia, 15g of Uncaria and 15g of Radix Puerariae.

## Observation indicators and methods
### Safety observations

In both groups, hematuria and stool routine, liver and kidney function, electrocardiogram and coagulation function were performed once within 24 hours and 14 days after hospitalization, respectively. Adverse reactions were recorded at any time.

### Efficacy observations

(1) To observe the related symptoms and the changes of tongue pulse and TCM syndrome integral;

(2) 16S SrDNA high-throughput sequencing technique was used to monitor the intestinal microbe status of stroke patients at 24 hours and 14 days after stroke onset.

## Sampling and high throughput sequencing of 16SrDNA V4 region
### Fresh sampling

Remove the urine firstly, use a sterile stool collector to respectively collect the stool samples of patients in control group and treatment group within 24 hours after onset and 14 days after onset, immediately place the stool samples on ice in the laboratory, use a sterile spoon to take 3-10g of the middle part of sample and place it in a sterile centrifuge tube, immediately place it in a -80° refrigerator for preservation, and use dry ice for transportation.

Main reagents and instruments: MiSeq Reagent Kit v3 (Illumina, USA), AgencourtAMPureXPPCR Purification Beads (Beckman Coulter, USA), TopTaq DNA Polymerase kit (Transgen, China). Main instruments: NanoDrop 2000 (Thermo Fisher Technologies Inc, USA), Invitrogen Qubit3.0 Spectrophotometer (Thermo Fisher Technologies Inc., USA), ABI 2720 Thermal Cycler (Thermo Fisher Technologies Inc., USA), Agilent 2100 bioanalyzer (Agilent Technologies Inc., USA),

Illumina MiSeqBenchtop Sequencer (Illumina Inc., USA), Eppendorf 5810R Centrifuge (Eppendorf, Hamburg, Germany)

## Analysis of faecal flora detection
### Genomic DNA testing

After obtaining the samples, Genomic DNA Quality Detection was performed using agarose gel electrophoresis by the company.

## Target region detection amplification of samples

High-fidelity PCR amplification of the hypervariable region V4 in the 16S rDNA of the qualified sample was performed with 3 replicates and a standard bacterial / fungal genomic DNA, Mix, as a positive control. The amplification primers are determined according to the selected detection region, and the specific sequences are as follows: Agarose gel electrophoresis is used to detect whether the amplification products are single and specific. Three replicates of the amplification products from the same sample were mixed and each sample was purified by adding an equal volume of AgencourtAMpure XP nucleic acid purification beads. Adapter sequence1 = CTGTCTCTTATACACATCTCCGAGCCCACG AGAC; Adapter sequence2 = CTGTCTCTTATACACATCTGACGCTGCCGA CGA.

## Add specific tag sequence for each sample

After amplification, the product was detected by agarose gel electrophoresis, and the amplified product was purified with magnetic beads of nucleic acid purification to obtain the original library of a sample.

## Library quantification and mixing

Based on the preliminary quantitation results of agarose gel electrophoresis, the sample library concentrations already labeled with their respective Index were diluted appropriately, then the library was accurately quantified using Qubit, and the samples were mixed in the appropriate ratio (molar ratio) according to the sequencing flux requirements of the different samples.

## Library quality detection

After mixing, the library was tested by Agilent

2100 Bioanalyzer to determine the size of the inserted fragment of the sequenced library, to confirm that there was no non-specific amplification between 120 and 200 bp, and to accurately quantify the concentration of the sequenced library.

## Sequencing on MiSeq

The library was sequenced using a 2 × 250 bp two-terminal sequencing strategy based on the Miseq platform, followed by bioinformatics analysis. The sequence data of each sample are used to analyze the relationship between bacterial species and the difference among species, so as to obtain the classification of bacteria and the relative abundance of bacteria (the relative abundance of microorganisms is the proportion of a certain microbial species in a sample to all microbial species. According to the morphological structure and physiological function of organisms, organisms can be divided into boundary, door, class, order, family, genus and species with different grades) and interrelation of bacterial communities. Library construction and sequencing were performed by Shanghai Genesky Biotechnology Co., Ltd.

