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Effect of Local Mild Hypothermia Therapy Combined with Early Continuous Nursing on Nerve Function and Inflammatory Factors in Patients with Subarachnoid Hemorrhage

Xuan Lv [1,#,*], Hua Shan [2,#], Suijun Zhu [1]

1. Department of Neurosurgery, The First People's Hospital of Linping District, Hangzhou, 311100 Hangzhou, Zhejiang, China

2. Department of Medical Affairs, The First People's Hospital of Linping District, Hangzhou, 311100 Hangzhou, Zhejiang, China

# These authors contributed equally to this work.

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* **Correspondence**

Xuan Lv

Department of Neurosurgery, The First People's Hospital of Linping District, Hangzhou, 311100 Hangzhou, Zhejiang, China

E-mail: Abc_237385512@outlook.com

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Abstract

Objective: To investigate the effect of local mild hypothermia combined with early continuous nursing on nerve function and inflammatory factors in patients with subarachnoid hemorrhage. **Methods:** 40 patients with subarachnoid hemorrhage receiving local mild hypothermia combined with early continuous nursing in our hospital from January 2023 to December 2023 were included as the combination group, and meanwhile 40 patients with subarachnoid hemorrhage receiving early continuous nursing were included as the control group. Neurological function, levels of inflammatory factors, cerebral artery blood flow velocity and psychological state were compared between the two groups before and after treatment, and complications were recorded between the two groups during treatment. **Results:** After treatment, National Institutes of Health Stroke Scale score, anterior blood flow velocity in cerebral artery, posterior cerebral artery and middle cerebral artery, interleukin-8, high-sensitivity C-reactive protein, tumor necrosis factor-α, and Hamilton depression and anxiety scores were decreased in both groups, and the decrement was more apparent in the combination group than the control group ($p < 0.05$). The Glasgow outcome score was elevated after treatment in both groups, which was higher in the combination group than the control group ($p < 0.05$). The complication rate in combination group was lower than that in control group ($p < 0.05$). **Conclusion:** Local mild hypothermia combined with early continuous nursing can effectively improve the nerve function and cerebral artery blood flow velocity, reduce the level of inflammatory factors, and regulate the psychological state of patients with subarachnoid hemorrhage under good safety.

1 Introduction

Subarachnoid hemorrhage is a serious cranial disease caused by the rupture and bleeding of intracranial aneurysms, and blood infiltration into the subarachnoid space may lead to delayed cerebral hemorrhage and serious neurological damage, resulting in a high possibility of poor prognosis [1,2]. Patients with subarachnoid hemorrhage often present with clinical symptoms such as sudden and severe headache, nausea, and vomiting, and the progressive headaches may be worsened during intense activity. Without timely and effective nursing interventions, this symptom will seriously impact the patient's daily life, health, and psychological state [3,4].

In the management of subarachnoid hemorrhage, nursing care plays a pivotal role. Early continuous nursing is a nursing intervention method with strict nursing sequence and accurate time requirements, which can effectively enhance the quality of patient recovery, accelerate recovery, and improve prognosis [5]. It has also been found that applying early continuous nursing to the rehabilitation care of patients with brain diseases can promote neurological and limb function [6]. Beyond standardized nursing, specific neuroprotective strategies are being explored to improve outcomes. Local mild hypothermia therapy has garnered attention as a potential intervention to protect vulnerable brain tissue following an injury. Previous research has demonstrated the safety and neuroprotective efficacy of mild hypothermia in various brain injury models, such as, establishing a strong rationale for its clinical application [7-10]. It has been reported that early transient mild hypothermia attenuated neurologic deficits and brain damage after experimental subarachnoid hemorrhage in rats [11]. Local mild hypothermia can protect ischemic brain tissue and reduce brain injury by maintaining deep hypothermia, thereby potentiating the overall rehabilitation outcome of patients with subarachnoid hemorrhage [12]. Local mild hypothermia therapy can effectively protect the brain and has a definite therapeutic effect on patients with brain diseases [13].

Therefore, based on the complementary benefits of structured nursing and neuroprotection, this study investigated the combined application of local mild hypothermia and early continuous nursing in patients with subarachnoid hemorrhage. We examined its effects on neurological function, cerebral artery blood flow velocity, inflammatory response, and psychological state. The aim is to explore the synergistic nursing effects of this combined regimen and to provide more robust evidence and reference for optimizing clinical nursing strategies for patients with subarachnoid hemorrhage.

