Original Article
Observations on effects of Heihu ointment combined with routine therapy on cerebral infarction cases

Jian Guo1*, Xiao-Hua Hu2*, Sheng-Gen Liu3, Li-Qin Wang1, Ren-Shi Xu4

Departments of 1Traditional Chinese Medicine, 4Neurology, The First Affiliated Hospital of Nanchang University, Jiangxi, P.R. China; 2Department of Chinese Integrated with Western Medicine, Nanchang University, Jiangxi, P.R. China; 3Department of Chinese Integrated with Western Medicine, Hospital of Jiangxi Provincial Armed Police Corps, Jiangxi, P.R. China. *Equal contributors.

Received August 18, 2017; Accepted May 24, 2018; Epub September 15, 2018; Published September 30, 2018

Abstract: Cerebral infarction (CI) is one of the most common diseases in cerebrovascular diseases, and the mortality rate and disability rate was high. There are a lot of western medicines and Chinese traditional medicines for the treatment of it, but the effects are not ideal. However, the combination of traditional Chinese and western medicine treatment showed better effects on it. In this paper, we selected 30 cases of typical cerebral infarction patients, and applied external application of the Heihu ointment, together with western medicine routine treatments. The patients were grouped according to age, gender, side of brain involvement, and the severity of CI. The neurological deficit scores and activities of daily living scores (Barthel Index scores) between before and after treatments were compared. Neurological deficit scores and activities of daily living scores and craniocerebral magnetic resonance image (MRI) were compared before and after treatments on patients, and also we evaluated the clinical efficacies. The results revealed that the effective rate was 86.67%, and MRI showed reduction on the brain infarction areas on 22 cases, and Magnetic Resonance Angiography (MRA) showed increased cerebrovascular branches on 9 cases. Meanwhile, the Barthel Index scores between before and after treatments had significant differences (P<0.05). However, the neurological deficit scores and the activities of daily living scores had no significant difference (P > 0.05) on the age, gender, and the side of brain involvements, while they were significant differences on the severity of CI (P<0.05). In conclusion, the external application of the Heihu ointment combined with western medicines’ routine therapy should be regarded as an effective treatment for cerebral infarction patients. While a lighter condition, and a better effect. And also, the Heihu ointment may have the recanalization effect on CI.

Keywords: Cerebral infarction, Heihu ointment, combine with, western medicine, the clinical efficacy

Introduction

Cerebral infarction (CI) is a cerebrovascular disease, and the supply of blood flow obstacles in the brain, which leads to irreversible injuries to brain tissues for ischemia and anoxia in corresponding regions, then it causes ischemic necrosis or encephalomalacia, which can result in relevant neurological function disorders [1, 2]. Adamas divided CI involvement into lacunar infarction, small-area infarction and large-area infarction. According to etiology and pathogenesis, CI can be divided into cerebral thrombosis, cerebral embolism and lacunar infarction, which are called cerebral ischemic stroke. As a common neurological disease, CI may attack people at any age in any season. It has high morbidity, disability rate, lethality and recurrence rate; it has been found that CI was one of the highest lethality three diseases among middle-aged and elder healthy populations [3]. In few hours (3-6 h) after the occurrence of CI, ischemic necrosis of the brain cells in the center of the involvement region will appear. The surrounding edge zone at the ischemia state, there is a surrounding edge zone found, which is called edema zone or ischemic penumbra, and the normal ionic balance and complete structure remains in this zone. Reasonable therapies can prevent the CI regions from expansion, and the related functions might recover or relieve soon [4-6]. There are a lot of therapies for CI, such as thrombolysis, encephala-edema control, anticoagulation, fiber reduction, neuro-protection and rehabilitation [7, 8]. However, there is still no special safe therapy for it. Thus, complex therapies are highly appreciated.
Traditional Chinese medicine has explored the etiology and pathogenesis of CI deeply. According to literature reviews, traditional Chinese medicine has achieved outstanding treatment effects on cerebral apoplexy. There are many Chinese medicine therapies, including traditional Chinese medicine decoction, injection of Chinese medicine, Chinese patent medicine, acupuncture and moxibustion, external application of traditional Chinese medicine, manipulation, etc [9-11]. It is good and prospect to use traditional Chinese medicine in the CI treatment, for the good tolerance compliance of patients, slight toxic and side effects, and also low costs [12]. The Heihu ointment is a traditional Chinese external ointment, from the classic ancient herb book-<<Pu Ji Fang>>, it has the effects on removing stasis, dredging collaterals and activating blood circulation. Moreover, it was convenient, and had good compliance of patients. In this research, we selected 30 CI patients, and used the Heihu ointment together with common therapies, and then we observed the effects in different groups. The results found the combination treatment had obvious curative effects on CI patients. This outcome provided a new treatment project for CI.

