Research Paper

Observation of the Clinical Effect of Ureklin and Aspirin Combined with Rehabilitation Training in Patients with Acute Cerebral Infarction

JIE LIN, GUANGJIE LI[1], YICHEN ZHANG[2], HUAIYING SHI[3], XUN GONG[4], LIBO ZHANG[5], XUANXUAN WANG[6]* AND XIAOWEI WU[7]

Department of Emergency Medicine, Wuhan No. 6 Hospital, Affiliated Hospital of Jianghan University, Wuhan, [1]Medical Administration Division, Cadre Sanatorium of Hainan and Geriatric Hospital of Hainan (CSH), Haikou, [2]Department of Biology, Shenzhen MSU-BIT University, Shenzhen, Guangdong, [3]Nursing Department of Cadre Sanatorium of Hainan and Geriatric Hospital of Hainan (CSH), Haikou, [4]School of Materials Science and Engineering, Shenyang Ligong University, [5]Imaging Department, The General Hospital of Northern Theatre, Chinese People's Liberation Army, Shenyang, [6]Department of Integrated Traditional Chinese and Western Medicine, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, [7]Department of Thoracic Surgery, Tongji Hospital Affiliated to Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

To observe the clinical effect of ureklin and aspirin combined with rehabilitation training in patients with acute cerebral infarction. A total of 120 patients with acute cerebral infarction admitted to our hospital from January 2018 to January 2021 were randomly divided into control group and observation group. Both groups received conventional treatment. On this basis, the control group was treated with aspirin combined with rehabilitation training and the observation group was treated with aspirin combined with rehabilitation training and ureklin. The clinical efficacy after 2 w of treatment and safety during treatment of the two groups were counted and the level of serum cytokine, hemorheology, neurological function and quality of life were compared between the two groups before and after 2 w of treatment. After 2 w of treatment, the total effective rate of control group was lower than that of observation group ($p<0.05$). After 2 w of treatment, level of serum vascular endothelial growth factor and scores of activity of daily living and Barthel index in both groups were higher than before treatment and there was statistical difference between observation group and control group ($p<0.05$). After 2 w of treatment, levels of serum homocysteine, cystatin-C, plasma viscosity, platelet aggregation rate, hematocrit, fibrin and score of National Institutes of Health Stroke Scale in both groups were lower than those before treatment and there was statistical difference between observation group and control group ($p<0.05$). During treatment, the total incidence of adverse reactions in the observation group was 6.67 % and there was no significant difference between the observation group and the control group (11.67 %, $p>0.05$). Ureklin and aspirin combined with rehabilitation training could effectively improve the synthesis of serum cytokines, hemorheology and neurological function in patients with acute cerebral infarction and improve the quality of life of patients, with better clinical efficacy.

Key words: Acute cerebral infarction, ureklin, aspirin, rehabilitation training, hemorheology

Acute Cerebral Infarction (ACI) is mainly caused by impaired blood oxygen supply in the local brain tissue of the patient, which leads to ischemia and hypoxia of the patient's brain tissue and eventually results in the patient's neurological deficit and it has the characteristics of acute onset, high disability and fatality rate[1]. In the current clinical treatment of patients with ACI, in addition to regulating lipids, anticoagulation, controlling blood pressure and improving cerebral circulation, aspirin and conventional rehabilitation training are used to respectively carry out anti-platelet aggregation and promote the blood circulation of the patient's body and improve the function of the patient's limbs. However, none of the above treatment options

***Address for correspondence**
E-mail: mei8383451@163.com

can promptly alleviate the patient's neurological damage[2].

Ureklin can inhibit vasoconstriction in patients and help patients to establish collateral circulation in the ischemic area of the brain. Relevant studies[3,4] have used ureklin in the treatment of patients with cerebrovascular disease and confirmed that it can effectively improve the neurological function and limb function of patients. However, the relevant mechanism of ureklin in the treatment of ACI is not yet fully understood. Based on above, this study used ureklin and aspirin combined with rehabilitation training for the treatment of patients with ACI.

