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Lumbrokinase in Treatment of Primary Hypertension in 51 Patients

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Lumbrokinase in traditional Chinese medicine as Di Long (earthworms) has been studied through animal experiments and clinical observations to confirm the fibrinolytic and thrombolytic effects and anticoagulation activities. It also helped to improve blood flow and has achieved more than the desired results. Compared with similar kinds of drugs, lumbrokinase is safer and has fewer side effects, higher efficacy and lower production costs. To further study the uses of lumbrokinase, in May 2006 to August 2006, clinical trail was conducted on the use of lumbrokinase in treatment of hypertension. Report is as follows:

1. DATA & MEHTOD

1.1 Test Sample: For the ease of intake, lumbrokinase was capsulated at 0.35g/capsule. The recommended human intake is 4.3g/d, which translates to roughly six capsules twice daily.

1.2 Subjects: Chose 102 outpatients with hypertension and divided into experimental group and control group, 51 patients each. Standards were as follows: systolic blood pressure (SBP) ≥ 140mmHg (18.7kPa) or diastolic blood pressure (DBP) ≥ 90mmHg (12kPa). All patients do not have complications of hypotension and have normal living and working life styles.

1.3 Groups: Randomly divided outpatients into experimental group and control group. There should be a balance in sex, age, course of disease and disease conditions in both groups. Please see Table 1 for the two groups' sex, age, and course of disease, and Table 2 for two groups' disease conditions.

Table 1 Patients' sex, age and course of disease in two groups

Group	n	Male		Female		age (x±s)	course of disease (yr) ($\bar{x}$ ±s)
		n	Ratio %	n	Ratio %		
Control	51	31	60.78	20	39.22	52±9	4.4 ±2.9
Exp't	51	30	58.82	21	41.18	52±7	4.3 ±3.3

Note: Statistic evaluation between two groups: sex: x^2=0.000, P>0.05; age: t=0.192, P=0.848; course of disease: t=0.160, *P*=0.873

Table 2 Patients' disease conditions in two groups ($\bar{x}$ ± s)

Group	n	SBP (mmHg)	DBP (mmHg)
Control	51	156±8	93±5
Experiment	51	156±10	92±5

Note: Comparison between two groups: SBP: t=0.218, P=0.829; DBP: t=0.501, P=0.619

1.4 Method

1.4.1 Eating Habits: During the trial period, patients should maintain their usual living, working and eating habits. Clinical physicians would let patients know the objective of the experiment, introduce lumbrokinase' properties and relevant information, and let them understand the experiment's requirements and arrangements. Patients needed to be willing to take the experiment and to agree to corporate. Double blinded method was used to give out samples. Experimental group was given lumbrokinase capsules; control group was given placebo (starch). Administration method: twice daily, six capsules each time, 0.35g per capsule, experimental period was 30 days.

1.4.2 Observations: Before and after treatment, observe blood pressure and other related symptoms (headache, vertigo, palpitation, tinnitus, insomnia, irritable, sore

waist and knees) and tally points according to severity of symptoms (severe 3 points, moderate: 2 points, mild: 1 point). Compile integral statistics and effective rate (symptom improvement has 1 point or more marked as effective) before and after experiment. Other than blood pressure, please include blood lipid tests (triglyceride and total cholesterol). Each item should be measured once before and after experiment, and blood pressure should be checked once every week.

1.4.3 Blood Pressure Measurement: Have the same person checking the blood pressure before and after experiment at a specific time. Before measurements, have patient sit and rest for 15min or more. Use the GB3053-82 model of desktop mercury sphygmomanometer to measure blood pressure.

1.5 Efficacy and Statistic Method

1.5.1 Evaluation: Effective and Ineffective. Effective: met any one of the following criteria. ① Reduction in diastolic pressure ≥ 10mmHg or back to normal; ② Reduction in systolic pressure ≥ 20mmHg or back to normal. Ineffective: did not meet any of the above criteria.

1.5.2 Statistic Method: Use Excel database and the SPSS10.0 statistic software to perform a chi-square test and a t-test.

2. RESULTS

2.1 Observation: See Table 3 & 4 for the symptom integrals and the subjective symptom improvement numbers (improvement rate) in the experimental group and the control group. From Table 3, there was significant difference in disease symptoms before and after treatment in the experimental group (P<0.01); when compared with control group, there was significant difference as well (P<0.01). From Table 4, there was significant difference in improvement of disease conditions: vertigo, palpitation and sore waist and knee, between experimental group and control group (P<0.05 and P<0.01, respectively)

Table 3 Disease symptoms before and after treatment in both groups ($\bar{x} \pm s$)

Group	n	Before treatment	After treatment
Control	51	2.9±1.2	2.6±1.3
Experimental	51	2.8±2.0	1.4±1.4$^{*\#}$

Note:
*compared with before treatment: t=6.128, *P*=0.000;
$^{\#}$ compared with control group: t=4.411, *P*=0.000

2.2 Changes in Blood Pressure

2.2.1 Comparison of Systolic Pressure Level Before and After Treatment: See Table 5 for results. There was significant difference (P<0.01) in comparing before and after treatment in the experimental group. When the experimental group compared with the control group, there was significant difference as well (P<0.01); an average reduction of (21±12)mmHg, compared with the control group (3±11)mmHg, there was significant difference (P<0.01) in reduction.

