Efficacy of Butylphthalide Injection in Conjunction with Citicoline Sodium in Treating Ischemic Stroke

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To observe the clinical efficacy of butylphthalide injection in conjunction with citicoline sodium in treating ischemic stroke. From January 2022 to January 2023, our hospital admitted and randomly assigned 100 patients with acute ischemic stroke into two groups, control group and observation group. Each group consisted of 50 patients. Routine neurological treatment was administered to the control group, involving interventions such as fluid replacement, blood pressure control, lipid regulation, anticoagulation, correction of electrolyte imbalance, and intravenous infusion of butylphthalide injection. In addition to the standard treatment received by the control group, the observation group orally received citicoline sodium tablets. The assessment of therapeutic efficacy took place after duration of 2 w in both groups. Assessment of neurological injury repair was conducted using the national institutes of health stroke scale, while cognitive function recovery was evaluated through the implementation of the Montreal cognitive assessment scale. Utilizing computed tomography scan, cerebral blood volume and cerebral blood flow were quantified. The evaluation of activities of daily living was carried out employing the activities of daily living scale. Moreover, any adverse reactions occurring during the treatment period were duly documented. The occurrence of adverse reactions did not show a significant difference between the two groups, as reflected by a ($p>0.05$) that indicated no noteworthy disparity. When used in conjunction, butylphthalide injection and citicoline sodium exhibit a synergistic effect in treating ischemic stroke. This integrated treatment approach effectively promotes the repair of neurological injury and enhances cognitive function recovery. Furthermore, it improves cerebral blood flow perfusion and enhances daily life functionality, while maintaining a high level of safety.

Key words: Butylphthalide, citicoline sodium, ischemic stroke, clinical efficacy

Impaired blood flow to the brain resulting in ischemic and hypoxic damage to brain tissue characterizes ischemic stroke as a clinically critical condition. Prevalent symptoms of this condition encompass dizziness and impaired consciousness. Neglecting prompt treatment may result in profound deficits in neurological function and a heightened susceptibility to disability and death[1,2]. Currently, clinical management of ischemic stroke focuses on early restoration of cerebral blood circulation and alleviation of neural damage to prevent disease progression and relieve clinical symptoms[3,4]. Butylphthalide inhibits multiple pathological processes associated with ischemic brain injury in acute ischemic stroke[5,6]. With an increasing body of reports, evidence from evidence-based medicine continues to strengthen the case for the positive influence of butylphthalide on improving central nervous system function and enabling functional recovery in patients with acute ischemic stroke[7,8]. Acting as a coenzyme in phospholipid synthesis, citicoline sodium plays a critical role in activating brain metabolism[9]. It promotes brain function, enhances the ascending reticular activating system, decreases cerebral vascular resistance, and improves cerebral blood circulation, oxygenation, and brain metabolism. Moreover, within the human body, citicoline sodium assumes a vital role as an essential building block of biological membranes[10,11]. Despite research exploring the effectiveness of combining butylphthalide and citicoline sodium for ischemic stroke treatment, the current findings lack consensus. Consequently, this study seeks to perform an in-depth analysis of the combined therapeutic efficacy

