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Cerebral hemodynamic changes assessment by transcranial doppler ultrasound in patients with acute cerebral infarction before and after treatment with butylphthalide

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Abstract: To assess cerebral hemodynamic changes by transcranial doppler ultrasound in patients with acute cerebral infarction before and after treatment with butylphthalide, A total of 90 patients with acute cerebral infarction admitted to our hospital from January 2019 to January 2020 were selected and equally divided into the control group and the experimental group according to the order of admission. The control group was treated with conventional treatment, while the experimental group was additionally given butylphthalide drug treatment. The experimental group obtained better hemodynamic indexes as compared with the control group (P<0.05). The experimental group yielded a notably higher total clinical effective rate after treatment in contrast with the control group (P<0.05). After treatment, the serum indexes of the experimental group were evidently lower than those of the control group (P<0.05). After treatment, a remarkably lower NIHSS score of the experimental group than the control group was observed (P<0.05). The BI index score of the experimental group after treatment was considerably higher than that of the control group (P<0.05). After treatment, the MMSE score in the experimental group was significantly higher than it was in the control group (P<0.05). The treatment of butylphthalide in patients with acute cerebral infarction can effectively improve the clinical symptoms of the patients, and the cerebral hemodynamics of the patients tested by TCD found that this treatment yields an excellent therapeutic effect and is worthy of promotion and application.

Keywords: Transcranial doppler ultrasound, acute cerebral infarction, butylphthalide, cerebral hemodynamics.

INTRODUCTION

As a common disease in neurology, cerebral infarction, also called ischemic stroke, is more likely to affect middle-aged and elderly people. It is a blood supply disorder to the brain consequent to a variety of factors, resulting in hypoxic necrosis of local brain tissue, and further symptoms of neurological deficit (Park *et al*., 2019; Yuan *et al*., 2019; Zhang *et al*., 2019b). Providing no timely and effective treatment, symptoms such as dizziness and nausea are prone to occur. In severe cases, brain herniation, cerebral edema and other complications may arise, seriously threatening the patient's life and undermining their quality of life (Duan *et al*., 2019; Yang *et al*., 2019; Zhang *et al*., 2019a). In addition, acute cerebral infarction, arising in one month, is normally treated with thrombolytic therapy and brain protection therapy after being confirmed by cranial CT. It aims to control the development of the patient's condition, alleviate negative emotions, and mitigate clinical symptoms (Lei *et al*., 2019; Mofors *et al*., 2019; Wang Y. *et al*., 2019). Albeit the conventional treatment can produce certain curative effects, it remains clinically unsatisfactory due to its limited safety (Cheng *et al*., 2019; Liu *et al*., 2019). Related studies have found that butylphthalide generates an excellent clinical effect in the treatment of acute cerebral infarction. In this regard, we intended to explore the changes in cerebral hemodynamics in patients with acute cerebral infarction before and after treatment with butylphthalide drugs by transcranial Doppler ultrasound, by enrolling 90 patients with acute cerebral infarction admitted to our hospital from January 2019 to January 2020.

MATERIALS AND METHODS

Subjects

A total of 90 patients with acute cerebral infarction admitted to our hospital from January 2019 to January 2020 were selected and equally divided into the control group and the experimental group according to the order of admission.

Inclusion criteria

(1) Met the diagnostic criteria of acute cerebral infarction; (2) The onset time was less than 24h; (3) This study was approved by the hospital ethics committee, and the patient and his family members knew the purpose and process of the study and signed an informed consent form.

Exclusion criteria

(1) Patients with mental disorders; (2) Patients with other intracranial lesions or hemorrhage; (3) Patients with severe infection within 14 days before the onset.

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Methods

The control group was treated with conventional treatment, and the patients were given 10mg of atorvastatin (manufacturer: Pfizer Pharmaceutical Co., Ltd.; SFDA approval No.H20051407; specification: 10mg*7 tablets), once a day. In addition, patients were given aspirin (manufacturer: Bayer Healthcare Co., Ltd.; SFDA approval No.J20171021; Specification: 100mg*30 tablets), with first dose of 300mg, and addition of 100mg/d-200mg/d in the later period. Finally, on this basis, 75mg clopidogrel bisulfate tablets (manufacturer: Dr. Reddy`s Laboratories Limited; SFDA approval No. H20180074; specification 75mg*20 tablets) were given once a day.

In accordance with this treatment, the experimental group was additionally given butylphthalide drug treatment. 25mg butylphthalide sodium chloride injection (manufacturer: CSPC Enbipu Pharmaceutical Co., Ltd.; SFDA approval No. H20100041; Specification: 100ml : Butylphthalide 25mg and sodium chloride 0.9g) was intravenously given, 2 times a day, installation time>50min, interval time>6h; after the patient's condition was stable, 0.2g Butylphthalide soft capsule (manufacturer: Shiyao Group Enbipu Pharmaceutical Co., Ltd.; SFDA approval No.H20050299; Specification: 0.1g*24 capsules/bottle) was given 3 times a day.