Materials and methods

Subjects

The 30 CI (different types) patients were collected from the inpatients of Jiangxi Armed Police Force Hospitals from August, 2013 to April, 2016, including 20 males and 10 females. They were from 38 to 87 years old, averaging at (61.30±13.16) years old. Among these cases, 17 patients had complications of hypertension, 5 patients had diabetes mellitus and 2 patients had coronary heart diseases. And 6 cases of them didn’t reexamine the MRI (Table 1). Meantime, 15 cases happened in basal ganglia region, 8 cases in lobe, 4 cases in both basal ganglia region and lobe, 1 patient in brainstem, 1 in epencephalon and the last one in thalamus (Figure 1).

Selection standards

① Essentials for Diagnosis of All Cerebrovascular Diseases passed on the 4th National Cerebrovascular Disease Academic Conference of Chinese Medical Association in 1996. ② Criteria of Disease Diagnosis and Therapeutic Effect of Traditional Chinese Medicine. ③ Obvious neurological deficits, focal signs of nervous system (e.g. difficulty in speaking, poor physical activity of the affected side, accompanied with numbness, inability or paralysis), more than 6 h’s course of the disease, clinical neurologic impairment score ≥ 4. ④ Blood pressure is higher than 130/80 mmHg and can be controlled below 180/100 mmHg. ⑤ Vital signs are stable and patients can eat, without evident skin allergy or serious injury. ⑥ The western medicine treatment has no obvious effects.

Exclusion criteria

Patients with transient ischemic attack, cerebral hemorrhage and subarachnoid hemorrhage; patients with disturbance of conscious-
Heihu ointment on cerebral infarction

Several cases of cerebral infarction were excluded from the study due to serious primary diseases such as heart, lung, liver, kidney, hematopoietic system and endocrinium diseases; pregnant and lactating women; patients with serious skin allergy and injuries against external application of ointment. Informed consent was obtained from all patients before external application of the Heihu ointment.

Therapy

The western medicine routine treatments were given to all cases, including cerebral protection, dehydration, blood pressure reduction, regulation of blood sugar level, antilipemic agents and treatments of complications. Meanwhile, they were given external application of Heihu ointment (Batch No.: Wu L2007005) along the facial nerves. Ingredients of the Heihu ointment are: 10 g Angelica sinensis, 10 g Saposhnikovia divaricata, 10 g radix clematidis, 10 g Zaocys dhumnades, 10 g Angelica dahurica, 6 g Carthamus tinctorius, 4 g Myrrh, 15 g Cape jasmine and 8 g cassia twig (all these ingredients are ground and blended with matrix). External application positions are: ① cervical vessels, including internal carotid, external carotid artery, supraclavicular arterial and subclavian artery; ② corresponding meridian points, including Dazhui Point, Jianjing Point on two shoulders, Fengchi, Fengfu, Yifeng, Tianrong and Tiantu. The external application of the Heihu ointment was adopted according to their brain involvement: we applied it at the right cervical vessels and acupoints when left hemiplegia appeared, and inversely. The usually ointment used period was 1-3 d (until skin bubbles at the application place) and 7 d as one course of the treatment. And it was planned four courses in total, with an interval of 3-4 d between two courses.

