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Correlations of 25(OH)D level with blood lipid, inflammatory factors and vascular endothelial function in diabetic patients

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Abstract. – OBJECTIVE: To investigate the correlation between 25-hydroxyvitamin D [25(OH) D] and the lipid profile, inflammatory cytokines, and endothelial function in diabetic patients.

PATIENTS AND METHODS: A total of 77 patients with type 2 diabetes mellitus treated in our hospital from January 2015 to March 2017 and 73 healthy volunteers were selected. The 25(OH)D, lipids, inflammatory factors, and endothelial function were compared between the two groups. The levels of 25(OH)D in diabetic patients were also compared to detect the levels of serum lipids and inflammatory cytokines in different groups. According to the inflammatory factors, patients with diabetes mellitus were divided into several groups. In addition, 25(OH) D, endothelial function indicators [nitrogen oxide (NO) and von Willebrand factor (vWF)], serum lipids [triglyceride (TG) and total cholesterol (TC)], high-density lipoprotein (HDL), and inflammatory factor tumor necrosis factor-alpha (TNF-α) were compared among different groups.

RESULTS: Compared with normal group, the 25(OH)D, NO, and HDL in the diabetic group were significantly lower than those in the normal group ($p<0.05$). Other lipids and inflammatory factors in the former were significantly higher than those in the normal group. Patients have lower HDL in those with less amount of 25(OH) D. Other blood lipid components such as TC and TG, LDL, and inflammatory factors significantly increased gradually as the 25(OH)D grows ($p<0.05$). For patients with more inflammatory cytokines, levels of 25(OH)D, NO, vWF, and ET-1 were significantly lower than those with normal inflammatory cytokines. Correlation analysis revealed that 25(OH)D was positively correlated with HDL and NO, but negatively correlated with TG, TC, TNF-α, and vWF.

CONCLUSIONS: In diabetic patients, the level of 25(OH)D is decreased and the inflammatory factors are increased. In patients with proper supplementation of 25(OH)D, the inflammation can be reduced and endothelial function can be improved.

Key Words:
Diabetes mellitus, Lipid, 25-hydroxyvitamin D, Inflammation.

Introduction

Diabetes mellitus, as an endocrine disease with a high clinical incidence rate, has a lot of adverse reactions, such as excessive intake of food and excessive urination, and it can even cause symptoms, such as cataract and diabetic foot, which can seriously affect the life and quality of patients[1-3]. Type 2 diabetes mellitus is the main type of diabetes, and its incidence rate will not be increased with age. Clinical studies[4-7] found that in this kind of disease, hyperlipidemia, inflammatory reactions and vascular endothelial damage can be caused. It is found that vitamin D is associated with diabetes metabolism. This study was performed to explore the relationships of vitamin D with blood lipids, and inflammation and vascular endothelial function of the diabetic patients[8-10].

Patients and Methods

Patients

A total of 77 patients with type 2 diabetes mellitus in our hospital from January 2015 to March 2017 were enrolled. 73 healthy volunteers were selected as the research objects, among which there were 40 men and 33 women aged 30-59 years old, with an average age of (48.42±5.43) years old in the normal group. All patients with type 2 diabetes mellitus conformed to the WHO diagnostic criteria for diabetes. There were no significant differences in age and sex between the

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two groups, and data were comparable. This study was approved by the Ethics Committee of Anhui Provincial Hospital. Signed written informed consents were obtained from the patients and/or guardians.

Diagnostic criteria for type 2 diabetes mellitus: the glucose concentration was greater than 11.1 mmol/L, the concentration of FPG was greater than 7.0 mmol/L, and all the above tests were performed after the fasting for 8 h.

Exclusion criteria: patients with damaged heart, liver, kidney, or other important organs, patients with osteoporosis, and patients with serious allergic reactions.