MATERIALS AND METHODS

General information:

The 120 patients with ACI admitted to our hospital were randomly divided into a control group and an observation group, with 60 cases in each group. Characteristics of infarcts in the control group were: 43 cases of single infarction, 17 cases of multiple infarction; 33 males and 27 females; the time from onset to consultation was 0.5 h to 5 h, with an average of 2.69±0.57 h; the age was 55 to 73 y old, with an average of 63.89±3.21 y old. Characteristics of infarcts in the observation group were: 41 cases of single infarction, 19 cases of multiple infarction; 35 males and 25 females; the time from onset to consultation was 0.4 h to 5 h, with an average of 2.73±0.53 h; the age was 55 to 72 y old, with an average of 63.11±3.28 y old.

Inclusion and exclusion criteria:

Inclusion criteria: Those who met the diagnostic criteria of ACI[5] and gave informed consent to this study, as well as those who have normal coagulation function, etc.

Exclusion criteria: Those with malignant tumors; those with a history of brain surgery or trauma; those who have recently undergone arterial puncture; those with liver and kidney dysfunction; those who have used anticoagulants and heparin 1 mo before the onset of ACI.

Treatment methods:

Both groups received conventional treatment, including controlling blood sugar levels, improving cerebral circulation and anticoagulation. On this basis, the control group was treated with aspirin (Beijing Zhongxin Pharmaceutical Co., Ltd., SFDA approval No. H13022754, 100 mg) combined with rehabilitation training, in which aspirin was taken orally, 300 mg/time in the 1st w and 100 mg in the 2nd w per time with 1 time/d. The rehabilitation training content includes standing training, muscle strength training, early sitting training, gait training, weight transfer training, passive joint movement training, etc., with 40 min/time, 1 time/d and 6 times/w.

The observation group was treated with ureklin on the basis of conventional treatment and aspirin. 0.15 Particle Nano-Ampere (pnA) units of ureklin were dissolved in 100 ml of saline and intravenously infused to the patients 1 time/d. Both groups were treated for 2 w.

Observation indicators:

Clinical efficacy after 2 w of treatment: The treatment effects were divided into significantly effective, effective and ineffective according to the "Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China 2014". Significantly effective: The patient's clinical symptoms are markedly improved and the patient can take care of his life completely and the National Institutes of Health Stroke Scale (NIHSS) [6] score is reduced by more than 50 %; effective: the patient's clinical symptoms have improved and part of his/her life can be taken care by himself/herself and the NIHSS score is reduced by 20 %-50 %; ineffective: does not meet the above criteria.

Serum cytokine levels before treatment and after 2 w of treatment: 5 ml of the patient's venous blood was drawn and centrifuged (3500 rpm, 10 min) to prepare serum and enzyme-linked immunosorbent assay was used to detect the patient's serum Vascular Endothelial Growth Factor (VEGF), Homocysteine (Hcy), Cystatin-C (Cys-C) levels.

Hemorheology before treatment and 2 w after the treatment: Blood collection was conducted the same as above and the platelet aggregation rate and hematocrit of the two groups were detected by the pulse thin tube method (Dongguan Chengzhuo Optoelectronics Technology Co., Ltd.). After adding the anticoagulant, the whole blood was centrifuged at 3500 rpm for 10 min and the plasma was collected. The plasma viscosity of the two groups was measured by the pulse thin tube method and the patient's peripheral blood fibrinogen level was measured by the automatic biochemical analyzer.

Neurological function and quality of life of patients: Before treatment and after 2 w of treatment, NIHSS was used to evaluate the neurological function of patients; Activities of Daily Living (ADL)[7] and Barthel Index

(BI) scores[8] were used to respectively evaluate patients daily routine ability and life quality.

Safety during the treatment period: The occurrence of adverse reactions in the two groups was counted.

Statistical methods:

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) 21.0 statistical software and $p<0.05$ indicated that the difference was statistically significant. The measurement data included serum cytokine levels, hemorheology, neurological function and quality of life. The data was expressed by the mean±standard deviation ($x\pm s$) and the t-test was used for comparison. The enumeration data including clinical efficacy and safety was indicated by case (percentage) [n (%)] and we used the χ^2 test for comparison.

RESULTS AND DISCUSSION

Clinical efficacy between the two groups was compared. After 2 w of treatment, there was a statistical difference in the total effective ratio of the observation group and the control group ($p<0.05$) (Table 1).

Serum cytokine levels between the two groups were compared. After 2 w of treatment, the serum Hcy and Cys-C levels of the two groups decreased compared with the levels before treatment, there was a statistical difference between the observation group and the control group ($p<0.05$). The serum VEGF level increased and the observation group and the control group had statistical difference ($p<0.05$) (Table 2).