2.2.2 Comparison of Diastolic Pressure Level Before and After Treatment: See Table 6 for results. There was significant difference before and after treatment in the experimental group (P<0.01); compared with control group, there was difference as well (P<0.01), an average reduction of (5±6)mmHg, compared with control group (1±5), the difference in reduction was significant (P<0.01).

2.3 Blood Lipid Changes: See Table 7 for results. There was no significant changes in patient's cholesterol, triglyceride and HDL levels in the experimental group (P>0.05). Also, there was no significant difference between the experimental group and the control group (P>0.05).

2.4 Comparison of Efficacy of Treatment in Both Groups: See Table 8 for results. Experimental group was more effective in reducing blood pressure compared with the control group (P<0.01).

Table 4 Subjective symptoms comparisons in both groups

Symptoms	Control (51)			Exp't (51)			Improvement rate (%)		X^2	*P*
	n	effective	Ineffec-tive	n	effectiv e	Ineffec-tive	Control group	Experimental group		
Headache	12	3	9	11	7	4	25.00	63.63	2.091	>0.05
Vertigo	36	6	30	38	26	12	16.66	68.42	18.121	<0.01
Palpitation	22	6	16	23	13	10	27.27	56.52	3.943	<0.05
Tinnitus	13	1	12	10	3	7	7.69	30.00	0.713	>0.05
Insomnia	13	3	10	8	3	5	23.07	37.50	0.045	>0.05
Irritable	17	4	13	14	5	9	23.52	35.71	0.120	>0.05
Sore waist & knees	23	5	18	28	18	10	21.73	64.28	7.594	<0.01

Table 5 Systolic pressure changes in the two groups before and after treatment (mmHg, $\bar{x} \pm s$)

Group	n	Before treatment	1st wk of treatment	2nd wk of treatment	3rd wk of treatment	4th wk of treatment	After treatment
Control	51	156 ± 8	154 ± 8	154 ± 9	154 ± 10	154 ± 13	153 ± 11
Experimental	51	156 ± 10	152 ± 10	147 ± 9	144 ± 9	138 ± 9	135 ± 11*#

Note: *compared with before treatment: t=12.683, *P*=0.000; #compared with control group: t=9.417, *P*=0.000

Table 6 Diastolic pressure changes in the two groups before and after treatment (mmHg, $\bar{x} \pm s$)

Group	n	Before treatment	1st wk of treatment	2nd wk of treatment	3rd wk of treatment	4th wk of treatment	After treatment
Control	51	93 ± 5	92 ± 5	92 ± 6	92 ± 6	92 ± 6	91 ± 6
Experimental	51	92 ± 5	90 ± 5	90 ± 6	89 ± 5	88 ± 6	87 ± 6*#

Note: *compared with before treatment: t=5.986, *P*=0.000; #compared with control group: t=3.459, *P*=0.001

Table 7 Blood lipid comparisons between two groups before and after treatment (mmol/L, $\bar{x} \pm s$)

Group	n	Before treatment			After treatment		
		TC	TG	HDL-C	TC	TG	HDL-C
Control	51	4.56 ± 0.73	1.89 ± 1.24	1.30 ± 0.30	4.60 ± 0.63	1.82 ± 1.08	1.33 ± 0.27
Experimental	51	4.58 ± 0.68	1.88 ± 1.28	1.26 ± 0.28	4.57 ± 0.59	1.81 ± 1.06	1.26 ± 0.26

Table 8 Comparison of treatment efficacy in both groups

Group	n	Effective	ineffective	Effective rate (%)
Control	51	6	45	11.76
Experimental	51	30	21	58.82#

Note:
#compared with control group: x^2=22.27, *P*<0.01

3. DISCUSSIONS

Early in the 1596, purpose and uses of earthworms were recorded in the "Compendium of Materia Medica". In 1878, a French researcher discovered that secretions from earthworm's digestive system helped to degrade fibrin. In 1983, division of Mihara discovered the activating enzyme in earthworm extractions and named it as lumbrokinase; Chinese, Japanese, and Korean scientists studied the zymology and physicochemistry of lumbrokinase and conducted clinical researches [1]. In 1992, oral intake of lumbrokinase have officially used in clinical practice. It was mainly used for preventing and controlling ischemic cerebrovascular disease. Recently, lumbrokinase had an unceasing development in the clinical practice. Reports showed effective use of lumbrokinase to treat infarction [2], angina pectoris [3] and etc. In here, we used to treat hypertension and the results were effective: improvements in subjective symptoms such as vertigo, palpitations, sore waist and knees; reduction in patient's symptom index (P<0.01); reduction in systolic and diastolic

pressure levels ($P<0.01$); clinical effective rate was 63.63%; there was significance in results compared with the control group ($P<0.01$). These proved that lumbrokinase is effective in lowering blood pressure; however, the mechanism of this function needed to be further studied.

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