Clinical Effect of Butylphthalide Combined with Rt-PA Intravenous Thrombolysis in the Treatment of Acute Cerebral Infarction

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Objective. To assess the clinical effect of butylphthalide combined with rt-PA intravenous thrombolysis in the treatment of acute cerebral infarction (ACI).

Methods. Totally, 312 acute cerebral infarction patients were included in this research. Those in the group for experiment received butylphthalide (25 mg QD) combined with rt-PA intravenous thrombolysis (0.9 mg/kg QD), while the control group received rt-PA intravenous (P < 0.05). Moreover, NIHSS (NIH Stroke Scale/Score) and Barthel index scores in the two groups improved, NIHSS score had ameliorated, and Barthel index score was higher than that in the reference group (P < 0.05).

Conclusion. The combination of butylphthalide and recombination plasminogen activator alteplase (rt-PA) intravenous thrombolysis has a significant clinical effect in the treatment of acute cerebral infarction. It can alleviate the inflammatory symptoms, accelerate the recovery of neurological function, and improve the ability of daily living.

1. Introduction

Acute cerebral infarction is one of the common diseases in neurology, most of which are ischemic stroke [1]. Its clinical characteristics are acute onset and severe symptoms, with a high disability rate and high mortality rate [2, 3]. At present, drug treatment is still the main treatment for acute cerebral infarction all over the world. The need for intravascular treatment is determined after the evaluation and screening of cranial CTA, but thrombolysis and intravascular treatment are still limited by time [4, 5]. Even after thrombolysis and thrombectomy, some patients still cannot recover their function quickly or their neurological function deteriorates [6]. At present, the ideal time for the treatment of cerebral infarction is the brain [7]. Appropriate drugs are used to improve the blood supply in the infarct area in the early stage of the disease protect brain cells improve neurological deficit. At present, for the early stage of cerebral infarction, butylphthalide is also one of the recommended drugs to improve neurological symptoms in addition to the routine use of antiplatelet and stabilizing drugs [8, 9].

Butylphthalide is a drug extracted from celery seed [10]. It targets multiple pathophysiological mechanisms in the pathogenesis of cerebral infarction [11]. Among them, the effect of improving brain tissue circulation has been confirmed. Butylphthalide treatment within a few hours after the occurrence of acute cerebral infarction stroke model can improve the maintenance of blood vessel diameter at the normal level and reduce thrombosis, and local cerebral blood flow improved [12]. Neurite growth is the basis of nervous system development, and a good connection between neurons is the cornerstone of normal neural function [13]. For patients with cerebral infarction, promoting the growth of neuronal synapses and accurate good connection might improve the prognosis, while NBP can increase the expression of growth-related protein 43 (GAP43) to activate the SHH signaling pathway [14, 15]. It can promote the extension of neurites and the growth of branches and improve the complexity of neurites and the plasticity of neuronal development, so as to improve the prognosis [16].

In our research, we compared the hs-C-reaction protein (CRP), IL-6, NIHSS Barthel index, clinical therapeutic
To process data, and the counting and measuring data are expressed in N/%, X ± s, and χ². T-test was used for comparison data between two groups. P < 0.05, the difference was statistically significant.

### 2. Data and Methods

#### 2.1. Clinical Data

This study was conducted at Lanzhou People’s Hospital from July 2019 and July 2021. This study has gained recognition from the ethics department in our hospital.

##### 2.1.1. Inclusion and Exclusion Standard

1. **Inclusive Standard.** (1) The onset ≤ 72 h; (2) the patients were diagnosed with acute ischemic stroke; (3) compliance with thrombolytic indications; (4) signed the consent form for voluntary participation.

2. **Exclusion Standard.** (1) Treated with intravenous thrombolysis after admission; (2) had malignant tumor or mental disease; (3) had to sever liver, kidney, and heart disorder; (4) had contraindications to thrombolysis.

#### 2.2. Method

In the experimental group, the patients received the combination of butylphthalide (Shijiazhuang Pharmaceutical Group Enbipu Pharmaceutical Co., Ltd.) (25 mg QD) and rt-PA intravenous thrombolysis (China Resources and Biological Pharmaceutical Co., Ltd.) (0.9 mg/kg QD) once a day at the left arm. This control lasted up to 14 days.

In the control group, the patients received rt-PA intravenous thrombolysis (China Resources and Biological Pharmaceutical Co., Ltd) (0.9 mg/kg QD) once a day at the left arm. This control lasted up to 14 days.

##### 2.3. Observation Index

After treatment, biochemical detection and inflammatory and oxidative stress indicators were collected. Moreover, we recorded NIHSS and Barthel index scores to assess patients’ activities of daily living.