Patients in both groups were treated for 2 months.

Observation indicators

A TCD detector (manufacturer: Nanjing Aosite Biotechnology Co., Ltd.; model: KJ-2V6M+) was used to check the hemodynamics of the two groups of patients, with a frequency of 2MHz. The hemodynamics included mean velocity (Vm), cranial arterial peak velocity (Vp) and pulsation index (PI).

The clinical efficacy of the two groups was compared and was considered markedly effective if the patient's NIHSS score reduced by ≥90%, and the limb dysfunction and cognitive dysfunction significantly disappeared; treatment was deemed effective if 45% ≥ NIHSS score <90%, and the limb dysfunction and cognitive dysfunction improved; on the other hand, it was regarded as ineffective if the patient's NIHSS score was less than 45%, and there was no change or aggravation of limb dysfunction and cognitive dysfunction.

3ml of venous blood was collected from the two groups of patients and sent to the clinical testing center for centrifugation within 30minutes after routine anticoagulation treatment. The enzyme-linked immunosorbent assay was used to detect the levels of Hcy and CysC of the two groups.

The *National Institute of Health Stroke Scale (NIHSS)* (Lyu *et al*., 2019) was used to evaluate and observe the brain nerve function of the two groups of patients before and after treatment. The total score of the scale was 42 points. The higher the score, the more severe the neurological damage of the patient.

The *Barthel Index (BI)* (Pego-Perez *et al*., 2019) was used to assess the patient's ability for daily living before and after treatment. The total score of the scale is 100 points. The higher the score, the better the ability of daily living of the patient.

The *mini-mental state examination (MMSE)* (Bhattacharyya *et al*., 2019) was used to assess the patient's mental state before and after treatment. The full score was 30 points. Higher scores indicated a better mental state.

Statistical analysis

All data were analyzed by SPSS20.0, and the graphics were plotted by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The count data and measurement data were examined by x^2 test, *t*-test and normality test. A *P*-value of <0.05 was claimed as statistically significant.

RESULTS

Comparison of general information of the two groups of patients

The two groups were not statistically different in terms of age, gender, BMI, average time of onset and diagnosis and treatment, past medical history, and place of residence (P>0.05) and they were comparable. See table 1.

Comparison of hemodynamic indexes between the two groups

The experimental group obtained better hemodynamic indexes as compared with the control group (P<0.05), see table 2.

Comparison of clinical efficacy between the two groups

The experimental group yielded a notably higher total clinical effective rate after treatment in contrast with the control group (P<0.05), as listed in table 3.

Comparison of serum indexes between the two groups

After treatment, the serum indexes of the experimental group were evidently lower than those of the control group (P<0.05), see table 4.

Comparison of NIHSS scores between the two groups

After treatment, a remarkably lower NIHSS score of the experimental group than the control group was observed (P<0.05), as displayed in fig. 1.

Comparison of BI index scores between the two groups

Fig. 2 showed that the BI index score of the experimental group after treatment was considerably higher than that of the control group (P<0.05).

Table 1: Comparison of general information of the two groups of patients

	Experimental group (n=45)	Control group (n=45)	x^2 or t	P
Age (year)			1.550	0.125
	60.25±3.32	61.33±3.29		
Gender			0.194	0.660
Male	30(66.67)	28(62.22)		
Female	15(33.33)	17(37.78)		
BMI(kg/m^2)			1.119	0.266
	26.27±1.59	25.89±1.63		
Average time of onset and treatment (h)			0.041	0.968
	4.12±1.21	4.13±1.11		
Disease history				
hypertension	27(60.00)	25(55.56)	0.182	0.670
diabetes	10(22.22)	9(20.00)	0.067	0.796
Hyperlipidemia	8(17.78)	11(24.44)	0.600	0.438
Place of residence			0.050	0.822
Town	31(68.89)	30(66.67)		
Rural area	14(31.11)	15(33.33)		

Table 2: Comparison of hemodynamic indexes between the two groups (x±s)

Groups	N	Vm(cm/s)		Vp(cm/s)		PI	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	45	25.88±2.25	38.27±2.88	55.27±3.12	69.21±4.23	0.91±0.07	0.53±0.05
Control group	45	25.79±2.31	31.15±2.42	55.31±3.07	61.35±3.89	0.89±0.09	0.89±0.07
t		0.187	12.697	0.061	9.175	1.177	28.073
P		0.852	<0.001	0.951	<0.001	0.242	<0.001

Table 3: Comparison of clinical efficacy between the two groups [n(%)]

