ORIGINAL RESEARCH

Clinical Efficacy of Angong Niuhuang Pills in the Treatment of Severe Heat Stroke and its Impact on the Rescue Efficiency of Patients

Ye Tian, MD; Yuna Shi, MD; Bo Zhang, MD; Xiaoyan Zhou, MD; Yahui Yang, MD

ABSTRACT

Objective • To study the clinical curative effects of Angong Niuhuang Pills in the treatment of severe heat stroke and its influence on the rescue efficiency of patients.

Methods • A total of 76 patients with severe heat stroke who were treated in our hospital were selected from January 2021 to December 2022. According to the sequence of admission, 38 patients in the control group (2021.1-12) received comprehensive western medicine therapy, and 38 sufferers in the observation group (2022.1-12) received Angong Niuhuang Pills on this basis. The body temperature monitoring results at 120 minutes after admission, inflammatory factor levels, relevant biochemical indicators, brain injury indicators, acute physiology and chronic health evaluation system II (APACHE II) score, clinical curative effect, clinical related recovery indicators, and the occurrence of organ function damage were compared between the 2 groups.

Results • The body temperature of patients in the observation one was less than that of the control one at 60 minutes, 90 minutes, and 120 minutes after admission, and the distinction had statistical significance (all $P < .05$); after the therapy, the levels of IL-1, IL-6, hs-CRP, TNF-α, ALT, BUN, Cr, MYO, S-100β protein, NSE, APACHEII score were all lower than those of the control one, and the distinction had statistical significance (all $P < .05$); the total clinical effective rate of the observation group (97.37%) was higher than that of the control group (81.58%), the recovery time of consciousness, rectal temperature recovery time and length of stay were all shorter than the control group, and the incidence of organ function damage (7.89%) was less than that of the control one (26.32%), and the distinction had statistical significance (all $P < .05$).

Conclusion • Angong Niuhuang Pills are safe and effective in the treatment of severe heatstroke sufferers, and can make the patients' body temperature return to the normal range in a short time, help to reduce inflammation reactions and play a protective role in the brain, and can shorten the recovery time of patients' consciousness and length of stay, with relatively high rescue efficiency. (*Altern Ther Health Med.* [E-pub ahead of print.])

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Heat stroke generally occurs under conditions such as high humidity, high temperature, or prolonged heat radiation, which can damage the body's body temperature regulation center, cause water and electrolyte metabolism disorders and neurological dysfunction, with no sweating and high fever as the main symptoms.[1,2] Severe heatstroke is severe and progresses rapidly, which will not only lead to the occurrence of systemic inflammatory response syndrome, but may also lead to the occurrence of multiple organ dysfunction syndrome, which will lead to the death of the patients. Even if the patients survive after treatment, the proportion of sequelae is around 30%.[3,4] Severe heat stroke is a frequent emergency in summer. If it is not treated in time, it will seriously endanger the life and health of patients. A single treatment is not effective for severe heat stroke patients. It is necessary to actively protect the patients' organs while controlling the temperature reduction. Therefore, Western medicine often implements comprehensive symptomatic treatment, but the effects have not reached expectations.[5,6] Traditional Chinese medicine includes heatstroke into the category of "summer-heat febrile disease", and believes that the occurrence of the disease is related to the invasion of heat, the blockage of the heart orifice, and the inability to express the heart yang and so on. Therefore, TCM treatment

pays attention to dispelling heat qi and resuscitating the mind. Angong Niuhuang Pill is a kind of Chinese patent medicine (internal medicine) in the "National Essential Drugs List 2018 Edition". It is mostly used in the treatment of cerebrovascular diseases. This article retrospectively analyzed the effects of Angong Niuhuang Pill on severe heat stroke patients, aiming to provide a reference for clinically achieving higher curative effects.

MATERIALS AND METHODS

Information

The study sample consisted of 76 patients with severe heat stroke admitted to our hospital. The start time of sample inclusion was January 2021 and the deadline was December 2022. According to the sequence of admission, the patients were divided into a control group and an observation group, with 38 cases/group.

