A Clinical Study of Therapeutic Effectiveness in Treating Ischemic Cerebrovascular Disease With Lumbrokinase

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Abstract: We treated 303 patients with cerebral infarction using Lumbrokinase in the treated group. We had 150 cases in the control group. Random sampling and the double blind method were employed in this research. There was no significant difference between the two groups in age, sex, state of illness, time of medication, anamnesis and complications. The results revealed that the overall effective rate was 93.7%, the markedly effective rate 73.6%. Fibrinogen, euglobulin lysis time, blood viscosity, plasma viscosity and platelet aggregating function were reduced in the treated group. It suggests that lumbrokinase can serve as an effective drug of preventing thrombosis and a safe and beneficial antithrombotic agent.

Key word: Cerebral infarction Lumbrokinase

Boluoke is the commercial product name of Lumbrokinase researched and developed by the Faculty of Biophysics of Chinese Academy of Sciences. Boluke is a new antithrombotic drug, mainly composed of two groups of enzymes: plasminogen activator and plasmin, and it contains t-PA-like ingredient[1] . Since we don't have a clear picture about Boluoke's clinical effect on cerebrovascular disease, during May 1990 to March 1991, we observed 453 patients with cerebral infarction (303 in treated group and 150 in control group) under random sampling and double blind method, and conducted a comprehensive research of clinical cases and hemorheology change. The results show that Boluoke is a new drug with preventative and therapeutic effects on cerebral infarction.

Materials and Methods

1. General condition:

453 patients with cerebral infarction were divided into treated group (303 patients) and control group (150 patients). All patients were diagnosed under the diagnostic standards passed by the Second National Cerebrovascular Conference. All patients are in acute stage of cerebral infarction of carotic artery system, and have different degree of paralysis. Infarction sites can be seen via CT scan. There was no statistically significant difference between two groups in age, gender, state of illness, onset of illness, time of medication, anamnesis and complications. Therefore, the two groups can be compared (Table 1); and the state of illness and time of medication of the two groups can be compared as well ($P>0.25$, $P>0.01$).

Table 1 Result of treated and control groups ($\bar{X} \pm s$)

	Age	Patient No.		Complication	Anamnesis
		M	F		
Treated	63 ± 9	203	100	5.6 ± 4.2	5.5 ± 2.6
Control	62 ± 9	101	49	5.9 ± 3.8	5.9 ± 2.6
P value*	>0.05	>0.05		>0.5	>0.1

* Comparison between treated and control groups

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2. Medication administration and result assessment:

Capsule I and capsule II (one is Boluoke, and the other is starch) are given to patients via random sampling and double blind method. Patients took two capsules half hour after meal, three times a day for total 21 days. Low molecular dextran, 500ml a day for 14 days, was also given via intravenous injection from the beginning of medication. The assessment of clinical nerve function deficiency before and after medication is based on the "clinical nerve function deficiency assessment standards of stroke patients" passed by the Second National Cerebrovascular Conference: 0~15 is mild, 16~30 is moderate, and 31~45 and above is serious. The final effectiveness assessment utilizes "Clinical effectiveness assessment standards of stroke patients of Beijing".(If the grades lowers more than 90.0%, it means fully recover; 46.0%~89.0% means significant progress; 18.0%~45% means progress; below 18.0% or increases no more than 18% means no change; deficiency grade increases more than 18.0% means deteriorate.) In addition, homorheology is also observed before and after medication. Venous blood was taken during 8~8:30am for test of euglobulin lysis time. Assessments of liver and kidney function, platelet, bleeding time, coagulation time were taken before and after treatment as well.

3. Data analysis

t analysis and X^2 analysis were applied, and the statistic software of the Math department of Capital University of Medical Sciences was utilized. All the data was processed by IBM-PC.

Result

The result shows that both overall effective rate and significant effective rate have significant difference ($P<0.01$), see table 2.

Table 2 Clinical effectiveness assessment of Bolouke and control group (Percentage assessment)

	Treated group 303 subjects	Control group 150 subjects
	No. (%)	No. (%)
Fully recover	68(22.4)	10(6.6)
Significant progress	155(51.2)	32(21.3)
Progress	61(20.1)	61(40.7)
No change	19(6.3)	38(25.3)
Deteriorate	0(0.0)	8(5.3)
Death	0(0.0)	1(0.6)
Overall effective rate	284(93.7)	103(68.6)
Significant effective rate	223(73.6)	42(28.0)

Via X^2 Analysis, overall effective rate $P<0.01$, significant effective rate $P<0.01$

The assessment results of the treated group show the fibrinogen, euglobulin lysis time, blood viscosity, plasma viscosity, platelet aggregating function were significantly reduced after treatment (Table 3). As to the control group, there was no significant difference between before and after treatment (Table 3).

