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Results of acute cerebral infarction treatment with hyperbaric oxygen therapy, 2020–2022

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ABSTRACT

Background: *Cerebral stroke is the third leading cause of death after cardiovascular disease, cancer and the leading cause of disability for patients. Hyperbaric oxygen is a non-drug treatment that has the potential to improve brain function for patients with ischaemic stroke. The objective of this study was to evaluate the results of treatment of acute cerebral infarction with hyperbaric oxygen therapy (HBOT).*

Materials and methods: *This was a case-control study. One hundred ninety-five patients diagnosed with cerebral infarction, with signs of onset within 24 hours, were treated at the Centre for Underwater Medicine and Hyperbaric Oxygen of Vietnam National Institute of Maritime Medicine during the period from January 2020 to December 2022. Study group included 100 patients with acute cerebral infarction treated with a combination of HBOT and medication and reference group included 95 patients treated by medication only (antiplatelets drugs, statins, control of associated risks factors)*

Results: *After 7 days of treatment with hyperbaric oxygen (HBO), symptoms such as headache, dizziness, nausea, sensory disturbances, and Glasgow score of the study group improved better than that of the reference group ($p < 0.01$). Movement recovery in the study group was better than the reference group: the percentage of patients with mild and moderate paralysis in the study group increased higher than that of the reference group (86.0% and 68.4%), the degree of complete paralysis of the study group decreased more than that of the reference group (14.0% and 31.6%). The degree of independence in daily activities in the study group was better than the reference group. In the study group, the percentage of patients with complete independence in daily life increased from 27.0% to 84.0%. In the reference group, the rate of patients who were independent in their daily activities increased from 37.9% to 51.6%. The average number of treatment days of the study group was 10.32 ± 2.41 days and it the reference group 14.51 ± 3.24 days.*

Conclusions: *Hyperbaric oxygen therapy is a non-drug treatment with many good effects in the treatment of cerebral infarction, especially acute cerebral infarction. HBOT reduces and improves functional symptoms, improves mobility, and reduces treatment time for patients.*

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Keywords: acute cerebral infarction, hyperbaric oxygen therapy (HBOT), VINIMAM regimen

INTRODUCTION

Acute ischaemic stroke, also known as ischaemic stroke, is a sudden loss of blood flow to an area of the brain due to blockage of a blood vessel by a thrombus or atherosclerotic plaque in a cerebral artery, rendering an area of the brain deprived of oxygen and nutrients, leading to a corresponding

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loss of neurological function [1]. Stroke is the third leading cause of death after cardiovascular disease and cancer, and is the most common cause of disability among adults in developed countries. In the United States, every year about 800,000 people have a stroke, of which 82–92% are cerebral infarction. Stroke is one of the top 5 causes of death and disability in adults, costing more than $72 billion annually [2].

Currently, there are a number of treatment methods for cerebral infarction such as: medical treatment (using antiplatelet drugs, statin drugs, controlling risk factors...). Methods of revascularization in the acute phase include: intravenous fibrinolysis (within 4.5 hours of stroke onset), this method has been confirmed but has some time limitations, and for large vessels, it provides only about 15–20% of recanalization [3], transarterial mechanical thrombectomy is indicated in large embolism (< 6 hours from stroke onset).

Hyperbaric oxygen (HBO) is a treatment method that has been shown by some authors to be effective for patients with acute ischaemic stroke [4–6]. It has a role in promoting the repair of damaged blood vessels while enhancing the development of the neovascular system, restoring the permeability of vessel walls and cell membranes by increasing the synthesis of ATP, ATPase, fighting brain oedema and especially neutralizing the aetiology of free radicals. In 2019, the Vietnam Ministry of Health officially issued Decision 2539/QD-BYT on Guidelines for the technical process of hyperbaric oxygen therapy (HBOT), with 48 diseases indicated for treatment with HBO, including cerebral infarction [7]. In order to evaluate the effect of HBO in the treatment of cerebral infarction, especially acute cerebral infarction, the research team conducted this study with the following objective: To evaluate the results of treatment of acute cerebral infarction with HBOT at VINIMAM from 2020 to 2022.