Diagnostic criteria: Western medicine: That conformed to the classification criteria for severe heat stroke in the 5th edition of "Internal Medicine"; Chinese medicine: That met the relevant diagnostic criteria in the "Diagnosis and Curative Effect Criteria for Diseases and Syndromes of Traditional Chinese Medicine", and the syndrome differentiation type was Shujue Syndrome (heat stroke sick).

Inclusion criteria: (1) Those who were clearly diagnosed with severe heat stroke by clinical examination; (2) Those whose body temperature exceeded 39°C when they were admitted to hospital; (3) Those who were in a coma; (4) Those with non-allergic constitution.

Exclusion criteria: (1) Patients with heatstroke caused by elevated body temperature due to other diseases or drugs; (2) Patients with a history of disturbance of consciousness and mental disorders; (3) Patients with a history of cerebrovascular accidents and severe multiple organ dysfunction; (4) Those with coagulation dysfunction and cancer; (5) Those with allergic reactions to related therapeutic drugs; (6) Those who died within one week of admission.

The control group was admitted from January to December 2021: there were 26 men cases, accounting for 68.42%, and 12 women cases, accounting for 31.58%; the minimum age was 37 years old, the maximum was 70 years old, and the mean age was (49.54 ± 3.66) years old. The body weight was 52-80 kg, with an average value of (63.52 ± 2.11) kg. The time from onset to visit was 49-138 minutes, with an average value of (78.29 ± 4.35) minutes. The mean respiratory rate was (24.77 ± 3.41) times/min, the mean heart rate was (128.54 ± 10.94) times/min, and the mean arterial pressure was (58.46 ± 6.27) mmHg.

The observation group was admitted from January to December 2022: there were 27 men cases, accounting for 71.05%, and 11 women cases, accounting for 28.95%; the minimum age was 39 years old, the maximum age was 73 years old, and the mean age was (50.16 ± 3.84) years old. The body weight was 51-81kg, with an average value of (64.03 ± 2.24) kg. The time from onset to visit was 51-143 minutes, with an average value of (78.46 ± 4.71) minutes. The mean respiratory rate was (24.86 ± 3.50) times/min, the mean heart rate was (128.75 ± 11.13) times/min, and the mean arterial pressure was (59.21 ± 6.40) mmHg.

The information data obtained by the 2 groups were balanced ($P > .05$).

Methods

Control group: Western medicine comprehensive treatment. Immediately after the patients were admitted to the hospital, methods such as ice caps, ice blankets, and alcohol scrub baths were used to cool down. When the body temperature did not drop, lytic cocktail (promethazine hydrochloride injection, Shanghai Hefeng Pharmaceutical Co., Ltd., SFDA approval number: H31021490, Chlorpromazine hydrochloride injection, Shanghai Hefeng Pharmaceutical Co., Ltd., SFDA approval number: H31021060) was pumped continuously for 24 hours, during which temperature monitoring and airway management were strengthened, and respiratory support was given. Intravenous infusion of glucose injection (Jichuan Pharmaceutical Group Co., Ltd. , SFDA approval number: H32024826) was given to correct the water and electrolyte disturbance and acid-base imbalance. Broad-spectrum antibiotics (cefuroxime sodium, Kangtian Pharmaceutical Zhongshan Co., Ltd., SFDA approval number: H20065669) were given to avoid secondary infection. For patients with relatively high intracranial pressure, dehydration therapy (20% mannitol injection, Qingdao Shouhe Jinhai Pharmaceutical Co., Ltd., SFDA approval number: H37020364) was implemented; for patients with urine output <30ml/h, potassium supplementation therapy (10% Potassium Chloride Injection, Hubei Kelun Pharmaceutical Co., Ltd., SFDA approval number: H42021164) was implemented; for patients with persistent coma, naloxone (Beijing Yongkang Pharmaceutical Co., Ltd., SFDA approval number: H20059406) was used to implement wake-up treatment; in case of shock, anti-shock treatment (Pehyclidine hydrochloride, Chengdu Lisite Pharmaceutical Co., Ltd., SFDA approval number: H20051948) should be carried out as soon as possible. Nutritional support and symptomatic support were given according to the changes in the sufferers' vital signs.