Groups	N	Markedly effective	Effective	Ineffective	Total effective rate
Experimental group	45	66.67%(30/45)	31.11%(14/45)	2.22%(1/45)	97.78%(44/45)
Control group	45	46.67%(21/45)	26.67%(12/45)	26.67%(12/45)	73.33%(33/45)
x^2					10.879
P					<0.05

Table 4: Comparison of serum indexes between the two groups (x±s)

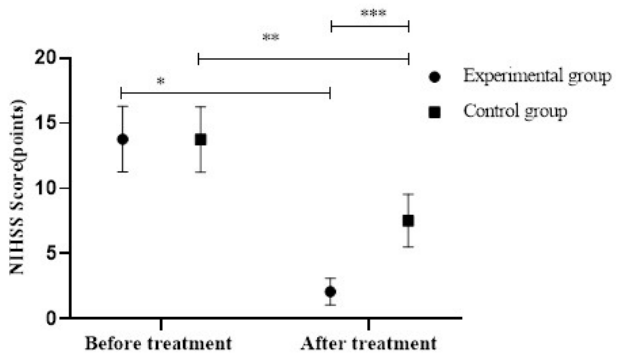
Groups	N	Hcy(μmol/L)		CysC(mg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Experimental group	45	26.11±3.72	13.25±2.13	1.91±0.41	0.89±0.16
Control group	45	26.12±3.69	18.96±3.02	1.92±0.43	1.51±0.27
t		0.013	10.365	0.113	13.252
P		0.989	<0.001	0.910	<0.001

Comparison of MMSE scores between the two groups

After treatment, the MMSE score in the experimental group was significantly higher than it was in the control group (P<0.05), as shown in fig. 3.

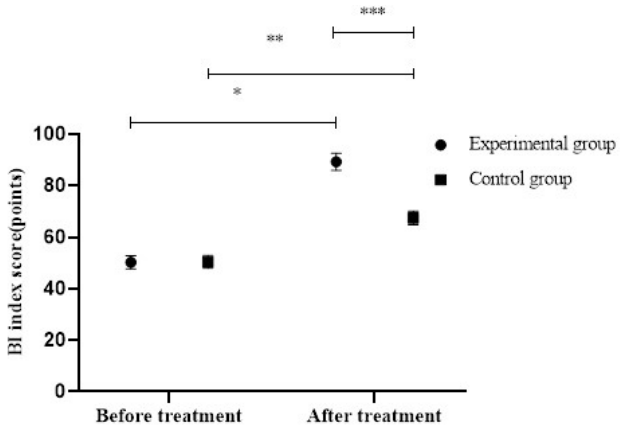
DISCUSSION

Cerebral infarction is characterized by rapid onset and rapid progress, with major manifestations such as limb hemiplegia and atherosclerosis is the main factor leading to cerebral infarction (Gao *et al*., 2019; Li *et al*., 2019; Wang Q. *et al*., 2019). In addition, brain lesions can easily damage the patient's frontal lobe, temporal lobe and peripheral systems and even lead to long-term oxygen and blood supply insufficiency in the patient's brain with the disease advancement, severely damaging the patient's nerve function (Galadanci *et al*., 2019; Vervliet *et al*., 2019). In light of this, an appropriate treatment plan should be urgently addressed that plays a crucial role in the prognosis of patients.



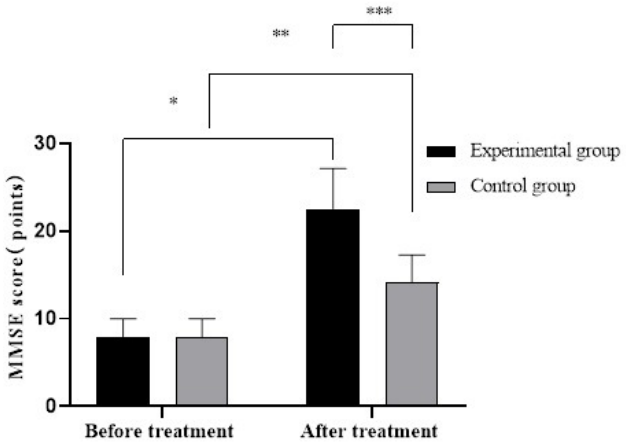
Note: The abscissa indicates before and after treatment, and the ordinate indicates the NIHSS score points;
The NIHSS scores of patients in the experimental group before and after treatment were (13.77±2.52) points and (2.09±1.02) points, respectively;
The NIHSS scores of the control group patients before and after treatment were (13.75±2.51) points and (7.53±2.02) points, respectively;
*indicates that the NIHSS scores of the experimental group patients before and after treatment are significantly different (t=28.821, P<0.001);
** indicates that there is a significant difference in the NIHSS scores of the control group before and after treatment (t=12.951, P<0.001);
***indicates that the NIHSS scores of the two groups of patients after treatment are significantly different (t=16.126, P<0.001).