Methods

Blood lipids, inflammatory factors and vascular endothelial function indicators of all participants were detected after fasting for 8 hours. The patients with diabetes were further grouped according to the level of 25(OH)D and, then, blood lipids, inflammatory factors, and endothelial function indices were compared among groups. Also, patients were divided according to the degree of inflammation (TNF-α content), and the blood lipid and endothelial function were compared between normal group and abnormal group.

Observation Indicators

Blood lipid indices, including triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL), were measured by Roche electrochemiluminescence.

Inflammatory factors, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), were measured by enzyme-linked immunosorbent assay (ELISA).

Vascular endothelial function indicators, including Endothelin-1 (ET-1), diastolic factor NO and von Willebrand factor (vWF), ET-1 were measured by ELISA kits.

Table I. Comparisons of 25(OH)D, blood lipids, inflammatory factors and endothelial functions between normal group and diabetic group.

Index	Results	
	Normal group (n=73)	Diabetic group (n=77)
25(OH)D (ng/mL)	31.3±5.4	10.2±3.2*
TNF-α (ng/mL)	8.23±2.5	19.01±6.3*
IL-6 (ng/mL)	8.16±2.5	18.93±5.7*
ET-1 (ng/mL)	63.21±12.2	98.31±12.7*
NO (ng/mL)	78.2±12.1	40.5±10.8*
vMF (ng/mL)	65.5±9.8	123.2±11.8*
TG (ng/mL)	1.42±0.21	1.83±0.30*
TC (ng/mL)	4.82±0.32	5.23±0.29*
LDL (ng/mL)	2.63±0.26	2.98±0.27*
HDL (ng/mL)	1.72±0.12	1.63±0.12*

Note: *compared with the normal group, $p<0.05$.

Statistical Analysis

All data were processed by Statistical Product and Service Solutions (SPSS) 20.0 software (IBM, Armonk, NY USA). Measurement data were expressed as ($\bar{x}\pm s$) and the enumeration data were expressed as [n (%)]. The correlation analysis was performed by Pearson correlation. $p<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of 25(OH)D, Blood Lipids, Inflammatory Factors and Endothelial Functions Between the Normal Group and the Diabetic Group

25(OH)D, blood lipids, inflammatory factors, and endothelial functions between the normal group and the diabetic group were compared. It was found that the levels of 25(OH)D, NO, and HDL in diabetic group were significantly lower than those in normal group ($p<0.05$), and the levels of other blood lipids and inflammatory factors in the former were significantly higher than those in the latter (Table I).

Comparisons of Blood Lipids and Inflammatory Factors Among Different 25(OH)D Groups

It was found in different 25(OH)D groups that as the decrease of the content of 25(OH)D in the patient's body, the content of blood lipid HDL was getting lower. Other lipid components, such as TC, TG, LDL, and inflammatory factors, such as TNF-α, were getting higher. The differences were statistically significant ($p<0.05$) (Table II).

Comparisons of 25(OH)D and Endothelial Function Among Groups with Different Levels of Inflammation

Compared with those in the normal group, the contents of 25(OH)D and NO in the group with high levels of inflammatory factors were decreased ($p<0.05$), while the vascular endothelial function indexes vWF and ET-1 were significantly decreased ($p<0.05$), and the differences were statistically significant (Table III).

Table II. Comparisons of blood lipids and inflammatory factors among different 25(OH)D groups.

Group	n	TC (ng/mL)	TG (ng/mL)	LDL (ng/mL)	HDL (ng/mL)	TNF-α (ng/mL)
Normal 25(OH)D	23	4.81±0.7	1.40±0.03	2.59±0.32	1.89±0.12	10.21±1.43
Insufficient 25(OH)D	25	4.98±0.38	1.69±0.02	2.87±0.21	1.73±0.11	15.46±2.43
Lack of 25(OH)D	29	5.43±0.56*	1.90±0.15*	2.99±0.21*	1.60±0.23*	19.89±3.33*

Note: *compared with the 25(OH)D normal group, $p<0.05$.