2 Materials and methods

2.1 General information

40 patients with subarachnoid hemorrhage receiving local mild hypothermia combined with early continuous nursing in our hospital from January 2023 to December 2023 were included as the combination group, and meanwhile 40 patients with subarachnoid hemorrhage receiving early continuous nursing were included as the control group. There were no significant differences in gender, age, time of emergent diagnosis, Hunt-Hess classification between the two groups, which were comparable ($p > 0.05$, Table 1).

2.2 Exclusion and inclusion criteria

2.2.1 Inclusion criteria

(1) Subarachnoid hemorrhage confirmed by head Computed Tomography (CT) or Magnetic Resonance Imaging (MRI); (2) Onset within 24 hours and the expected survival time more than 3 months; (3) Complete clinical data, and no participation in other clinical or academic research during the intervention.

2.2.2 Exclusion criteria

(1) Hypotension; (2) Malignant tumors; (3) Serious diseases such as heart, liver, and kidneys; (4) Immune and coagulation dysfunction; (5) Mental disorders, and poor compliance with intervention; (6) Pregnant and lactating women.

Table 1 Comparison of general information between the two groups.

Project	Combination group (n = 40)	Control group (n = 40)	X^2/t	p
Gender [case (%)]			0.453	0.501
Male	23 (57.50)	20 (50.00)		
Female	17 (42.50)	20 (50.00)		
Age (years)	45.33 ± 4.68	45.63 ± 5.11	-0.274	0.785
Time of emergent diagnosis (h)	5.78 ± 0.96	5.63 ± 1.19	0.626	0.533
Hunt-Hess classification [case (%)]			0.067	0.967
Ⅱ stage	15 (37.50)	14 (35.00)		
Ⅲ stage	15 (37.50)	16 (40.00)		
Ⅳ stage	10 (25.00)	10 (25.00)		

2.3 Methods

2.3.1 Control group

This group adopted early continuous nursing, mainly including: (1) a comprehensive nursing intervention group with 2 supervisors, 2 senior nurses, and 3 junior nurses was established to formulate a reasonable nursing plan. Responsible nurses evaluated and implemented daily plans of patients according to the nursing schedule on a daily basis; (2) psychological nursing: responsible nurses actively communicated with patients and their families, grasped the ideological changes of patients and their families, and improved their confidence in recovery and cooperation with intervention through active communication of the condition; (3) early function rehabilitation training: responsible nurses helped patients to conduct rehabilitation training in the early stages (24-48 hours after stable vital signs) to promote the recovery of patients' limb and consciousness functions; and (4) prevention of complications: patients' conditions were comprehensively evaluated strictly following aseptic procedures, and the patients' vital signs were detected through electrocardiography and other instruments. The above nursing intervention lasted for 14 days.

2.3.2 Combination group

Based on the control group, used a medical intelligent pressure low-temperature treatment instrument. At the beginning of the study, the patients' heads were placed in ice caps to maintain the brain temperature at 34-36 ℃, and this was maintained continuously for 72 hours.

2.4 Clinical indicators

2.4.1 Neurological function

Before and 14 days after intervention, the National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the neurological function of patients in the two groups. The scale includes 11 items such as consciousness level, gaze, and field of view, and its scores are positively correlated with the degree of neurological dysfunction [14]. The Glasgow Outcome Scale (GOS) was applied to assess the consciousness status of two groups of patients, which is 5-point rating scale with scores ranging from 1 to 5, and the scores are positively correlated with consciousness status [15].

2.4.2 Cerebral artery blood flow velocity

Before and 14 days after intervention, the average blood flow velocity of anterior, posterior and middle cerebral arteries was measured by LOGIQ7 Doppler ultrasonic detector (GE, USA).