Evaluation standard of therapeutic efficiency

Therapeutic effect indexes: ① Main therapeutic effect index: the neurologic impairment score, which is evaluated according to Clinical Neurologic Impairment Scoring of Stroke Patients (1996). ② Minor therapeutic effect index: the activities of daily life (Barthel Index (BI)), symptoms, signs and MRI changes which were evaluated by 2 image doctors with intermediate professional level or above).

All the indexes were assessed both before and after the treatment separately.

Therapeutic efficiency judgment: Therapeutic effect indexes of CI patients were evaluated according to Clinical Neurologic Impairment Scoring of Stroke Patients (1996).
Heihu ointment on cerebral infarction

Scoring of Stroke Patients (1996). And the therapeutic efficiency was judged by changes of neurological deficit scores before and after the treatments.

Basic cure: hemiplegia and difficult sluggish speech are eliminated; muscle strength reaches IV-V, be able to have an independent living and walking; neurological deficit score reduces by 91%-100% and the invalidism level is 0.

Remarkable progress: improvement in speaking difficulty; hemiplegia limbs recovers to II or higher muscle strength; partial life-independent; neurological deficit score decreases by 46%-90% and the invalidism level is 1-3.

Progress: improvement in hemiplegia and speaking difficulty; life-dependent; neurological deficit score decreases by 18%-45%.

Non-change: no significant improvement in symptoms and signs; neurological deficit score decreases or increases by less than 17%.

Worsening: neurological deficit score increases by 18% or higher.

Die: The patient dies.

Among them, basic cure and remarkable progress are called excellent therapeutic efficiency. Progress is called therapeutic efficiency. Non-change, worsening and die are called invalid. Total efficiency = excellent therapeutic efficiency + therapeutic efficiency. Total effective rate = Total efficiency/total cases × 100%.

Side effects: Maybe some patients will cause local skin reactions, but we found that no special treatment needs to perform on them, such as local redness, exudation, pruritus and rash. The applied ointment therapy can continue. At the same time, we have not yet found any side effects on liver and kidney functions, and the others.

### Statistical analysis

All experimental data are showed as the mean ± the standard deviation (SD); single factor analysis of variance (ANOVA) was performed using SPSS 19.0 statistical software, followed by Tukey’s test. In this study, the value at $P<0.05$ was considered statistically significant.

### Results

Among the 30 cases, as in (Figure 2), 24 of them had MRI reexamination and 22 cases had progresses on the area of CI. 14 cases had MRA reexamination and 9 of them showed increases of blood vessel branches in the brain. The neurological deficit scores and BI between before and after treatments had significant difference ($P<0.05$, Table 2). The gender, age and the side of brain involvement between before and after treatments were compared among groups, and the results indicated no statistical significance ($P > 0.05$, Tables 3-5 and Figures 3-6). Then, the patients who had neurological deficit scores ≥ 10 (serious) and <10 (mild) before and after treatments were compared, it showed statistical signifi-

| Table 3. Comparison of neurological deficit scores and BI of gender groups between before and after treatment ($\bar{x} \pm s$) |
|-----------------|-----------------|-----------------|-----------------|
| Neurological deficit scores | Before | After | Before | After |
| Male (20 cases) | 8.05±4.17 | 4.30±4.54 | 63.00±14.09 | 79.75±20.42 |
| Female (10 cases) | 7.50±3.89 | 2.70±2.45 | 65.00±12.02 | 84.00±12.20 |
| $P$ value | 0.731 | 0.310 | 0.704 | 0.551 |

| Table 4. Comparison of neurological deficit scores and BI of left and right brain involvement groups between before and after treatment ($\bar{x} \pm s$) |
|-----------------|-----------------|-----------------|-----------------|
| Neurological deficit scores | Before | After | Before | After |
| Left (15 cases) | 7.13±2.75 | 3.33±3.58 | 64.67±10.60 | 82.33±16.89 |
| Right (15 cases) | 8.60±4.98 | 4.20±4.46 | 62.67±15.80 | 80.00±19.55 |
| $P$ value | 0.327 | 0.562 | 0.687 | 0.729 |

| Table 5. Comparison of neurological deficit scores and BI of different age groups between before and after treatment ($\bar{x} \pm s$) |
|-----------------|-----------------|-----------------|-----------------|
| Neurological deficit scores | Before | After | Before | After |
| <60 (13 cases) | 7.92±4.03 | 4.15±4.74 | 64.61±14.06 | 80.77±21.59 |
| ≥ 60 (17 cases) | 7.82±4.14 | 3.47±3.45 | 62.94±13.00 | 81.47±15.39 |
| $P$ value | 0.948 | 0.651 | 0.738 | 0.918 |
Heihu ointment on cerebral infarction

