



Correlation of serum vitamin E content with insulin resistance and oxidative stress response in patients with type 2 diabetes mellitus

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ABSTRACT

Objective: To study the correlation of serum vitamin E content with insulin resistance and oxidative stress response in patients with type 2 diabetes mellitus. **Methods:** Patients who were diagnosed with type 2 diabetes mellitus in Xining Second People's Hospital between February 2016 and February 2017 were selected as T2DM group, healthy volunteers who received physical examination during the same period were selected as control group, oral glucose tolerance test was conducted to detect insulin resistance indexes, and fasting venous blood was collected to detect oxidative stress indicators. **Results:** Serum VitE, 2 h-Ins, 2 h-CP, Trx, Txnip, SOD and GSH-Px levels of T2DM group were significantly lower than those of control group while F-Ins, F-CP, MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels were significantly higher than those of control group; serum VitE level in T2DM patients was positively correlated with serum 2 h-Ins, 2 h-CP, Trx, Txnip, SOD and GSH-Px levels, and negatively correlated with serum F-Ins, F-CP, MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels. **Conclusion:** The decrease of serum vitamin E in patients with type 2 diabetes mellitus can lead to the aggravation of insulin resistance and the activation of oxidative stress response.

1. Introduction

Type 2 diabetes is a common endocrine system disease in China and the incidence is increasing year by year. The insulin resistance and the relative insufficiency of the islet β cell secretion function are the basic characteristics of the disease. In recent years, the study has found that excessive activation of oxidative stress reaction is an important characteristic of type 2 diabetes mellitus, and the activation of oxidative stress in patients with type 2 diabetes mellitus can not only directly cause islet β cell function damage and affect peripheral tissue sensitivity to insulin, but can also cause damage to glomeruli, neurons, endothelial cells and son on, and result in the corresponding diabetic complications[1,2]. Therefore, oxidative

stress is considered as the key factor to cause the occurrence of type 2 diabetes mellitus and the progression of complications, and the anti-oxidation is an important target to treat type 2 diabetes mellitus and prevent diabetic complications[3]. Vitamin E is a type of fat-soluble antioxidant nutrient located in the cell membrane, which can enhance the antioxidant capacity of the body and protect the cellular structure from oxidative stress injury[4,5]. In the following studies, we specifically analyzed the correlation between serum vitamin E content and insulin resistance as well as oxidative stress response in patients with type 2 diabetes mellitus.

2. Research subjects and methods

2.1 General information of research subjects

Patients who were diagnosed with type 2 diabetes mellitus in Xining Second People's Hospital between February 2016 and February 2017 were selected as T2DM group, and all patients

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conformed to the diagnosis of type 2 diabetes mellitus after oral glucose tolerance test. Healthy volunteers who received physical examination during the same period were selected as control group, and they were without metabolic diseases or genetic diseases. There were 78 cases in T2DM group, including 42 men and 36 women that were 42-65 years old; there were 45 cases of healthy subjects, including 25 men and 20 women that were 41-64 years old. There was no statistically significant difference in general information between the two groups ($P>0.05$).

2.2 Research methods

2.2.1 Insulin resistance evaluation

Two groups of subjects received the oral glucose tolerance test after inclusion, fasting venous blood specimen was collected to determine the contents of F-Ins and F-CP by electrochemical luminescence kit, and the venous blood sugar 2 h after the oral glucose was collected to determine the content of 2 h-Ins and 2 h-CP by electrochemical luminescence kit.

2.2.2 Oxidative stress response evaluation

Fasting venous blood samples were collected to detect the contents of vitamin E (VitE) according to the operation instructions of high-performance liquid mass spectrometer (LCM-8040) and the supporting reagents. The contents of MDA, AOPP, 8-OHdG, AGEs and LOX-1 were determined by enzyme-linked immunosorbent assay kit, and radioimmunoprecipitation kit was used to detect the contents of Trx, Txnip, SOD and GSH-Px.

2.3 Statistical methods

SPSS 16.0 software was used to input data, differences in measurement data between two groups were by t test, the correlation between two measurement data was by Pearson test and $P<0.05$ indicated statistical significance in differences in test results.

