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Research Article

Effects of Kudiezi injection on diabetes patients complicated with cerebral infarction and bone mineral density

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Objective: To observe the clinical effects of Kudiezi injection on diabetes patients complicated with cerebral infarction and their bone mineral density.

Methodology: One hundred diabetes patients complicated with cerebral infarction were randomly divided into a control group and a treatment group. The control group was intravenously injected with 250 ml of 0.9% NaCl injection containing 0.5 g meclofenoxate (qd). The treatment group was intravenously administered with 250 ml of 0.9% NaCl injection containing 40 ml of Kudiezi injection (qd). The two groups were treated for 21 d to observe the therapeutic effects and safety.

Results: There were no intra-group or inter-group difference between the clinical and biochemical indices of the two groups on the 21st day ($P>0.05$). The overall effective rate of the treatment group was significantly higher than that of the control group ($P<0.05$), and the neurological deficit score was significantly lower ($P<0.05$). The blood rheology indices and cerebral blood flow of the treatment group were better than those of the control group ($P<0.05$). Both treatments significantly elevated the bone mineral density ($P<0.05$), and the treatment group enjoyed significantly better outcomes ($P<0.05$). No adverse reactions occurred.

Conclusion: Kudiezi injection in combination with meclofenoxate could treat diabetes complicated with cerebral infarction safely and effectively.

Keywords: Kudiezi injection; diabetes mellitus; cerebral infarction; bone mineral density.

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Introduction

As one of the independent risk factors of cerebral infarction, diabetic mellitus severely endangers human life and health. Diabetes patients are prone to cerebral infarction simultaneously with increasing prevalence of diabetes and population ageing[1]. Such patients are commonly treated by thrombolysis, fibrinolysis and inhibition of platelet aggregation. However, these protocols

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are limited in clinical practice due to the harsh requirements of time window[2]. Recently, acute cerebral infarction has been successfully treated by promoting brain metabolism, increasing cerebral blood flow and mitigating neurological disorders, etc[3].

Kudiezi injection, which is refined with a *Brassicaceae* family herb *Thlaspi arvense*, mainly contains adenosine and flavonoids[4,5]. Kudiezi injection can scavenge oxygen free radical, prevent ischemia-reperfusion injury, dilates blood vessels, increase cardiac cerebral blood flow, elevate fibrinolytic activity, and improve microcirculation[6]. Besides, Kudiezi injection is capable of relieving clinical symptoms such as ischemic cardiovascular and cerebrovascular diseases, and angioneurotic headache[7]. Moreover, Kudiezi injection positively affects the microcirculation, peripheral neuropathy, diabetic nephropathy and bone mineral density of diabetes patients[8].

Therefore, this study aimed to evaluate the effects of Kudiezi injection on the diabetes patients complicated with cerebral infarction as well as their bone mineral density.

Table 1. Clinical and biochemical indices before and after treatment

Index	Treatment		Control	
	Before	After	Before	After
BMI (kg/m^2)	26.3±7.6	25.9±7.2	26.5±8.1	26.0±7.6
HOMA-IR	8.24±1.13	8.31±1.61	8.28±1.08	8.26±1.71
PT (s)	12.7±2.1	12.5±2.0	12.6±2.1	12.4±1.9
APTT (s)	28.3±5.7	28.1±5.6	28.2±5.6	28.0±5.4
TT (s)	19.2±3.4	19.6±3.5	19.3±3.4	19.6±3.3
FIB (g/L)	2.92±0.54	2.88±0.48	2.90±0.49	2.85±0.43

Methodology

General information

One hundred diabetes patients complicated with cerebral infarction who were diagnosed conforming to relevant standards within 3 days were selected. Cerebral infarction was confirmed by cranial CT. They were divided by random sampling into a treatment group and a control group. The treatment group included 27 males and 23 females aged 35-70 years old [mean: (52.8 ± 16.3)], and the control group included 26 males and 24 females aged 36-72 years old [mean: (54.2±15.7)]. The gender, age, risk factors of cerebrovascular diseases and disease severity of the two groups were similar (P>0.05).

Written consent has been obtained from all patients. Exclusion criteria: 1) Severe liver and kidney diseases, other bone metabolism disorders and administration of drugs affecting bone metabolism; 2) administration of calcium-containing drugs, lipid-lowering drugs and active vitamin D; 3) unwilling to take required drugs or incomplete clinical data.