The observation one was treated with Angong Niuhuang Pills (Huatuo Sinopharm Co., Ltd., SFDA approval number: Z34020859) additionally when nutritional support was given to the patients. Angong Niuhuang Pills were added to warm water at 40-60°C to dissolve, and administered through nasal feeding, 1 pill at a time, three times a day.

Both groups continued treatment for 7 days.

Evaluation indicators and judgment criteria

1. The changes of body temperature of two groups of patients were closely monitored within 120 minutes after admission.
2. When the patients were admitted to the hospital and after the therapy, 5 mL of venous blood from the elbow

was collected for routine anticoagulant treatment and centrifuged at a speed of 3000 rpm for a total of 10 minutes. The supernatant was separated, and the instrument was an automatic biochemical analyzer. The levels of inflammatory factors [serum interleukin-1 (IL-1), IL-6, hypersensitive C-reactive protein (hs-CRP) and tumor necrosis factor-α (TNF-α)], brain injury indicators [S-100β protein, neuron-specific enolase (NSE)] were all measured by enzyme-linked immunosorbent assay; alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (Cr), myoglobin (MYO), and D-dimer (DD) were all determined by enzyme-linked immunoassay. The APACHE II score includes 12 physiological parameters, including acute physiology score, age score and chronic health score. The theoretical minimum value is 0 points and the maximum value is 71 points. A lower score indicates a milder condition.

3. The clinical curative effect was evaluated with reference to the "Technical Manual for Prevention and Treatment of Heat Stroke". Specific criteria: within 3 days of treatment, the temperature of the patients' anus returned to the normal range, and the consciousness recovered, which was considered to be markedly effective; within 3 to 7 days of treatment, the temperature of the patients' anus was less than 39°C but higher than the normal temperature, and the patients were awake but in a trance, which was considered to be effective; if none of the above standards were met, severe complications or even death occurred, it was invalid. The sum of the significantly effective percentage and the effective percentage was the total effective rate.
4. The clinically relevant recovery indicators of the two groups, namely the recovery time of consciousness, the time for rectal temperature to return to normal, and the length of hospital stay were observed, and whether there were any organ function damage symptoms such as increased creatinine, hematuria or proteinuria, liver function damage, and multiple organ dysfunction syndrome were recorded, the total incidence rate of organ function damage was the sum of the percentages of each damage.

Statistical processing

Data analysis was carried out by SPSS 25.0 software. The count data and measurement data involved were respectively used: χ^2 test and t test, and the expression forms were: [n (%)], ($\bar{x} \pm s$). If the difference was statistically significant, then $P < .05$.

RESULTS

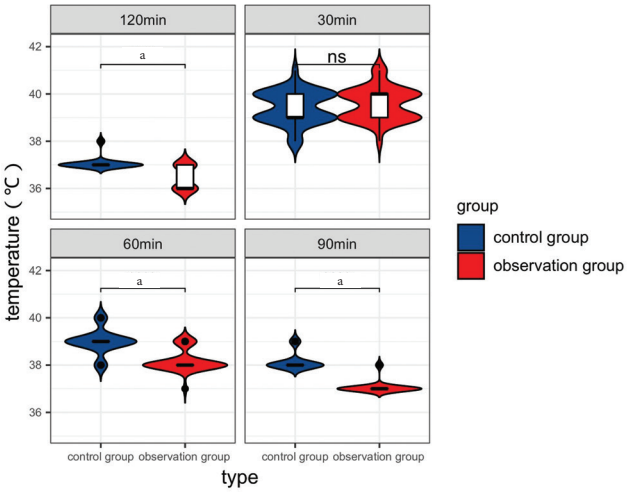
Body temperature monitoring results within 2 hours of admission

Except for the body temperature at 30 minutes after admission, the body temperature monitoring data at other time periods in the observation group were obviously less than those in the control one ($P < .05$). See Table 1.

