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Ultra-early electroacupuncture rehabilitation for intravenous thrombolysis-induced cerebral infarction

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Abstract. – OBJECTIVE: The purpose of this research was to investigate whether it is possible to perform ultra-early interventional electroacupuncture on individuals who had experienced intravenous thrombolysis prior to receiving therapy for acute cerebral infarction.

PATIENTS AND METHODS: Patients who have undergone intravenous thrombolysis between July 2019 and March 2021 were eligible for participation in this study. The participants were divided into two groups; one group received electroacupuncture therapy 24 hours after their condition became stable, while the other group received treatment 48 hours after their condition became stable. Both groups received the same therapy for their respective forms of rehabilitation. The Fugl-Meyer Motion Assessment Scale (FMA) was used to assess the patients' motor function before and after therapy, as well as two weeks and one month after treatment. The scores of the FMA were recorded before and after treatment.

RESULTS: After therapy, the FMI scores were higher in both groups ($p<0.05$), and the researchers found that the ultra-early electroacupuncture intervention was related to higher FMI ratings 2 weeks and 1 month after treatment ($p<0.05$). In neither of the two study groups was there any sign of a major adverse response or consequence ($p>0.05$).

CONCLUSIONS: This research offers evidence that ultra-early interventional electroacupuncture rehabilitation therapy may be an effective and safe method of treatment for individuals who have had a cerebral infarction after receiving intravenous thrombolysis. The results lend credence to the notion that this kind of therapy should be taken into consideration as an adjunctive model for rehabilitation in patients of this type.

Key Words:
Electroacupuncture, Cerebral infarction, Intravenous thrombolysis, Ultra-early rehabilitation.

Introduction

Cerebral infarction, also known as ischemic stroke, is a disorder of the blood supply to local brain tissue that can arise due to several reasons[1]. High disability and mortality rates are hallmarks of cerebral infarction[2]. Localized cerebral ischemia in cerebral infarction can result in the irreversible damage of neurons and lead to energy failure, acidosis, increased release of glutamate, elevated intracellular Ca2+ levels, increased production of free radicals following ischemia and reperfusion, damage to the blood-brain barrier (BBB), inflammation, and ultimately, many excitatory cell deaths through necrosis, apoptosis, and autophagy, which affects the function of several neural networks[3-5]. Approximately 15 million people worldwide experience stroke each year, and 6 million die as a result, with half of the surviving patients potentially suffering permanent disability[6]. Approximately 85% of stroke patients suffer from cerebral infarction and reducing the mortality and disability rates of these patients remains a significant challenge[7,8].

As a common cerebrovascular disease in clinical practice, cerebral infarction is often seen in middle-aged and elderly individuals, greatly impacting their ability to care for themselves and placing a significant burden on their families[9,10]. Currently, the primary aim of clinical treatment for cerebral infarction is to enhance cerebral microcirculation and improve blood supply in the ischemic region, as well as to prevent the progression of the disease. Pharmacological interventions such as antiplatelet therapy, blood lipid reduction, enhancement of blood circulation, and mitigation of blood stasis have been identified as potential treatment options[11,12]. Failure to receive

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thrombolytic therapy within the designated timeframe can elevate the likelihood of experiencing problems. In patients with acute cerebral infarction undergoing thrombolytic therapy, the brain tissue is susceptible to ischemia and reperfusion injury. This can cause an overproduction of free radicals or a lack of antioxidant capacity, resulting in cellular damage to brain tissue. Thrombolytic therapy and neurorehabilitation therapy have been validated as the most efficacious approaches for decreasing disability rates, according to evidence-based medicine. The use of thrombolytic therapy in the acute phase is a commonly accepted practice, but there is presently no agreement on the most favorable timing for the initiation of rehabilitation treatment. According to established protocols[13,14], it is recommended to commence rehabilitation intervention within 48 hours after the stabilization of the condition. Several studies have suggested that the initiation of rehabilitation promptly following the onset of cerebral infarction may yield greater benefits[15,16].