## EFFICACY ASSESSMENTS

According to the standard of the 4th National Academic Conference on Cerebrovascular Diseases and the "Criteria for the Diagnosis and Efficacy Evaluation of Stroke" developed by the National Scientific Cooperation Group on Encephalopathy and Acute Diseases of China Food and Drug Administration [3].

## Criteria for evaluating the curative effect of TCM syndromes

Use a unified sentence to ask questions. According to the Chinese medicine ischemic stroke syndrome scoring table and Chinese medicine Qi deficiency syndrome scoring table, the symptoms were classified into severe, moderate, mild and no obvious symptoms, and the scores were 6,4,2 and 0 respectively.

Clinical recovery: The clinical symptoms and physical signs of TCM disappeared or disappeared basically, and the integral of syndrome decreased by ≥ 95%. Significant effect: The clinical symptoms and physical signs of TCM were significantly improved, and the integral of syndrome was reduced

by ≥ 70%. Effective: The clinical symptoms and physical signs of TCM were improved, and the integral of syndrome was reduced by ≥ 30%. Ineffective: The clinical symptoms and physical signs of TCM were not significantly improved or even aggravated, and the integral of syndrome was reduced by less than 30%. The calculation formula is nimodipine method: [(integral before treatment – integral after treatment) ÷ integral before treatment] × 100%.

### Criteria for scoring the degree of neurological deficit

Evaluation of neurological deficit: After enrollment, the degree of neurological defect of study objects was evaluated with National Institutes of Health Stroke Scale (NIHSS) score [5]. The total score was 42. The higher the score, the more severe the neurological defect was indicated. According to NIHSS score, the range is divided into mild deficit (NIHSS score <7 points), moderate deficit (NIHSS score 7-15 points) and severe deficit (NIHSS score> 15 points).

### STATISTICAL METHODS

SPSS 13.0 statistical software was used. The measurement data were expressed by x ± s, and the difference was statistically significant when P<0.05.

## RESULTS OF TREATMENT
### Colony analysis of intestinal flora at phylum level

The maximum relative abundance of intestinal flora in the first 6 positions at phylum level was in the following order: Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, Tenericutes, and Cyanophyta. The relative abundance was 0.4234 ± 0.2191, 0.2987 ± 0.1236, 0.2391 ± 0.1146, 0.0216 ± 0.0025, 0.0115 ± 0.008, 0.0010 ± 0.0001 in the early cerebral infarction control group and 0.4233 ± 0.2180, 0.2991 ± 0.1228, 0.2389 ± 0.1142, 0.0217 ± 0.0023, 0.0114 ± 0.008, 0.0010 ± 0.0002 in the early cerebral infarction treatment group. There was no significant difference in the abundance of intestinal flora between the two groups (P>0.05). After 14 days of treatment, 0.4106 ± 0.2312, 0.2994 ± 0.1426, 0.2505 ± 0.1165, 0.0226 ± 0.0019, 0.0118 ± 0.063, 0.0017 ± 0.0008 in the combined Chinese and Western medicine treatment group and 0.4147 ± 0.2236, 0.2731 ± 0.1347, 0.2712 ± 0.1189, 0.0223 ± 0.0022, 0.0114 ± 0.0088, 0.0024 ± 0.0009 in the Western medicine treatment group, the abundance of Bacteroidetes was up-regulated, Firmicutes and Proteobacteria was down-regulated in the two groups. However, the adjustment range of combined Chinese and western medicine treatment group was larger, with statistical difference (P<0.05).