Figure 3. A. Difference of neurological deficit scores of different gender groups between before and after treatment has no statistical significance. B. Difference of BI of different gender groups between before and after treatment has no statistical significance.

Figure 4. A. Difference of neurological deficit scores of left and right brain involvement groups between before and after treatment has no statistical significance; B. Difference of BI of left and right brain involvement groups between before and after treatment has no statistical significance.

Figure 5. A. Difference of neurological deficit scores of different age groups between before and after treatment has no statistical significance; B. Difference of BI of different age groups between before and after treatment has no statistical significance.

cance ($P<0.05$, Table 6 and Figures 9, 10). Among 30 cases, 3 cases were basic cure, 20 cases were remarkable progress, 3 cases were progress and 4 cases were invalid. Therefore, the total efficiency cases were 26 and the total effective rate was 86.67% (Figure 7).

Typical cases

(1) The patient, Gong, male, 43 years old, was hospitalized with chief complaints of “left-side body weakness for 10 d”. The patient had left-side body weakness and numbness of left fin-
Heihu ointment on cerebral infarction

The upper body weakness was obvious, accompanied with numbness of left corners of the mouth, occasional pains in the left head and neck, as well as walking instability. The specialized examination showed that the muscle strength of the right arm was IV, muscle strength of the left arm was III, muscle strength of the left leg was IV and muscular tension of two legs increased slightly. Neurological deficit scores were 8 and BI was 60. In MRI (Figure 8), in the right basal ganglia and the right frontal lobe, multiple DWI high signal shadow was observed, which might cause acute or sub-acute multiple CI. Diagnosis: acute CI. Symptomatic and supportive treatments were given, including external application of the Heihu ointment for promoting blood circulation to remove meridian obstruction, Xingnaojing for improving brain blood circulation, Panax notoginseng Saponins for blood activation and removing blood stasis, Edaravone eliminate oxygen free radicals, Bayaspirin anti-platelet drugs, Nimotop for improving brain blood supply, Citicoline Sodium as nutrient to brain cells and Dextran 40 for glucose dilatation. Symptom improvement was observed after 3 d’s treatments. The left-side body weakness improved compared to the conditions before the treatment. The patient discharged after 9 d’s treatments and the muscle strength of the left arm recovered. Muscle strengths of the left arm and left leg were evaluated as 4- and 4+, together with slightly high muscle tension. At the meantime, the neurological deficit score was 4 and BI was 80. The MRI+MRA reexamination (Figure 9) showed that the multiple DWI high signal shadow in the right basal ganglia and the right frontal lobe decreased significantly, and the artery blood vessel branches in the right brain increased compared with the signs before the treatment.

(2) The patient, Hu, female, 74 years old, was hospitalized with main complaints of "dizziness.
Heihu ointment on cerebral infarction

Figure 8. Before treatment.

Figure 9. Reexamination 40 d after treatment.

Figure 10. Before treatment.

