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# Analysis of the Clinical Effect of Naomaili Granules in the Treatment of Acute Ischemic Stroke

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**Abstract:** *Objective*: To explore the clinical efficacy and safety of Naomaili granules in the treatment of acute ischemic stroke. *Methods*: Eighty-eight patients were randomly divided into a treatment group and a control group, with 44 patients in each group. The control group received conventional Western medicine treatment, while the treatment group was additionally administered Naomaili granules at 10g per time, 3 times per day, for 20 days. Neurological function (NIHSS), activities of daily living (BI), inflammatory factors (hs-CRP, IL-6) levels, and adverse reactions were observed before and after treatment. *Results*: After 20 days of treatment, the NIHSS score of the treatment group decreased from (9.20 ± 2.10) to (5.12 ± 1.30), the BI index increased from (52.30 ± 8.50) to (78.60 ± 9.20), and hs-CRP and IL-6 decreased to (3.12 ± 1.10) mg/L and (18.20 ± 4.20) pg/mL, respectively, all significantly better than the control group ($P < 0.01$). The incidence of adverse reactions in the treatment group was 4.55%, lower than the 15.91% in the control group ($P < 0.05$). *Conclusion*: Naomaili granules can improve neurological function and living ability, reduce inflammatory response, and have good safety in patients with acute ischemic stroke.

**Keywords:** Naomaili granules; Ischemic stroke; Acute phase; Neurological function; Inflammatory factors; Safety

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## 1. Introduction

Ischemic stroke is a clinically common disease, and effective treatment during the acute phase is of great significance. Currently, conventional Western medicine treatment, mainly including antiplatelet aggregation, lipid-lowering and plaque stabilization, and symptomatic support, is the basic approach. However, monotherapy still has room for improvement in reducing neurological deficits, inhibiting inflammatory responses, and promoting neurological repair. According to traditional Chinese medicine theory, Qi deficiency and blood stasis are important pathogenesis of acute ischemic stroke. During this stage, implementing Qi-invigorating and blood-activating therapy can achieve satisfactory results. Modern pharmacological studies have shown that Naomaili granules,

derived from Buyang Huanwu Decoction, can exert neuroprotective effects through multiple pathways, such as improving cerebral blood circulation, inhibiting oxidative stress, and regulating immune and inflammatory responses [1]. The high-concentration active ingredient extraction process of the drug provides an important material basis for the clinical treatment of acute stroke patients. However, large-sample clinical studies on the treatment of acute ischemic stroke with Naomaili granules are still relatively limited, and its specific effects on neurological function, activities of daily living, and inflammatory markers need further validation. Based on this, this article analyzes the clinical effect of Naomaili granules in the treatment of acute ischemic stroke.

## 2. Materials and methods

### 2.1. Baseline information

Eighty-eight patients with acute ischemic stroke admitted from January 8, 2023, to January 8, 2024, are selected. All patients met the diagnostic criteria of the "Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018". The inclusion criteria are onset time ≤ 72 hours, NIHSS score of 5–15, and syndrome differentiation belonging to Qi deficiency and blood stasis type (consistent with the "Guidelines for the Diagnosis and Treatment of Common Diseases in Traditional Chinese Medicine Internal Medicine"). Patients who received thrombolytic or thrombectomy treatment, or had severe liver and kidney dysfunction, are excluded. They are randomly divided into a treatment group and a control group, with 44 patients in each group. The treatment group consisted of 24 males and 20 females, with an average age of (62.50 ± 8.30) years and an average NIHSS score of (9.20 ± 2.10). The control group consisted of 22 males and 22 females, with an average age of (61.80 ± 7.90) years and an average NIHSS score of (9.50 ± 1.90). There were no significant differences in baseline data between the two groups ($P > 0.05$), making them comparable.

### 2.2. Methods

The control group received conventional Western medicine treatment, specifically including oral administration of Aspirin Enteric-coated Tablets (100mg/time, once a day) for antiplatelet aggregation, Atorvastatin Calcium Tablets (20mg/time, once a day) for lipid-lowering and plaque stabilization. At the same time, targeted control measures are provided based on patients' blood pressure and blood glucose levels (target blood pressure < 140/90mmHg, target blood glucose 7.8–10.0mmol/L), along with symptomatic treatments such as nutritional support and maintenance of water and electrolyte balance. The treatment group received Naomaili Granules (produced by Hefei Heyuan Pharmaceutical Co., Ltd., approval number: Guo Yao Zhun Zi Z20200023) in combination with the control group's treatment, with a dosage of 10g/time, three times a day, dissolved in warm water and taken orally. Continuous administration for 20 days constituted one treatment course. Both groups received interventional treatment for 20 days, during which medication compliance and adverse reactions were strictly recorded. A 3-month outpatient follow-up was conducted after the treatment, including neurological function evaluation, laboratory index detection, and clinical event recording.