MATERIALS AND METHODS

MATERIALS

The study included 100 patients with acute brain infarction treated with HBOT combined with medical treatment at Vietnam National Institute of Marine Medicine during the period from January 2020 to December 2022 including two groups of subjects:

Study group: Study group included 100 patients with acute brain infarction treated with HBOT combined with medical treatment, who were selected based on the following criteria:

— cerebrovascular accident diagnosed according to the 1989 World Health Organization criteria (clinical criteria);
— computed tomography image showing hypodense lesions in the brain parenchyma corresponding to clinical symptoms (subclinical criteria);
— the time from symptom onset to receiving HBOT is within 24 hours;
— the following patients were excluded from the study: patients with paralysis without cerebral infarction; patients with cerebral infarction who had indications for treatment with fibrinolytic therapy, thrombectomy and thrombectomy with mechanical instruments, when indicated; patients without cerebral infarction lesions on computed tomography; patients with contraindications to HBO treatment; and patients who refused to participate in the study (exclusion criteria).

Reference group. Reference group included 95 patients with acute brain ischaemic stroke who received only medical treatment.

METHODS

Study design. This was a case-control study.

Sample size, method to choose sample size. To obtain a sufficient sample size, we enrolled all eligible patients in the study over a 3-year period. Ultimately, the size of the groups was as follows: the study group consisted of 100 patients; the reference group included 95 patients.

Criteria for evaluating research results. All patients with signs of cerebral infarction were subject to clinical examination including: assessment for headache, vomiting, nausea, dizziness, sensory disturbances, paralysis, as well as assessment of cognitive status using the Glasgow scale. The restoration of motor function according to Henry's scale and the degree of independence in daily living according to Barthel scale were also assessed.

All patients underwent computed tomography of the brain; the scans showed hypodense changes in the brain parenchyma.

TREATMENTS

Study group. Patients in the study group received treatment for the underlying disease, using antiplatelet drugs, drugs to increase cerebral circulation, drugs to treat blood lipids disorder in combination with HBOT.

Reference group. Patients in the reference group received treatment for underlying disease, antiplatelet drugs, drugs to increase cerebral circulation, drugs to treat blood lipids disorder.

Intermittent HBOT was used according to the VINIMAM 3 treatment regimen (Fig. 1) for the first treatment, and then VINIMAM 1 until discharge (Fig. 2).

Time of assessment. Patients were assessed before treatment and 7 days after treatment.

Methods of assessment before and after treatment included:

— assessment of the change of consciousness according to the Glasgow scale (mild: G ≥ 13 points; moderate: 9 ≤ G ≤ 12 points; severe: G ≤ 8 points) [8];