Figure 11. Reexamination 20 d after treatment.
and left-side body activity disorder for 2 d" (She had treated in a local hospital, but had no significant improvement). Blood pressure: 140/80 mmHg; shallow left nasolabial groove, incomplete eye close, slurred speech and tongue left. The muscle strength of the left arm was III+ at the distal end, together with IV at the proximal end. The muscle strength of the left leg was IV. The muscle tensions of other limbs were normal. The patient couldn’t complete finger-to-nose test, quick alternating movement test, heel-knee-tibia test and Romberg test. The two-side tendon reflex was positive (+). Neurological deficit score was 14 and BI was 50. MRI (Figure 10) of head prompted acute cerebral infarction in the right basal ganglia region. Diagnosis: acute CI. We chose external application of the Heihu ointment for promoting blood circulation to remove meridian obstruction, accompanied with the western medicine treatments as follows: mannitol for dehydration and intracranial pressure reduction, Xingnaojing, Xueshuangtong, Alprostadil for circulation improvement, Vitamin C, Vitamin B6 and mecobalamine as nutrient to nerves. After 6 d’s treatments, the patient could make clear expression and have no bucking, and also obvious improvements on the left-side body activities. She discharged after 15 d’s treatments, with articulation and muscle strength of the left leg was IV+. Neurological deficit score was 3 and BI was 85. According to the reexamination of head MRI+MRA (Figure 11), it showed that the DWI high signal shadow in the right basal ganglia region reduced significantly and the blood vessels in the distal end increased slightly.

Discussion

CI is one of the major diseases which can threaten the human health. It has high lethality and disability rate. As we all know, the brain is very sensitive to ischemia and anoxia. Continuous blood supply is the essential condition for maintaining the normal functions of the brain. So, brain blood supply obstacle, ischemia and anoxia can cause injuries to local brain tissues, and then cerebral infarction. There are still brain cells with complete morphological structure and reversible dysfunction in the ischemic penumbra surrounding the cerebral infarction. In clinic, recanalization is used to recover the blood supply in infarcted regions, and to reverse functions of the brain cells. So, it is very important to reduce the lethality and disability rate of CI.

Recanalization by western medical therapy-thrombolytic therapy

It is well known that common pathogeneses of acute CI includes thrombosis, embolus detachment, plaque formation on vessel walls and hemadostenosis. The main cause of CI is local brain vascular occlusion caused by acute thrombosis or thrombus transfer from other positions, which accounts for 75% in clinical [13]. This is the main basic of thrombolytic therapy for CI in western medical treatment. Commonly, there are several western medical therapies on CI, including thrombolytic therapy, reduction of intracranial pressure, anticoagulation, fiber reduction, neuroprotection, and so on. Among these methods, thrombolytic therapy is a more effective recanalization way and attracts wide research attentions. It is crucial to give instant thrombolysis recanalize blood vessels before the necrosis of brain tissues, for it can reverse the functions of the brain tissues in ischemic penumbra and reducing anoxi, and also ameliorate the ischemic injuries on the brain tissues. Thrombolytic therapy not only has complications of hemorrhage, reperfusion injury and arterial reocclusion, but also has a narrow time window limit, and it is about 5.5 h which is the ultimate time that nerve cells in penumbra can tolerate [14] and is the key time for thrombolytic. At present, the widely accepted thrombolysis intervention took the time window of 3-6 h as the main reference index. Since there were few patients receiving thrombolytic therapy clinically in 6 h after the occurrence of CI, most patients missed the best time of thrombolytic therapy. As a result, studying recanalization after the 6 h occurrence of CI is more important [15].

“Recanalization in traditional Chinese medicine” activating blood circulation, removing blood stasis and dredging collaterals

We have studied CI for a long time in traditional Chinese medicine. There are records about it in Huangdi’s Internal Classics, and the relative mature knowledge on CI has been formed in Ming and Qing Dynasty after the development in Tang, Song and Jin Dynasty. CI belongs to “stroke” category in traditional Chinese med-
Heihu ointment on cerebral infarction

