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Evaluation of the Therapeutic Effect of Cerebrospinal Fluid Replacement in Subarachnoid Hemorrhage and Study on the Endpoint of Replacement Volume

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Abstract: *Objective*: To evaluate the therapeutic effect of cerebrospinal fluid (CSF) replacement in subarachnoid hemorrhage (SAH) and analyze the endpoint of replacement volume. *Methods*: 36 patients with spontaneous or traumatic SAH and intracerebral hemorrhage breaking into the subarachnoid space received by the hospital from August 2024 to April 2025 were selected. Different volumes of CSF were replaced with routine operation, and the clinical efficacy was analyzed. *Results*: All 36 patients were effective without any complications. In terms of replacement volume, the patients in the clear CSF replacement group had a greater decrease in VAS scores immediately and at 48 hours, and their symptom relief was more significant. The difference was statistically significant by *t*-test. Regarding the average frequency of CSF replacement, the control group had a higher average frequency than the clear group, but there was no statistical difference by the rank sum test. *Conclusion*: CSF replacement therapy can effectively improve clinical symptoms in patients with SAH. In terms of replacement volume, patients in the clear CSF replacement group had a greater decrease in VAS scores immediately and at 48 hours, with more significant symptom relief. Therefore, CSF replacement should be thorough, has high safety, and is worthy of clinical promotion.

Keywords: Subarachnoid hemorrhage; Cerebrospinal fluid replacement; Different replacement volumes; Clinical efficacy

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1. Introduction

Subarachnoid hemorrhage (SAH) is a severe neurological disease primarily caused by the rupture of intracranial aneurysms. It manifests as a sudden and severe headache, often accompanied by consciousness disorders, intense headache, nausea and vomiting, meningeal irritation, and increased intracranial pressure. In severe cases, it can

also be complicated by cerebral vasospasm, hydrocephalus, delayed cerebral ischemia, and other complications, which seriously affect the prognosis and quality of life of patients [1]. Currently, the treatment of SAH includes surgical clipping of aneurysms or interventional therapy targeting the etiology, cerebrospinal fluid (CSF) replacement therapy, drug therapy, and combination therapy for subarachnoid hemorrhage. CSF replacement therapy is a commonly used method for the clinical treatment of SAH in China. It reduces the incidence of SAH complications by replacing the accumulated blood in the subarachnoid space, which is a practical and effective method.

This article mainly focuses on 36 patients with spontaneous or traumatic subarachnoid hemorrhage and cerebral hemorrhage breaking into the subarachnoid space admitted to the hospital from August 2024 to April 2025 as data collection subjects. The study subjects were selected based on inclusion and exclusion criteria. Both the patients and their families were informed of the study content and signed informed consent forms. This study was reviewed and approved by the medical ethics committee of the hospital. Inclusion criteria: patients diagnosed with subarachnoid hemorrhage and cerebral hemorrhage breaking into the subarachnoid space through cranial CT, magnetic resonance imaging, and other examinations, as well as patients who meet the indications for cerebrospinal fluid replacement surgery. Exclusion criteria: patients with combined liver and kidney dysfunction, spontaneous subarachnoid hemorrhage without interventional or craniotomy surgery, patients with expandable intracranial hypertension, and patients with respiratory and circulatory failure, thrombocytopenia, and coagulation dysfunction. The analysis was conducted, and the main contents are reported as follows.

2. Materials and methods

2.1. General information

During the period from August 2024 to April 2025, 36 patients with spontaneous or traumatic subarachnoid hemorrhage and cerebral hemorrhage breaking into the subarachnoid space admitted to the hospital were selected. They were divided into a control group and a study group (clear group) according to the random number method. Among them, the control group consisted of 9 males and 12 females, with a minimum age of 23 years, a maximum age of 84 years, and an average age of 64.0 years. The observation group consisted of 9 males and 5 females, with a minimum age of 43 years, a maximum age of 79 years, and an average age of 62.7 years.