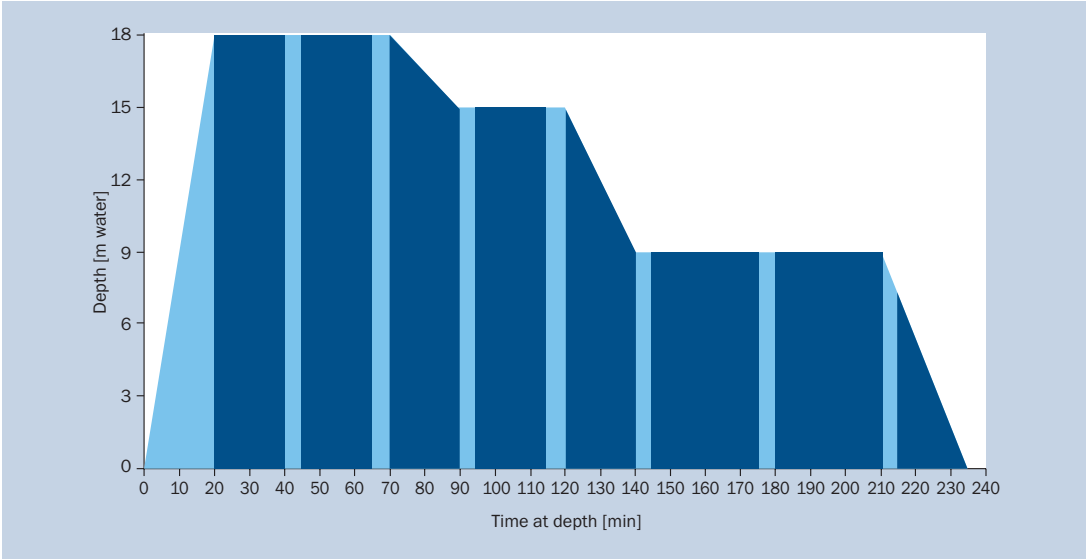

Figure 1. VINIMAM regimen 3. Treating pressure: 2.8 absolute atmospheric pressure; Total treatment time: 235 minutes; Total oxygen breathing time: 180 minutes: 20 minutes × 5 + 30 minutes × 2 + 20 minutes breathe and ascent; Between oxygen breaths rest: 5 minutes; Breathing flow: free

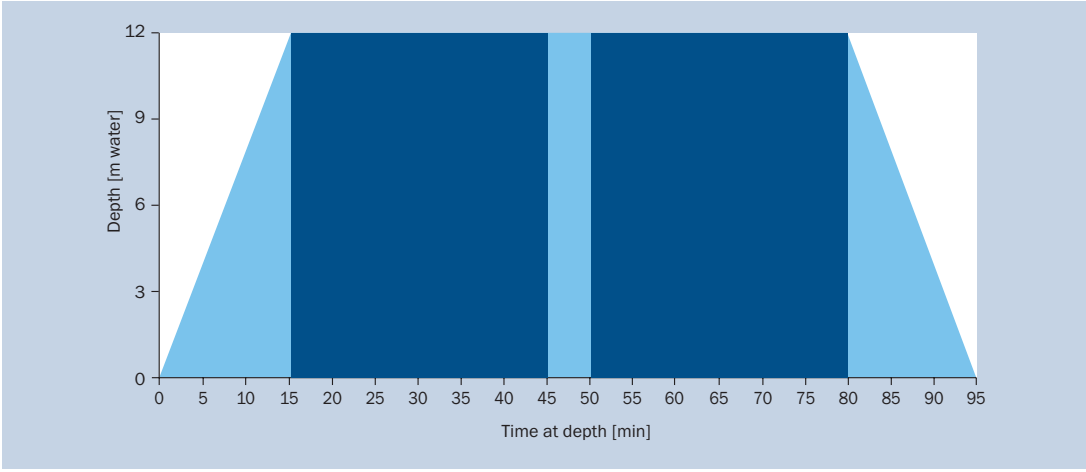

Figure 2. VINIMAM regimen 1. Treating pressure: 2.2 absolute atmospheric pressure; Total treatment time: 95 minutes; Total oxygen breathing time: 30 minutes × 2 = 60 minutes; Between 2 oxygen breaths rest: 5 minutes; Breathing flow: free

— results of recovery of independence in daily activities according to Barthel independent: 95–100 points; slightly dependent: 65–94 points; highly dependent: 30–64 points; fully dependent: 0–29 points) [9];
— results of motor recovery according to Henry: mild paralysis (reduced muscle force, motor function still present); moderate paralysis (can lift arms and legs off the bed); severe paralysis (can still stretch limbs when there is pressure point); very severe paralysis (only slight muscle contractions); completely paralyzed (no movement at all) [10].

DATA PROCESSING

Data were entered and processed by the statistical software SPSS 20.0.

ETHICS IN RESEARCH

The research topic was approved by the research ethics committee of the Vietnam National Institute of Marine Medicine before conducting the research. Participation in the study was completely voluntary.