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of butylphthalide and citicoline sodium in treating ischemic stroke. By providing more accurate and reliable evidence, this research strives to enhance the utilization of these treatments, leading to improved patient prognosis and life quality. This study included 100 individuals with acute ischemic stroke who received treatment at our hospital between January 2022 and January 2023. A random assignment was made, allocating the individuals into either the control group or the observation group, where each group consisted of 50 cases. With ages ranging from 35 y to 69 y and an average age of (57.49±22.15) y, the control group consisted of 24 males and 26 females. The mean Body Mass Index (BMI) was (24.32±3.56) kg/m^2, and the duration of the disease was (29.68±6.34) h. Within the observation group, there were 27 male and 23 female participants, aged between 38 y and 72 y, with a mean age of (59.52±21.58) y. The BMI averaged (24.33±3.76) kg/m^2, and the disease duration was (31.34±6.07) h. The general data did not exhibit any noteworthy distinctions between the two groups ($p>0.05$). The Hospital Ethics Committee granted approval for this study. Inclusion criteria includes, meeting the diagnostic criteria for acute ischemic stroke outlined in the 8th edition of "Internal Medicine"[12]; onset of first-ever stroke within ≤48 h from symptom onset to hospital admission; absence of any coagulation function abnormalities and no recent use of medications that influence coagulation function, such as warfarin. In exclusion criteria, the patients experiencing gastrointestinal bleeding; patients with known allergies to the study medications and patients with a prior history of intracerebral hemorrhage were excluded. As part of their management, patients in the control group underwent routine treatment within the neurology department. This included fluid supplementation, blood pressure control, lipid-lowering therapy, anticoagulation, electrolyte imbalance correction, and symptomatic management. Simultaneously, within 48 h of symptom onset, patients also received intravenous infusion of butylphthalide and sodium chloride injection (manufactured by Shiyao Group Enbipu Pharmaceutical Co., Ltd., with a specification of 100 ml:25 mg:0.9 g and National Medical Products Administration Approval Number: H20100041). Administered twice daily, each infusion consisted of a dosage of 25 mg, with a required minimum interval of 6 h between infusions. The infusion process itself lasted a minimum of 50 min. This treatment regimen was continued for a period of 2 w. The observation group received citicoline sodium tablets (manufactured by Sichuan Zitonggong Pharmaceutical Co., Ltd.) orally, with a specification of 0.2 g×12 tablets. These tablets were administered alongside the treatment provided to the control group. Administered three times daily, the observation group received a dosage of 0.2 g per time for 2 w. After this treatment duration, the efficacy of both groups was evaluated. The evaluation of neurologic recovery and cognitive function improvement involved the use of the National Institutes of Health Stroke Scale (NIHSS)[13] and the Montreal Cognitive Assessment (MoCA)[14], conducted before and after the 2 w treatment period. NIHSS scores span from 0 to 42, denoting varying degrees of impairment. Normal function is represented by a score of 0-1, while mild impairment is indicated by a score of 2-4. Scores ranging from 5-15 suggest moderate impairment, 16-20 denote moderate-to-severe impairment, and scores exceeding 20 reflect severe impairment. With a total score of 30, the MoCA evaluates 8 cognitive domains through 11 items. A score of 26 or higher is considered within the range of normal cognitive function. Prior to and after the 2 w treatment period, dynamic scanning in the transverse plane was carried out using a Siemens SOMATOM definition AS64 64-slice spiral Computed Tomography (CT) machine. Post-acquisition, the images were transferred to the workstation for processing and analysis. Regions of Interest (ROI) were carefully designated, with CT values exceeding 120 Hu or below 30 Hu being disregarded to mitigate the influence of the skull and cerebrospinal fluid. The mean values obtained from four ROIs were documented as the final measurements for Cerebral Blood Volume (CBV) and Cerebral Blood Flow (CBF). The Activities of Daily Living (ADL) scale was administered for evaluation both prior to and following the 2 w treatment period[15]. This scale encompasses two sections; physical self-care ability and instrumental ADL. In the assessment, there are 6 items in the section evaluating physical self-care ability, while the section encompassing instrumental ADL includes 8 items. Scoring was conducted on a 4-point scale, with a score of 14-16 indicating normal function, 17-21 denoting some degree of impairment, and a score of 22 or higher indicating significant impairment. During the treatment period, the occurrence of adverse reactions was carefully tracked and documented, facilitating a