Research method: Both groups received conventional treatment, including interventional or craniotomy surgery, infusion of mannitol, reduction of intracranial pressure, spasmolysis, antibiotics, hemostatic agents, blood pressure control, maintenance of acid-base balance, and bed rest. Cerebrospinal fluid replacement therapy was performed after the acute phase of bleeding.

2.2. VAS score

VAS pain scale was used to evaluate patients five times before surgery, immediately after surgery, 24 hours after surgery, 48 hours after surgery, and at the end of the entire replacement cycle. VAS is one of the commonly used pain scoring criteria, and its full name is Visual Analog Scale. A 10 cm horizontal line is drawn on paper, with one end marked as 0, indicating no pain; the other end marked as 10, indicating severe pain; and the middle section representing varying degrees of pain. Patients are asked to mark on the line according to their perceived level of pain. **Table 1** shows the VAS scoring criteria.

Table 1. VAS scoring criteria

Description of pain	Score	Patient's rating
Minor pain, tolerable	0–3 points	
Moderate pain affecting sleep, but still tolerable	4–6 points	
Severe pain strongly felt by the patient, affecting appetite and sleep	7–10 points	

2.3. Cerebrospinal fluid replacement therapy

Based on the amount of subarachnoid hemorrhage and the shade of bloody color in the cerebrospinal fluid, replacement was performed once every 1–2 days until the hemorrhage was basically cleared.

In the control group, lumbar puncture was performed on the patients to measure intracranial pressure. Cerebrospinal fluid was slowly released in 5~10 mL aliquots for testing, and 0.9% sodium chloride injection was slowly infused in 10 mL aliquots. This was followed by another slow release of 10 mL of cerebrospinal fluid. This process was repeated, with a total replacement volume of 40 mL.

In the experimental group, lumbar puncture was similarly performed to measure intracranial pressure. Cerebrospinal fluid was also slowly released in 5~10 mL aliquots for testing, followed by slow infusion of 10 mL of 0.9% sodium chloride injection. This was repeated until the cerebrospinal fluid became clear or significantly lighter in color, with a maximum total replacement volume of 120 mL. Observations were made after the completion of the entire cerebrospinal fluid replacement cycle.

2.4. Observation indicators

(1) Comparison of efficacy between the two groups. Complete recovery: Clinical symptoms such as vomiting, dizziness, and headache disappear, intracranial pressure returns to normal, consciousness recovers, and there is no recurrence of bleeding or other complications; Improvement: Clinical symptoms such as vomiting, dizziness, and headache show significant improvement, intracranial pressure returns to normal, and complications are controlled after intervention; Ineffective: No significant improvement in clinical symptoms such as vomiting and dizziness, and there are complications such as recurrence of bleeding. Total effective rate of treatment = (Number of complete recoveries + Number of improvements) / Total number of cases × 100% (2) Comparison of the number of treatments required between the two groups. (3) Comparison of the degree of headache relief within 48 hours between the two groups. (4) Comparison of the incidence of complications between the two groups.

3. Results

3.1. Statistical methods

Statistical analysis was performed using SPSS 22.0 software. Quantitative data conforming to a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared using the *t*-test. For non-normally distributed data, the rank sum test was used for comparison. Qualitative data were expressed as rates or proportions and compared using the chi-square test. The significance level was set at 0.05.

3.1.1. Comparison of replacement frequency between the two groups

The average frequency in the control group was 2.10, and the average frequency in the clear group was 1.53. There was no statistically significant difference between the two groups according to the rank sum test ($z = 1.32$, $P = 0.187$) (**Figure 1**).