Previous medical literatures have elaborated pathogenesis of CI, and they have emphasized on different points. Generally, there are several understandings of its pathogenesis, including phlegm, stasis, internal heat and Qi asthenia [16]. Together with some therapeutic methods, such as traditional Chinese medicine decoctions, Chinese patent medicines, acupuncture and moxibustions, acupuncture catgut embeddings, et al. Zhou Zhongying [17] believed that the cerebral arterial occlusion caused by phlegm stagnation was the main pathogenesis of stroke. Liu Qinglin [18] believed that splenic asthenia, liver depression, deficiency of Qi and blood, adipagia, fat, thick taste and heavy drinking were easy to cause phlegm stagnation in orifice, which leaded to vein obstructions. Li Yongping [19] pointed out that phlegm was the direct pathological factor and the pathomechanism were Yin deficiency, Qi deficiency, internal heat and phlegmatic hygrosis. According to the therapeutic principle of diagnosis and treatment, which based on a holism of the illness and the patient's condition, we conferred specific therapeutic methods for them, such as nourishing Yin, suppressing hyperactive Yang, calming liver wind, resolving phlegm and relaxing bowels, promoting blood circulation, eliminating heat and phlegm, invigorating the spleen and eliminating dampness, replenishing Qi and blood, and so on. Guo Jian and Liu Shenggen had devoted themselves to the understanding of traditional Chinese medicine on diseases and found that wind-phlegm stasis stagnant on orifice is the main pathogenesis of CI, which could be treated by promoting blood circulation, and this was known as recanalization in traditional Chinese medicine. Based on the previous treatment experience of traditional Chinese medicine, Guo Jian and Liu Shenggen developed the Heihu ointment [20] with modern science and technology. And they applied the Heihu ointment to patients with CI through basic researches on traditional Chinese medicines and clinical experiments. All the 30 cases in this paper had a course longer than 6 h and they missed the optimal time for thrombolytic therapy. The external application of the Heihu ointment combined with western medicine routine therapy was given, and we obtained some results, firstly, on the skin where the Heihu ointment was applied had local redness, exudation, pruritus and rash, which didn’t need special treatment. Secondly, 24 cases had MRI reexamination. Among them, 22 cases showed DWI signal reduction and narrowing, 1 case remained the same DWI signal and involvement size, and 1 case suffered increase of DWI signal and involvement size. 14 cases had MRA reexamination, in which 9 cases showed increase of blood vessel branches in brain and 5 cases had no changes. Thirdly, 26 cases achieved excellent therapeutic efficiency, manifested by improvement in symptoms and sings, reduction of neurological deficit scores and severity of illness as well as an increase of BI. The rest 4 cases were identified invalid. The total effective rate of external application of the Heihu ointment combined with western medicine route treatment was 86.67%. It concluded that the Heihu ointment was effective to CI. The imageological showed that external application of traditional Chinese medicine could increase blood vessel branches in brain. Therefore, we concluded that the Heihu ointment might realize “recanalization in traditional Chinese medicine” on CI through two mechanisms: (1) It can regulate the immune system, through stimulating the reticuloendothelial cells-mononuclear phagocyte system and inducing immune phagocytes to eliminate the thrombus and foreign matters in occluded blood vessels; (2) It can dilate some blood vessels, by enhancing endothelial cell proliferation and stimulating vascular proliferation to promote the formation of collateral circulation surrounding the CI involvement.

Ingredient analysis of the Heihu ointment

Myrrh, Angelica sinensis and Carthamus tinctorius in the Heihu ointment has the functions of blood circulation promotion and recanalization. Radix clematidis, Zaocys dhumnades and Saposhnikovia divaricata can relieve rheumatic pains, colds and have recanalization effects. Angelica dahurica, cassia twig and Cape jasmine can warm Yang, get rid of dampness and also analgesics. So we can conclude the combination functions of these ingredients as circulation promotion, stasis removing and xeransis. The azone in the substrate of the Heihu ointment has the functions as follow: it can increase the permeability of skin to accelerate the drug absorption, and it can enhance the circulation of blood, together with relieving pain and carrying drugs to diseases directly along

Int J Clin Exp Med 2018;11(9):8965-8977
the facial nerves [21]. Our preliminary researches have confirmed that when the local skin occurred bubbles, redness, exudation, they meant the following effects: regulate immune, trophic nerve and multiple humoral factors, stimulate reticuloendothelial cells-mononuclear phagocyte system, induce phagocytes to devour damaged, degeneration, necrosis and proliferous cells and tissues; ② promote local angiectasis, improve local microcirculation and blood supply for local tissues and cells; ③ promote local metabolism; ④ facilitate formation of collateral circulation and change functions of corresponding organs as well as metabolism. Moreover, external application can avoid side effects by oral application on digestive tract and liver and kidney [22, 23].