##### 2.4. Statistical Analysis

SPSS22.0 statistical software is used to process data, and the counting and measuring data are expressed in N/%, X ± s, and χ². T-test was used for comparison data between two groups. P < 0.05, the difference was statistically significant.

### 3. Results

#### 3.1. Clinical Characteristics

Table 1 shows the characteristics of subjects. The results showed that there had no statistical difference in age, gender, BMI, history of smoking, drinking, etc. (P > 0.05).

#### 3.2. Comparison between the Experimental and Control Groups before and after Intervention

The NIHSS (scores) in the experimental group after intervention were lower than that in the control group, 8.44 ± 2.17 and 15.19 ± 2.07, respectively. While the Barthel index score in the experimental group after intervention was significantly higher than that in the control group, 79.77 ± 6.19 and 15.19 ± 2.07, respectively (P < 0.05, Table 2).

#### 3.3. Comparison of Inflammatory Indicators between the Experimental and Control Groups

The NIHSS score and Barthel index score of the two groups were improved after intervention (P < 0.05, Table 2). The level of hs-CRP and IL-6 in the experimental group after intervention were lower than that in the control group, 8.44 ± 2.17 and 15.19 ± 2.07, respectively (P < 0.05, Table 2). The level of hs-CRP and IL-6 in the experimental group was lower than in the control group (P < 0.05, Table 2). The level of hs-CRP and IL-6 in the experimental group was lower than in the control group (P < 0.05, Table 2). The level of hs-CRP and IL-6 in the experimental group was lower than in the control group (P < 0.05, Table 2).

#### 3.4. Comparison of Clinical Therapeutic Effect and Safety Index between the Experimental and Control Groups

As shown in Table 4, the total effective rate was improved after butylphthalide was combined with rt-PA intravenous thrombolysis treatments (P < 0.05 *). After the intervention, the safety index had no statistical difference after intervention between the two groups (P > 0.05). This treatment is safe for participants (Table 5).

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**Table 1: Comparison of clinical characteristics of acute cerebral infarction complicated with microhemorrhage patients between two groups.**

|                   | Experimental group (n = 164) | Control group (n = 148) | t/χ²   | P   |
|-------------------|-------------------------------|-------------------------|--------|-----|
| Age (years)       | 54 ± 4.15                     | 55 ± 2.75               | 2.25   | 0.61|
| Sex               |                               |                         |        |     |
| Male (n%)         | 89 (54.3%)                    | 77 (52.0%)              | 4.68   | 0.58|
| Female (n%)       | 75 (45.7%)                    | 71 (48.0%)              | 4.49   | 0.43|
| BMI               | 22.5 ± 3.16                   | 23.35 ± 2.43            | 1.39   | 0.34|
| Smoking           | 78 (47.6%)                    | 72 (48.6%)              | 6.71   | 0.55|
| Alcohol intake    |                               |                         |        |     |
| More than 14 alcohol units | 75 (45.7%) | 69 (46.6%) | 2.96 | 0.42|
| Less than 14 alcohol units | 89 (54.3%) | 79 (53.4%) | 6.18 | 0.37|
| Hypertension      | 67 (40.9%)                    | 59 (39.9%)              | 1.79   | 0.16|
| Diabetes          | 58 (35.4%)                    | 49 (33.1%)              | 1.29   | 0.49|
| Coronary heart disease | 48 (29.3%) | 44 (29.7%) | 0.63 | 0.51|

Note: compared with control group, significant difference as P < 0.05.
Table 2: Comparison of NIHSS and Barthel index score between the two groups before and after intervention (x ± s).

|                     | Experimental group (n = 164) | Control group (n = 148) | t/χ² | P      |
|---------------------|------------------------------|-------------------------|------|--------|
| NIHSS (scores)      |                              |                         |      |        |
| Before intervention | 23.08 ± 3.19                 | 22.14 ± 3.13            | 4.76 | 0.17   |
| After intervention  | 8.44 ± 2.17                  | 15.19 ± 2.07            | 7.25 | ≤0.001*|
| Barthel index score (scores) |                |                         |      |        |
| Before intervention | 55.62 ± 5.71                 | 59.77 ± 6.19            | 0.21 | 0.87   |
| After intervention  | 79.77 ± 6.19                 | 71.44 ± 5.62            | 7.94 | ≤0.001*|

Note: compared with control group, significant difference as P < 0.05. NIHSS: National Institutes of Health Stroke Scale.