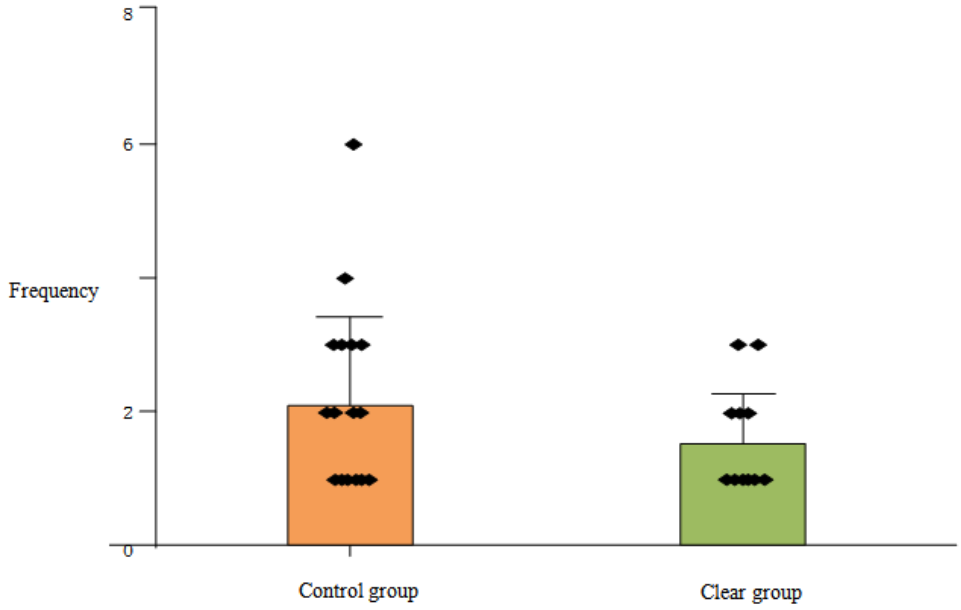

Figure 1. Comparison of frequencies between two groups

3.1.2. Comparison of immediate VAS score reduction between the two groups

The VAS score reduction in the control group was 1.41 ± 0.57, while the VAS score reduction in the clear group was 2.75 ± 0.58. The difference was statistically significant according to the t-test ($t = 6.28$, $P < 0.001$) (**Figure 2**)

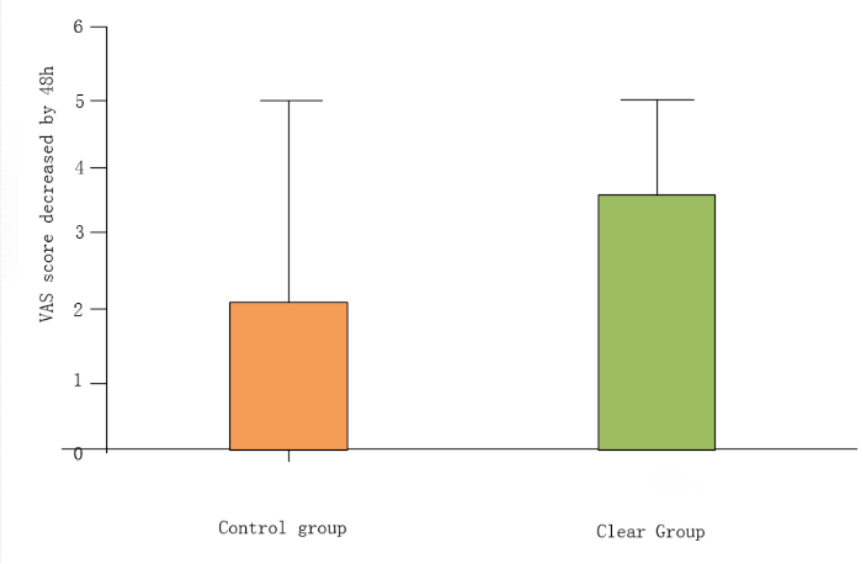

Figure 2. Comparison of immediate VAS score reduction between the two groups

3.1.3. Comparison of VAS score reduction at 48h between the two groups

The VAS score reduction at 48 hours in the control group was 2.17 ± 1.04, while the VAS score reduction at 48 hours in the clear group was 3.67 ± 1.23. The difference was statistically significant according to the *t*-test ($t = 3.59$, $P = 0.001$) (**Figure 3**).