Electroacupuncture (EA) is a treatment modality that combines conventional acupuncture techniques with electrical stimulation. It is commonly utilized as an adjunctive therapeutic modality. The implementation of this therapeutic approach is distinguished by improved management, uniformity, and empirical measurement. Owing to its uncomplicated nature, practicability, and economic viability, it has garnered extensive recognition in clinical environments. Research[17] has indicated that electroacupuncture has the potential to improve hemiplegia, spasm, neuralgia, and cognitive function following a stroke. Furthermore, prior research[18] has demonstrated its ability to regulate mental and psychological conditions. Electroacupuncture has been observed[19] to result in noteworthy enhancements in neurological function among numerous patients. Electroacupuncture has been observed[20] to enhance cerebral ischemic injury recovery, stimulate endogenous recovery mechanisms post-nerve injury, and elicit an ischemic tolerance response in the body, which is known to exert significant anti-inflammatory, anti-oxidative stress, and anti-apoptotic effects. Additionally, electroacupuncture has demonstrated[21] clear effects on the recovery of nerve function, promoting vascular regeneration, and nerve regeneration and activating the release of neurotrophic factors, thus playing a neuroprotective role. Electroacupuncture, as a traditional Chinese medicine-based treatment, is widely used in the rehabilitation of cerebral infarction. The utilization of traditional medical electroacupuncture in China has been shown[22,23] to be an effective method for reducing dysfunction after acute cerebral infarction with no reported adverse reactions. The implementation of ultra-early rehabilitation management, including rehabilitation training and acupuncture intervention, has been verified[24] to enhance the recovery of physical function in patients. The literature supports the notion that early initiation of electroacupuncture intervention has a significant impact on cerebral infarction; thus, it is recommended[25] to commence treatment as soon as the condition is stabilized if feasible. However, there is limited research exploring the benefits of ultra-early interventional electroacupuncture treatment on patient's post-intravenous thrombolysis. The present study aims to examine the effect of ultra-early electroacupuncture intervention on motor function recovery in patients with cerebral infarction who have undergone intravenous thrombolysis.

Patients and Methods

We selected 78 patients with acute cerebral infarction who received intravenous thrombolytic therapy with recombinant tissue plasminogen activator from the Department of Neurology, Binzhou People's Hospital, Shandong Province, from July 2019 to March 2021. Inclusion criteria: all patients who met the diagnostic criteria of cerebral infarction according to the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke (2010) and the treatment criteria of alteplase thrombolysis. They had no sequelae of stroke, especially motor function sequelae, and could cooperate with rehabilitation treatment. All patients have signed the informed consent form, and the hospital Ethics Committee has approved and agreed to implement our study.

Exclusion criteria: Patients with the following conditions were excluded from the study:

- Severe cerebral infarction treated in the intensive care unit.
- Severe cardiorespiratory disease.
- Psychosis or dementia, and other conditions that may affect rehabilitation treatment.
- Severe cognitive and speech dysfunction, which would hinder cooperation with rehabilitation treatment.
- Bone and joint diseases that significantly affect motor function.

Study Design

This is a prospective cohort study. The participants were divided into two groups: a treatment group that received electroacupuncture 24 hours after stabilization, and a control group that received electroacupuncture 48 hours after stabilization. Both groups underwent identical rehabilitation treatment, and the motor function of the patients was evaluated using the Fugl-Meyer Motion Assessment Scale (FMA) before and after treatment, as well as 2 weeks and 1 month after treatment.

Treatment Methods

Our research team consisted of neurologists, rehabilitation doctors, therapists, and traditional Chinese medicine doctors who intervened in different periods. We evaluated the patients' condition on admission, and according to the diagnosis and treatment criteria, we performed intravenous thrombolytic therapy with alteplase and gave routine drug treatment such as nutritional nerve, lipid regulation and plaque stabilization, and control of risk factors. The patients' vital signs remained stable and there was no progression of their condition; in fact, there were indications of improvement, leading to a determination that the condition was stable.

The treatment group received electroacupuncture 24 hours after the initial treatment, while the control group received acupuncture 48 hours after. Chinese medicine doctors performed dialectical acupuncture on both groups, targeting shoulder and hand three li, Waiguan, Hegu for upper limb failure, and Huantiao, Fengshi, Zusanli, Jiexi, and Sanyinjiao for lower limb failure. Intensity was adjusted based on tolerance, with a continuous wave frequency of 100 times/min, lasting for 25 minutes, once per day. Rehabilitation doctors and therapists evaluated and treated both groups, including: (1) comprehensive training of hemiplegic limbs such as placing them in good positions in bed, active and passive joint activities, and neuromuscular facilitation technology; (2) neuromuscular electrical stimulation; (3) standing bed, sitting balance, walking training; (4) operation training; (5) daily living ability training; (6) psychological counseling. Rehabilitation treatment was conducted once a day for 30 minutes, five times a week. The same rehabilitation physician evaluated the patients' motor function rehabilitation before treatment, 14 days after treatment, and 30 days after treatment. Adverse reactions and complications related to rehabilitation were recorded, including needle sickness, shoulder and hand syndrome, and shoulder pain.