2.4.3 Inflammatory factors

Before and 14 days after intervention, 5 mL fasting peripheral venous blood was extracted from two groups of patients in the morning, placed at room temperature for 30-60 min, and centrifuged at 3000 r/min for 10 min to separate the serum. The serum was stored at -20 ℃ for testing. Enzyme-linked immunosorbent assay (ELISA) was used to detect interleukin-8 (IL-8), high-sensitivity C-reactive protein (hs-CRP), and tumor necrosis factor (TNF)-α level using the appropriate kit (Shanghai Enzyme-linked Biotechnology Co., Ltd., China) in accordance with the instructions. The information of the kit is as follows: human IL-8 ELISA kit (ml027375), human hs-CRP ELISA kit (ml106583) and human TNF-α ELISA kit (ml077385).

2.4.4 Psychological state

Before and 14 days after intervention, the Hamilton Depression Rating Scale (HAMD) and Hamilton Anxiety Rating Scale (HAMA) were employed to evaluate the psychological status of two groups of patients. HAMD and HAMA were five-point rating scales ranging from 0 to 4 points, with the former consisting of 17 items and the latter consisting of 15 items. The scores of the two scales were positively correlated with the degree of depression and anxiety, respectively [16].

2.4.5 Complications

The occurrence of cerebral spasm, hydrocephalus, rebleeding, arrhythmia, pulmonary infection, intracranial infection, lower limb venous thrombosis, and cerebral herniation were statistically recorded in two groups.

2.5 Statistical methods

SPSS 26.0 was used for statistical analysis, and Kolmogorov-Smirnov test was for normality analysis of measurement data. Continuous variables that conformed to normal distribution were expressed as mean ± standard deviation. Independent sample t-test was applied for comparison between two groups, and paired sample t-test was for comparison between two time points within the same group. Continuous variables that did not conform to a normal distribution were represented using the quartile method [M (P25, P75)]. Mann Whitney U test was conducted for comparison between two groups, and Wilcoxon signed rank sum test was for comparison between two time points within the same group. Classified data were expressed as rates or composition ratios, and comparisons were performed using a χ^2 test. A bilateral $p < 0.05$ was considered statistically significant.

3 Results

3.1 Comparison of neurological function between the two groups before and after intervention

Before intervention, there was no statistically significant difference in NHISS and GOS scores between the two groups ($p > 0.05$). After intervention, the NIHSS scores of both groups were decreased ($p < 0.05$), while the GOS scores of both groups were increased ($p < 0.05$), and the changing trends were more remarkable in the combination group than the control group ($p < 0.05$, Table 2).

3.2 Comparison of cerebral artery blood flow velocity between the two groups before and after intervention

Before intervention, there was no statistically significant difference in blood flow velocity of anterior cerebral artery, posterior cerebral artery, and middle cerebral artery between the two groups ($p > 0.05$).

Post intervention, the blood flow velocity of the anterior cerebral artery, posterior cerebral artery, and middle cerebral artery was decreased in both groups ($p < 0.05$), and the decrement was more apparent in the combination group than the control group ($p < 0.05$, Table 3).

Table 2 Comparison of neurological function between the two groups before and after intervention.

Group	Case	NIHSS score		GOS score	
		Before intervention	After intervention	Before intervention	After intervention
Combination group	40	15.00 (14.00, 16.00)	7.00 (7.00, 7.25) *	3.00 (2.00, 4.00)	5.00 (4.00, 5.00) *
Control group	40	15.00 (14.00, 16.00)	12.50 (12.00, 13.00) *	3.00 (2.75, 3.00)	4.00 (3.00, 4.25) *
Z		-1.063	-7.984	-0.332	-2.607
p		0.288	< 0.001	0.740	0.009

Note: Compared to before intervention within the same group, * $p < 0.05$.

Table 3 Comparison of cerebral artery blood flow velocity between the two groups before and after intervention (mean ± standard deviation, cm/s).

Group	Case	Anterior cerebral artery		Posterior cerebral artery		Middle cerebral artery	
		Before intervention	After intervention	Before intervention	After intervention	Before intervention	After intervention
Combination group	40	114.79 ± 7.96	73.86 ± 4.54 *	80.22 ± 5.02	51.97 ± 1.71 *	103.31 ± 7.81	80.39 ± 4.90 *
Control group	40	116.53 ± 6.50	98.74 ± 5.83 *	78.12 ± 6.06	67.92 ± 3.90 *	106.76 ± 8.52	98.10 ± 9.77 *
t		-1.069	-21.289	1.687	-23.678	-1.891	-10.253
p		0.288	< 0.001	0.096	< 0.001	0.062	< 0.001

Note: Compared to before intervention within the same group, * $p < 0.05$.