Table 3: Comparison of inflammatory indicators between the two groups before and after intervention (x ± s).

|                     | Experimental group (n = 164) | Control group (n = 148) | t/χ² | P      |
|---------------------|------------------------------|-------------------------|------|--------|
| hs-CRP (mg/L)       |                              |                         |      |        |
| Before intervention | 5.09 ± 1.03                  | 4.97 ± 1.03             | 3.26 | 0.08   |
| After intervention  | 4.08 ± 1.06                  | 4.60 ± 0.99             | 10.75| ≤0.001*|
| IL-6 (ng/L)         |                              |                         |      |        |
| Before intervention | 9.82 ± 1.83                  | 9.78 ± 1.74             | 0.238| 0.093  |
| After intervention  | 3.57 ± 0.89                  | 6.32 ± 1.15             | 6.323| 0.0002*|

Note: compared with control group, significant difference as P < 0.05. hs-CRP: high sensitivity C-reactive protein.

4. Discussion

Acute cerebral infarction usually occurs when the blood flows to the brain tissue. Hypoxia causes the primary injury of a certain region of the brain. The amount of blood flow passing through brain tissue in a unit of time largely depends on the lumen thickness of blood vessels and the abundance of collateral circulation vessels. Because the brain cannot store energy, once hypoxia leads to energy supply disorder, it will cause irreversible damage [21]. The longer the duration of cell ischemia and the more serious the degree of ischemia, the more cell necrosis will occur [22]. In this study, the total effective rate of treatment in the experimental group was significantly higher than that in the control group. Moreover, NIHSS scores and Barthel index scores in the two groups improved, and the NIHSS score in the study group was lower than that in the reference group, and the Barthel index score was higher than that in the reference group (P < 0.05). The safety index had no statistical difference from those without accepting the intervention.

Intravenous thrombolysis is an important method for the clinical treatment of acute ischemic cerebral infarction. It can effectively restore cerebral blood perfusion and remove arterial thrombosis. rt-PA is a glycoprotein with a high affinity with fibrin. The combination of the two shows high activity. It can activate plasminogen to become plasmin, so as to dissolve thrombus [24]. rt-PA has no antigenicity and can be reused. It has the characteristics of antiplatelet aggregation, improving microcirculation and increasing arterial blood flow. Sodium butylphthalide chloride is a synthetic racemic n-butylphthalide, which can significantly improve brain nerve injury and has a strong anti-ischemic effect [25]. It can reduce the area of cerebellar infarction, alleviate the symptoms of brain edema, improve brain energy metabolism, blood flow, and microcirculation, and prolong the life cycle slow nerve cell apoptosis, antiplatelet aggregation, so as to protect brain nerves [26, 27].

Relevant studies have also pointed out that the secondary injury caused by inflammatory factors is an important factor leading to the deterioration of patients with cerebral infarction [28]. Serum hs CRP and IL-6 play an important role in the development of cerebral infarction, and their levels are positively correlated with the area of cerebral infarction. The level in the experimental group was lower than that in the control group, indicating that the combined treatment has a definite effect, can effectively alleviate inflammatory symptoms, and help to avoid secondary injury. The results also showed that after treatment, the NIHSS score and

Table 4: Comparison of clinical therapeutic effect between the two groups (n(%)).

|                     | Experimental group (n = 164) | Control group (n = 148) | χ²  | P      |
|---------------------|------------------------------|-------------------------|-----|--------|
| Significant effective| 54 (32.6%)                   | 32 (21.4%)              | 7.268| 0.007*|
| Effective           | 92 (55.8%)                   | 42 (28.6%)              | 9.737| 0.012*|
| Ineffective         | 19 (11.6%)                   | 74 (50.0%)              | 4.061| 0.003*|
| Total effective rate| 146 (88.4%)                  | 74 (50.0%)              | 6.378| 0.002*|
| t                  | 4.857                        | 5.732                   | —   | —      |
| P                  | 0.13                         | 0.21                    | —   | —      |

Note: compared with control group, significant difference as P < 0.05.
Barthel index score of the two groups were improved, indicating that the combined treatment can accelerate the recovery of neurological function and improve the ability of daily life, which was consistent with Wang et al.’s research [29].

The advantage of this study was to demonstrate the combination of butylphthalide and rt-PA intravenous thrombolysis on the treatment of acute cerebral infarction. It is undeniable that this study has many deficiencies, such as regional, racial, single, accidental, and small numbers. As a retrospective study, the results are biased. In addition, the model lacks large sample population verification, and its effectiveness needs to be tested. This study further explored the evaluation of the severity of cerebral infarction and provided a clinical reference for large-scale marker screening and combination.