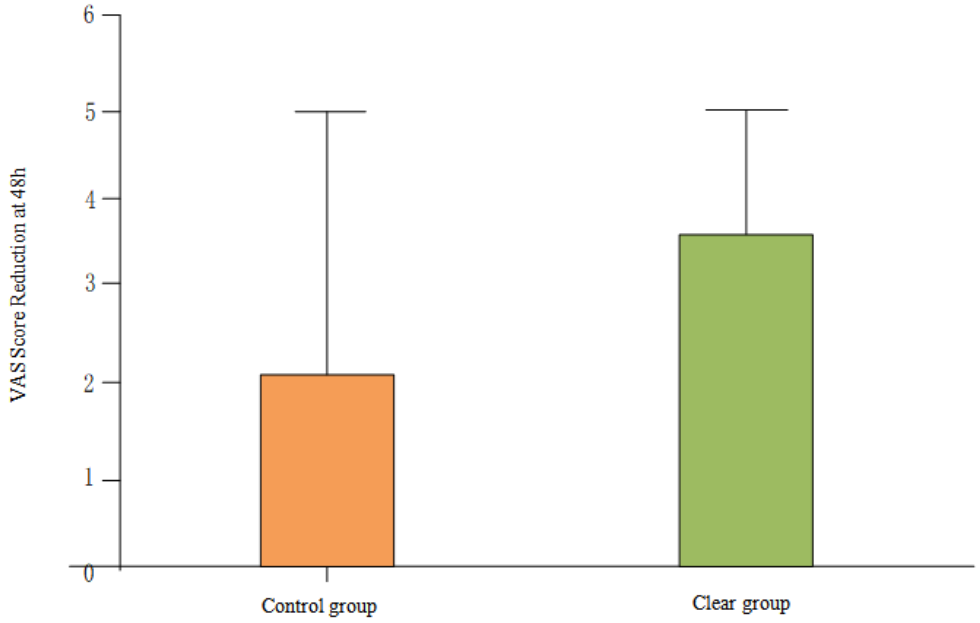

Figure 3. Comparison of VAS score reduction at 48h between the two groups

3.1.4. Comparison of average VAS score reduction at 48h between the two groups

The average VAS score reduction at 48 hours in the control group was 2.15 ± 0.95, while the average VAS score reduction at 48 hours in the clear group was 3.36 ± 1.47. The difference was statistically significant according to the *t*-test ($t = 2.75$, $P = 0.01$) (**Figure 4**).

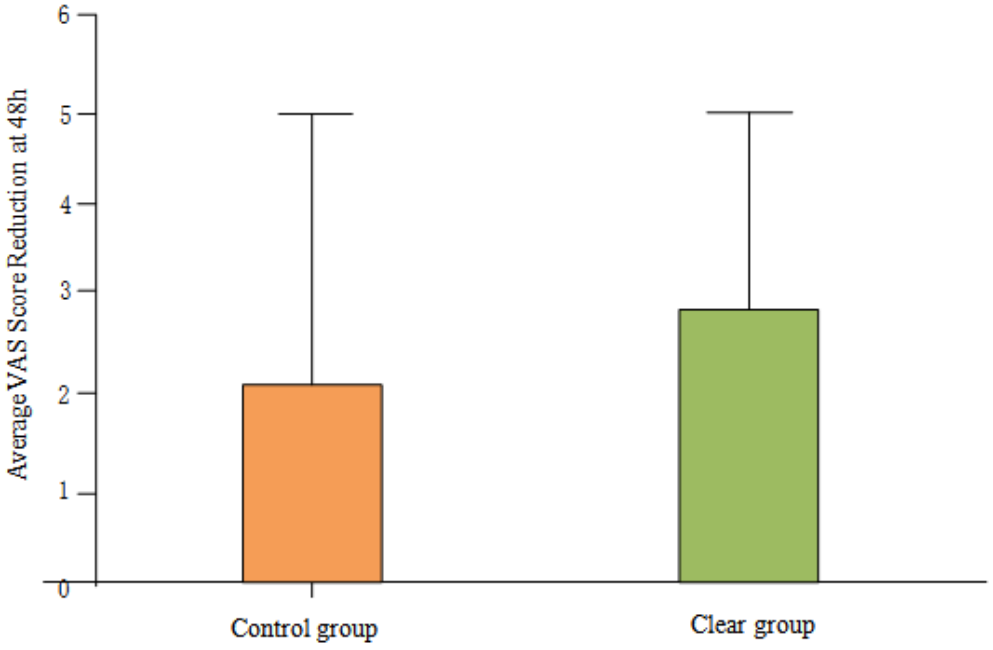

Figure 4. Comparison of average VAS score reduction at 48h between the two groups

3.2. SPSS calculation results

3.2.1. Comparison of replacement frequency between two groups

The comparison of replacement frequency between the two groups is shown in **Tables 2** and **3**.