comparison of the incidence between the two groups. Statistical Package for the Social Sciences (SPSS) 25.0 will be employed to perform the statistical analysis in this research. Continuous variables will be presented as means and standard deviations, and their analysis will be conducted using t-tests. Categorical variables, on the other hand, will be expressed as frequencies and percentages (n (%)) and assessed using Chi-square (χ^2) tests. To establish statistical significance, a threshold of $p<0.05$ will be utilized. Before treatment, no remarkable differences in NIHSS and MoCA scores was identified between the two groups ($p>0.05$). However, following a 2 w treatment period, both groups exhibited a noteworthy reduction in NIHSS scores and improvement in MoCA scores. Notably, the observation group demonstrated a remarkable difference as opposed to the control group ($p<0.05$) (Table 1). Prior to treatment, no marked differences in CBV and CBF was found between the two groups ($p>0.05$). However, following a 2 w treatment period, both groups exhibited remarkable increases in CBV and CBF, with the observation group displaying notably higher values when compared to the control group ($p<0.05$) (Table 2). Prior to treatment, no noteworthy differences in ADL scores for physical self-care ability and instrumental ADL was observed between the two groups ($p>0.05$). Following a 2 w treatment period, both groups exhibited a remarkable decrease in scores for physical self-care ability and instrumental ADL. Notably, the observation group displayed a more pronounced reduction when compared to the control group ($p<0.05$) (Table 3). Throughout the treatment period, both groups encountered adverse reactions such as nausea, decreased appetite, headache, and insomnia. Nevertheless, the incidence of adverse reactions did not exhibit any notable difference between the observation group (16.0 %) and the control group (14.0 %) ($p>0.05$) (Table 4). An acute cerebrovascular disorder, ischemic stroke is marked by the sudden compromise of cerebral blood circulation, which subsequently triggers ischemic and reperfusion damage to brain tissue. The main causes of brain injury are reduced CBF and secondary damage caused by inflammation processes, among others. Severe injury or untreated cases can result in varying degrees of residual neurological impairments, such as motor dysfunction, speech impairment, and swallowing difficulties. Thus, the reduction and prevention of reperfusion injury, along with minimizing ischemic damage, play a critical role in improving patient outcomes[16-18]. According to the study findings, the combined use of butylphthalide and citicoline sodium demonstrated a notable therapeutic effect in patients with ischemic stroke. The improvements observed in NIHSS and MoCA scores following treatment suggest the potential advantages of the combination therapy in promoting neurologic recovery and cognitive function improvement. Following treatment, noticeable disparities were observed between the observation group (receiving butylphthalide and citicoline sodium) and the control group (receiving standard therapy) in terms of CBV and CBF, as determined by spiral CT imaging. Notably, the observation group exhibited significantly higher values of CBV and CBF, indicating the positive impact of the combined therapy on enhancing cerebral perfusion. Furthermore, ADL were assessed, including physical self-care ability and instrumental ADL. The scores for both physical self-care ability and instrumental ADL remarkably decreased in both groups after treatment, with a more pronounced reduction observed in the observation group, indicating a positive impact of the combination therapy on improving patient's daily life functions. Several adverse reactions, such as nausea, decreased appetite, headache, and insomnia, were observed during the treatment period, but the incidence of adverse reactions did not differ substantially between the observation and control groups. Based on the obtained results, it can be inferred that the combination therapy of butylphthalide and citicoline sodium demonstrates a definite therapeutic effect in patients with ischemic stroke. This treatment approach has the potential to promote neurologic recovery, cognitive function improvement, cerebral perfusion, and daily life functions. Although some adverse reactions may occur during treatment, overall, the combination therapy appears to be safe. However, it should be acknowledged that this study has limitations, including a limited sample size and a relatively short duration of observation. Hence, it is essential to conduct extensive and prolonged clinical trials to thoroughly evaluate the efficacy and safety of the combination therapy. Moreover, further investigation is warranted to determine optimal medication dosages, treatment duration, and considerations regarding indications and contraindications.

TABLE 1: NIHSS AND MoCA SCORES

Group (n=50)	NIHSS		MoCA	
	Before	After	Before	After
Observation	21.54±5.09	9.88±2.54*	15.58±4.92	24.8±4.38*
Control	20.80±5.10	17.36±4.42*	15.78±4.95	18.56±4.43*
t	-0.726	10.370	0.203	-7.082
p	0.469	0.000	0.840	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 2: CEREBRAL PERFUSION INDEXES

Group (n=50)	CBV (ml/100 g)		CBF (ml/(100 g/min))	
	Before	After	Before	After
Observation	1.76±0.32	2.32±0.20*	17.95±2.59	24.26±2.86*
Control	1.79±0.29	2.00±0.21*	17.05±2.57	20.28±2.60*
t	0.465	-7.660	-1.732	-7.284
p	0.643	0.000	0.086	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 3: ADL SCORE BETWEEN THE TWO GROUPS

Group (n=50)	Self-care ability		Instrumental ADL	
	Before	After	Before	After
Observation	20.44±4.50	10.68±3.80*	25.80±5.28	13.36±3.91*
Control	21.48±4.53	17.04±4.81*	25.96±5.03	17.64±4.88*
t	1.152	7.329	0.155	4.841
p	0.252	0.000	0.877	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 4: ADVERSE REACTIONS n (%)

Group (n=50)	Nausea	Loss of appetite	Headache	Insomnia	Overall incidence
Observation	2 (4.0)	2 (4.0)	3 (6.0)	1 (2.0)	8 (16.0)
Control	3 (6.0)	2 (4.0)	1 (2.0)	1 (2.0)	7 (14.0)
χ^2					0.078
p					0.779

In summary, the combination therapy of butylphthalide and citicoline sodium exhibits potential as a therapeutic intervention for patients diagnosed with ischemic stroke. This study serves as an important reference point for the exploration of innovative treatment modalities and the advancement of patient outcomes in the field of ischemic stroke.

Conflict of interests:

The authors declared no conflict of interests.

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This article was originally published in a special issue, "Recent Progression in Pharmacological and Health Sciences" Indian J Pharm Sci 2024:86(2) Spl Issue "284-288"