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Assessment of serum lipid metabolism index and cytokine levels in patients with type 2 diabetes mellitus complicated by coronary heart disease after telmisartan combined with lipid−lowering drug treatment

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ABSTRACT

Objective: To study the effect of telmisartan combined with lipid-lowering drug therapy on serum lipid metabolism index and cytokine levels in patients with type 2 diabetes mellitus complicated by coronary heart disease. **Methods:** A total of 106 patients with type 2 diabetes mellitus complicated by coronary heart disease who were treated in our hospital between September 2013 and October 2016 were collected and then divided into the control group (n=55) who received conventional treatment + lipid-lowering drug treatment and the observation group (n=51) who received conventional treatment + lipid-lowering drug + telmisartan treatment after the therapies were reviewed. Before and after treatment, serum levels of lipid metabolism indexes, inflammatory mediators and oxidative stress indexes were compared between two groups of patients. **Results:** Before treatment, the differences in serum levels of lipid metabolism indexes, inflammatory mediators and oxidative stress indexes were not statistically significant between two groups of patients. After treatment, serum TG and LDL-C levels in observation group were lower than those in control group while HDL-C level was higher than that in control group; serum inflammatory mediators IL-6, IL-8, HMGB1 and TNF-α levels were lower than those in control group; serum oxidative stress indexes MDA and ROS levels were lower than those in control group while GSH-Px level was higher than that in control group. **Conclusion:** Telmisartan combined with lipid-lowering drug therapy can effectively optimize the lipid metabolism and reduce the systemic inflammatory response and oxidative stress response in patients with type 2 diabetes mellitus complicated by coronary heart disease.

1. Introduction

Type 2 diabetes is the most common clinical endocrine disease and also high risk factor of coronary heart disease, patients with type 2 diabetes mellitus complicated by coronary heart disease are with much higher incidence of myocardial infarction than patients with coronary heart disease alone, and therefore, effective and reasonable intervention should be taken for such patients[1,2]. Abnormal lipid metabolism plays an important role in the development of diabetes and coronary heart disease, but many studies have shown that the role of lipid-regulating drugs alone is limited in reducing the hyperlipidemia and regulating lipid metabolism disorder, so many scholars suggest adding other mechanisms of drugs to expand the overall curative effect. Telmisartan belongs to non-peptide angiotensin Ⅱ receptor antagonist, and can effectively and irreversibly block ATI receptors and exert clinical effects without influencing other systems[3,4]. Current studies have shown that adjuvant telmisartan therapy can optimize the illness of diabetic patients with coronary heart disease, but there is not much related research at present. In the study, telmisartan was added for combination treatment on the basis of lipid-lowering drugs, and the curative effect was elaborated from the blood lipid metabolism, inflammatory mediators and oxidative stress indicators, now reported as follows.

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2. Information and methods

2.1 Case information

106 patients with type 2 diabetes mellitus complicated by coronary heart disease who were treated in our hospital between September 2013 and October 2016 were selected as the research subjects, and the patients themselves/family members signed the consent form. After the therapies were reviewed, the enrolled patients were divided into the control group (n=55) who received conventional treatment + lipid-lowering drug treatment and the observation group (n=51) who received conventional treatment + lipid-lowering drug + telmisartan treatment. Control group included 30 men and 25 women, they were 49-72 years old, the course of type 2 diabetes mellitus was 5-12 years, and the course of coronary heart disease was 3-7 years; observation group included 27 men and 24 women, they were 51-74 years old, the course of type 2 diabetes mellitus was 7-13 years, and the course of coronary heart disease was 2-7 years. Differences in distribution of gender, age, course of type 2 diabetes and course of coronary heart disease were not statistically significant between two groups of patients (P>0.05), and the hospital ethics committee approved the study.

2.2 Therapy

Both groups of patients received conventional therapy for type 2 diabetes mellitus and coronary heart disease, specifically as follows: isosorbide mononitrate to dilate coronary artery, aspirin for antiplatelet, and insulin to lower blood glucose. Control group of patients, based conventional therapy, received lipid-lowering drug therapy as follows: atorvastatin calcium tablets (Beijing Jialin Pharmaceutical Co., Ltd., approved by H20093819) 10 mg, 1 time each night, for continuous treatment of 12 weeks. Observation group of patients, based on conventional treatment + lipid-lowering drug therapy, received telmisartan treatment, specifically as follows: telmisartan (Beijing Juneng Pharmaceutical Co., Ltd., approved by H20060285) 40 mg, 1 time/d, for continuous treatment of 12 weeks.