Table 2. The comparison of replacement frequency between the two groups

Rank				
group		**N**	**Mean rank**	**Sum of ranks**
Frequency	Control group	21	20.31	426.50
	Clear group	15	15.97	239.50
	Total	36		

Table 3. Summary of the independent sample Mann-Whitney U test

Total N	36
Mann-Whitney U	119.500
Wilcoxon W	239.500
Test statistic	119.500
Standard error	28.777
Standardized test statistic	-1.320
Asymptotic significance (2-tailed test)	.187
Exact significance (2-tailed test)	.226

3.2.2. Comparison of VAS score reduction between the two groups

The comparison of VAS score reductions between the two groups is shown in **Tables 4** and **5**.

Table 4. Comparison of VAS score reduction between the two groups

Group statistics					
	Group	**N**	**Mean**	**Standard deviation**	**Standard error of the mean**
Decrease in VAS score	Control group	18	1.4074	.56656	.13354
	Clear group	12	2.7500	.58387	.16855

Table 5. Independent samples test

	Independent samples test										
	Levene's test for equality of variances			***t*-test for equality of means**							
						Significance				**95% confidence interval of the difference**	
		F	Significance	t	Degrees of freedom	One-tailed *P*-value	Two-tailed *P*-value	Mean difference	Standard error of the difference	Lower limit	Upper limit
Decrease in VAS score	Assuming equal variances	.097	.758	-6.283	28	<.001	<.001	-1.34259	.21370	-1.78034	-.90484
	Not assuming equal variances			-6.243	23.223	<.001	<.001	-1.34259	.21504	-1.78720	-.89799

3.2.3. Comparison of VAS score reduction at 48 hours between the two groups

The comparison of VAS score reduction at 48 hours between the two groups is shown in **Tables 6** and **7**.

Table 6. Comparison of VAS score reduction at 48 hours between the two groups

Group Statistics					
	Group	**N**	**Mean**	**Standard deviation**	**Standard error of the mean**
VAS score reduction at 48 hours	Control group	18	2.1667	1.04319	.24588
	Clear group	12	3.667	1.23091	.35533

Table 7. Independent samples test

Independent samples test										
	Levene's test for equality of variances		**t-test for equality of means**							
					Significance				**95% confidence interval of the difference**	
	F	Significance	t	Degrees of freedom	One-tailed *P*-value	Two-tailed *P*-value	Mean difference	Standard error of the difference	Lower limit	Upper limit
VAS score reduction at 48 hours	Assuming equal variances	.168	.685	28	<.001	.001	-1.50000	.41766	-2.35553	-6.4447
	Not assuming equal variances			20.948	.001	.002	-1.50000	.43211	-2.39876	-6.0124

3.2.4. Comparison of the average reduction in VAS scores at 48 hours between the two groups

The comparison of the average reduction in VAS scores at 48 hours between the two groups is shown in **Tables 8** and **9**.

Table 8. The comparison of the average reduction in VAS scores at 48 hours between the two groups

Group statistics					
	Group	**N**	**Mean**	**Standard deviation**	**Standard error of the mean**
VAS score reduction at 48 hours	Control group	18	2.1481	.95296	.22461
	Clear group	12	3.3611	1.47339	.42533

Table 9. Independent samples test

	Independent samples test									
	Levene's test for equality of variances		t-test for equality of means							
					Significance				95% Confidence interval of the difference	
	F	Significance	t	Degrees of freedom	One-tailed *P*-value	Two-tailed *P*-value	Mean difference	Standard error of the difference	Lower limit	Upper limit
VAS score reduction at 48 hours	Assuming equal variances	2.344	.137	28	.005	.010	-1.21296	.44162	-2.11758	-.30834
	Not assuming equal variances			17.129	.001	.022	-1.21296	.48100	-2.22720	-.19873

