

A Clinical Study of Astragalus Injection in Preventing and Treating Stroke-Associated Pneumonia

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1. Abstract

Background and Purpose: Stroke-associated pneumonia (SAP) is a disease with a high incidence in Intensive Care Unit (ICU), which seriously threatens people's health. However, there is no effective prevention method for SAP. The purpose of this study was to explore the effectiveness and feasibility of astragalus injection to treat SAP. **Methods:** 240 patients with acute cerebral infarction were selected and randomly divided into 2 groups, the control group was given basic system therapy, and the treatment group was treated astragalus injection (20 ml for intravenous drip-ping once a day) in addition to the basic system therapy for 15 days. At the end of the 15-day treatment, the difference in the incidence of SAP and NIHSS score were evaluated, furthermore, the inflammatory mediators, including procalcitonin (PCT), c-reactive protein (CRP), interleukin-1 β (IL-1 β) and interleukin-6 (IL-6) were tested by ELISA.

Results: the incidence of SAP in the treatment group was statistically significantly lower at 8.3% (10 of 120) compared to 15.8% (19 of 120) in the control group; Compared with the control group, the levels of blood inflammatory mediators and NIHSS scores in the treatment group were significantly decreased, especially in patients

with cerebral infarction of Qi deficiency and blood stasis syndrome.

Conclusion: Astragalus injection showed therapeutic effect on SAP, which was mainly effective for stroke patients with Qi-deficiency and blood deficiency, but it was not effective for stroke patients with other syndromes.

2. Introduction

Stroke is a disease with high morbidity and mortality [1,2]. The incidence of pneumonia after stroke is 5-26%. and it is the most common complication after stroke [3,4]. Stroke-associated pneumonia (SAP) plays an important role in stroke. Studies have shown that compared with non-SAP patients, SAP patients showed a higher mortality rate [5]. Therefore, effective treatment of SAP is crucial to the survival rate of identifying patients. Since Hilker et al. [5] proposed the concept of stroke-associated pneumonia (SAP) in 2003 [6], a large number of scholars have carried out research on SAP, and the one with Chinese characteristics is the research on prevention and treatment methods of traditional Chinese medicine (TCM). TCM is the crystallization of Chinese wisdom. TCMs such as Da-cheng-qi [7] and Ligusticum [8] have been proven to play a vital role in the prevention and treatment of stroke. Astragalus as a TCM is an excellent tonic, modern medical research has shown that astragalus has a variety of effects such as enhancing immune function, inducing interferon production, antibacterial and antiviral effects, and reducing ischemic brain injury [9,10],

However, the effect of astragalus on SAP patients has not been reported in the literature.

In addition, studies have confirmed that the inflammatory response including the accumulation of inflammatory mediators is the core content of pathophysiology after ischemic stroke [11], and the release of inflammatory cytokines may lead to the occurrence of SAP after stroke. Therefore, in this study we discussed the effect of astragalus on the secretion of inflammatory factors in patients, we found astragalus, the sacred medicine for invigorating Qi, may have a certain preventive effect on the occurrence of SAP.

3. Methods

Patients

This study enrolled acute stroke patients who were admitted to the outpatient department and emergency department of Shanghai Blue Cross Brain Hospital hospital from January 2013 to December 2019 (n = 240).

Inclusion Criteria Were:

- 1) Age 40 years or older (male or female)
- 2) Admission in the hospital for treatment within 72 hours after the onset of symptoms, with a total hospital stay of no less than 15 days
- 3) No infection of lungs and other parts at the time of consultation
- 4) no history of previous strokes, or a history of stroke but no severe disability, National Institutes of Health Stroke Scale score (NIHSS) score ≥ 6 and ≤ 30

Exclusion Criteria Were:

Stroke patients with transient ischemic attack (TIA), psychosis, hematopathy, coagulation dysfunction, vasculitis, and other serious heart, liver and kidney diseases were excluded, stroke patients receiving interventional therapy were excluded, intravenous thrombolytic therapy was allowed, and strokes receiving other clinical trials patients, pregnant or breastfeeding women were excluded.