**Functions and modern pharmacology of *Angelica sinesis***

*Angelica sinesis* has sweet taste and warm property, which can replenish blood, activate blood circulation, regulate menstruation, relieve pains and relax bowels. It is often used in clinic on blood deficiency, dizziness, palpitation, irregular menstruation, rheumatic arthralgia and constipation [24]. *Angelica sinesis* contains more than 40 ingredients, including ferulic acid, *Angelica sinesis polysaccharide*, essential oils, amino acids, microelements, etc [25]. Essential oils can resist excitatory effects of epinephrine-hypophysin or histamine on uterus. *Angelica sinesis* extracts have the functions of dilating the isolated coronary and increasing its blood flow, which meant a remarkable protection on myocardial ischemia. Moreover, *Angelica sinesis* can promote generation of hemoglobin and red blood cells, strengthen body immunity, and also have the effects of anti-inflammation, anti-lipid peroxidation, antibiosis and anti-tumor, et al. [24]. *Angelica sinesis* decoction or essential oils can work on inhibiting myocardial contraction. Luo Huiying [26] also discovered that the essential oils of *Angelica sinesis* could protect experimental cerebral ischemia-reperfusion injury.

**Functions and modern pharmacology of *Angelica dahurica***

*Angelica dahurica* has an acrid flavor and warm property, which can relieve exterior syndromes, expel wind, alleviate pain, free nasal orifices, eliminate dampness, and also wind the swelling and empyema. Clinically, it is often used for cold, headache, toothache, rheumatic arthralgia, nasal congestion, runny nose, abnormal leucorrhoea, etc. It mainly contains coumarins essential oils [24]. Coumarins compounds can be used as anticoagulant and antithrombotic drugs. Meanwhile, they can promote lipolysis and inhibit fat synthesis, dilate coronary arteries, and so on. Therefore, *Angelica dahurica* can be used to treat hypertension disease. Zhao Wanhong [27] studied the effects of compounds of the *Angelica dahurica* capsule, they found that it could promote blood circulation and remove blood stasis, meantime, these effects could also be applicable to prevent complications of hypertension and cardiovascular accidents.

**Functions and modern pharmacology of *Carthamus tinctorius***

*Carthamus tinctorius* has an acrid flavor and warm property, which can activate blood flow to promote menstruation, remove blood stasis and relieve pain. In clinic, it is often used to treat amenorrhea and dysmenorrheal, lochia and abdominal pain, chest stuffiness, pain, heat and blood stasis, which were caused by blood stasis, *Carthamus tinctorius* contains carthamin yellow, uranidin, carthamone, neocarthamin and safflower oil [24]. Carthamin yellow can dilate coronary arteries, improve myocardial ischemia, dilate blood vessels to reduce blood pressure, resist arrhythmia, inhibit platelet aggregation, enhance fibrinolysis to reduce whole blood viscosity, ease pains and calm down central nervous system, and also anti-convulsion. *Carthamus tinctorius* decoction can excite smooth muscle. Zhao Jinning [28] found that *Carthamus tinctorius* could inhibit platelet aggregation, increase plasmin activity, dilate blood vessels, improve blood circulation in the brain, and have the effects of anticoagulations as well as anti-thrombosis.

**Functions and modern pharmacology of *Cape jasmine***

*Cape jasmine* is bitter in taste and cold-natured, which can clear heat, promote diuresis and remove the blood heat and toxic materials in vivo. The external application of it can relieve swelling and pain. *Cape jasmine* contains flavo-
Heihu ointment on cerebral infarction

Heihu ointment contains gardenin, iridoids, organic acid esters (e.g., chlorogenic acid and crocetin), essential oils and polysaccharide. It has many functions, such as anti-inflammatory, antipyretic, cholangogue sedative-phypnotic and antihypertensive. And researchers found that active substances in extracts of Cape jasmine fruit could enhance the proliferation of endothelial cells in vitro and prevented atherosclerosis as well as thrombosis [25].