Treatment methods

All patients were administered with diabetic diet while taking part in moderate exercises to control the fasting blood glucose level at 5.5-6.5 mmol/L and the postprandial glucose level at 6.5-9.5 mmol/L by injecting insulin and/or orally administering antidiabetic agents. The patients with high blood pressure level, high blood lipid level, intracranial hypertension and infections were first treated correspondingly. In addition, the control group was intravenously injected with 250 ml of 0.9% NaCl injection containing 0.5 g meclofenoxate (Nanjing Hicin Pharmaceutical Co., Ltd.) (qd). The treatment group was intravenously administered with 250 ml of 0.9% NaCl injection containing 40 ml of Kudiezi injection (ShenYang Shuangding Pharmacy Co., Ltd.) (qd). The two groups were treated for 21 d to observe the therapeutic effects and safety.

Main clinical indices

The changes of blood rheology, cerebral blood flow, blood test items, electrolyte levels and liver, kidney functions before and after treatment were compared. The

plasma levels of C-reactive protein (CRP) and interleukin-6 (IL-6) were detected. Moreover, adverse reactions were observed and recorded.

Bone mineral density was measured by OSTEOCORE dual-energy X-ray absorptiometry (MEDILINK, France) at the the neck, Torch and Ward's triangle of femur of the non-dominant side, as well as the 1st-4th lumbar vertebrae. The machine was corrected daily before measurements (accuracy: 1%; measurement error: <1%).

Table 2. Therapeutic effects

Group	Case No.	Basically cured	Significantly improved	Improved	Unchanged	Aggravated	Overall effective rate (%)
Treatment	50	6	29	8	7	0	86.00%
Control	50	3	23	6	13	5	64.00%

Evaluation criteria for therapeutic effects

The therapeutic effects were graded according to the following criteria. Basically cured: Neurological deficit score decreases by 91%-100% (degree of disability: 0); significantly improved: neurological deficit score decreases by 46%-90% (degree of disability: 1-3); improved: neurological deficit score decreases by 18%-45%; unchanged: neurological deficit score decreases by approximately 17%; aggravated: neurological deficit score increases by over 18%. Overall effective rate = (Case number of basically cured patients + case number of significantly improved patients + case number of improved patients)/(total case number) × 100%[9].

Statistical analysis

All data were analyzed by SPSS 15.0 and expressed as $\bar{x}$ ±s (means ± standard deviation). The two groups were compared by t test. $P<0.05$ was considered statistically significant.

Results

Clinical and biochemical indices before and after treatment

The BMI, PT, APTT, TT and FIB of the two groups (both inter-group and intra-group) were similar after 21 days of treatment ($P>0.05$) (Table 1).

Table 3. Blood rheology indices

Index	Treatment		Control	
	Before	After	Before	After
Whole blood viscosity/mpa·s High cut	7.42±0.68	6.07±0.56*#	7.38±0.62	5.51±0.66*
Whole blood viscosity/mpa·s Low cut	18.05±2.81	14.52±2.04*#	17.92±2.76	11.90±2.31*
Plasma viscosity/%	2.02±0.18	1.61±0.17	2.04±0.20	1.81±0.14
Hematocrit/%	64.33±8.29	51.62±7.16*#	63.98±7.91	52.83±7.24*
Platelet viscosity/%	70.51±9.91	51.29±8.38*#	72.48±9.15	55.34±8.92*
Fibrinogen level/%	5.13±0.39	4.06±0.34*#	5.22±0.36	4.41±0.35

Compared with the results before treatment, *P<0.05; compared with the control group, #P<0.05.

Therapeutic effects

The overall effective rates of the treatment group and the control group were 86.00% and 64.00% respectively, which were significantly different (P<0.05) (Table 2).

Blood rheology indices

Whole blood viscosity, hematocrit and platelet viscosity were significantly different before and after treatment (P<0.05), and the fibrinogen level of the treatment group after treatment was also significantly different from that before treatment (P<0.05). After treatment, the whole blood viscosity, hematocrit, platelet viscosity and fibrinogen level of the treatment group were significantly different from those of the control group (P<0.05) (Table 3).

Cerebral blood flow

Both groups had significantly different cerebral blood flows after treatment compared with those before treatment (P<0.05). Moreover, most associated indices of the two groups were also significantly different (P<0.05) (Table 4).

Table 4. Cerebral blood flow

Position	Treatment			Control		
	Before	After	Difference	Before	After	Difference
Frontal lobe	51±5	58±7	7.1±1.7*#	52±4	53±4	1.1±0.4*
Parietal lobe	53±6	58±5	5.2±0.8*#	52±5	54±4	2.0±1.2*
Temporal lobe	51±4	59±4	8.7±0.6*#	51±5	55±3	3.8±1.7*
Occipital lobe	52±6	58±5	6.2±1.2*#	51±4	53±3	2.2±0.9*
Central sulcus	55±5	57±6	1.9±0.4*	54±6	53±5	1.8±1.1
Brainstem	57±5	66±3	9.2±1.5*#	56±3	60±3	4.2±0.5*
Focus	47±3	53±3	5.9±0.6*#	46±4	50±4	3.7±0.6
Peripheral focus	48±6	54±4	6.0±1.7*#	48±4	51±3	2.9±1.1
Cerebral hemisphere	50±4	56±5	6.2±1.1*#	49±5	53±4	3.0±1.2

Compared with the results before treatment, *P<0.05; compared with the control group, #P<0.05.