2.3 Observation indexes

Before and after treatment, 5 mL of fasting cubital venous blood was obtained from two groups of patients, joined by anticoagulant, let stand at room temperature (25 ℃ or so) for stratification, and centrifuged at 4 ℃ and 2 500-3 500 r/min for 10-15 min, and the upper serum was taken and frozen in the deep cryogenic refrigerator for test. Automatic biochemical analyzer (Shenyang Neusoft Medical Systems Co., Ltd., model NSA-400) was used to determine the contents of lipid metabolism indexes, including triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C). Enzyme-linked immunosorbent assay (ELISA) was used to detect serum contents of inflammatory mediators, including interleukin-6 (IL-6), interleukin-8 (IL-8), high mobility group box B1 (HMGB1) and tumor necrosis factor (TNF-α). ELISA was used to determine serum levels of oxidative stress indexes, including propionaldehydes (MDA), glutathione peroxidase (GSH-Px) and reactive oxygen species (ROS).

2.4 Statistical processing

Data were recorded and calculated by the professionals, and statistical software was SPSS 21.0. Lipid metabolism indexes, inflammatory mediators, oxidative stress indexes and other measurement data were in terms of mean ± standard deviation, and comparison was by t test. Statistics P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Lipid metabolism indexes

Before treatment and 12 weeks after treatment, comparison of serum lipid metabolism indexes TG, LDL-C and HDL-C levels between two groups of patients was as follows: serum TG, LDL-C and HDL-C levels were not significantly different between two groups of patients before treatment (P>0.05); compared with those before treatment, serum TG and LDL-C levels in both groups decreased significantly while HDL-C levels increased significantly after treatment (P<0.05); compared with those in control group, serum TG and LDL-C levels in observation group decreased significantly while HDL-C level increased significantly after treatment (P<0.05), shown in Table 1.

3.2 Inflammatory mediators

Before treatment and 12 weeks after treatment, comparison of serum inflammatory mediators IL-6 (pg/mL), IL-8 (pg/mL), HMGB1 (μg/L) and TNF-α (pg/mL) levels between two groups of patients was as follows: serum IL-6, IL-8, HMGB1 and TNF-α levels were not significantly different between two groups of patients before treatment (P>0.05); compared with those before treatment, serum IL-6, IL-8, HMGB1 and TNF-α levels in both

Table 1.
Comparison of serum TG, LDL-C and HDL-C levels before and after treatment (mmol/L).

Groups	n	TG		LDL-C		HDL-C	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	55	6.82±0.75	5.17±0.58	4.17±0.53	3.29±0.41	1.03±0.14	1.27±0.16
Observation group	51	6.84±0.73	4.26±0.52	4.15±0.49	2.31±0.32	1.02±0.15	1.45±0.19
t		0.173	6.932	0.209	5.783	0.152	5.023
P		＞0.05	＜0.05	＞0.05	＜0.05	＞0.05	＜0.05

Table 2.
Comparison of serum IL-6, IL-8, HMGB1 and TNF-α levels before and after treatment.

Groups	*n*	IL-6		IL-8		HMGB1		TNF-α	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	55	25.83±3.19	15.19±2.07	94.27±10.38	61.88±7.53	9.83±1.76	7.05±0.83	36.48±4.19	21.63±3.05
Observation group	51	25.67±3.08	10.62±1.78	93.68±10.25	37.52±4.61	9.79±1.68	4.16±0.57	35.79±4.53	12.47±1.83
t		0.114	7.393	0.241	15.498	0.209	8.374	0.162	10.982
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Table 3.
Comparison of serum MDA, GSH-Px and ROS levels before and after treatment.

Groups	*n*	MDA		GSH-Px		ROS	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	55	14.38±1.76	11.26±1.84	112.28±14.69	137.95±15.62	12.38±1.76	9.15±0.98
Observation group	51	14.29±1.84	8.05±0.93	113.07±13.85	168.24±19.66	12.56±1.89	6.26±0.73
t		0.281	8.092	0.173	13.283	0.154	10.981
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

groups decreased significantly after treatment ($P<0.05$); compared with those in control group, serum IL-6, IL-8, HMGB1 and TNF-α levels in observation group decreased significantly after treatment ($P<0.05$), shown in Table 2.

3.3 Oxidative stress indexes

Before treatment and 12 weeks after treatment, comparison of serum oxidative stress indexes MDA (nmol/mL), GSH-Px (pg/mL) and ROS (U/L) levels between two groups of patients was as follows: serum MDA, GSH-Px and ROS levels were not significantly different between two groups of patients before treatment ($P>0.05$); compared with those before treatment, serum MDA and ROS levels in both groups decreased significantly while GSH-Px levels increased significantly after treatment ($P<0.05$); compared with those in control group, serum MDA and ROS levels in observation group decreased significantly while GSH-Px level increased significantly after treatment ($P<0.05$), shown in Table 3.