Table III. Comparisons of 25(OH)D and endothelial functions in different levels of inflammation.

Groups	n	25(OH)D (ng/mL)	NO (ng/mL)	vMF (ng/mL)	ET-1 (ng/mL)
Normal group	23	19.4±4.2	77.6±5.4	69.4±6.7	102.3±9.6
Abnormal group	54	10.9±2.1	40.5±6.4	139.3±10.6	66.3±3.5

Note: *compared with the normal group, $p<0.05$.

Correlations of 25(OH)D with Blood Lipids, Inflammatory Factors, and Endothelial Functions in Diabetic Patients

The correlation of 25(OH)D with blood lipid indicators (TG, TC, and HDL), inflammatory factor (TNF-α) and endothelial function indicators (NO and vWF) in diabetic patients were compared, respectively. It was found that 25(OH)D was negatively correlated with TG, TC, TNF-α and vWF (r=-0.3465, r=-0.6432, r=-0.8743, r=-0.7532, $p<0.05$), but positively related to HDL and NO (r=0.6532, r=0.5427, $p<0.05$; Figure 1 A-F).

Discussion

Type 2 diabetes mellitus is the main type of diabetes, which will bring a heavy burden to life and work of patients. As a chronic endocrine

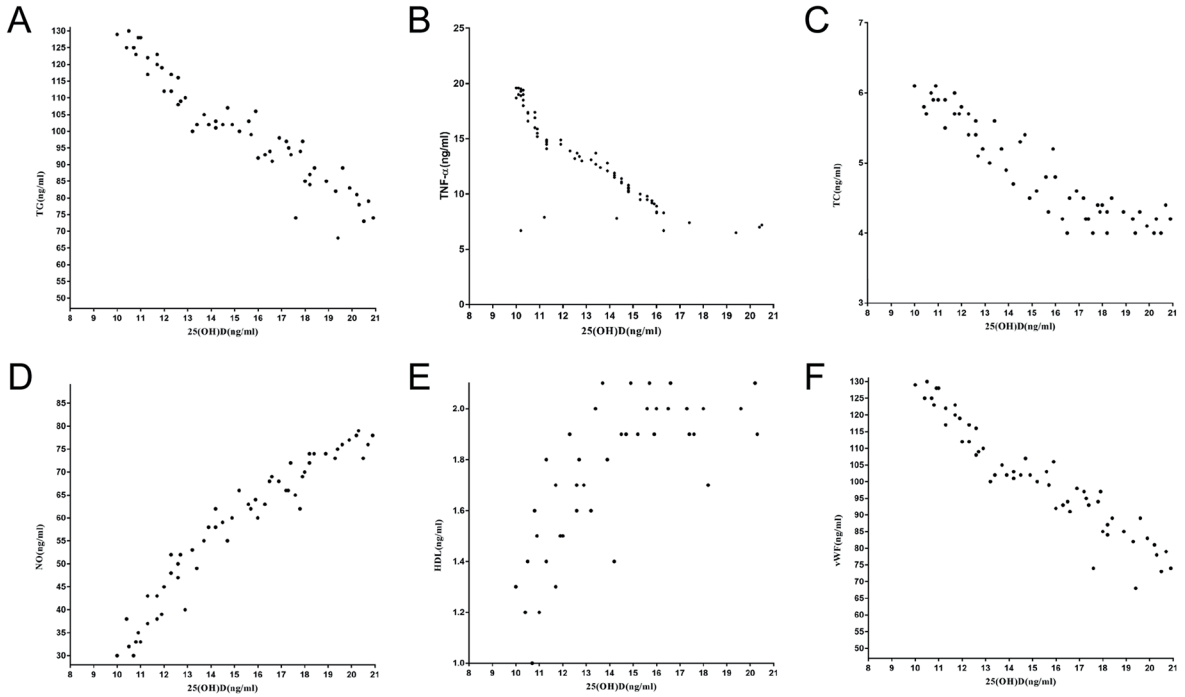

Figure 1. Correlations of 25(OH)D with blood lipids, inflammatory factors and endothelial functions in diabetic patients. ***A,*** The correlation between 25 OH)D and TG. ***B,*** The correlation between 25(OH)D and TNF-α. ***C,*** The correlation between 25(OH)D and TC. ***D,*** The correlation between 25(OH)D and NO. ***E,*** The correlation between 25(OH) D and HDL. ***F,*** The correlation between 25(OH)D and vWF.

disease, it can cause serious damage to the endocrine system[11,12]. A clinical research has found that type 2 diabetes mellitus is a chronic inflammatory disease, and after the onset, there will be a series of inflammatory reactions. Therefore, many inflammatory factors play very important roles in this disease, in which the TNF-α and IL-6, as the common factors, play important roles in inflammatory reactions[13]. Diabetic patients also have the symptom of vascular damage. Abnormal secretions of endothelial contraction factor ET-1 and diastolic factors often occur in patients. They will lead to vasospasm contraction and occurrence of adverse reactions of endothelial ischemia and hypoxia, thus thickening the vascular wall and causing smooth muscle spasm[14,15]. In addition, as a kind of polysaccharide protein in vascular endothelial function indices, vWF is secreted by endothelial cells *in vivo*, which can play an important role in the physiological process of coagulation. When the blood vessel wall is damaged, the secretion of vWF will be increased, so it can be used as an indicator of the damage degree of the vascular wall. Diabetes is also related to dyslipidemia. When patients suffer from type 2 diabetes mellitus, they will have a series of dyslipidemia symptoms, which will lead to the changes in blood lipid level and cause abnormal lipid composition in the body[16].