Serum CRP and IL-6 levels

CRP levels of both groups were reduced by 18.5% and 45.9% respectively after treatment, and IL-6 levels were decreased by 13.1% and 9.3% respectively (P<0.05). After treatment, CRP levels of the two groups were also significantly different (P<0.05) (Table 5).

Bone mineral density

Bone mineral densities of both groups were significantly raised after 21 days of treatment (P<0.05), and the two groups also had significantly different outcomes after treatment (P<0.05) (Table 6).

Table 5. Serum CRP and IL-6 levels

Index	Treatment		Control	
	Before	After	Before	After
CRP (mg/L)	15.62±3.31	8.33±1.59*#	15.48±3.27	11.64±2.94*
IL-6 (μg/L)	0.88±0.010	0.67±0.009*	0.89±0.012	0.62±0.008*

Compared with the results before treatment, *P<0.05; compared with the control group, #P<0.05.

Table 6: Bone mineral density

Index	Treatment		Control	
	Before	After	Before	After
L1-L4	0.73±0.04	0.95±0.04*#	0.72±0.05	0.87±0.06*
Neck	0.68±0.07	0.89±0.06*#	0.66±0.04	0.82±0.05*
Torch	0.52±0.06	0.85±0.05*#	0.53±0.05	0.74±0.06*
Ward	0.50±0.06	0.82±0.06*#	0.51±0.07	0.72±0.04*

Compared with the results before treatment, *P<0.05; compared with the control group, #P<0.05.

Discussion

Diabetes complicated with cerebral infarction occurs owing to complicated reasons, for which hyperglycemia may be a crucial risk factor. Besides, abnormal blood flow pattern and flow rate may also contribute to the devastating disease, and cerebral microcirculation can be reflected by dynamic blood rheological changes[10,11] that are closely associated with the aggregation and deformability of red blood cells and platelets, as well as plasma composition. After cerebral infarction, cerebral vascular occlusion decreases blood flow by inducing regional hypoperfusion or drying up and cerebral edema. Therefore, brain cell functions are severely damaged due to long-term ischemia that weakens the oxygen storage capacity, thus jeopardizing partial functions of normal cells and metabolism[12,13].

As an age-related disease, osteoporosis is mainly manifested as reduced mechanical strength of bone and loss of coupling between bone formation and resorption[14]. It has previously been reported that elderly men with type 2 diabetes suffered from significant decrease in bone mineral density, with the bone metabolism characteristics of increased bone resorption and decreased bone formation[15]. In addition, the patients with diabetic nephropathy were prone to bone fracture. As secondary osteoporosis, diabetic osteoporosis may be another chronic complication of diabetic mellitus, which has not been verified hitherto though[16]. However, bone fracture is bound to affect the quality of life of diabetes patients[17,18]. Hence, it is of great significance to treat diabetic osteoporosis.

Kudiezi injection, which is extracted, separated and refined from the whole herb of a *Brassicaceae* family plant *Thlaspi arvense*, mainly contains adenosine and flavonoids[19]. The injection can resist platelet aggregation, inhibit thrombosis, enhance fibrinolytic activity, promote thrombolysis, dilate blood vessels, reduce vascular resistance, increase cardiac cerebral blood flow, stabilize cell membrane and protect nerve functions[20].

In this study, the blood rheology indices and cerebral blood flows of both groups were significantly improved after treatment (P<0.05). In the meantime, the treatment group had significantly better outcomes than the control group did (P<0.01 or P<0.05). The overall effective rates of the treatment group and the control group were 86.00% and 64.00% respectively, which were significantly different (P<0.05).

In summary, Kudiezi injection could resist platelet aggregation, facilitate thrombolysis, improve cerebral circulation, protect nerve functions, effectively decrease the levels of serum CRP and IL-6, and suppress the release of inflammatory mediator. This injection gave rise to satisfactory outcomes for diabetes complicated with cerebral infarction while being fairly secure. Furthermore, it elevated the bone mineral density of type 2 diabetes patients without inducing coagulopathy, and it could be used to treat type 2 diabetes complicated with osteoporosis in combination with calcium reagents.

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None

Conflict of Interest

The authors declare no competing financial interest.

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