Fig. 1: Comparison of NIHSS scores between the two groups (x±s)



Note: The abscissa represents before and after treatment, and the ordinate represents the BI index score points;
The BI index scores of patients in the experimental group before and after treatment were (50.32±2.56) points and (89.35±3.33) points, respectively;
The BI index scores of the control group before and after treatment were (50.45±2.47) points and (67.52±2.67) points, respectively;
* indicates that there is a significant difference in the BI index scores of the experimental group before and after treatment (t=62.334, P<0.001);
** indicates that there is a significant difference in the BI index scores of the control group before and after treatment (t=31.482, P<0.001);
*** indicates that there is a significant difference in the BI index scores of the two groups of patients after treatment (t=34.309, P<0.001).

Fig. 2: Comparison of BI index scores between the two groups (x±s)



Note: The abscissa represents before and after treatment, and the ordinate represents MMSE score points;
The MMSE scores of patients in the experimental group before and after treatment were (7.83±2.15) points and (22.53±4.61) points, respectively;
The MMSE scores of the control group before and after treatment were (7.85±2.17) points and (14.22±3.07) points, respectively;
*indicates that there is a significant difference in the MMSE scores of the experimental group before and after treatment (t=19.386, P<0.001);
**indicates that there is a significant difference in the MMSE scores of the control group before and after treatment (t=11.366, P<0.001);
***indicates that the MMSE scores of the two groups of patients after treatment are significantly different (t=10.065, P<0.001).

Fig. 3: Comparison of MMSE scores between the two groups (x±s)

Despite that conventional treatment emanates certain therapeutic effects, it remains clinically undesirable. Phthalide, as the first domestically developed and internationally innovative drug that acts on multiple pathological aspects of acute ischemic stroke, plays a role in improving cerebral perfusion and neurological deficits in ischemic areas (Galadanci *et al*., 2019; Hussain *et al*., 2019). Butylphthalide is a synthetic racemic n-butyl phthalide, which can block multiple pathological processes caused by cerebral ischemia, protect nerve cells, scavenge free radicals, increase antioxidant enzyme activity and improve central nervous system function (Wong *et al*., 2019). Relevant studies have found that butylphthalide has garnered a notable clinical effect in the treatment of acute cerebral infarction, with respect to improving brain energy metabolism and microcirculation of ischemic brain regions and promoting recovery. In the current study, the NIHSS score of the experimental group after treatment was significantly lower than that of the control group and the BI index obtained opposite results,

indicating that butylphthalide can effectively improve the brain nerve function of patients and patient's ability of daily living. TCD, characterized by reproducibility and non-invasiveness, can accurately detect changes in the patient's cerebral vascular hemodynamics. It can also detect the presence of occlusion and stenosis of the patient's intracranial blood vessels to provide an accurate reference for later treatment, thus it is widely used in neurosurgery (Herbert *et al*., 2019). The clinical manifestations of patients with cerebral infarction are mainly abnormal cerebrovascular reserve capacity and abnormal cerebral hemodynamics, and treatment with butylphthalide can effectively increase patient's blood perfusion and also optimize cerebral ischemia, stabilizing blood supply to the brain and accelerating patient's recovery. Our study found that the hemodynamic indicators of the experimental group were significantly better than those of the control group after being tested by TCD, suggesting that butylphthalide produces a promising result in improving the clinical indicators of patients of cerebral infarction.

In recent years, it has been clinically discovered that the development of acute cerebral infarction is closely related to the Hcy and CysC in the serum. With the presence of vascular damaging amino groups, more Hcy deposited in the blood vessel would cause an over-reaction and peroxidation stress response of the endoplasmic reticulum stress mechanism, leading to vascular endothelial cell damage and dysfunction symptoms, thereby inducing vasoconstriction. CysC, as a non-glycosyl molecule basic protein, can damage vascular endothelium and cause thickening of the vascular wall, resulting in the formation of atherosclerotic plaques. In the present study, the experimental group that was treated with butylphthalide witnessed a substantially lower Hcy index and CysC index, indicating that the butylphthalide drug can drastically inhibit the serum Hcy index and CysC expression in patients. Remarkably, we found that a higher total clinical effective rate was observed in the experimental group in comparison with the control group, which was in line with the results of NING *et al*. (Ning *et al*., 2019) who pointed out that the total effective rate of treatment in the observation group was better than the control group (96.00% vs 75.00%). Taken together, it indicates that butylphthalide yields an excellent therapeutic value for patients with acute cerebral infarction beyond the conventional treatment.

CONCLUSION

To sum up, butylphthalide is a boon for patients with acute cerebral infarction in terms of improving the patient's brain nerve function, enhancing the patient's daily activity ability and mental state. It is therefore worthy of promotion and application.

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