Table 1. Comparison of body temperature monitoring results within 2 hours of admission between the two groups (°C)

group	n	30 min	60 min	90 min	120 min
control group	38	39.42 ± 0.68	39.00 ± 0.52	38.16 ± 0.37	37.08 ± 0.27
observation group	38	39.58 ± 0.68	38.18 ± 0.46	37.08 ± 0.27	36.47 ± 0.51
t value	-	0.653	9.047	16.687	13.671
P value	-	.516	<.001	<.001	<.001

Figure 1. Comparison of body temperature monitoring results within 2 hours of admission between the two groups



[a]$P < .0001$

Table 2. Comparison of the levels of inflammatory factors in each group

group	IL-1 (pg/mL)		IL-6 (ng/L)	
	on admission	after treatment	on admission	after treatment
Control group (n=38)	214.44 ± 32.60	144.34 ± 16.70[a]	9.64 ± 1.10	7.20 ± 0.74[a]
Observation group (n=38)	215.57 ± 33.26	94.45 ± 13.57[a]	9.72 ± 1.16	5.06 ± 0.40[a]
t value	0.150	14.292	0.308	15.682
P value	.882	<.001	.759	<.001

group	hs-CRP (mg/L)		TNF-α (pg/mL)	
	on admission	after treatment	on admission	after treatment
Control group (n=38)	7.33 ± 1.28	4.48 ± 0.69[a]	281.65 ± 41.57	176.52 ± 20.16[a]
Observation group (n=38)	7.41 ± 1.35	3.07 ± 0.51[a]	282.36 ± 42.40	105.45 ± 14.33[a]
t value	0.265	10.130	0.074	17.713
P value	.792	<.001	.941	<.001

[a]Compared with the admission data of this group, $P < .05$.

Levels of inflammatory factors

After therapy, the inflammatory factors levels in the 2 groups were obviously lower than those at admission ($P < .05$). Compared with the control group, the levels of IL-1, IL-6, hs-CRP, TNF-α of the observation group were significantly reduced ($P < .05$). See Table 2.

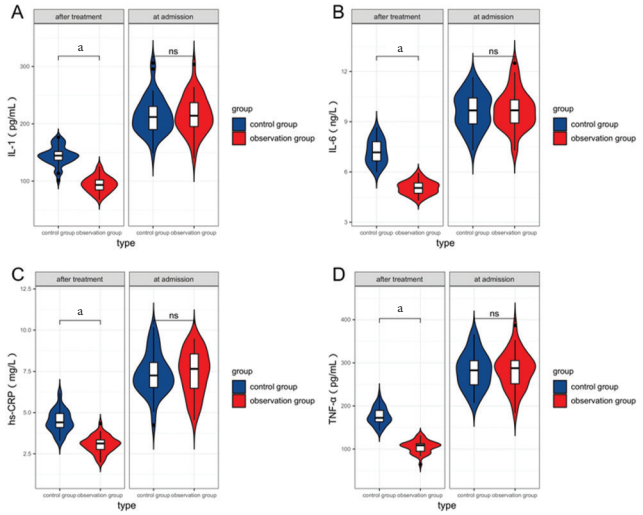
Related biochemical indicators

There was difference in the relevant biochemical indicators of the two groups between the time at admission and after the therapy ($P < .05$). At the end of therapy, there was difference in the relevant biochemical indicators between the observation group and the control group ($P < .05$). See Table 3.

Brain injury indicators and APACHE II score

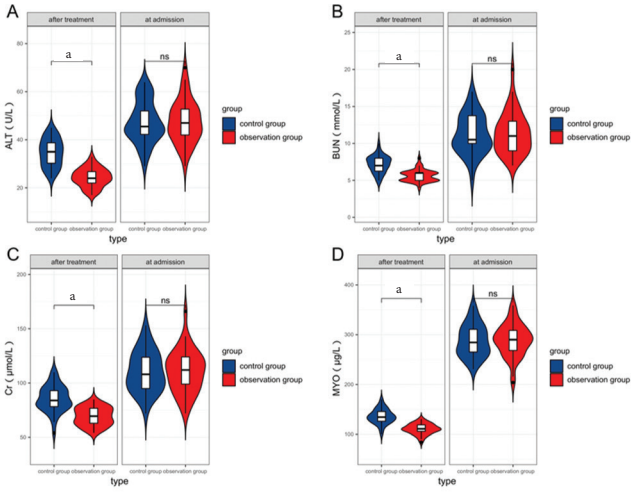
After the treatment, the brain injury indicators and APACHE II score in the observation group were less than