Metabolic abnormalities in diabetic patients are associated with vitamin D, but there is relatively little research on the relationship between them. Therefore, the relationships of vitamin D with blood lipid indices, inflammatory factors, and vascular endothelial indicators were explored in this study. Compared with those in healthy people, vitamin D, HDL, and NO in diabetic patients were decreased, while lipid indices (TG, TC, and LDL), inflammatory factors (TNF-α and IL-6), and vascular endothelial factors (vWF and ET-1) were increased significantly[17], suggesting that the vitamin D secretion in diabetic patients is decreased, the inflammatory factors are increased, the prevalence rate of inflammatory reaction is also increased and damage to vascular endothelial wall is aggravated[18,19]. After grouping diabetes patients according to vitamin D, it was found that HDL and NO were also significantly decreased with the decrease of vitamin D content, but other blood lipid indexes, inflammatory factors, and vascular endothelial factor indices were significantly increased. Moreover, according to the correlation analysis, vitamin D was positively correlated with HDL and NO, but negatively correlated with blood lipid indexes (TG, TC, and LDL), inflammatory factors (TNF-α and IL-6), and vascular endothelial factors (vWF and ET-1). Clinical studies have revealed that the existing form of the vitamin in the body, 25(OH)D, can promote the secretion of nuclear factor-kappa B (NF-κB) inhibitor, which will lead to the abnormal formation of inflammatory factors such as TNF-α. Relevant studies on vitamin D and blood lipids have shown that when the secretion of vitamin D reduces, the level of PTH *in vivo* will increase, resulting in the increased secretion of active vitamin D and adipocyte calcium influx *in vivo*, thus promoting the expression of lipase. Finally, the synthesis of lipids is increased and all kinds of blood lipid factors will also be increased in patients.

Conclusions

Vitamin D is significantly reduced in diabetic patients, and it is negatively related to blood lipid indicators, inflammatory factors, and vascular endothelial functional factors. Therefore, in order to reduce the adverse effects in diabetic patients, such as hyperlipidemia and endothelial wall damage, vitamin D can be taken properly for appropriate prevention and treatment.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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