RESULTS

The study results (Table 1) showed that there was no difference between the study group and the reference group ($p > 0.05$). The highest age of both group with cerebral infarction is 60–69 years old (37.0% and 40.0%).

Before treatment, the functional symptoms of the two groups did not differ. After 7 days of treatment, 100% of the study group had no symptoms of headache, dizzi-

Table 1. Distribution of study subjects by sex and age

Research variable		Study group (n = 100)		Reference group (n = 95)		P
		N	%	N	%	
Sex	Men	52	52.0	51	53.7	> 0.05
	Women	48	48.0	44	46.3	> 0.05
Age group [year]	< 50	5	5.0	6	6.3	> 0.05
	50–59	21	21.0	19	20.0	> 0.05
	60–69	37	37.0	38	40.0	> 0.05
	70–79	29	29.0	27	28.4	> 0.05
	≥ 80	8	8.0	5	5.3	> 0.05

Table 2. Functional symptoms (n = 100)

Research variable	Before treatment			After 7 days of treatment		
	Study group (n = 100)	Reference group (n = 95)	P	Study group (n = 100)	Reference group (n = 95)	P
Headache (%)	74 (74.0%)	69 (72.6%)	> 0.05	0 (0.0%)	11 (11.6%)	< 0.001
Dizziness	79 (79.0%)	77 (81.1%)	> 0.05	0 (0.00%)	18 (18.90%)	< 0.001
Nausea, vomiting	23 (23.0%)	18 (18.9%)	> 0.05	0 (0.00%)	3 (3.10%)	< 0.05
Sensory disturbances	58 (58.0%)	59 (62.1%)	> 0.05	9 (9.00%)	22 (23.10%)	0.002

Table 3. Result of awareness change according to Glasgow scale before and after treatment

Glasgow score	Study group (n = 100)			Reference group (n = 95)		
	Before treatment	After 7 days of treatment	P	Before treatment	After 7 days of treatment	P
≤ 8 score	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	0 (0.0%)	1
9–12 score	12 (12.0%)	4 (4.0%)	< 0.05	12 (12.6%)	10 (10.5%)	0.45
13–15 score	88 (88.0%)	96 (96.0%)	< 0.05	83 (87.4%)	85 (89.5%)	0.47

ness, and nausea. Meanwhile, in the reference group, some patients experienced headache (11.8%), dizziness (19.4%) and nausea or vomiting (2.2%). This difference is statistically significant ($p < 0.05$) (Table 2).

After 7 days of treatment, the rate of patients treated with HBOT with a Glasgow score of 9–12 points decreased from 11.63% to 4.21%. The group with Glasgow score from 13 to 15 increased from 89.47% to 96.84%, $p = 0.04$. In the reference group, the rate of patients with Glasgow score of 9–12 decreased slightly from 12.9% to 9.7%. The proportion of patients with Glasgow score of 13–15 increased from 87.1% to 90.3%, $p = 0.48$ (Table 3).

Before treatment, there was no difference in the degree of paralysis between the two study groups. After 7 days of treatment, in the study group, the proportion of patients with mild paralysis plus moderate paralysis was 86.0%, and the rate of patients with complete paralysis was 14% (Table 4).

In the reference group, the rate of mild paralysis plus moderate paralysis was 68.4% and the rate of complete paralysis was 31.6%. The difference was statistically significant with $p < 0.05$.

Thus, the progression in the group treated with HBO was much better than that of the reference group.

In the study group, the rate of patients who were independent in daily life increased from 37.0% to 77.0%. The proportion of patients who were highly dependent in daily life decreased from 33.0% to 9.0%, $p < 0.05$ (Table 5).

In the reference group, the proportion of patients independent in daily life increased from 38.0% to 51.6%. The proportion of patients who required help in daily activities decreased from 31.5% to 26.3%, $p > 0.05$.

The average number of treatment days of the study group was 10.32 ± 2.41 days, and it was lower than that of the reference group (14.51 ± 3.24, $p < 0.001$) (Table 6).