Table 1.
## Comparison of the relative abundance of intestinal flora before and after treatment in the two groups

| Intestinal flora | Fecal samples collected at 24 hours after onset | | | | | Fecal samples collected after 14 days | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | Control group | | Treatment group | | | Control group | | Treatment group | | |
| | Mean value | Variance | Mean value | Variance | P | Mean value | Variance | Mean value | Variance | P |
| Bacteroidetes | 0.2391 | 0.1146 | 0.2389 | 0.1142 | 0.011 | 0.2731 | 0.1347 | 0.2994 | 0.1426 | 0.004 |
| Firmicutes | 0.4234 | 0.2191 | 0.4233 | 0.2180 | 0.008 | 0.4147 | 0.2236 | 0.4106 | 0.2312 | 0.003 |
| Proteobacteria | 0.2987 | 0.1236 | 0.2991 | 0.1228 | 0.013 | 0.2712 | 0.1189 | 0.2505 | 0.1165 | 0.009 |
| Actinobacteria | 0.0216 | 0.0025 | 0.0217 | 0.0023 | 0.022 | 0.0223 | 0.0022 | 0.0226 | 0.0019 | 0.014 |
| Verrucomicrobia | 0.0014 | 0.0008 | 0.0013 | 0.0009 | 0.001 | 0.0042 | 0.0019 | 0.0028 | 0.0021 | 0.008 |
| Cyanophyta | 0.0010 | 0.0001 | 0.0010 | 0.0002 | 0.009 | 0.0024 | 0.0009 | 0.0017 | 0.0008 | 0.009 |
| Tenericutes | 0.0115 | 0.0079 | 0.0114 | 0.0080 | 0.021 | 0.0114 | 0.0088 | 0.0118 | 0.0063 | 0.010 |
| Planctomycetales | 0.0001 | 0.0000 | 0.0001 | 0.0000 | 0.018 | 0.0003 | 0.0001 | 0.0002 | 0.0001 | 0.018 |
| Fusobacteria | 0.0002 | 0.0001 | 0.0002 | 0.0001 | 0.0170 | 0.0004 | 0.0001 | 0.0003 | 0.0001 | 0.014 |

### Comparison of TCM syndrome integral after treatment between the two groups

Table 2.
## Comparison of curative effect of TCM syndrome after treatment between the two groups

| Group | Number of cases | Rate of recovery | Significant effect rate | Effective rate | Total effective rate | Inefficiency |
| --- | --- | --- | --- | --- | --- | --- |
| Treatment group | 30 | 10.00% | 26.67% | 53.33% | 90.33% | 10.00% |
| Control group | 30 | 6.67% | 20.00% | 53.33% | 82.14% | 20.00% |

Statistical treatment showed that the scores of TCM syndromes in the two groups were significantly improved after treatment compared with those before treatment (P<0.05), but the integrals of TCM syndromes in the treatment group were significantly improved compared with those in the control group (P<0.01), indicating that the therapeutic effect of the treatment group was significantly better than that of the control group.

## Comparison of neurological deficit between two groups before and after treatment

| Table 3. Comparison of neurological deficit between two groups before and after treatment | | | |
|---|---|---|---|
| Group | Number of cases | Before treatment | After treatment |
| Treatment group | 30 | 21.65±2.04 | 6.64±4.22 |
| Control group | 30 | 21.46±2.03 | 9.87±6.09 |
| Note: The statistical treatment showed that there was no significant difference in the scores of neurological deficits between the two groups before treatment (P>0.05), and there was significant difference between the treatment group and the control group after treatment (P<0.05), indicating that the therapeutic effect of the treatment group was significantly superior to that of the control group. | | | |

## Adverse reactions

The blood, urine, stool routine, liver and kidney function and ECG showed no abnormality before and after treatment in both groups. No patient complained of rash, hemorrhage, gastrointestinal discomfort and abnormal defecation after medication, suggesting the safety of Yiqi Huoxue Huatan Recipe was good.

## DISCUSSION

The healthy human gut is a very rich microenvironment with up to $10^{14}$ bacteria and more than 500 species, which together form a complex microbial ecosystem, the microecology of the gut [6]. The types of intestinal microbes are complex, and their mechanisms of action on the occurrence and development of metabolic and inflammatory diseases are not well understood. At present, there is some consensus on the theory of "microbiome-gut-brain axis" [7], but further study is needed on how intestinal microbiota participate in the pathogenesis of cerebral infarction and its interaction [8].