Elimination Criteria:

Those who failed to receive adequate treatment as required, those who asked to withdraw or be discharged halfway through, and those who had obviously incomplete medical records. All patients voluntarily accepted the experiment and signed the informed consent. acute stroke patients included cerebral thrombosis, acute lacunar infarction, and cerebral embolism, and were not included in cerebral hemorrhage, subarachnoid hemorrhage patients and cerebral infarction patients with interventional therapy. The diagnosis of cerebral thrombosis, acute lacunar infarction, and cerebral embolism must meet the criteria in "Diagnosis Essentials of Various Cerebrovascular Diseases" (Chinese Journal of Neurology, 1996) formulated by the Fourth National Cerebrovascular Disease Conference.

4. Grouping and Intervention

All 240 patients with acute stroke that met the criteria were randomly divided into two groups. The control group was given basic system therapy, the treatment group was given basic system therapy and intravenously infused 20 ml of astragalus injection (Zhengda Qingchunbao Pharmaceutical Company, Hangzhou, China) every day (equivalent to 40 g of raw astragalus) for 15 days. The basic system treatment refers to the "Guidelines for the Prevention and Treatment of Cerebrovascular Diseases in China" promulgated in 2005. The SAP diagnostic criteria were based on the standards proposed in the 2010 "Chinese Expert Consensus on the Diagnosis and Treatment of Stroke-related Pneumonia"[12].

Subgroup: Among all the syndromes of cerebral infarction in traditional Chinese medicine, patients with Qi deficiency and blood stasis account for about 60% of the total (between 50%-70%). Therefore, in this experiment, patients with deficiency and blood stasis were classified as subgroups were used for further observation.

The classification was determined by traditional Chinese medicine doctors in accordance with the "Diagnosis and Efficacy Standards for Diseases and Syndromes of traditional Chinese medicine"[13]. The symptoms of this type of syndrome were as follows: hemiplegia, paralysis of the limbs, numbness of the body, poor speech, slanted tongue, or with pale complexion, shortness of breath and fatigue, palpitation and spontaneous sweating, lavender tongue, thin white or greasy fur, thin pulse. In addition, patients with Qi deficiency and blood stasis are often elderly and physically frail. All subjects were systematically numbered and a database was established to collect clinical and laboratory testing and auxiliary testing data before and after treatment in the treatment group and the control group.

Observation and Evaluation Indicators

- a. The incidence of SAP in each group and subgroup
- b. Before starting systemic treatment on the day of the first visit or admission, blood was obtained for the first time, At the end of the 15-day treatment (fasting at 6 am on the 16th day), the second blood draw was performed on the patient, the level of C-reactive protein (CRP), procalcitonin (PCT), blood interleukin 1 β (IL-1 β) and interleukin 6 (IL-6) were detected by enzyme-linked immunosorbent assay (ELISA) (B & D). ELSA analysis was performed according to the manufacturer instructions.

5. Statistical Analysis

Comparison of rates between two samples---u test was used to analyze the incidence of SAP between groups. the hypothesis test of the overall mean of the large sample completely randomized design data between groups---u test was performed to analyze the comparison of laboratory observations between groups and subgroups. All data in this experiment were expressed by mean \pm SD and all statistical tests were two-sided tests, and P value < 0.05 was considered to be a significant difference.

6. Results

Comparison of the Incidence of SAP between the Two Groups

The treatment group and the control group had 120 patients with acute cerebral infarction, respectively. After 15 days of hospitalization, the incidence of SAP in the treatment group was statistically significantly lower at 8.3% (10 of 120) compared to 15.8% (19 of 120) in the control group. In addition, the incidence of SAP in the treatment group was significantly at 6.9% (5 of 73) in patients with Qi deficiency and blood stasis, and was significantly lower than that in the control group at 15.2% (12 of 79).