Table 3 The analysis results of two groups of patients

	No	Before medication	After medication	P Value
Treated Group				
Fibrinogen (g/L)	294	3.91 ± 1.09	3.27 ± 0.80	<0.001
Euglobulin lysis time (min)	203	217.07 ± 82.53	172.73 ± 65.70	<0.01
Plasma viscosity	222	1.84 ± 0.21	1.73 ± 0.14	<0.01
Blood viscosity	221	5.94 ± 2.47	5.23 ± 1.44	<0.01
Hematocrit	219	47.20 ± 29.30	43.27 ± 3.51	>0.05
Blood reduction viscosity	220	10.45 ± 4.37	10.08 ± 5.75	>0.2
Homeostatic sedimentation	217	22.44 ± 11.35	21.70 ± 11.05	>0.2
Platelet aggregating function	182	58.98 ± 22.45	53.83 ± 16.96	<0.02
Control Group				
Fibrinogen (g/L)	146	3.73 ± 1.02	3.61 ± 0.98	>0.2
Euglobulin lysis time (min)	69	194.33 ± 87.19	169.69 ± 62.48	>0.05
Plasma viscosity	118	1.88 ± 0.25	1.83 ± 0.19	>0.1
Blood viscosity	119	5.72 ± 1.22	5.57 ± 1.23	>0.2
Hematocrit	119	44.49 ± 4.11	44.06 ± 4.04	>0.2*
Blood reduction viscosity	118	10.28 ± 2.34	9.79 ± 2.00	>0.05
Homeostatic sedimentation	118	26.84 ± 10.35	26.05 ± 11.10	>0.5
Platelet aggregating function	116	59.26 ± 23.92	56.17 ± 17.85	>0.2

Discussion:

Our ancient medicine has recorded “DiLong”(earthworm) as a single herb in the Compendium of Materia Medica (BenCaoGangMu). Dilong has the property of expelling wind and relieving spasm, therefore can be used in symptoms caused by pathogenic factors obstructed in meridians and paralysis. In 1983, a Japanese scholar, Mihara, once reported this drug in the International Thrombosis Anti-Hemorrhage Conference, and named the drug Lumbrokinase[4] . In 1986, the Drug Administratrion of South Korea permitted to produce lumbrokinase, and the product was extensively used in the world. Boluoke is a multi-enzyme drug, contains t-PA-like ingredient, and has thombolytic ability. The mechanisms of its function are: First, it has the function of plasminogen activator, and second is its special affinity with fibrin which can degrade fibrin rapidly. Mihara reported that oral administration of Boluoke can significantly dissolve thrombus in the Saphenous vein of Beagle, better than 200 thousand units of urokinase. We observed 303 patients with cerebral infarction taking Boluoke orally, and the results show that the overall effective rate is 93.7%, and significant effective rate is 73.6%, which are higher than the control group (overall effective rate 68.8%, significant effective rate 28.0%). It explains that Boluoke has significant effect on patient with acute cerebral infarction. There is no side effect or complication. Compared with urokinase and streptokinase, Boluoke has special affinity with fibrin and possesses greater advantage. It is convenient, and won’t induce hemorrhage during application. From hemorheology change and euglobulin lysis point of view, the treated group’s fibrin content, plasma viscosity, blood viscosity and euglobulin lysis time reduced significantly after treatment, but there is no change in the control group. This result indicates that Boluoke has significant fibrinolytic ability, and can reduce blood viscosity; it has anti-aggregating ability for platelet, anti-coagulating and vascular system relaxation ability. The result of our research is in accordance with the report of the Japanese scholar: Boluoke moderates the aggregating function of platelet. Boluoke not only can dissolve thrombus formed inside the body, but also can moderate blood coagulation in great degree, therefore improves local or the whole body circulation, makes it more beneficial in recovering lost function. The results indicate that Boluoke can be extensively used as therapeutic and preventative drug for thrombus formation.

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