4. Discussion

Subarachnoid hemorrhage (SAH) includes spontaneous SAH and traumatic SAH, with traumatic brain injury being the main cause of traumatic SAH (tSAH). Traumatic vasoconstriction observed in animal models can lead to secondary ischemic injury, as well as changes in intracranial pressure and mean arterial blood pressure, which largely explain the clinical course of tSAH and may ultimately result in neurological deterioration, increased morbidity, and mortality [3]. Approximately 85% of non-traumatic SAH cases are typically associated with the rupture of intracranial aneurysms, with nearly 500,000 patients worldwide suffering from aneurysmal SAH (aSAH) each year [4–5]. The main symptom of aSAH is sudden severe headache, often described as "the worst headache of my life," which may be accompanied by transient loss of consciousness, nausea or vomiting, pseudomeningocele, and epileptic seizures [6]. During aSAH, blood accumulates between the arachnoid and pia mater layers, leading to rapid increases in intracranial pressure and deprivation of oxygen to brain tissue, ultimately causing brain tissue damage and neurological dysfunction. Additionally, neurotoxins released from the hematoma can also cause cell death [7]. Blood breakdown products in the cerebrospinal fluid (CSF) can also block the arachnoid villi, leading to hydrocephalus and vasospasm, which can exacerbate neurological dysfunction [1]. The 30-day mortality rate for aSAH is approximately 20%, and up to 50% of survivors may become functionally dependent [8]. Currently, the etiology of SAH remains unknown for 10% of patients, making it impossible to determine the correct source of bleeding. This condition is known as angiographically negative SAH (naSAH), which has a more benign prognosis and better outcome compared to aSAH [9]. Therefore, for the clinical treatment of spontaneous SAH, rapid clearance of subarachnoid hematoma is key after addressing the underlying causes, such as aneurysms or vascular malformations, through craniotomy clipping or interventional therapy [10]. Conventional treatment cannot quickly clear the subarachnoid hematoma within a short period, while combined CSF replacement therapy for aneurysmal SAH can effectively control the disease and improve prognosis [11–12, 15]. In terms of efficacy and safety, both groups in this study were effective. Comatose patients were evaluated by head CT, showing a significant reduction in subarachnoid or ventricular hematoma, resulting in a 100% effectiveness rate. Regarding safety, lumbar puncture is a routine procedure in neurosurgery [2]. The safety of CSF replacement was assessed through preoperative evaluation (including medical history, physical examination, laboratory tests, and imaging

studies), strict aseptic techniques during surgery, lateral puncture techniques, strict control of CSF release and 0.9% sodium chloride injection rates, maintenance of intracranial pressure stability, and postoperative monitoring and care (including vital signs, neurological function, and CSF pressure). There were no complications in this group, demonstrating safety and efficacy. Currently, CSF replacement therapy is widely used to treat SAH due to its advantages of minimal trauma and rapid recovery. It can effectively improve clinical symptoms without increasing the risk of adverse reactions, exhibiting high safety [13–14]. Regarding replacement volume, patients in the clear CSF replacement group showed a greater decrease in VAS scores immediately and at 48 hours, with more significant symptom relief. The difference was statistically significant, indicating the importance of thorough CSF replacement [10]. This finding is consistent with previous literature reports. Regarding the average frequency of CSF replacement, the control group had a higher average frequency than the clear group, but there was no statistical difference, possibly due to the small sample size, necessitating further large-scale studies.

5. Conclusion

In summary, patients with SAH and hypertensive intracerebral hemorrhage with ventricular rupture who receive CSF replacement therapy can effectively improve clinical symptoms. In terms of replacement volume, patients in the clear CSF replacement group showed a greater decrease in VAS scores immediately and at 48 hours, with more pronounced symptom relief. Therefore, thorough CSF replacement is crucial and demonstrates high safety, making it worthy of clinical promotion.

Disclosure statement

The authors declare no conflict of interest.

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