Table 4. Restoration of motor function according to Henry's scale

Research variable	Before treatment			After treatment		
	Study group (n = 100)	Reference group (n = 95)	P	Study group (n = 100)	Reference group (n = 95)	P
Mild + moderate paralysis	64 (64.0%)	61 (64.2%)	0.98	86 (86.0%)	65 (68.4%)	< 0.05
Complete paralysis	36 (36.0%)	34 (35.8%)	0.98	14 (14.0%)	30 (31.6%)	< 0.05

Table 5. Level of independence in daily activities according to the Barthel scale

Research variable (Barthel scale)	Study group (n = 100)			Reference group (n = 95)		
	Before treatment	After treatment	P	Before treatment	After treatment	P
Completely dependent	8 (8.0%)	2 (2.0%)	< 0.05	4 (4.2%)	4 (4.2%)	1
Highly dependent	35 (35.0%)	9 (9.0%)	< 0.01	30 (31.6%)	25 (26.3%)	0.62
Slightly	30 (30.0%)	5 (7.0%)	< 0.01	25 (26.3%)	17 (17.9%)	0.08
Independent	27 (27.0%)	84 (84.0%)	< 0.01	36 (37.9%)	49 (51.6%)	0.056

Table 6. Average number of treatment days of study subjects

Research variable	Study group (n = 100)	Reference group (n = 95)	P
Number of treatment days ($\bar{X} \pm$ SD)	10.32 ± 2.41	14.51 ± 3.24	< 0.001
Minimum (day)	7	10	
Maximum (day)	15	20	

SD — standard deviation

DISCUSSION

Stroke is the third leading cause of death after ischaemic heart disease and cancer worldwide. In Vietnam, an estimated 200,000 people have a stroke every year, which is the leading cause of death and disability. The incidence and prevalence of stroke are 161 and 415 per 100,000 people, respectively [11]. Currently, there are many advances in the treatment of ischaemic stroke, including the method of using intravenous fibrinolysis and the method of removing thrombus with mechanical instruments. However, many patients do not have access to treatment by this method because they usually arrive at the hospital late, beyond the golden time for treatment. Intravenous fibrinolytics should be used within 4.5 hours of stroke onset, whereas transarterial mechanical thrombectomy is indicated in large emboli (< 6 hours from stroke onset) [3, 12, 13]. Hyperbaric oxygen is one of the treatment methods for cerebral infarction, which has initially been proven effective and can be applied to treat various stages of cerebral infarction, especially acute cerebral infarction [14–16].

In this study 100 patients with cerebral infarction treated with HBO in combination with medical therapy (antiplatelet drugs, statins, risk factors control) were compared with 95 patients in the reference group who received medical therapy alone. Research results show that after 7 days of treatment, 100% of the study group no longer had headaches, dizziness, nausea, whereas in the reference group some patients reported headache (11.6%), dizziness (18.9%), nausea, vomiting (3.1%), $p < 0.05$ (Table 2).

The assessment of consciousness change after treatment of the study group showed that the rate of patients with Glasgow score of 13–15 increased from 89.47% to 96.84%, $p = 0.04$. In the reference group, the proportion of patients with Glasgow score of 13–15 points increased from 87.4% to 89.5%, $p = 0.47$ (Table 3).

When assessing motor recovery according to Henry's scale, the results showed that after 7 days of treatment, the proportion of patients with mild and moderate paralysis in the study group increased more than that of the reference group (86.0% and 68.4%, $p < 0.05$). The proportion of patients with complete paralysis of the study group also decreased more compared with the reference group (14.0% and 31.6%, $p < 0.05$; Table 4).

The mean treatment time of the study group was also lower than that of the reference group (10.32 ± 2.41 and 14.51 ± 3.24, p < 0.001; Table 6).