Hemorheology between the two groups was compared. After 2 w of treatment, the two group's plasma viscosity, platelet aggregation rate, hematocrit and fibrinogen decreased. There were statistical differences between the observation group and the control group ($p<0.05$) (Table 3).

Neurological function and quality of life between the two groups were compared. The NIHSS scores of the two groups decreased after 2 w of treatment compared with NIHSS scores before treatment and the observation group and the control group had statistical differences ($p<0.05$). The ADL and BI scores increased after 2 w of treatment, there were statistical differences between observation group and the control group ($p<0.05$) (Table 4).

The safety of the two groups was compared. During the treatment period, the observation group and the control group had a statistically significant difference in the incidence of total adverse reactions ($p>0.05$) (Table 5).

TABLE 1: COMPARISON OF CLINICAL EFFICACY BETWEEN THE TWO GROUPS [n (%)]

Group	n	Significantly effective	Effective	Ineffective	Total effective ratio
Control	60	28 (46.67)	20 (33.33)	12 (20.00)	48 (80.00)
Observation	60	33 (55.00)	23 (38.33)	4 (6.67)	56 (93.33)
χ^2	-	-	-	-	4.615
p	-	-	-	-	0.032

TABLE 2: COMPARISON OF SERUM CYTOKINE LEVELS BETWEEN THE TWO GROUPS ($\bar{x}\pm s$)

Time	Group	n	VEGF (ng/l)	Hcy (μmol/l)	Cys-C (mg/l)
Before treatment	Control	60	226.24±36.78	24.13±2.36	1.84±0.26
	Observation	60	223.76±37.14	24.76±2.31	1.81±0.27
	t	-	0.368	1.478	0.620
	p	-	0.714	0.142	0.536
2 w after treatment	Control	60	317.36±22.64*	17.74±1.63*	1.11±0.23*
	Observation	60	373.73±16.31*	11.23±1.31*	0.73±0.22*
	t	-	15.648	24.114	9.248
	p	-	<0.001	<0.001	<0.001

Note: Compared with the levels before treatment, *p<0.05

TABLE 3: COMPARISON OF HEMORHEOLOGY BETWEEN THE TWO GROUPS ($\bar{x}\pm s$)

Time	Group	n	Plasma viscosity (mPa·s)	Platelet aggregation rate (%)	Hematocrit (%)	Fibrinogen (g/l)
Before treatment	Control	60	3.10±0.71	67.33±7.17	46.13±6.16	336.86±44.77
	Observation	60	3.07±0.64	66.63±7.43	45.76±6.32	336.43±44.32
	t	-	0.243	0.525	0.325	0.053
	p	-	0.808	0.600	0.746	0.958
2 w after treatment	Control	60	1.81±0.43*	52.37±5.14*	37.83±7.32*	276.36±37.23*
	Observation	60	1.33±0.33*	41.43±4.64*	31.73±5.31*	232.44±23.74*
	t	-	6.859	12.238	5.225	7.705
	p	-	<0.001	<0.001	<0.001	<0.001

Note: Compared with the values before treatment, *p<0.05

TABLE 4: COMPARISON OF NEUROLOGICAL FUNCTION AND QUALITY OF LIFE BETWEEN THE TWO GROUPS ($\bar{x}\pm s$ SCORE)

Time	Group	n	NIHSS	ADL	BI
Before treatment	Control	60	12.47±3.36	33.81±3.63	33.37±16.32
	Observation	60	12.36±2.87	33.64±3.72	34.62±13.43
	t	-	0.193	0.253	1.347
	p	-	0.847	0.800	0.181
2 w after treatment	Control	60	7.44±1.66*	51.77±7.36*	47.74±6.73*
	Observation	60	4.36±1.37*	70.73±7.41*	53.36±3.36*
	t	-	11.085	14.062	5.787
	p	-	<0.001	<0.001	<0.001

Note: Compared with the scores before treatment, *p<0.05

TABLE 5: COMPARISON OF THE SAFETY OF THE TWO GROUPS [n (%)]