5. Conclusion

The combination of butylphthalide and rt-PA intravenous thrombolysis has a significant clinical effect in the treatment of acute cerebral infarction. It can alleviate the inflammatory symptoms, accelerate the recovery of neurological function, and improve the ability of daily living.

Data Availability

The data used to support this study is available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] W. Huijun and L. Maikou, "Correlation analysis between serum procalcitonin and infarct volume in young patients with acute cerebral infarction," Neurological Sciences, vol. 42, no. 8, pp. 3189–3196, 2021.

[2] G. Xiaohong, W. Liping, W. Chenglong, H. Wang, and J. Kong, "Prognosis of subtypes of acute large artery atherosclerotic cerebral infarction by evaluation of established collateral circulation," Journal of Stroke and Cerebrovascular Diseases, vol. 29, no. 11, article 105232, 2020.

[3] W. Qiang, Y. Dan, L. Ji, Q. Cheng, F. Zhou, and H. Lin, "Significance of expression of AIM2, IL1β, and IL18 in plasma of patients with acute cerebral infarction," Zhong Nan Da Xue Xue Bao. Yi Xue Ban, vol. 46, pp. 149–155, 2021.

[4] X. Min, H. Xiao-Ying, and H. Pan, "The relationship between the mean platelet volume and carotid atherosclerosis and prognosis in patients with acute cerebral infarction," BioMed Research International, vol. 2020, Article ID 6685740, 2020.

[5] Z. Yuan, Z. Yongbo, and Y. Yishu, "Acute cerebral infarction with adenomyosis in a patient with fever: a case report," BMC Neurology, vol. 20, no. 1, p. 210, 2020.

[6] X. Min, H. Xiao-Ying, and H. Pan, "The value of combined detection of D-dimer and CD62p in judging the severity of acute cerebral infarction and short-term prognosis," BioMed Research International, vol. 2021, Article ID 6620311, 2020.

[7] W. Zi-Yi, W. Meng, G. Jiao-Jiao, Y. Gao, and X. F. Yu, "Acute bilateral cerebral infarction in the presence of neuro-myelitis optica spectrum disorder," Medicine (Baltimore), vol. 99, no. 40, article e22616, 2020.

[8] R.-X. Hu, D.-D. Yu, H. M. Li et al., "Exploring efficacy of Chinese medicine injection for promoting blood circulation and removing blood stasis in treatment of acute cerebral infarction based on two complex network analysis methods," Zhongguo Zhong Yao Za Zhi, vol. 46, pp. 3722–3731, 2021.

[9] L. Zongqin, R. Xiaoxia, L. Jun, T. Zeng, P. Huang, and X. Xu, "A single-center clinical study to evaluate Shenziong glucose injection combined with edaravone in the treatment of acute large-area cerebral infarction," BioMed Research International, vol. 2021, 2021.

[10] Z. Xiao-Lei, Y.-T. Dong, L. Yi, Y. Zhang, T. T. Li, and F. Y. Hu, "Effects of dl-3-n-butyphthalide on serum lipoprotein-associated phospholipase A2 and hypersensitive C-reactive protein levels in acute cerebral infarction," Brain and Behavior, vol. 9, p. e01469, 2019.

[11] M. Wang, Y. Feng, Y. Yuan et al., "Use of l-3-n-butyphthalide within 24 h after intravenous thrombolysis for acute cerebral infarction," Complementary Therapies in Medicine, vol. 52, article 102442, 2020.

[12] S.-C. Tang, C.-J. Luo, K.-H. Zhang et al., "Effects of dl-3-n-butyphthalide on serum VEGF and bFGF levels in acute cerebral infarction," European Review for Medical and Pharmacological Sciences, vol. 21, no. 19, pp. 4431–4436, 2017.

[13] L. Cunfang, C. Aijun, G. Yongchao, X. Qi, and X. Zheng, "Combination of tetrandrine and 3-n-butyphthalide protects against cerebral ischemia-reperfusion injury via ATF2/TLR4

### Table 5: Comparison of safety index between two groups (x ± s).

| Group               | Time          | AST       | ALT       | CK         | Cr         |
|---------------------|---------------|-----------|-----------|------------|------------|
|                     | Before intervention | 29.63 ± 5.62 | 29.38 ± 6.20 | 82.04 ± 5.97 | 80.48 ± 6.84 |
|                     | After intervention | 29.92 ± 5.52 | 29.84 ± 5.54 | 82.61 ± 7.03 | 81.94 ± 7.05* |
| t                   | 2.458         | 3.071     | 1.837     | 4.972      |            |
| P                   | 0.86          | 0.79      | 0.88      | 0.24       |            |
| Control group (n = 148) | Before intervention | 29.27 ± 5.21 | 30.04 ± 4.97 | 79.83 ± 6.38 | 80.03 ± 5.97 |
|                     | After intervention | 29.67 ± 4.97 | 30.64 ± 6.48 | 79.46 ± 6.58 | 81.31 ± 4.39 |
| t                   | 1.278         | 2.131     | 1.921     | 4.549      |            |
| P                   | 0.63          | 0.45      | 0.83      | 0.19       |            |

Note: compared with the control group, P < 0.05 *. AST: aspartate aminotransferase; ALT: alanine aminotransferase; CK: creatine kinase; Cr: creatinine.
pathway,” *Immunopharmacology and Immunotoxicology*, vol. 43, no. 6, pp. 749–757, 2021.