### 2.3. Observation indicators

(1) Neurological function evaluation

The National Institutes of Health Stroke Scale (NIHSS) is used to evaluate the degree of neurological impairment before and after 20 days of treatment. The scale includes 11 items such as level of

consciousness, gaze, facial paralysis, and limb movement, with a total score ranging from 0 to 42. A lower score indicates less severe neurological impairment and better recovery.

(2) Daily life ability evaluation

Concurrently, the Barthel Index (BI) is used to evaluate patients' self-care ability in daily life, covering 10 daily activities such as eating, dressing, walking, and toileting. The total score ranges from 0 to 100, with a higher score indicating stronger independent living ability.

(3) Inflammatory factor detection

Before and after 20 days of treatment, 3ml of fasting venous blood is collected to detect serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels using Enzyme-Linked Immunosorbent Assay (ELISA). The instrument used is a fully automated biochemical analyzer (model: Cobas8000), and the kit is purchased from a biotechnology company in Shanghai. Operations are strictly performed according to the instructions.

(4) Safety observation

During the treatment and within 3 months of follow-up, adverse events such as gastrointestinal reactions (e.g., abdominal distension, nausea, vomiting) and allergic reactions are recorded. Additionally, blood routine tests (red blood cell count, platelet count, neutrophil ratio) and liver and kidney function indicators [alanine aminotransferase (ALT), serum creatinine (Scr), blood urea nitrogen (BUN)] are detected before and after 20 days of treatment to observe any abnormal fluctuations or clinically significant abnormalities.

### 2.4. Statistical analysis

SPSS 26.0 software is used for data analysis. Measurement data are expressed as mean ± standard deviation (x±s), and comparisons between groups are performed using the t-test. Count data are expressed as rates (%), and the $\chi^2$ test is used for comparison. A $P$-value < 0.05 is considered statistically significant.

## 3. Results

### 3.1. Neurological function evaluation results

The comparison of NIHSS scores between the two groups before and after treatment is shown in **Table 1**. Before treatment, there was no statistically significant difference in NIHSS scores between the two groups ($P > 0.05$). After 20 days of treatment, the NIHSS scores in both groups were significantly lower than before treatment ($P < 0.01$), and the reduction was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$), as shown in **Table 1**.

**Table 1.** Comparison of NIHSS scores between the two groups before and after treatment (x±s, scores)

| Group | *n* | Before treatment | After treatment | *t* | *P* |
|---|---|---|---|---|---|
| Treatment group | 44 | 9.20 ± 2.10 | 5.12 ± 1.30 | 14.231 | < 0.001 |
| Control group | 44 | 9.50 ± 1.90 | 6.83 ± 1.50 | 9.872 | < 0.001 |
| *t* | | 0.745 | 5.862 | | |
| *P* | | 0.458 | < 0.001 | | |

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

## 3.2. Evaluation results of daily living abilities

The comparison of Barthel Index (BI) scores before and after treatment between the two groups is shown in **Table 2**. Before treatment, there was no statistically significant difference in BI scores between the two groups ($P > 0.05$). After 20 days of treatment, the BI scores of both groups were significantly higher than those before treatment ($P < 0.01$), and the increase was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$), as shown in **Table 2**.

**Table 2.** Comparison of Barthel Index scores before and after treatment between the two groups (x±s, points)

| Group | *n* | Before treatment | After treatment | *t* | *P* |
|---|---|---|---|---|---|
| Treatment group | 44 | 52.30 ± 8.50 | 78.60 ± 9.20 | 16.123 | < 0.001 |
| Control group | 44 | 51.50 ± 8.20 | 65.40 ± 8.70 | 10.345 | < 0.001 |
| *t* | | 0.482 | 6.231 | | |
| *P* | | 0.631 | < 0.001 | | |

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

## 3.3. Inflammatory factor test results

The comparison of serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels before and after treatment between the two groups is shown in **Table 3**. Before treatment, there was no statistically significant difference in inflammatory factor levels between the two groups ($P > 0.05$). After 20 days of treatment, the levels of hs-CRP and IL-6 in both groups were significantly lower than those before treatment ($P < 0.01$), and the reduction was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$).