Benakis et al. [9] showed that intestinal flora and IL-17 positive T cells play an important role in the occurrence and development of cerebral infarction. Singh [10] et al. studied the relationship between brain injury, intestinal microbe disturbance and immune system after cerebral infarction. It was found that cerebral infarction could disrupt the intestinal microbe environment, thus impairing the function of gastrointestinal microbiota. In contrast, the change of intestinal microbiota could also affect the brain injury and prognosis through the change of inflammation. Liao Shuoxi [11] analyzed the correlation between intestinal microflora and its metabolites in patients with cerebral infarction. The results showed that the intestinal microflora in patients with cerebral infarction were significantly different from those in normal controls. The intestinal pathogenic bacteria in patients with cerebral infarction were more abundant, but the probiotic abundance was obviously decreased.

Intestinal flora, as a large number of microbes living in human digestive tract, is an important environmental factor in the process of human health and disease conversion. It has been found that Firmicutes are the most dominant bacteria in human and higher mammal intestines, accounting for about 50% ~ 60% of the total bacterial population. Firmicutes are a class of intestinal bacteria that are associated with obesity and are capable of degrading insoluble fibers. Studies have shown that normal intestinal flora may be involved in diet-induced obesity, and that when the amount of Firmicutes in the gut exceeds that of Bacteroidetes, the absorption of calories from the diet is more effective, leading to obesity [12]. The gut is also known as the human "second brain" or "gut brain". Intestinal brain and brain are two-way interconnected, and they are connected through the brain-gut axis. Intestinal brain can affect central nervous system, then affect people's emotion, cognition and behavior. Various forms of stress can alter the changes of intestinal flora and flora, cause inflammatory reaction of host's nerve, and thus cause nervous system dysfunction.

Cerebral infarction is a cerebrovascular circulation disorder. The pathogenesis and progression of cerebral infarction are not fully

understood. In recent years, animal experiments have suggested that intestinal microbes have an important effect on the prognosis of acute ischemic stroke, such as the degree of brain damage and dysfunction caused by acute middle cerebral artery occlusion in mice; therapeutic fecal flora transplantation can restore the ecological dysregulation caused by brain damage and improve the prognosis of stroke; the diversity of intestinal flora is reduced and the bacteroides grow too much after stroke; it also causes dysfunction of the intestinal barrier and decreased intestinal motility [13]. The severity of stroke symptoms in mice treated with antibiotics was only 40% of that in the control group [14]. These findings suggest that acute brain lesions cause ecological dysregulation of microbial flora, and changes in gut flora can subsequently exacerbate brain damage and post-stroke neuritis and have a severe impact on stroke prognosis.

Zhu Dongchen [15] found that the relative abundance, community structure and species richness of main microbes in intestinal flora of patients with cerebral infarction and transient cerebral ischemia all changed. It was speculated that this change may play an important role in the occurrence and development of cerebrovascular diseases and may be a potential pathogenic factor in cerebral ischemic diseases. They found that the relative abundance of Bacteroidetes was significantly lower in the stool of patients with cerebral infarction than in the transient ischemic group, i.e., the relative abundance of Bacteroidetes was correlated with the degree of cerebral ischemia. The relative abundance of Bacteroidetes in intestinal flora was negatively correlated with the serum ApoE level in the healthy group, transient ischemic group and cerebral infarction group, but there was no significant correlation between other major microbe species and the serum ApoE level. Therefore, it was considered that Bacteroidetes might influence the occurrence and development of cerebral ischemic diseases by regulating ApoE metabolism.

The pathological factor of ischemic stroke is phlegm-dampness, which is caused by unequal distribution of lung, spleen and renal dysfunction and water metabolism disorder. Jing Cai [16] et al. used 16rs DNA high-throughput sequencing technique to analyze the colony composition and abundance of intestinal flora in phlegm-dampness and peaceful subjects. The results showed that the diversity of intestinal flora in phlegm-dampness was different in the structure and abundance level of bacterial flora, and the relative abundance of Bacteroides, Rothia, Fecobacterium and Macromonas was significantly decreased.