Comparison of Inflammatory Factors Between the two Groups

Inflammation plays an indispensable role in the occurrence and development of SAP. In this experiment, the levels of PCT, CRP, IL-1 β , and IL-6 in the two groups were tested by ELISA. Table 1 shows the levels of PCT, CRP, IL-1 β and IL-6 in the first blood test between the treatment group and the control group. The results proved that there was no significant difference in the levels of inflammatory mediators between the treatment group and the control group ($p>0.05$). At the end of the 15-day treatment, PCT, CRP, IL-1 β , and IL-6 were tested for the second time. The results are shown in table 2. The results showed that compared with the control group, the treatment group PCT, CRP, IL-1 β and IL-6 levels were significantly reduced ($p<0.05$); in addition, after 15 days of treatment, PCT, CRP, IL-1 β , and IL-6 in the Qi deficiency and blood stasis subgroup were also tested (table 3). As expected, compared with the control group, the levels of PCT, CRP, IL-1 β and IL-6 in the subgroup of Qi deficiency and blood stasis subgroup in the treatment group were significantly decreased ($p<0.05$). These results indicated that astragalus injection effectively inhibited the secretion of PCT, CRP, IL-1 β , and IL-6.

Table 1: The first test of blood inflammatory indicators in the two groups of patients.

Group	PCT	CRP	IL-1 β	IL-6
	(ng/ml)	(mg/ml)	(pg/ml)	(pg/ml)
Treatment group (n=120)	10.7 \pm 3.1	35.1 \pm 15.7	65.4 \pm 25.9	116.1 \pm 23.3
Control group (n=120)	10.4 \pm 3.0	41.8 \pm 16.1	71.1 \pm 21.4	121.4 \pm 24.3
P value	>0.05	>0.05	>0.05	>0.05

Table 2: The second blood inflammatory index test for the two groups of patients.

Group	PCT	CRP	IL-1 β	IL-6
	(ng/ml)	(mg/ml)	(pg/ml)	(pg/ml)
Treatment group (n=120)	3.0 \pm 2.2	14.7 \pm 14.2	33.5 \pm 17.9	68.2 \pm 18.3
Control group (n=120)	6.5 \pm 2.6	24.1 \pm 10.0	48.7 \pm 18.0	94.2 \pm 23.1
P value	<0.05	<0.05	<0.05	<0.05

Table 3: The second blood inflammatory index of the two groups of patients with Qi deficiency and blood stasis type.

Group	PCT	CRP	IL-1 β	IL-6
	(ng/ml)	(mg/ml)	(pg/ml)	(pg/ml)
Treatment group (n=73)	2.7 \pm 1.9	12.9 \pm 10.1	31.2 \pm 15.2	66.4 \pm 16.9
Control group (n=79)	7.1 \pm 2.5	22.4 \pm 7.8	50.1 \pm 17.1	95.9 \pm 23.5
P value	<0.01	<0.01	<0.01	<0.01

7. Discussion

SAP refers to the symptoms of fever, cough, sputum, dyspnea and other symptoms in clinically diagnosed acute stroke patients, which are diagnosed according to specific diagnostic procedures. At present, factors such as basic patient status (age, gender, smoking), factors related to aspiration after stroke (lesion location and size, NIHSS score, state of consciousness) and decreased systemic immune function caused by stroke can induce the occurrence and development of SAP. The selective digestive tract purification training, drug use management, and feeding management are recognized as the main measures to effectively prevent the occurrence of SAP. And with the in-depth study of Chinese medicine, the preventive effect of Chinese medicine on stroke has also been verified [14,15]. Astragalus is an important medicinal plant in traditional Chinese medicine. It is rich in isoflavones and triterpene saponins [16]. It has been reported that ulinastatin combined with astragalus injection showed a good clinical effect on inflammatory response after PCI, which reduced the expression level of inflammatory factors in patients and reduced myocardial injury caused by ischemia-reperfusion [17]. Astragalus had important clinical application value. In this study, the levels of inflammatory factors in our treatment group were significantly lower than those in the control group, consistent with previous research. These results indicated that astragalus inhibited the occurrence of inflammation. In general, the application of astragalus to prevent and treat SAP

had a theoretical basis in terms of pharmacology, and it was also very appropriate through our clinical observations. At the same time, although astragalus was the holy medicine for invigorating Qi, its price was very low compared to various western medicines for the treatment of infection or stroke, and it was suitable for ordinary patients. In addition, the standardized astragalus injection was convenient to administer, simple to operate, easy to establish dose-effect standards, and was very suitable for clinical promotion. of course, the specific mechanism of astragalus invigorating Qi still need in-depth study.

8. Conclusion

In conclusion, Astragalus reduced the incidence of SAP in patients with acute cerebral infarction by reducing the expression of inflammatory mediators.

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