Observation Indicators

The study evaluated changes in motor function of patients in both groups before and after rehabilitation treatment using the Fugl-Meyer Assessment Scale (FMA). The FMA scale consists of two parts: the upper limb assessment, which includes 33 items with a score range of 0-2 points per item, for a maximum score of 66 points; and the lower limb assessment, which includes 17 items with a score range of 0-2 points per item, for a maximum score of 34 points. The score reflects the patient's motor function of the limb, with a higher score indicating better motor function.

During the study, adverse reactions and complications, such as shoulder pain, shoulder-hand syndrome, and limited joint movement, were recorded. Inter-group and intra-group statistical analysis was performed on the data collected from both groups, and the incidence of adverse reactions and complications was recorded and analyzed statistically.

Statistical Analysis

We used SPSS 26.0 statistical software (IBM Corp., Armonk, NY, USA) for statistical analysis, and the measurement data were expressed by $\pm$ s, while the independent sample *t*-test was employed for inter-group comparison. Paired *t*-test was used for intra-group comparison, counting data were expressed in percentage. The Chi-squared test (χ^2) is used for inter-group comparison, and $p<0.05$ was the evaluation standard with statistically significant difference.

Results

Demographic Characteristics of All Patients

We collected the age, gender, smoking history, drinking history, previous hypertension history, diabetes history of all patients, and the motor function score of Fugl Meyer exercise assessment scale (FMA) of the two groups before rehabilitation treatment. There was no significant difference between the two groups in the above indicators ($p>0.05$) (Table I).

Comparison of Clinical Efficacy

There was no significant difference in FMA scores between the two groups before rehabilitation ($p>0.05$). The FMA score of the treatment group was better than that of the control group after 2 weeks of treatment ($p<0.05$). After one month of treatment, the FMA score of the treatment group was significantly better than that of

Table I. Demographic characteristics.

Items	Treatment group (n=39)	Control group (n=39)	*p*
Age (years)	59.82±9.28	58.71±7.57	0.258
Gender (male/female)	27/12	28/11	0.80
History of smoking	18	25	0.11
History of drinking	8	12	0.30
Hypertension	23	19	0.36
Diabetes	7	8	0.77
Pre-treatment FMA	70.00±18.66	69.28±19.28	0.87

FMA: The Fugl-Meyer Motion Assessment Scale.

Table II. Comparison of FMA scores of motor function between the two groups [points, ($\bar{\chi}$±s)].

Group	Before rehabilitation	Rehabilitation for 14 days	Rehabilitation for 30 days
Treatment group (n=39)	70.00±18.90	86.72±14.85	93.79±13.87
Control group (n=39)	69.28±19.53	76.79±14.82	82.87±14.12
t	0.301	0.534	0.733
p	0.870	0.004	0.001

FMA: The Fugl-Meyer Motion Assessment Scale.

the control group ($p<0.05$). Compared with before treatment, the FMA scores of patients in the two groups increased at 2 weeks and 1 month after treatment ($p<0.05$) (Table II and Figure 1).

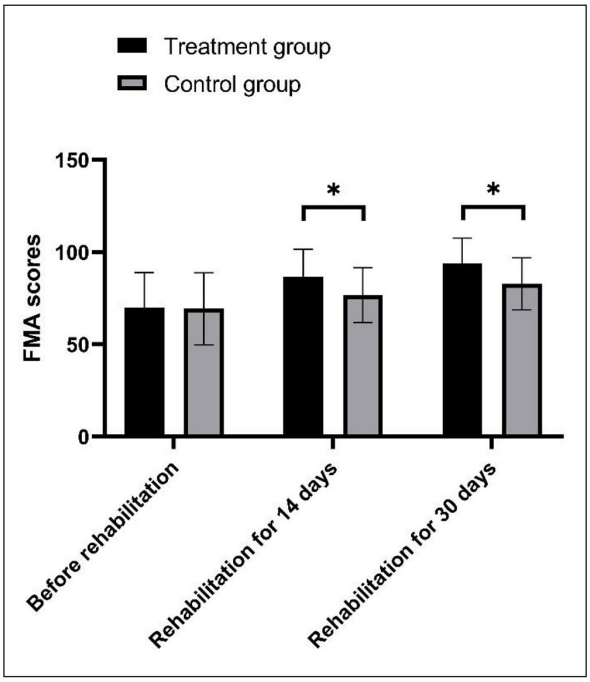

Figure 1. FMA scores of motor function. *indicates the values where $p<0.05$.