Group	n	Nausea/ vomiting	Chest distress	Dizziness	Rash	Incidence of total adverse reactions
Control	60	2 (3.33)	3 (5.00)	1 (1.67)	1 (1.67)	7 (11.67)
Observation	60	1 (1.67)	1 (1.67)	2 (3.33)	0 (0.00)	4 (6.67)
χ^2	-	-	-	-	-	0.901
p	-	-	-	-	-	0.343

ACI is a common disease in neurology and one of the main types of stroke. Patients show hypotonia or loss of muscle tone at the early stage of onset. Most patients will still have different degrees of neurological deficit symptoms even after clinical treatment[9,10]. The clinical treatment of patients with ACI mainly includes anticoagulation, lipid regulation, blood sugar control, etc. Aspirin is one of the basic drugs for treatment of patients with ACI in clinic, which can improve the blood supply to the brain of patients with ACI through anti-platelet aggregation. Rehabilitation training can effectively promote the body's blood circulation and prevent further loss of muscle tone of the patient's limbs[11]. However, the combination of the above therapies cannot effectively control the patient's condition, which limits its clinical application and emerges a requirement of other drugs in therapeutic practice.

VEGF is a pro-angiogenesis substance that can effectively promote the repair of damaged vascular endothelium and angiogenesis in patients with ACI. Hcy and Cys-C have the ability to promote vascular damage in patients with ACI and affect the blood oxygen supply of the brain. Especially, Hcy was found to trigger an increase of inflammatory response in patients by mediating it in the body, thus aggravating the neurological damage in patients with ACI[12]. The results of this study showed that after 2 w of treatment, the clinical efficacy and serum VEGF levels of the observation group were higher than those of the control group and the serum Hcy and Cys-C levels, plasma viscosity, platelet aggregation rate, hematocrit and

fibrinogen were lower than those of the control group.

The findings above show that ureklin and aspirin combined with rehabilitation training can effectively improve the clinical symptoms of patients with ACI, relieve vascular endothelial damage and improve the body's blood rheology. The reason may be that as a tissue-type kininogenase, ureklin could convert kininogen into kinin, selectively expand arteries in ischemic sites inhibit platelet aggregation, improve blood supply in infarcts and promote the angiogenesis as well as establishment of collateral circulation in surrounding lesions, stimulate blood flow in cerebral ischemic tissues, thereby effectively alleviate the damage of vascular endothelial function and improve the body's blood rheology[13,14].

Impaired neurological function is the most important clinical manifestation of patients with ACI, accompanied by varying degrees of limb dysfunction. The main manifestations of patients are weakened limb motor ability, reduced ability of daily routines and quality of life. The results of this study showed that after 2 w of treatment, the NIHSS score of the observation group was lower than that of the control group and the ADL and BI scores were higher than those of the control group, indicating that ureklin and aspirin combined with rehabilitation training can alleviate the neurological damage in patients with ACI and improve the ability of daily living and quality of life. The reason may be that, on the one hand, ureklin can improve blood supply to the brain tissue of the lesion in patients with ACI by alleviating the vascular endothelial damage around the lesion and promoting angiogenesis.

On the other hand, ureklin can effectively ameliorate the deformation ability and oxygen dissociation ability of red blood cells, improve the blood oxygen supply of brain tissue around the patient's lesion, reduce the anaerobic degradation of damaged brain tissue and alleviate the secondary damage of brain tissue cells and nerve cells. Furthermore, ureklin can enhance the utilization of glucose by cells in order to promote the repair of damaged lesions and eventually improve the quality of life for the patients with ACI[15,16]. In addition, ureklin treats patients with ACI mainly by repairing cerebrovascular damage, therefore, it will not bring about other effects on the body. Hence adding ureklin on the basis of conventional treatment will not increase the occurrence of adverse reactions.

In summary, ureklin and aspirin combined with rehabilitation training can effectively improve serum cytokine synthesis, hemorheology and neurological function in patients with ACI and improve the quality of life of patients. The practice has good clinical efficacy and is worthy of clinical promotion. Our study did not specifically investigate the recovery of neurological function in patients with ACI, therefore, follow-up statistics on changes in brain waves, neurotransmitters and other indicators of patients before and after treatment can be carried out, in order to further analyze the effects of ureklin and aspirin combined with rehabilitation training in improving the neurological function of patients with ACI.

Author's contributions:

Jie Lin and Guangjie Li have contributed equally to this work.

Conflicts of interest:

The authors declared no conflict of interest.

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