**Table 3.** Comparison of inflammatory factor levels before and after treatment between the two groups (x±s)

| Group | *n* | Indicator | Before treatment | After treatment | *t*-value | *P*-value |
|---|---|---|---|---|---|---|
| Treatment group | 44 | hs-CRP (mg/L) | 6.85 ± 1.60 | 3.12 ± 1.10 | 13.245 | < 0.001 |
| | | IL-6 (pg/mL) | 28.50 ± 5.30 | 18.20 ± 4.20 | 10.123 | < 0.001 |
| Control group | 44 | hs-CRP (mg/L) | 6.72 ± 1.50 | 5.05 ± 1.40 | 5.872 | < 0.001 |
| | | IL-6 (pg/mL) | 27.80 ± 5.10 | 24.30 ± 5.10 | 3.215 | 0.002 |

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

## 3.4. Complication rate

The occurrence of complications during treatment in the two groups is shown in **Table 4.** The total incidence of complications in the treatment group was 4.55% (2/44), mainly manifesting as mild abdominal distension (1 case) and nausea (1 case), which resolved spontaneously without special treatment. The total incidence of complications in the control group was 15.91% (7/44), including gastrointestinal reactions (abdominal distension in 3 cases, nausea in 2 cases), and thrombocytopenia (2 cases, platelet count < $100 \times 10^9$/L). There was a statistically significant difference in the total incidence of complications between the two groups ($\chi^2$=3.968, $P$=0.046), and no severe liver or kidney damage or bleeding events occurred in either group.

**Table 4.** Comparison of complication rates between the two groups [n(%)]

| Group | *n* | Gastrointestinal reactions | Abnormal blood routine | Abnormal liver/Kidney function | Total incidence |
|---|---|---|---|---|---|
| Treatment group | 44 | 2 (4.55) | 0 (0.00) | 0 (0.00) | 2 (4.55) |
| Control group | 44 | 5 (11.36) | 2 (4.55) | 0 (0.00) | 7 (15.91) |
| $\chi^2$ | | | | | 3.968 |
| *P* | | | | | 0.046 |

Note: Compared with the control group, $P < 0.05$.

# 4. Discussion

## 4.1. Multi-dimensional interpretation of the mechanism of Naomaili granules in the intervention of acute ischemic stroke

The ischemic and hypoxic damage to nerve cells caused by the interruption of cerebral blood flow is a critical core of acute ischemic stroke, accompanied by the synergistic deterioration of inflammatory cascade activation and microcirculation dysfunction [2]. In this study, the significant improvement of neurologic function by Naomaili granules combined with conventional therapy stems from the synergistic effect of multiple components based on Buyang Huanwu Decoction. *Astragalus* promotes the formation of collateral circulation by regulating vascular endothelial growth factor (VEGF). Motherwort alkaloids reduce blood-brain barrier damage by inhibiting neutrophil adhesion molecules. Paeoniflorin reduces levels of proinflammatory factors such as IL-6 and hs-CRP by blocking the NF-κB signaling pathway. Qian *et al.* confirmed that Naomaili granules can comprehensively improve perfusion in ischemic areas of the brain by regulating hemorheology and coagulation function, which is closely related to the presence of notoginsenoside [3]. Cao *et al.* demonstrated that the application of Naomaili granules in patients with this disease can increase VEGF levels and decrease endothelin-1 (ET-1) expression, correcting vascular endothelial dysfunction [5]. This provides mechanistic support for its use as a "heavy agent for emergency" during the acute phase at the vascular protection level. The multi-target intervention characteristics of this traditional Chinese medicine compound on the ischemic cascade reaction were fully verified in the study by Zhang *et al.* [7]. Their research showed that these drugs have a significant effect on improving neurologic function in patients with large artery atherosclerotic cerebral infarction, representing a precise correspondence between relevant drug components and ischemic lesions.

## 4.2. Hierarchical association of clinical value between neurologic function restoration and improvement of daily living abilities

In clinical practice, the NIHSS score and Barthel Index are commonly used to evaluate the effectiveness of disease treatment. These scores accurately reflect the neurologic function restoration and reconstruction of patients' living abilities. In this study, the reduction in NIHSS score (4.08 ± 1.20 points) and the increase in BI index (26.30 ± 9.10 points) in the treatment group were significantly better than those in the control group. This result is consistent with the conclusion reported by Qian *et al.* that Naomaili granules can increase the BI index by 23.6% [3]. From a mechanistic perspective, drugs mediate neural plasticity through dual pathways: total notoginsenosides and *Astragalus saponins* can improve cerebral blood perfusion and increase local oxygen content in the brain. Additionally, paeoniflorin can activate the BDNF-TrkB signaling pathway, promoting presynaptic vesicle release and axonal myelination. Wang *et al.*'s study further confirmed that Naomaili granules can increase serum BDNF

levels by 41.2% [8]. This factor enhances hippocampal neurogenesis by regulating cAMP response element-binding protein (CREB) phosphorylation. Clinically, this cascade effect of neuroprotection-functional reconstruction has a temporal advantage. Early intervention within 72 hours of onset in the treatment group can shorten the duration of subsequent interventions entering the treatment time window, thereby achieving the goal of continuous treatment.

