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Effect of resistance + aerobic exercise on insulin resistance, plaque properties and lipid metabolism in patients with diabetic macroangiopathy

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ABSTRACT

Objective: To study the effect of resistance + aerobic exercise on insulin resistance, plaque properties and lipid metabolism in patients with diabetic macroangiopathy. **Methods:** Patients with type 2 diabetes mellitus complicated by macroangiopathy who were treated in Zigong Third People′s Hospital between February 2015 and April 2016 were selected as the research subjects and randomly divided into exercise group and the control group who received resistance + aerobic exercise combined with hypoglycemic therapy and routine hypoglycemic therapy respectively. The insulin resistance indexes, plaque property indexes and lipid metabolism indexes were detected before intervention and 16 weeks after intervention. **Results:** 16 weeks after inclusion, serum F-Ins, MCP-1, YKL-40, MMP9, CatK, Caspase-3, TG, LDL, Resistin, Leptin and Visfatin contents of both groups of patients were significantly lower than those before inclusion, and serum F-Ins, MCP-1, YKL-40, MMP9, CatK, Caspase-3, TG, LDL, Resistin, Leptin and Visfatin contents of exercise group were significantly lower than those of control group. **Conclusion:** Resistance + aerobic exercise can improve the insulin resistance and lipid metabolism and stabilize the plaque properties in patients with diabetic macroangiopathy.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a common endocrine disease in our country, its important characteristics are the insulin resistance and relatively insufficient insulin secretion, and comprehensive treatment is needed to control blood glucose to reach the target[1,2]. Exercise is an important part of the comprehensive treatment for patients with type 2 diabetes mellitus, the common way of exercise is the resistance exercise and aerobic exercise, and moderate exercise on the basis of drug treatment can improve blood glucose control in patients with type 2 diabetes[3]. Diabetic macroangiopathy is the most common complication in patients with type 2 diabetes, it is basically characterized by macrovascular atherosclerosis and plaque formation, and there is no report about the effect of exercise on macroangiopathy characteristics and process in patients with type 2 diabetes. In the following studies, we analyzed the effect of resistance + aerobic exercise on insulin resistance, plaque properties and lipid metabolism in patients with diabetic macroangiopathy.

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2. Research subjects and methods

2.1 General information of research subjects

A total of 106 cases of patients with type 2 diabetes mellitus complicated by macroangiopathy who were treated in Zigong Third People′s Hospital between February 2015 and April 2016 were selected as the research subjects, all patients were diagnosed with type 2 diabetes mellitus by oral glucose tolerance test, and they were diagnosed with carotid atherosclerosis by carotid ultrasound examination. Patients with diabetic nephropathy and those with exercise contraindications were excluded. The 106 enrolled patients were divided into two groups by random number table, each with 53 cases. Exercise group included 32 men and 21 women that were

42-64 years old; control group included 30 men and 23 women that were 41-65 years old. There was no statistically significant difference in general information between the two groups (P>0.05).

2.2 Clinical intervention

Both groups received oral hypoglycemic drugs and/or insulin therapy, and the hypoglycemic target was fasting blood glucose < 6.0 mmol/L, and 2 h postprandial blood glucose 8 mmol/L. Exercise group received resistance + aerobic exercise intervention, and resistance exercise intervention method was as follows: after single maximum resistance load test, 60%-80% of the maximum resistance load was referred to selected the corresponding pounds of elastic rope, arms upward and standing crouching were finished in turn, repeating 5 times was as one group, 18-22 group were completed each time, and the exercise was conducted three times a week; exercise training method was as follows: the training included warm-up training, aerobics as well as the basic training and relaxation training of aerobic dance, each training lasted for 60 min, and the training was conducted three times a week.

2.3 Serum biochemical index detection

Fasting venous blood before inclusion and 16 weeks after inclusion were taken and centrifuged to separate serum, radioimmunoprecipitation kit was used to determine F-Ins contents, enzyme-linked immunosorbent assay kit was used to determine MCP-1, YKL-40, MMP9, CatK, Caspase-3, Resistin, Leptin and Visfatin contents, and automatic biochemical analyzer was used to detect the contents of TG and LDL.