Functions and modern pharmacology of Myrrh

Myrrh has acid-bitter flavor and mild property, which can remove stasis, relieve pain, reduce swelling and resolve mass. It is often used for stasis pain, and traumatic injuries. Myrrh contains bdellium, gum, myrrholoic acid, essential oils, and so on. Greases in Myrrh can reduce lipids and prevent atheromatous plaque in endarterium. Besides, Myrrh has curative effects on antibacterial and anti-inflammation, antitumor, liver protection and inhibition of uterine smooth muscle contraction [24].

Functions and modern pharmacology of cassia twig

Cassia twig has an acid-bitter flavor and mild property, which can relieve exterior syndromes, invigorate pulse-beat, and warm meridian to activate Yang. Practically, it is always used to treat cold, pain, amenorrhea, joint pains, phlegm, edema, palpitation, etc. The main active substances in cassia twig are as follow: essential oils, organic acids, polysaccharides, coumarins and tannin [24]. Cinnamic acids in cassia twig have many curative effects, they are antibiosis, increasing leucocyte, cholangogue, antimutation and anti-invasion. Cinnamaldehyde not only has the function of obvious calm and abirrlation, but also can excite sweat gland and salivary gland, stimulate gastric secretion, relax bronchi smooth muscle to realize antipyresis, invigorate stomach and antiasthma, and improve peripheral circulation. Huang Jingqun [29] discovered that cinnamaldehyde had remarkable antiplatelet aggregation and in-vivo antithrombosis functions.

The Heihu ointment is prepared with these medicines by using modern pharmacology technologies and has curative effects on CI through recanalization effects and promoting the blood circulation. It can eliminate the brain arteriospasm, dilate blood vessels to recover blood supply for the injured brain tissues, inhibit cellular edema and thereby reduce injuries to the brain tissues; stimulate revascularization and promote establishment of collateral circulation, further improving blood supply in the brain vessels; improve metabolic disorders of brain tissues, reduce inflammatory response, interrupt cascade injuries of ischemia and anoxia to brain tissues, thus recovering functions of paralysis limbs gradually.

In western basic treatment, anticoagulation, circulation improvement, cranial nerve protection and rehabilitation all play important roles in improving blood supply of damaged central nervous, nourishing brain cells and promoting neural functional recovery. In our study, we found that the external application of the Heihu ointment combined with western medicine route treatment could reduce brain injury size, promote establishment of collateral circulation in the CI involvement region, reduce damages to neurological function and facilitate recovery of neurological functions, thus improving curative effect of patients with CI and lowering occurrence of untoward effects and sequelae. It can increase the self-respect and activity of daily living for patients.

Conclusions

Based on above statistical data, it could come to conclusions that the external application of the Heihu ointment combined with western medicine routine therapy should be regarded as an effective treatment for CI. The curative effects had no obvious difference in patients with different gender, age, and the involvement of left or right brain. However, observations exhibited that the lighter condition of patients, the better effects. Meantime, the Heihu ointment could recanalize the embolic cerebrovascular, which might require further researches.

Acknowledgements

Supported by The National Science Foundation of Jiangxi Province (No. 20181BAB215036) and Chinese Medicine Research Project of Health and family planning Commission of Jiangxi Province (No. 2017B091).

Disclosure of conflict of interest

None.
Heihu ointment on cerebral infarction

Address correspondence to: Dr. Li-Qin Wang, Department of Traditional Chinese Medicine, The First Affiliated Hospital of Nanchang University, No. 17 Yongwai Street, Nanchang 330006, Jiangxi, P.R. China. Tel: 86-0791-8869-2700; Fax: 86-0791-8862-3153; E-mail: wangliqin_0607@163.com; Ren-Shi Xu, Department of Neurology, The First Affiliated Hospital of Nanchang University, Jiangxi, P.R. China. Tel: 86-0791-8869-3419; E-mail: 13767015770@163.com

References

Heihu ointment on cerebral infarction