3. Results

3.1 Serum VitE levels

Serum VitE level of T2DM group was (28.52 ± 4.52) nmol/L and serum VitE level of control group was (43.78 ± 5.96) nmol/L. And t test showed that serum VitE level of T2DM group was significantly lower than that of control group. Differences in serum VitE levels were statistically significant between T2DM group and control group ($P<0.05$).

3.2 Insulin resistance indexes

Analysis of insulin resistance indexes F-Ins (U/mL), F-CP (ng/mL), 2 h-Ins (U/mL) and 2 h-CP (ng/mL) in OGTT test between two

groups of subjects was as follows: serum F-Ins and F-CP levels of T2DM group were significantly higher than those of control group while 2 h-Ins and 2 h-CP levels were significantly lower than those of control group. Differences in serum F-Ins, F-CP, 2 h-Ins and 2 h-CP levels were statistically significant between T2DM group and control group ($P<0.05$). Pearson correlation analysis showed that serum VitE level in T2DM patients was negatively correlated with F-Ins and F-CP levels, and positively correlated with 2 h-Ins and 2 h-CP levels.

Table 1.

Comparison of insulin resistance indexes between two groups of subjects.

Groups	n	F-Ins	F-CP	2 h-Ins	2 h-CP
T2DM group	78	12.31±1.84	1.32±0.17	28.75±3.35	1.93±0.25
Control group	45	5.52±0.77	0.78±0.15	66.61±8.25	6.62±0.83
T		12.741	8.398	13.426	32.589
P		<0.05	<0.05	<0.05	<0.05

3.3 Oxidative stress indexes

Analysis of anti-oxidation indexes Trx (ng/mL), Txnip (pg/mL), SOD (U/L) and GSH-Px (U/L) between two groups of subjects was as follows: serum Trx, Txnip, SOD and GSH-Px levels of T2DM group were significantly lower than those of control group. Differences in serum Trx, Txnip, SOD and GSH-Px levels were statistically significant between T2DM group and control group ($P<0.05$). Pearson correlation analysis showed that serum VitE level in T2DM patients was positively correlated with Trx, Txnip, SOD and GSH-Px levels.

Analysis of oxidation products MDA (nmol/L), AOPP (nmol/L), 8-OHdG (ng/mL), AGEs (μ g/mL) and LOX-1 (ng/mL) between two groups of subjects was as follows: serum MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels of T2DM group were significantly higher than those of control group. Differences in serum MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels were statistically significant between T2DM group and control group ($P<0.05$). Pearson correlation analysis showed that serum VitE level in T2DM patients were negatively correlated with MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels.

Table 2.

Comparison of anti-oxidation indexes between two groups of subjects.

Groups	n	Trx	Txnip	SOD	GSH-Px
T2DM group	78	33.52±5.21	14.51±1.89	65.61±7.68	58.69±6.74
Control group	45	48.59±6.25	20.34±2.41	104.52±13.28	109.33±12.46
T		7.498	7.912	8.762	9.672
P		<0.05	<0.05	<0.05	<0.05

Table 3.

Comparison of oxidation products between two groups of subjects.

Groups	n	MDA	AOPP	8-OHdG	AGEs	LOX-1
T2DM group	78	19.45±2.24	95.52±11.25	131.25±18.86	33.25±5.25	4.41±0.56
Control group	45	7.32±0.94	37.51±4.52	52.41±7.32	15.64±1.78	2.43±0.33
T		12.948	14.216	15.249	11.329	8.498
P		<0.05	<0.05	<0.05	<0.05	<0.05

4. Discussion

Oxidative stress is the key link causing disease progression in patients with type 2 diabetes mellitus. In the process of oxidative stress reaction activation, the massively generated reactive oxygen species can on the one hand, directly damage islet β cells and affect the secretion of insulin, and on the other hand, will influence the glucose uptake and metabolism by peripheral tissue and decrease the insulin sensitivity[6]. Vitamin E is a kind of antioxidant nutrient located in cell membrane and strongly fat-soluble, which can increase the antioxidant capacity of cells and protect cells from the damage of oxygen free radicals. Studies have reported that vitamin E supplementation can mitigate the oxidative stress reaction in patients with type 2 diabetes mellitus[7,8], but there is no clear report about vitamin E change in the course of type 2 diabetes mellitus. In the above study, analysis of serum VitE levels in patients with type 2 diabetes mellitus showed that serum VitE level of T2DM group was significantly lower than that of control group. This indicates that VitE content reduction is associated with the occurrence of type 2 diabetes mellitus, and the decreased antioxidant capacity as well as the insulin resistance and oxidative stress damage caused by VitE content reduction may be closely related to the incidence of type 2 diabetes mellitus.