Figure 2. Comparison of the levels of inflammatory factors in each group



[a]$P < .0001$

Figure 3. Comparison of relevant biochemical indicators between the two groups



[a]$P < .0001$

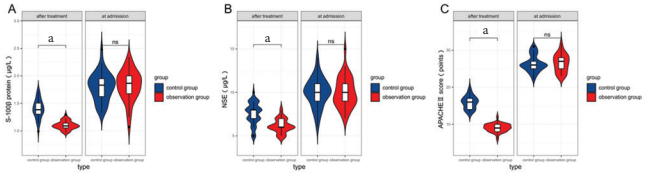
Table 3. Comparison of relevant biochemical indicators between the two groups

	ALT (U/L)		BUN (mmol/L)	
group	on admission	after treatment	on admission	after treatment
Control group (n=38)	47.37 ± 8.68	34.61±5.74[a]	11.24 ± 2.68	7.21 ± 1.14[a]
Observation group (n=38)	47.58 ± 8.97	24.34±3.86[a]	11.39 ± 2.80	5.63 ± 0.79[a]
t value	0.084	9.185	0.226	7.207
P value	.933	<0.001	.822	<.001

	Cr (μmol/L)		MYO (μg/L)	
group	on admission	after treatment	on admission	after treatment
Control group (n=38)	110.39±18.77	85.58 ± 12.12[a]	287.95 ± 32.15	135.71 ± 14.72[a]
Observation group (n=38)	110.73±19.59	69.29 ± 8.37[a]	289.03 ± 33.10	110.61 ± 10.59[a]
t value	0.059	6.821	0.151	8.534
P value	0.953	<.001	.880	<.001

[a]Compared with the admission data of this group, $P < .05$.

Figure 4. Comparison of brain injury indicators and APACHE Ⅱ score in each group



[a]$P < .0001$

those in the control one ($P < .05$), and the data of the above indicators in the two groups were obviously lower than those at admission ($P < .05$). See Table 4.

Clinical curative effect

According to the calculation of the total clinical effective rate, 97.37% of the observation group was higher than 81.58% of the control group, with $P < .05$. See Table 5.

Clinically relevant recovery indicators

The times of clinical related recovery indicators in the observation group were obviously shorter than those in the control one ($P < .05$). See Table 6.

Table 4. Comparison of brain injury indicators and APACHE II score in each group

	S-100β protein (μg/L)		NSE (μg/L)		APACHEII score (points)	
group	on admission	after treatment	on admission	after treatment	on admission	after treatment
Control group (n=38)	1.80 ± 0.26	1.40 ± 0.17[a]	10.00 ± 1.68	7.55 ± 1.25[a]	26.34 ± 2.23	15.89 ± 1.77[a]
Observation group (n=38)	1.82 ± 0.28	1.10 ± 0.08[a]	10.00 ± 1.74	6.16 ± 0.79[a]	26.53 ± 2.42	9.05 ± 1.09[a]
t value	0.323	9.843	0.180	5.684	0.314	21.385
P value	.748	<.001	.858	<.001	.755	<.001

[a]Compared with the admission data of this group, $P < .05$.

Table 5. Comparison of the clinical efficacy of each group [n (%)]

group	n	markedly effective	efficient	invalid	total effective rate
control group	38	16 (42.11)	15 (39.47)	7 (18.42)	31 (81.58)
observation group	38	26 (68.42)	11 (28.95)	1 (2.63)	37 (97.37)
χ^2 value	-	-	-	-	5.029
P value	-	-	-	-	.025