## 4.3. The core target effect of inflammation regulation in the treatment of ischemic stroke

After patients experience ischemic brain injury, changes occur in the levels of hs-CRP and IL-6 in the blood. Under the mediation of inflammatory factors, the blood-brain barrier is damaged, leading to severe neuronal apoptosis [3, 5]. In this study, the treatment group showed a 36.14% and 54.26% reduction in IL-6 and hs-CRP levels, respectively, which was significantly better than the control group's 12.60% and 24.85% reduction. These results are highly consistent with those reported by Qian *et al.*, where IL-6 decreased by 40.3% and hs-CRP decreased by 52.7% after treatment with Naomaili granules. From a mechanistic perspective, paeoniflorin in Naomaili granules can reduce the binding activity of the IL-6 promoter region by 63.2% by inhibiting the nuclear translocation of the NF-κB p65 subunit. Leonurine, on the other hand, targets the TLR4/MyD88 pathway, reducing TNF-α by 37.8%, thereby inhibiting both innate and adaptive immune pathways. This compensates for the drawbacks of using Western medicine alone. Aspirin only inhibits COX-2-mediated prostaglandin synthesis and does not directly affect the IL-6/JAK-STAT pathway. Studies by Cao *et al.* further confirm that combination therapy with Naomaili granules can reduce soluble intercellular adhesion molecule-1 (sICAM-1) levels by 29.4%, suggesting that it blocks the pathological process through the entire chain of "inflammation trigger-cascade amplification-tissue damage" by inhibiting leukocyte adhesion and vascular endothelial damage [5]. This integrated Chinese and Western anti-inflammatory strategy not only reduces neuroinflammatory damage during the acute phase (additional reduction of 1.71 points in NIHSS score) but also reduces the degree of vascular wall inflammation and the risk of stroke recurrence within 90 days.

## 4.4. Safety characteristics and precise application strategies for the clinical application of Naomaili granules

In this group, compared to the control group, the treatment group had a lower incidence of adverse reactions. Only a few patients in the treatment group experienced gastrointestinal adverse reactions, which is consistent with the conclusion reported by Qian *et al.*, that the adverse reaction rate of Naomaili granules is lower than that of the argatroban treatment group [3]. This safety characteristic is derived from three levels of protection: Firstly, the modern extraction process of membrane separation combined with macroporous resin adsorption effectively controls the active ingredients such as paeoniflorin (≥ 18.0mg/g) and astragaloside IV (≥ 0.30mg/g), achieving effective dose control while keeping impurity content below 0.5% [4]. Secondly, the combination of Astragalus and Glycyrrhiza in the prescription can buffer the stimulation of bitter and cold medicines on the gastrointestinal tract. Acute toxicity experiments have verified that its median lethal dose (LD50) is greater than 20g/kg, demonstrating high biosafety [6]. Thirdly, the drug does not affect platelet aggregation function. In this study, 2 cases of thrombocytopenia (4.55%) occurred in the control group, while no similar events occurred in the treatment group, which is consistent with the conclusion reported by He that combined thrombolytic therapy does not increase the risk of bleeding. In clinical application, the principle of syndrome differentiation and treatment should be followed. The improvement rate of TCM syndrome scores in patients with Qi deficiency and blood stasis syndrome is 31.7% higher than that in the non-syndrome differentiation medication group. Patients need to take the medication 30

minutes after eating to reduce gastrointestinal adverse reactions. Doctors should monitor biochemical indicators for patients with combined hepatorenal insufficiency to improve patient safety during medication.

## 5. Conclusion

Naomaili granules demonstrate significant therapeutic potential in the management of acute ischemic stroke (AIS). Clinical evidence indicates that this treatment not only improves neurological function and daily living ability but also reduces inflammatory responses, contributing to better patient outcomes. Furthermore, Naomaili granules exhibit a favorable safety profile, supporting their clinical applicability. These findings suggest that Naomaili granules could serve as a promising adjunct therapy for AIS, warranting further large-scale studies to validate long-term efficacy and mechanisms.

## Disclosure statement

The authors declare no conflict of interest.

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