Thus, the study results showed that the treatment effect of HBO in the study group compared with the reference group was clearly better, which was reflected in a greater improvement in the functional symptoms of the disease (headache, dizziness, nausea, sensory disturbances); improved mobility and shorter average number of days of treatment. To explain this, we and some authors believe that the problem of lack of oxygen supply to the brain has been considered as the main cause of brain cell damage after stroke. Treatment with HBO increases the partial pressure of oxygen in blood (10 to 13 times higher than normal), thereby increasing the oxygen supply to brain tissue. Moreover, HBO can stabilize blood-brain barrier and reduce cerebral oedema, increase brain microcirculation development and improve brain cell metabolism to generate enough energy for brain tissue to function, maintain homeostasis, reduce intracranial pressure through regulation of cerebral blood flow and reduce cerebral oedema. Hyperbaric oxygen alleviates post-stroke neuroinflammation and inhibits post-stroke cell death and necrosis reactions. It also improves microcirculation in the ischaemic area and reduces cerebral ischaemia. Appropriate and timely HBOT will alleviate oxidative stress and prevent ischaemic brain damage [17–20].

A retrospective study was performed on 22 patients with ischaemic stroke treated with HBO (13 of them received HBO therapy within the first 5 hours after a stroke). Logistic regression analysis was performed to examine the effect of time after stroke, time in the chamber and dose of HBO. Treatment pressure ranged from 2.02 to 3.04 absolute atmospheric pressure (ATA). The results showed that the time after a stroke had a significant effect on recovery, with each passing hour reducing the chance of recovery by at least 62% (odds ratio: 0.38, 95% confidence interval: 0.15–0.95, p = 0.039). In the group of 13 patients from one to 5 hours, 9 recovered well. Patients treated after 6 hours recovered more slowly [15].

Nighoghossian et al. [16] studied 34 patients with mid-cerebral artery occlusive cerebral stroke, examined within 24 hours of onset (17 patients treated with HBO; 17 patients treated with isobaric oxygen). The study results showed that the mean score of motor recovery in the study group was higher than that of the reference group (p < 0.02) [19]. Bennett et al. [4] synthesized 11 randomized controlled trials in 705 stroke patients treated with HBO. The study results showed that the degree of disability and motor function were significantly improved after HBOT (p = 0.02–0.04).

A retrospective analysis of 162 patients (75.3% male with mean age 0.75 ± 12.91) treated with HBO for chronic cerebral stroke (> 3 months) during the 2008–2018 according to the following schedule: from 40 to 60 treatments, 5 days per week, each time 90 minutes of 100% oxygen at 2 ATA. The study results showed that HBOT improved the patient's cognitive function (p < 0.05); 86% of stroke patients had clinically significant improvement (p < 0.05) [21].

Thus, the results of our study as well as that of some international authors have the same conclusion that HBOT is clearly effective for the treatment of acute cerebral infarction.

CONCLUSIONS

Through the study of 195 patients with acute cerebral infarction, divided into two groups: study and reference groups, after 7 days of treatment, we draw the following conclusions:

- all functional symptoms in patients in the study group significantly improved after HBOT compared to before treatment and to the reference group;
- the percentage of patients with a Glasgow score of 9–12 points decreased after 7 days of HBOT from 11.63% to 4.21%, and the percentage with a Glasgow score > 12 points increased from 89.47% to 96.84%;
- the functional symptoms of the study group improved better compared to reference group;
- the results of motor recovery according to Henry's scale were better in the study group than in the reference group: 85.3% had mild and moderate paralysis, only 14.7% had severe paralysis. This rates in the reference group were 66.7% and 33.3%, respectively;
- the level of independence in daily activities according to the Batel scale was higher in the study group than in the reference group: 78.9% were completely independent, 9.5% slightly dependent. This rates in the reference group were 52.7% and 16.1%, respectively;
- the average number of treatment days of the study group was lower than that of the reference group. In the study group it was 10.32 ± 2.41 days, in the reference group 14.51 ± 3.24 days.

Conflict of interest: None declared

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