[14] R. Du, J. F. Teng, Y. Wang, X. Y. Zhao, and Z. B. Shi, “Clinical study of butylphthalide combined with Xue Shuan Tong on serum inflammatory factors and prognosis effect of patients with cerebral infarction,” *Pakistan Journal Of Pharmaceutical Sciences*, vol. 28, pp. 1823–1827, 2015.

[15] K. Xie, Z. Shuzhi, and L. Xiaoning, “Efficacy and mechanism of butylphthalide combined with atorvastatin calcium tablets in the diagnosis of cerebral infarction using Iodol/Fe₃O₄ magnetic contrast agent,” *Journal of Nanoscience and Nanotechnology*, vol. 20, no. 12, pp. 7356–7361, 2020.

[16] Q. Fan-Xing, H. Ying, and W. Sen, “Clinical observation of thrombolytic effect of alteplase combined with butylphthalide in patients with acute anterior circulation cerebral infarction,” *Pakistan Journal of Medical Sciences*, vol. 37, no. 4, pp. 1145–1150, 2021.

[17] L. Yu-Xin, C. Qiu-Mei, and M. Bing-Chen, “Pathogens distribution and drug resistance in patients with acute cerebral infarction complicated with diabetes and nosocomial pulmonary infection,” *BMC Infectious Diseases*, vol. 19, no. 1, p. 603, 2019.

[18] L. Qun-Xi, Z. Xiao-Jing, P. Yan-Bo et al., “A prospective study of comparing the application of two generation scoring systems in patients with acute cerebral infarction,” *Advances in Therapy*, vol. 36, pp. 3071–3078, 2019.

[19] L. Ying-Ying, G. Shi-Jie, Q. Hui, Y. X. Zhao, and D. Y. Huang, “Donepezil improves gait performance in patients with an acute cerebral infarction: a prospective observational cohort study,” *Current Neurovascular Research*, vol. 17, no. 3, pp. 304–311, 2020.

[20] Y. Liu, M. Qu, N. Wang, and L. Wang, “Effects of an evidence-based nursing intervention on neurological function and serum inflammatory cytokines in patients with acute cerebral infarction: a randomized controlled trial,” *Restorative Neurology and Neuroscience*, vol. 39, no. 2, pp. 129–137, 2021.

[21] F. Sun, H. Liu, H. X. Fu et al., “Comparative study of intravenous thrombolysis with rt-PA and urokinase for patients with acute cerebral infarction,” *The Journal of International Medical Research*, vol. 48, no. 5, 2020.

[22] L. Gang, H. Chong, X. Xiangping, and S. Yao, “Relationship of uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide with acute cerebral infarction,” *Revista da Associação Médica Brasileira*, vol. 67, pp. 1639–1643.

[23] O. Ryo, N. Michikazu, N. Shinseuke et al., “Pretreatment blood pressure is a simple predictor of hemorrhagic infarction after intravenous recombinant tissue plasminogen activator (rt-PA) therapy,” *Journal of Stroke and Cerebrovascular Diseases*, vol. 28, no. 7, pp. 1979–1986, 2019.

[24] M. Atsunori, E. Toshihiro, N. Tomoya, and S. Terao, “Thrombolytic recombinant tissue plasminogen activator (rt-PA) treatment in the acute ischemic stroke with limb arterial embolism; three case reports,” *Rinshō Shinkeigaku*, vol. 60, no. 3, pp. 223–228, 2020.

[25] X.-R. Lee and X. Gui-Ling, “Effects of edaravone, the free radical scavenger, on outcomes in acute cerebral infarction patients treated with ultra-early thrombolysis of recombinant tissue plasminogen activator,” *Clinical Neurology and Neurosurgery*, vol. 167, pp. 157–161, 2018.

[26] Y.-J. Yu and W. Xiong, “Tirofiban combined with rt-PA intraarterial thrombolysis improves the recanalization rate of acute middle cerebral artery occlusion in rabbits,” *European