Comparison of Adverse Reactions and Complications

There were 2 cases of shoulder-hand syndrome in the treatment group (5.1%) and 3 cases of shoulder-hand syndrome in the control group (7.7%). There was no significant difference in the incidence of complications between the two groups ($p>0.05$) (Table III and Figure 2).

Discussion

A total of 39 people took part in the experiment, and each of them had an equal chance to be allocated to either the electroacupuncture group or the control group. The electroacupuncture group received the treatment first, followed by the control group. Patients who were assigned to receive electroacupuncture began their therapy during the first twenty-four hours after receiving intravenous thrombolysis. This treatment lasted for a total of fifteen days and consisted of electroacupuncture. It has been shown[25] that this treatment is superior to intravenous thrombolysis in terms of efficacy. The treatment that was administered to the patients in the control group was the conventional kind of medical attention that is given to individuals who are ill.

Table III. Comparison of incidence of shoulder-hand syndrome.

Group	N	With alteplase and gaveroutine drug treatment	Without alteplase and gave routine drug treatment	Incidence (%)
Treatment group	39	2	37	5.13%
Control group	39	3	36	7.69%
χ^2	78	5	73	0.214
p				1.000

FMA: The Fugl-Meyer Motion Assessment Scale.

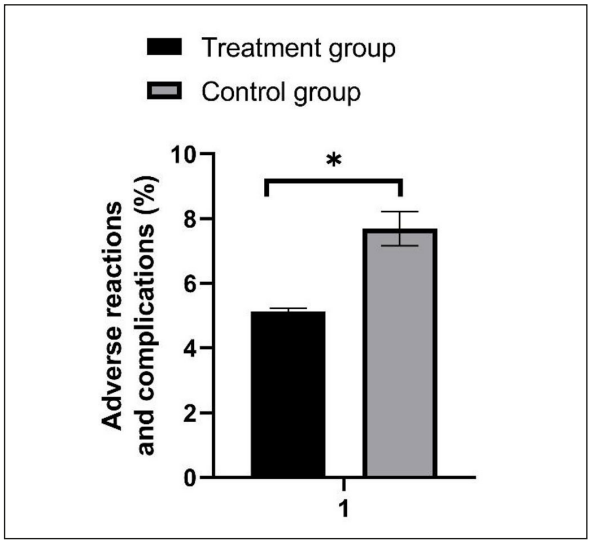

Figure 2. Comparison of adverse reactions and complications.

Table IV provides a summary of the statistical results of the study.

According to the findings of the research, the group that was given electroacupuncture treatment had outcomes that were significantly superior to those found in the control group. The electroacupuncture group had a reduced incidence of neurological deterioration, a shorter time of hospital stay, and a higher functional result at three months as compared to the other groups in the study.

A measuring technique known as the modified Rankin scale (mRS) is used in order to evaluate the functional outcome of stroke patients. A score of 0 indicates that the person in question does not have any form of restriction, whilst a score of 6 indicates that the person in question has already passed away. The group that received electroacupuncture had a functional outcome that was considerably better after three months, as evidenced by the mRS score. These findings originate from the research that was carried out and analyzed.

According to the findings of the research study, patients who had a cerebral infarction brought on by intravenous thrombolysis may benefit from an ultra-early rehabilitation therapy that includes electroacupuncture. This was shown to be the case in the treatment group. It has been shown that this treatment is not only safe but also effective when put to use. It was revealed that taking the medication was related to a decreased risk of neurological deterioration, a shorter length of time spent in the hospital, and a more positive functional result three months following treatment.

The technique used in the research was solid, and the findings, when seen from a statistical perspective, are intriguing to contemplate. The findings of the study should be viewed with some measure of care since the research was not carried out on a very large scale. It is required to do further research in order to determine whether or not the conclusions of this study can be relied upon.

Nerve injury following cerebral infarction can lead to a wide range of symptoms, including changes in consciousness, cognition, speech, swallowing, and motor function. Motor dysfunction is a prevalent phenomenon, as evidenced by the fact that more than half of the patients do not

Table IV. Summary of the statistical results of the study.

Outcome	Electroacupuncture Group	Control Group
Incidence of neurological deterioration	10%	25%
Length of hospital stay (days)	10	15
Functional outcome at 3 months (mRS score)	2	3

mRS: the modified Rankin scale.

achieve complete recovery[26]. Motor deficits not only curtail the patient's physical activities but also impose a considerable burden on their families[27]. As a result, the reduction of disability rates has emerged as a critical concern in medical investigations pertaining to acute cerebral infarction. The implementation of stroke units and the continuous enhancement of medical models have augmented the number of patients who are receiving prompt intravenous thrombolytic therapy, leading to a better overall prognosis for individuals with cerebral infarction[28].