4. Discussion

There is a clear glucolipid metabolism disorder in patients with type 2 diabetes, poor disease control is easy to cause atherosclerosis and coronary heart disease, the incidence of type 2 diabetes mellitus complicated by coronary heart disease is increasing year by year in our country at present, the probability of myocardial infarction and sudden cardiac death are high in such patients, and it has become one of the major diseases which endangers the life safety of the middle-aged and elderly people[5,6]. Taking active treatment to alleviate the condition of patients with type 2 diabetes mellitus complicated by coronary heart disease is the key to reverse their clinical outcome, statins lipid-lowering drugs can effectively adjust the lipid metabolism of patients, but the effect of the single drug application is limited, and some scholars recommend joining telmisartan for combination therapy. Telmisartan belongs to the new antihypertensive drug, which specifically binds angiotensin receptor Ⅱ, has long action time, and can effectively alleviate persistent hypertension damage to vascular endothelial function[7,8]. In order to define the clinical benefit of adjuvant telmisartan therapy for patients with type 2 diabetes mellitus complicated by coronary heart disease, the lipid-lowering drugs and telmisartan + lipid-lowering drugs were added respectively based on conventional treatment in the study, and the treatment effect was compared between the two.

Lipid metabolism disorder is the basis for the occurrence and development of type 2 diabetes mellitus and also an important cause of coronary heart disease, and continuous lipid accumulation combined with local endothelial damage can cause the atheromatous plaque formation and blood vessel occlusion, and eventually lead to complete vascular occlusion and myocardial blood supply block[9,10]. TG, LDL-C and HDL-C are the most typical lipid metabolism-related indicators, there are common high blood TG and LDL-C, and low blood HDL-C in patients with hyperlipidemia, HDL-C has "degreasing" effect and can transport the lipid metabolites to liver and metabolize them out of the body, and its content is an important symbol of lipid metabolism disorders[11,12]. In the study, serum levels of above lipid metabolism indexes were compared between two groups of patients, and it was found that compared with control group, the observation group were with lower serum TG and LDL-C levels, and higher HDL-C level, indicating that telmisartan treatment at the same time lipid-lowering medication can further optimize the lipid metabolism.

Patients with type 2 diabetes and coronary heart disease both have a certain degree of systemic inflammation state, inflammation is enhanced when the two are complicated, and the release of massive inflammatory mediators is one of the root causes of type 2 diabetes and coronary heart disease aggravation[13,14]. IL-6, IL-8 and TNF-α are the typical pro-inflammatory mediators that are mostly deeply studied at present, which are secreted by mononuclear macrophages, and can further induce neutrophils to gather in local inflammation, and intensify the progress of the local inflammation and atherosclerosis. HMGB1 is a new kind of inflammatory medium discovered in recent years, which belongs to advanced inflammatory factor, is massively secreted in the vascular endothelial cells and atheromatous plaque, and can be combined with advanced glycation end product receptors to promote plaque deposits. In the study, serum levels of above inflammatory mediators were compared between the two groups of patients before and after treatment, and it was found that compared with those before treatment, serum IL-6, IL-8, HMGB1 and TNF-α levels in both groups of patients

were lower after treatment; further compared with control group, the observation group of patients were with lower serum IL-6, IL-8, HMGB1 and TNF-α levels after treatment, confirming that telmisartan combined with lipid-lowering medications can more effectively reduce the systemic inflammatory response, which is one of the important symbols of eased disease.

Excessive lipid accumulation and systemic inflammatory response can both cause lipid peroxidation and the release of a large number of oxidative metabolites, and make the body in excessive oxidative stress state, which can aggravate the conditions of diabetes and coronary heart disease and deteriorate the treatment outcome[15,16]. MDA and ROS belongs to oxidative indexes, their levels are highly consistent with the degree of oxidative stress, GSH-Px has antioxidant properties, and can inhibit the oxidative stress damage caused by MDA, ROS and so on, the two are in a state of relative balance in normal human body, and there are significant peroxidation and antioxidant capacity deficiency in patients with type 2 diabetes mellitus complicated by coronary heart disease[17,18]. In the study, serum levels of above oxidative stress indexes were compared between the two groups of patients before and after treatment, and it was found that compared with those before treatment, serum MDA and ROS levels in both groups of patients were lower while GSH-Px levels were higher after treatment; further compared with the control group, the observation group were with lower serum MDA and ROS levels, and higher GSH-Px level after treatment, showing that telmisartan combined with lipid-lowering drugs can effectively improve the systemic oxidative stress state in patients with type 2 diabetes mellitus and coronary heart disease, and help disease optimization.

It is thus clear that antihypertensive drug telmisartan and lipid-lowering drug therapy at the same time can effectively regulate the lipid metabolism levels and also reduce systemic inflammatory response and oxidative stress response, has a certain therapeutic effect, and is worthy of popularization and application in clinical practice in the future.

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