Figure 5. Comparison of the clinical efficacy of each group

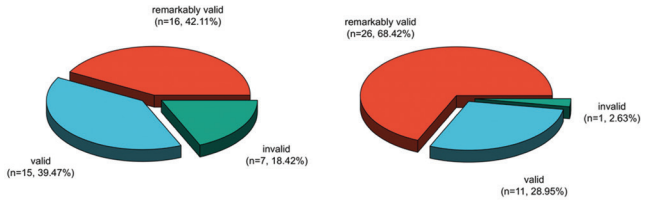
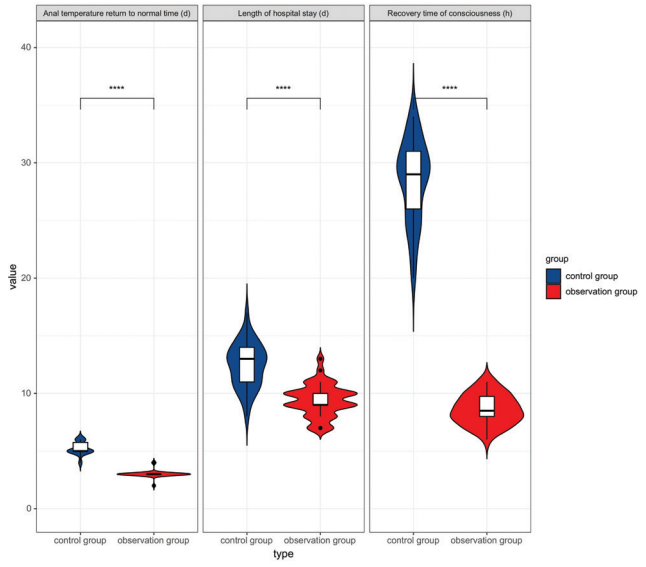


Table 6. Comparison of clinically relevant recovery indicators across groups

group	n	Consciousness recovery time (h)	Time for rectal temperature to return to normal (d)	Length of hospital stay (d)
control group	38	28.42 ± 3.54	5.18 ± 0.56	12.45 ± 1.91
observation group	38	8.61 ± 1.28	3.03 ± 0.28	9.39 ± 1.39
t value	-	32.369	22.025	8.324
P value	-	<.001	<.001	<.001

Figure 6. Comparison of clinically relevant recovery indicators across groups



[a]$P < .0001$

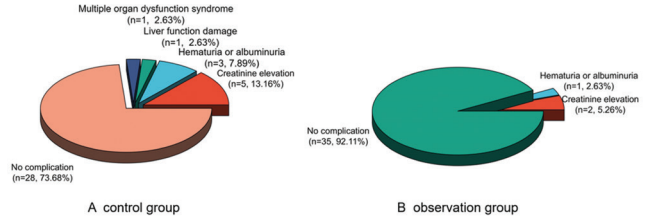
Occurrence of organ function damage

Compared with the control group, the incidence of the organ function damage in the observation group was significantly decreased ($P < .05$). See Table 7.

Table 7. Comparison of the incidence of organ dysfunction in each group [n (%)]

group	n	Increased creatinine	hematuria or proteinuria	Liver damage	multiple organ dysfunction syndrome	total incidence
control group	38	5 (13.16)	3 (7.89)	1 (2.63)	1 (2.63)	10 (26.32)
observation group	38	2 (5.26)	1 (2.63)	0 (0.00)	0 (0.00)	3 (7.89)
χ^2 value	-	-	-	-	-	4.547
P value	-	-	-	-	-	.033