Research[29] has indicated that the implementation of ultra-early rehabilitation within stroke units is both viable and secure and yields favorable outcomes in terms of neurological and motor functions, as well as overall quality of life. The integration of ultra-early rehabilitation with intravenous thrombolysis has been observed to optimize the enhancement of patients' neurological function, mitigate the occurrence of secondary complications, and expedite the development of typical, synchronized, and distinct motor patterns, as evidenced by previous studies[30]. Furthermore, it has been discovered[31] that implementing ultra-early rehabilitation can notably improve the neurological and motor capabilities of individuals who have suffered from a stroke.

Electroacupuncture therapy, which entails the use of filiform needles to apply pulse current, has gained popularity in post-stroke rehabilitation due to its ease of use, enhanced therapeutic effectiveness, and minimal occurrence of adverse effects. Studies[32] have substantiated the efficacy of electroacupuncture in managing dyskinesia linked with acute cerebral infarction (ACI). Furthermore, the amalgamation of ultra-early electroacupuncture and rehabilitation intervention has been found[33] to be more efficacious in enhancing neurobehavioral function and regulating autophagy compared to mere early rehabilitation training. This leads to better safeguarding of brain cells and improved neural function. Several studies[34] have explored the mechanism of electroacupuncture in treating ACI, with particular attention to its capacity to enhance oxidative stress responses, diminish inflammatory responses, modulate cerebral blood flow, and impede cellular apoptosis. The application of electroacupuncture has been observed[35] to have an impact on the neurovascular unit, leading to the regulation of protein and mRNA expression in the striatum of the remote section of anterior cerebral artery infarction. Additionally, electroacupuncture has been found to inhibit the Nogo-A/RhoA signal pathway, which is responsible for impeding central nerve regeneration, in the pons. These findings have been documented in previous research[36]. Consequently, this process facilitates the regeneration of nerves, diminishes the distant harm caused by acute cerebral infarction, and alleviates nerve protrusion injury.

A research investigation[37,38] was carried out to assess the impact of ultra-early electroacupuncture on the motor function of individuals diagnosed with ACI who had received intravenous thrombolysis treatment. The research sample comprised individuals diagnosed with mild to moderate ACI, while those with severe cognitive and speech impairment, communication impairment, or inability to complete the assessment were excluded from the study[37]. The study's findings indicate that there was no statistically significant distinction in the FMA motor function score between the treatment and control groups prior to the implementation of rehabilitation intervention ($p>0.05$). The study findings[39,40] indicate that the treatment group exhibited a significantly higher FMA motor function score compared to the control group on both the 14th and 30th day of rehabilitation treatment ($p<0.05$). Furthermore, no significant adverse events or life-threatening complications were observed in either cohort ($p>0.05$).

It is noteworthy that the examination expounded upon in this segment constitutes an initial inquiry into the amelioration of motor function and does not account for the rehabilitative impacts of other functional impairments, such as those affecting consciousness, cognition, and speech. The study's findings[41] suggest that a larger sample size, in-depth investigation, and additional exploration are necessary to comprehensively evaluate the viability of ultra-early intervention rehabilitation utilizing traditional Chinese medicine. Regrettably, the study's constraints are attributed to its limited sample size and single-center design, highlighting the necessity for future enhancements and substantiation *via* clinical controlled trials with large sample sizes and multiple centers.

Conclusions

In conclusion, the combination of intravenous thrombolysis and ultra-early electroacupuncture can improve the motor function of patients with ACI, and ultra-early interventional rehabilitation treatment with electroacupuncture has a positive effect on the improvement of motor function of patients with ACI without serious adverse reactions or complications.

Authors' Contributions

LL designed the study, collected and analyzed the data; LP performed the experiments; LX drafted the manuscript; LY provided useful advice on the design of this study, and supervised the experimental work and revision of this manuscript. All authors read and approved the final manuscript.

Data Availability

Data for this study is available from the corresponding author upon reasonable request.

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Ethics Approval

This research was approved by the Ethical Committee of Binzhou People's Hospital (No. 2021-292). The current study complies with the Declaration of Helsinki.

Informed Consent

The participants were fully informed about the purpose of the study and written informed consent has been obtained from them to publish this paper.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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