Yiqi Huoxue Huatan Recipe is composed of Radix Astragali, Ligusticum Wallichii, Salvia Miltiorrhiza, Pinellia Ternata, Arisaema Cum Bile, Angelica Sinensis, Hirudo and Rhizoma Acori Graminei. In the prescription, Radix Astragali reinforces vital energy most ("Materia Medica Seeking Truth"), "good treatment for limb impotence" (" Records of Tradition Chinese and Western Medicine in Combination · Drug "), and Radix Astragali is the fundamental of the disease mechanism of qi deficiency and blood stasis in this disease, which is used as the monarch drug. Chuanxiong Xiangchuan Xinsan is a kind of medicine of blood-qi, "the main stroke into the brain, headache, cold arousal, muscle clonus and relieve urgency" ("Sheng Nong's Herbal Classic"); "this medicine is used to specially treat the brain diseases" ("Compendium of Materia Medica"); Salvia Miltiorrhiza is used to remove blood stasis to produce new, adjust the menstruation, it is "into the blood, to reach the zang-fu organs, to remove stagnation of blood stasis"; Pinellia Ternata has the function of eliminating dampness and reducing phlegm, reducing nausea and arresting vomiting. "New Compilation of Materia Medica": "eliminating dampness and removing phlegm, saving violent stroke;" "Arisaema Cum Bile dispelling wind and stopping spasticity, eliminating dampness and resolving phlegm," "main stroke, eliminating phlegm and paralysis, dispelling qi, breaking strength and resolving swelling" ("Kaibao Materia Medica"); "Rhizoma Acori Graminei expelling phlegm and invigorating the mind, tranquilizing the mind and promoting mentality" and "opening wisdom and adding spirit" ("Zunsheng Bajian"), Angelica Sinensis can replenish blood, can attack and replenish blood, can remove blood stasis and not injure blood. The combination of traditional Chinese medicines has the effect of invigorating qi and activating blood circulation, eliminating phlegm and removing

turbid.

Modern pharmacological studies have shown that Radix Astragali can improve anti-hypoxia ability of brain tissue, inhibit platelet aggregation and neuron apoptosis, dilate cerebral vessels and increase cerebral blood flow [17]; Ligusticum Wallichii is mainly composed of Ligustrazine which can dilate blood vessels, improve microcirculation, inhibit platelet aggregation and reduce brain edema [18]. It can also resist lipid peroxidation and inhibit apoptosis [19]. Salvia Miltiorrhiza can significantly increase blood flow in cerebral ischemia area, inhibit inflammatory reaction and neuron necrosis in ischemic lesion, relieve brain edema, reduce the toxicity of NO and anti-lipid peroxidation, and have a good neuroprotective effect on ischemic brain injury [20]; Pinellia Ternata has the effects of lowering blood lipid, anti-lipid peroxidation and increasing the activity of antioxidant enzymes [21]; the volatile oil of Rhizoma Acori Graminei can increase the permeability of blood and brain, effectively increase the blood perfusion volume of brain, and make the drug have the maximum effect [22]; Hirudin contained in Hirudoid has a significant anticoagulant effect and is more effective in inhibiting thrombus growth than heparin, which accelerates the decomposition of thrombi that already exist on the wall of the vessel [23].

The results showed that cerebral infarction patients were treated by Western medicine combined with traditional Chinese medicine Yiqi Huoxue Huatan Tongluo Method for 14 days, intestinal flora is dominated by microorganisms at the phylum level, the relative abundance of Bacteroidetes was up-regulated and the relative abundance of Firmicutes and Proteobacteria were down-regulated more significantly. The improvement of TCM syndromes was more obvious, suggesting a better prognosis.

Based on the above study results, Yiqi Huoxue Huatan Recipe has a good therapeutic effect on patients with ischemic stroke. Its possible mechanism is related to the neuroprotective effect [2]. It is also possible to adjust the metabolism of environment in human body by regulating the relative abundance of intestinal flora to improve the constitution of patients, thus improving the prognosis of patients with cerebral infarction, or to play a comprehensive effect through multiple approaches.

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