2.4 Statistical methods

SPSS 19.0 software was used to input data, the data were analyzed by t test, and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Insulin resistance indexes

Before inclusion and 16 weeks after inclusion, F-Ins contents of exercise group were (14.58±2.05) U/mL and (9.68±0.93) U/mL respectively, and F-Ins contents of control group were (14.77±2.21) U/mL and (12.48±1.78) U/mL respectively. After t test, serum F-Ins contents were not statistically different between two groups of patients before intervention (P>0.05). 16 weeks after intervention, serum F-Ins contents of both groups of patients were significantly lower than those before intervention (P<0.05) and serum F-Ins contents of exercise group were significantly lower than those of control group (P<0.05).

3.2 Plaque property indexes

Before inclusion and 16 weeks after inclusion, analysis of serum plaque property indexes MCP-1 (pg/mL), YKL-40 (pg/mL), MMP9 (ng/mL), CatK and Caspase-3 (pg/mL) between two groups of patients was as follows: serum MCP-1, YKL-40, MMP9, CatK and Caspase-3 contents were not statistically different between two groups of patients before inclusion (P>0.05); 16 weeks after inclusion, serum MCP-1, YKL-40, MMP9, CatK and Caspase-3 contents of both groups of patients were significantly lower than those before intervention (P<0.05), and serum MCP-1, YKL-40, MMP9, CatK and Caspase-3 contents of exercise group were significantly lower than those of control group (P<0.05).

3.3 Lipid metabolism indexes

Before inclusion and 16 weeks after inclusion, analysis of serum lipid metabolism indexes TG, LDL, Resistin (ng/mL), Leptin (μg/mL) and Visfatin (ng/mL) between two groups of patients was as follows: serum TG, LDL, Resistin, Leptin and Visfatin contents were not statistically different between two groups of patients before

Table 1.
Changes in plaque property indexes before and after inclusion.

Groups	n	Time	MCP-1	YKL-40	MMP9	CatK	Caspase-3
Exercise group	53	Before inclusion	289.4±33.5	227.6±31.8	652.4±79.1	83.5±11.2	37.61±4.49
		16 weeks after inclusion	192.5±22.6^{*a}	178.3±20.3^{*a}	392.6±41.7^{*a}	60.7±8.7^{*a}	22.13±3.26^{*a}
Control group	53	Before inclusion	291.3±35.8	229.1±34.6	650.8±72.4	84.3±10.8	37.25±5.12
		16 weeks after inclusion	242.1±29.4^{a}	203.5±28.5^{a}	512.5±67.9^{a}	72.8±9.2^{a}	29.45±3.52^{a}

*: comparison between exercise group and control group, P<0.05; ^{a}: compared with those before inclusion, P<0.05.

Table 2.
Changes in lipid metabolism indexes before and after inclusion.

Groups	n	Time	TG	LDL	Leptin	Resistin	Visfatin
Exercise group	53	Before inclusion	6.16±0.79	3.52±0.52	29.51±4.24	93.1±10.2	53.1±6.7
		16 weeks after inclusion	4.88±0.62^{*a}	2.41±0.45^{*a}	18.93±2.42^{*a}	68.7±8.4^{*a}	30.2±4.7^{*a}
Control group	53	Before inclusion	6.22±0.83	3.49±0.49	29.94±3.89	92.8±10.2	52.7±7.1
		16 weeks after inclusion	5.62±0.78^{a}	3.11±0.37^{a}	23.41±3.20^{a}	80.1±9.5^{a}	41.9±6.2^{a}

*: comparison between exercise group and control group, P<0.05; ^{a}: compared with those before intervention, P<0.05.

inclusion (P>0.05); 16 weeks after inclusion, serum TG, LDL, Resistin, Leptin and Visfatin contents of both groups of patients were significantly lower than those before intervention (P<0.05), and serum TG, LDL, Resistin, Leptin and Visfatin contents of exercise group were significantly lower than those of control group (P<0.05).