3.3 Comparison of inflammatory factor levels between the two groups before and after intervention

Prior to intervention, no significantly statistical difference was detected in IL-8, hs-CRP and TNF-α levels in the two groups ($p < 0.05$), but due to intervention, the three levels were declined ($p < 0.05$), which were lower in the combination group than the control group ($p < 0.05$, Table 4).

Table 4 Comparison of inflammatory factor levels between the two groups before and after intervention (mean ± standard deviation, ng/mL).

Group	Case	IL-8		hs-CRP		TNF-α	
		Before intervention	After intervention	Before intervention	After intervention	Before intervention	After intervention
Combination group	40	3.68 ± 0.46	1.61 ± 0.46 *	256.89 ± 33.43	187.25 ± 20.28 *	0.56 ± 0.12	0.24 ± 0.07 *
Control group	40	3.75 ± 0.44	2.16 ± 0.19 *	252.66 ± 27.20	214.93 ± 26.99 *	0.57 ± 0.12	0.36 ± 0.11 *
t		-0.709	-6.858	0.621	-5.185	-0.109	-5.935
p		0.480	< 0.001	0.536	< 0.001	0.913	< 0.001

Note: Compared to before intervention within the same group, * $p < 0.05$.

3.4 Comparison of psychological state between the two groups before and after intervention

Before intervention, there was no statistically significant difference in HAMD and HAMA scores between the two groups ($p > 0.05$). In response to intervention, the HAMD and HAMA scores were diminished in both groups ($p < 0.05$), which were lower in the combination group than the control group ($p < 0.05$, Table 5).

Table 5 Comparison of HAMD and HAMA scores between the two groups before and after intervention (mean ± standard deviation).

Group	Case	HAMD		HAMA	
		Before intervention	After intervention	Before intervention	After intervention
Combination group	40	28.85 ± 4.78	14.38 ± 3.30 *	30.05 ± 5.19	17.75 ± 3.30 *
Control group	40	29.05 ± 4.51	18.95 ± 3.56 *	28.98 ± 4.81	21.50 ± 3.57 *
t		-0.193	-5.960	0.961	-4.874
p		0.848	< 0.001	0.340	< 0.001

Note: Compared to before intervention within the same group, *$p < 0.05$.

3.5 Comparison of complications between the two groups

The incidence of complication was lower in the combination group than the control group ($p < 0.05$, Table 6).

Table 6 Comparison of complications between the two groups [case (%)].

Complication	Combination group (n = 40)	Control group (n = 40)	χ^2	p
Cerebral spasm	0 (0.00)	1 (2.50)		
Hydrocephalus	0 (0.00)	1 (2.50)		
Rebleeding	2 (5.00)	3 (7.50)		
Arrhythmia	1 (2.50)	3 (7.50)		
Pulmonary infection	1 (2.50)	3 (7.50)		
Intracranial infection	1 (2.50)	4 (10.00)		
Thrombus of lower extremity veins	0 (0.00)	4 (10.00)		
Cerebral hernia	0 (0.00)	1 (2.50)		
Total incidence rate	5 (12.50)	15 (37.50)	6.667	0.010

4 Discussion

To improve the prognosis and quality of life of patients with subarachnoid hemorrhage, this study dissected the neurological function, inflammatory response, cerebral artery blood flow velocity, and psychological state of patients to explore the intervention effect of local mild hypothermia combined with early continuous nursing. The results suggested that compared with early continuous nursing intervention alone, the combination of local mild hypothermia can achieve more significant effects.

NHISS and GOS scores are commonly used clinical assessments of neurological function, with higher scores indicating more severe neurological impairment in patients. The anterior cerebral artery, posterior cerebral artery, and middle cerebral artery are all critical blood vessels in the brain, the blood flow velocity of which is clinically mainly determined to mirror the cerebral artery blood flow of patients. In this study, the data revealed that local mild hypothermia combined with early continuous nursing can ameliorate neurological function and cerebral artery blood flow of patients and was superior to early continuous nursing alone. Local mild hypothermia can maintain deep hypothermia and protect ischemic brain tissue by reducing brain metabolic rate, decreasing the release of excitatory neurotransmitters, and alleviating brain edema and intracranial pressure [12,17]. Local mild hypothermia can protect neurons by increasing their ubiquitin secretion, thereby mitigating neuronal damage, effectively inhibiting neuronal apoptosis, and enhancing neurological function [18]. Local mild hypothermia can also directly regulate brain blood flow and reduce blood flow velocity by lowering brain temperature [19]. Accordingly, local mild hypothermia combined with early continuous nursing had therapeutic efficacy in improving neurological function and cerebral artery blood flow of patients.