Figure 7. Comparison of the occurrence of organ dysfunction in each group



DISCUSSION

In recent years, due to the influence of many factors such as global climate change and the expansion of urban environment, the number of patients with heat stroke has been increasing, especially those who work in hot weather in summer are more prone to heat stroke.[7] Heatstroke can lead to symptoms such as high fever, coma, and convulsions in patients, as well as the occurrence of a series of complications, such as systemic inflammatory response syndrome.[8,9] According to the severity, heatstroke can be divided into premonitory heatstroke, mild heatstroke, and severe heatstroke. Severe heatstroke can also be divided into heat exhaustion, heat cramps, and heat apoplexy according to clinical manifestations, with the latter being the most serious.[10] Based on the heat imbalance mechanism, it can be divided into classic type and exertional severe heat stroke. The former usually occurs in infants and the elderly. It is caused by exposure to heat and poor heat dissipation mechanism of the body. The common manifestations are dry, pale or flushed skin, etc. If classic severe heatstroke occurs in elderly patients with underlying diseases, the fatality rate is higher.[11] The latter is common among athletes, long-term military trainees, laborers, etc. Metabolic heat production is beyond the tolerance range of the physiological heat dissipation mechanism, which causes thermal damage. Such patients will have moist skin and sweating profusely and other performance. The pathogenic mechanism of severe heat stroke lies in: inflammatory responses, cytotoxic effect caused by abnormal thermoregulation and elevated body temperature.[12,13] When the core body temperature of the patients' body rises, it will lead to a stress responses, causing an increase in the levels of pro-inflammatory and anti-inflammatory cytokines; in addition, long-term high fever will prompt patients to undergo acute physiological changes, which can aggravate cytotoxicity, and cause inflammatory responses. The inflammatory responses associated with severe heatstroke can exacerbate the condition and even lead to death.[14] Excessive body temperature and long duration of high fever are related to the mortality of the disease. The reasons are that high fever will damage the cell membrane of the body, change the intracellular structure, cause thermal denaturation of cellular proteases, which will damage oxygen-dependent metabolic pathways, and promote tissue cells undergo massive hypoxic necroptosis, eventually leading to the occurrence of multi-system organ dysfunction.[15,16] In addition, the first organ affected by severe heat stroke is the brain, which will damage the patients' nervous system and cause coma and other disturbance of consciousness. The key to the rescue of severe heatstroke lies in two points: early cooling and early organ protection.[17]

At present, western medicine mainly adopts cooling and symptomatic comprehensive treatment of western medicine to treat severe heatstroke, and uses ice caps, ice blankets, etc. to cool down. Although it can alleviate the high fever state of patients to a certain extent, it can only achieve good effect in patients with mild heat stroke. However, patients with severe heatstroke directly enter the period of organ function damage after onset, and it is difficult to achieve relatively good effects on important organ function damage by cooling, so it is necessary to pay attention to symptomatic treatment.[18,19] In traditional Chinese medicine, severe heat stroke is included in the category of febrile disease, heat stroke is classified as "summer-heat febrile disease" category, and heat exhaustion is included as "summer coma" category. The evil qi of summer heat will enter the human body, damage the function of the viscera, consume the Yin fluid, and also disturb the Jueyin with heat, heat sinks into the pericardium, and the heart orifice is blocked, resulting in high fever and coma in the patients. Compared with modern medicine, traditional Chinese medicine pays more attention to syndrome differentiation and

treatment. In clinical treatment, it pays attention to clearing away heat, nourishing yin and replenishing qi, refreshing the mind and resuscitating the mind. During the treatment period, it also needs to pay more attention to dynamic changes of dampness and heat in the patients' body, continuously and effectively control body temperature, and avoid adverse consequences caused by abnormal body temperature. The Angong Niuhuang Pills used in this study were developed from traditional Chinese medicinal materials such as bezoar, buffalo horn concentrated powder, artificial musk, pearl, cinnabar, realgar, coptis, scutellaria baicalensis, gardenia, turmeric, and borneol. It is often used clinically in groups such as fever and cerebrovascular diseases. The bezoar in the prescription has the effects of calming the liver and calming the wind, clearing the heart and resuscitation; the buffalo horn concentrated powder can clear away heat and cool the blood, and the compatibility with bezoar can relieve the fire of the pericardium; musk can awaken the mind, promote blood circulation and menstruation; pearl can calm the mind, nourish Yin and quench wind, and clear away heat; cinnabar can clear heart, calm convulsions, soothe nerves and detoxify; realgar can dry dampness and eliminate phlegm, and can promote the improvement of the detoxification effect of bezoar; Coptis chinensis, scutellaria, and gardenia can clear away heat and dampness, purify fire and detoxify; turmeric has the effects of clearing heart and cooling blood, promoting qi and relieving depression; borneol can open and close the orifices, and the combination with musk can help improve the refreshing effect. In addition, the application of honey to reconcile can exert the effects of regulating and nourishing the spleen and stomach. Modern pharmacological studies believe that Angong Niuhuang Pills can exert antipyretic, anticonvulsant, sedative, wake-promoting, anti-inflammatory and other effects. It can excite the cerebral cortex, improve the permeability of the blood-brain barrier, not only improve local microcirculation but also help to the regeneration of microvessels, and can also prevent thrombosis, which can reduce the body's oxygen consumption, regulate neurotransmitters, neuropeptides and other substances, and reduce the occurrence risk of organ damage and systemic inflammatory reactions. The traditional Chinese medicine of clearing heart and purging fire in the prescription has relatively good effects of strengthening the heart, clearing heat, calming, anti-inflammation, etc., and can regulate the permeability of blood vessels, protect the ultrastructure of brain cells, and can excite the cerebral cortex, which is conducive to improving the tolerance of brain tissue to inflammatory factors and hypoxia-ischemia, thereby relieving cerebral edema and protecting brain tissue. Blood-cooling and detoxifying traditional Chinese medicines can exert anti-inflammatory, antispasmodic, anti-pathogenic microorganisms and other effects, and the patients' cerebral vasospasm can be relieved. Aroma resuscitating traditional Chinese medicine can regulate the patients' central nervous system in two directions, reduce the damage to the nervous system caused by severe heatstroke, help restore the patients' mind, and also have anti-inflammatory and sedative effects. Calming and tranquilizing drugs can inhibit the reaction of oxygen free radicals, remove oxygen free radicals, protect the blood-brain barrier and improve brain metabolism, which is beneficial to the improvement of brain cell function in patients.