4. Discussion

Exercise is an important part of the comprehensive treatment plan for type 2 diabetes mellitus, which has positive value for controlling blood glucose. Resistance and aerobic exercise are common ways of exercise for diabetic patients[4,5]. Resistance exercise is the anaerobic exercise that exerts a certain resistance on particular muscle group during exercise, which can ensure the muscle volume and increase the muscular uptake and utilization for glucose, and is helpful to increase insulin sensitivity[6,7]; aerobic exercise is the exercise with equivalent oxygen uptake and oxygen consumption, which can increase the glucose utilization in peripheral tissues, and also help increase insulin sensitivity[8]. Diabetic macroangiopathy is a common type of complication of type 2 diabetes mellitus, insulin resistance is an important characteristic in patients with type 2 diabetes mellitus and also an important link causing macrovascular complications, and hyperinsulinemia and relatively insufficient insulin secretion are the outstanding performances of insulin resistance. Nontheless, there is no clear report about the effect of exercise on insulin resistance in patients with diabetic macroangiopathy, and the analysis of the changes in insulin resistance before and after the exercise intervention in the study showed that serum F-Ins contents and INS resistance levels of both groups of patients significantly decreased while Ins secretion levels significantly increased after intervention, and serum F-Ins content and INS resistance level of exercise group after intervention were significantly lower than those of control group while Ins secretion level was higher than that of control group. This shows that resistance + aerobic exercise can improve insulin resistance and relatively insufficient insulin secretion, and reduce insulin levels in patients with diabetic macroangiopathy.

The characteristics of diabetic macroangiopathy are arteriosclerosis and atherosclerotic plaque formation, and lipid metabolism disorder is closely related to the formation and deposition of atherosclerotic plaques. TG is an important component of blood lipid in the body, and LDL can transfer lipid to surrounding tissues and make it deposit; the LDL that is transferred to the endangium is oxidized into ox-LDL, which can be further swallowed by macrophages to form foam cells and then gradually form the atheromatous plaque[9,10]. The synthesis and secretion of various adipocytokines such as Resistin, Leptin and Visfatin are abnormal in the process of dyslipidemia. Resistin can affect the sensitivity of insulin and cause vascular endothelial injury, which can induce the local deposition of macrophages and form the foam cells[11]; Leptin has strong pro-inflammatory activity, and can cause the endangium inflammation activation and accelerate the plaque formation[12]; Visfatin can induce the adipocyte differentiation and maturation and promote the lipid deposition in the endometrium[13,14]. In the study, analysis of the changes in serum lipid metabolism indexes before and after the exercise intervention showed that serum TG, LDL, Resistin, Leptin and Visfatin contents of both groups of patients after intervention were significantly lower than those before intervention, and serum TG, LDL, Resistin, Leptin and Visfatin contents of exercise group after intervention were significantly lower than those of control group. This indicates that resistance + aerobic exercise can help improve blood lipid metabolism in patients with diabetic macroangiopathy and then improve the process of atherosclerosis.

In the process of atherosclerosis, the changed properties and the decreased stability of atherosclerotic plaques can result in local thrombosis, also increase the embolus dropping and cause the risk of vascular thrombosis. The change of atheromatous plaque stability is closely related to the inflammatory response activation within plaque and the degradation of fibrous cap, and MCP-1, YKL-40, MMP9, CatK, Caspase-3 and other molecules can mediate the activation of the inflammatory response and the degradation of fibrous cap[15]. MCP-1 is a type of protein that can cause monocyte chemotaxis, which can promote the monocyte infiltration in the endangium and accelerate the formation of atheromatous plaques[16]; YKL-40 is a new type of inflammatory mediator that can mediate the cascade activation of inflammatory response in the atheromatous plaque and accelerate the changes in the plaque properties[17,18]; MMP9 and CatK have the activity to hydrolyze extracellular matrix, which can degrade various components in the fibrous cap of the atheromatous plaque, thus result in the fiber cap fracture and decrease the plaque stability[19,20]; Caspase-3 is the common downstream molecule of multiple apoptotic signaling pathways in the body, which can directly execute cell apoptosis and affect the stability of the plaque[21]. In the study, analysis of the changes in serum plaque property indexes before and after the exercise intervention showed that serum MCP-1, YKL-40, MMP9, CatK and Caspase-3 contents of both groups of patients after intervention were significantly lower than those before intervention, and serum MCP-1, YKL-40, MMP9, CatK and Caspase-3 contents of exercise group after intervention were significantly lower than those of control group. This shows that resistance + aerobic exercise can help to stabilize the plaque properties of patients with diabetic macroangiopathy.

Above all, it can be concluded that resistance + aerobic exercise combined with hypoglycemic drug therapy can be more effective than routine hypoglycemic therapy in improving the insulin resistance and lipid metabolism, and stabilizing the plaque properties in patients with diabetic macroangiopathy.

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