It has been evidenced that subarachnoid hemorrhage results in the exposure of outer wall of blood vessels to substances released by the breakdown products of red blood cells such as oxygenated hemoglobin, which will cause a series of inflammatory cascade reactions such as leukocyte recruitment, infiltration, and activation, as well as a notable increase in the level of inflammatory factors [20,21]. IL-8, hs-CRP, and TNF-α are common inflammatory factors in clinical practice, with higher levels signifying more severe inflammatory response. The results of this study showed that local mild hypothermia combined with early continuous nursing can inhibit inflammatory response, outperforming early continuous nursing alone. Local mild hypothermia can reduce the oxygen content of brain tissue, and delay the consumption of adenosine triphosphate in ischemic tissues, thereby enhancing the tolerance of tissues to ischemia and hypoxia, and improving the levels of inflammatory factors on the basis of restoring supply-demand balance [22]. Besides, hypothermia was known to suppress the activation of microglia and astrocytes, curtailing the release of pro-inflammatory cytokines (IL-6, IL-8 and TNF-α) [23,24]. Hence, local mild hypothermia combined with early continuous nursing can effectively improve inflammatory response in patients with subarachnoid hemorrhage.

HAMD and HAMA are commonly used scales for clinical assessment of depression and anxiety, respectively, with higher scores implying greater degree of depression and anxiety. The results of this study showed that local mild hypothermia combined with early continuous nursing can alleviate negative emotions such as depression and anxiety and improve psychological state of patients, and have better effects compared to early continuous nursing alone. Local mild hypothermia can significantly alleviate patients' condition by improving their neurological function and inhibiting their inflammatory response, and as patients no longer suffer from the pain of the disease and have increased confidence in their physical recovery, their negative emotions such as depression and anxiety will gradually dissipate, and their psychological state will also improve significantly. Reportedly, evident clinical therapeutic efficacy can mitigate the negative emotion of patients and regulate psychological state to some extent [25]. Collectively, local mild hypothermia combined with early continuous nursing has shown efficacy in improving the psychological state of patients with subarachnoid hemorrhage.

In addition, patients with subarachnoid hemorrhage are at high risk of developing complications such as cerebral spasms, cerebral hemorrhage, rebleeding, and intracranial infections due to the tendency for brain tissue or nerve to adhere to blood vessels after bleeding, and the mortality rate is also extremely high

[26-29]. Herein, local mild hypothermia combined with early continuous nursing can reduce the incidence of cerebral spasm, hydrocephalus, rebleeding, arrhythmia, pulmonary infection, intracranial infection, lower limb venous thrombosis, and cerebral herniation in patients, indicating that this intervention method had high safety and was worthy of clinical promotion.

5 Conclusion

In conclusion, local mild hypothermia combined with early continuous nursing can effectively improve neurological function and cerebral artery blood flow velocity, reduce inflammatory factor levels, and regulate psychological state to some extent, with good safety. However, this study has several limitations that should be considered. The findings are based on a relatively small sample size from a single center, which may limit the generalizability of the results. Additionally, the assessments of NIHSS, GOS, and HAMD/HAMA scores were not performed in a blinded manner, which could introduce potential bias. Therefore, future multi-center, randomized controlled trials with larger sample sizes, longer observation periods, and blinded outcome assessments are warranted to confirm our findings and further validate the application value of this combined intervention for subarachnoid hemorrhage.

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Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Substantial contributions to conception and design: X.L. and H.S. Data acquisition, data analysis and interpretation: X.L., H.S. and S.Z. Drafting the article or critically revising it for important intellectual content: All authors. Final approval of the version to be published: All authors.

Ethics Approval and Consent to Participate

This study was approved by Medical Ethics Committee, and patients were informed and agreed.

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Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Supplementary Materials

Not applicable.

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