The sharp rise in the body temperature of patients with severe heat stroke in a short period of time will lead to an increase in endotoxins, inflammatory mediators and other substances secreted by muscle tissue and others, and these substances can enter the blood circulation system, eventually leading to the emergence of systemic inflammatory reactions, causing serious damage to important organs.[20] hs-CRP is a common inflammatory marker, and IL-1, IL-6, and TNF-α can all reflect the degree of inflammation in patients. The data of this research showed that the body temperature of the observation one gradually decreased from 30 minutes after admission, which was less than that of the control one, and the improvement degree of the inflammatory responses was greater, which fully demonstrates that the addition of Angong Niuhuang Pills can better control the body temperature of patients, enhance the inhibitory effect of inflammatory responses. The ALT, BUN, Cr, and MYO of the observation group improved greatly, and the occurrence of organ function damage was less, indicating that Angong Niuhuang Pills can better protect organ function. This is because Angong Niuhuang Pills can reduce damage to organs by inhibiting inflammatory factors and prevent progression to multiple organ failure. APACHE Ⅱ score can evaluate the severity and prognosis of critically ill sufferers; S-100β protein and NSE are indicators related to brain injury, and S-100β protein is mainly distributed in calcium-binding protein in serum. Under the normal physiological concentration, it can better nourish the nerves. And when the concentration is significantly increased, it will cause damage to nerve arrest, promote neuron apoptosis, and produce neurotoxicity. NSE is mainly distributed in nerve cells and released into the blood after brain tissue damage, which will increase the level of NSE in serum. The two indicators can predict brain damage caused by various reasons, and the decrease of their levels means that both methods can help relieve brain damage, while the data of the observation group were lower, which suggests that the addition of Angong Niuhuang Pills is more helpful to repair damaged nerve tissue, it can play a good role in brain protection, and help improve the prognosis of sufferers. The clinically relevant recovery indicators and total effective rate of the observation one were better than those of the control one, indicating that the addition of Angong Niuhuang Pills can improve the efficiency of disease rescue and treatment, and help patients recover as soon as possible. In addition, in this study, since the patients fell into a coma and were unable to routinely take medication by mouth, administering Angong Niuhuang Pills by nasal feeding can further improve the curative effects and lower the patients' body temperature as soon as possible.

All in all, the addition of Angong Niuhuang Pills to severe heat stroke patients not only has higher rescue

efficiency and curative effects, but also reduces inflammation and damage to organ functions, promotes faster cooling of patients and improves prognosis. Nevertheless, there are still deficiencies in this research. Due to the relatively short follow-up time, the long-term effects of the follow-up patients cannot be further tracked, so it is necessary to strengthen research in this area in the future. In future research , the mechanism of Angong Niuhuang Pills in treating severe heatstroke will be deeply explored, and at the same time, data accumulation and case analysis will be strengthened in combination with clinical practice, so as to give more scientific and effective guidance for its clinical application.

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