Insulin resistance is the main pathological feature of type 2 diabetes mellitus, and the reduced peripheral tissue sensitivity to insulin will affect blood glucose metabolism, and also lead to the increased compensatory secretion of insulin. To clarify whether the lower VitE content was associated with insulin resistance in the course of patients with type 2 diabetes, the insulin resistance indexes were analyzed in the study at first, and the results showed that serum F-Ins and F-CP levels of T2DM group were significantly higher than those of control group while 2h-Ins and 2h-CP levels were significantly lower than those of control group. This means that fasting insulin secretion increases and postprandial insulin secretion decreases in patients with type 2 diabetes mellitus, and the compensatory hyperinsulinemia and postprandial insulin deficiency also indicate that patients with type 2 diabetes mellitus have significant insulin resistance and poor postprandial reactivity of islet function. Further analysis of the correlation between VitE content and insulin resistance showed that serum VitE level in T2DM patients was negatively correlated with F-Ins and F-CP levels, and positively correlated with 2 h-Ins and 2 h-CP levels. This indicates that the decrease of VitE in patients with type 2 diabetes mellitus is associated with insulin resistance and poor islet function reactivity; decrease of VitE content can cause the excessive activation of oxidative stress reaction, lead to oxidative damage of β cells and affect the peripheral tissue sensitivity to insulin, resulting in insulin resistance and poor islet function reactivity.

In the process of oxidative stress reaction activation, the continuous generation of oxygen free radicals can cause the constant consumption of various antioxidants in the body. Trx is a small molecular protein with antioxidant effect, which can interact with Txnip to directly remove hydrogen peroxide and reactive oxygen species groups, and can also activate a variety of transcription factors to inhibit apoptosis and reduce cell damage[9,10]; SOD and GSH-Px are antioxidant enzymes with catalytic reduction in the body, which can eliminate oxygen free radicals and reduce oxidative stress response through reduction reactions[11,12]. In the study, analysis of anti-oxidation indexes showed that serum Trx, Txnip, SOD and GSH-Px levels of T2DM group were significantly lower than those of control group. This shows that there is an excessive consumption of antioxidant enzymes in type 2 diabetic patients, and then indicates that oxidative stress response is overactive. Further analysis of the correlation between VitE content and anti-oxidation indexes showed that serum VitE level in T2DM patients was positively correlated with Trx, Txnip, SOD and GSH-Px levels. This means that the decrease of VitE content in patients with type 2 diabetes mellitus is associated with the excessive consumption of antioxidant enzymes, and the reduction of VitE content can cause the excessive activation of oxidative stress reaction and the increased formation of oxygen free radicals, and increase the consumption of antioxidant enzymes.

The activation of oxidative stress response in diabetic patients is related to the substandard blood glucose control and excessive AGEs generation, and the excessively generated AGEs can be combined with the receptor RAGE to induce the formation of oxygen free radicals[13,14]. The generated oxygen free radicals can have oxidation reaction with the protein and lipid in the cell, which not only generates the oxidation products MDA, AOPP and LOX-1, and also causes cell structure and function damage[15–17]. In the study, analysis of serum oxidation product contents in subjects showed that serum MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels of T2DM group were significantly higher than those of control group. Further analysis of the correlation between VitE content and oxidative products showed that serum VitE level in T2DM patients was negatively correlated with MDA, AOPP, 8-OHdG, AGEs and LOX-1 levels. This means that the decrease of VitE content in patients with type 2 diabetes mellitus is associated with the excessive generation of oxidation products, and the reduction of VitE content can cause the excessive activation of oxidative stress reaction and the increased formation of oxygen free radicals, and increase the formation of oxidation products.

To sum up, it can be concluded that the serum vitamin E level significantly reduces in patients with type 2 diabetes mellitus; the decrease of vitamin E content can cause oxidative stress response activation, and result in insulin resistance and poor islet function reactivity.

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