

Correlation between Serum 25-Hydroxyvitamin D3 and Abnormal Insulin Secretion in Patients with Type 2 Diabetes Mellitus

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To investigate the correlation between serum 25-hydroxyvitamin D3 and abnormal insulin secretion in patients with type 2 diabetes mellitus. Eight type 2 diabetes mellitus patients treated from January 2018 to November 2020 (observation group) and another 80 healthy volunteers receiving physical examination in the same period (control group) were included. Fasting venous blood sample was collected to detect serum 25-hydroxyvitamin D3, fasting blood glucose, glycosylated hemoglobin, fasting insulin, insulin resistance index and insulin secretion index. According to insulin secretion index, observation group was divided into normal and abnormal insulin secretion groups and their serum 25-hydroxyvitamin D3, fasting blood glucose, glycosylated hemoglobin, fasting insulin and insulin resistance index were compared. Based on serum 25-hydroxyvitamin D3 level, observation group was divided into serum 25-hydroxyvitamin D3 positive and negative groups and their fasting blood glucose, glycosylated hemoglobin, fasting insulin, insulin resistance index and insulin secretion index were compared. The correlations of serum 25-hydroxyvitamin D3 with fasting blood glucose, glycosylated hemoglobin, fasting insulin, insulin resistance index and insulin secretion index were analyzed. Observation group had lower serum 25-hydroxyvitamin D3 level and insulin secretion index and higher fasting blood glucose, glycosylated hemoglobin, fasting insulin and

insulin resistance index than those of control group ($p<0.05$). Abnormal insulin secretion group had lower serum 25-hydroxyvitamin D3 level and higher fasting blood glucose, fasting insulin and insulin resistance index than those of normal insulin secretion group ($p<0.05$). Serum 25-hydroxyvitamin D3 positive group had higher fasting blood glucose, glycosylated hemoglobin, fasting insulin and insulin resistance index and lower insulin secretion index than those of serum 25-hydroxyvitamin D3 negative group ($p<0.05$). Serum 25-hydroxyvitamin D3 was negatively correlated with fasting blood glucose, glycosylated hemoglobin, fasting insulin and insulin resistance index, but positively correlated with insulin secretion index. In type 2 diabetes mellitus patients, the expression of serum 25-hydroxyvitamin D3 is down-regulated, which is closely related to abnormal insulin secretion. Serum 25-hydroxyvitamin D3 can be used to determine the insulin secretion function of type 2 diabetes mellitus patients.

Key words: Type 2 diabetes mellitus, insulin secretion, 25-hydroxyvitamin D3, correlation

Type 2 diabetes mellitus (T2DM), a common chronic metabolic disease, is mainly characterized by insulin resistance (IR) and it easily leads to a variety of complications, seriously harming the physical health of patients^[1-3]. In clinical practice, it is advocated to diagnose and treat T2DM as early as possible. However, in recent years, increasing studies have verified that 25-hydroxyvitamin D3 [25-(OH)D3] plays a vital role in the occurrence and development of T2DM^[4]. In this study, 80 T2DM patients treated in our hospital from January 2018 to November 2020 were compared with another 80 healthy volunteers to determine the correlation between serum 25-(OH)D3 and abnormal insulin secretion in T2DM patients, aiming to investigate the expression and clinical significance of serum 25-(OH)D3 in T2DM. Eight T2DM patients treated from January 2018 to November 2020 (observation group) and another 80 healthy volunteers receiving physical examination in the same period (control group) were included. In control group, there were 43 males and 37 females' aged 50-84 y old and (65.43±9.14) y old on average. In observation group, there were 44 males and 36 females' aged 50-85 y old and (65.68±9.32) y old on average. There were no significant differences in the age and gender between the two groups ($p>0.05$). This study was approved by the Ethics Committee of our hospital and all patients signed the informed consent. Inclusion criteria: Patients meeting the diagnostic criteria in the Chinese Guidelines for the Prevention and Treatment of T2DM (2017 Edition)^[5], confirmed by symptom observation and blood glucose test; those aged ≥ 50 y old; those who were conscious and would cooperate in the study. Exclusion criteria: Patients with consciousness disorder or mental disorder; those with severe infection, malignant tumor or hematological disease; or those with other chronic underlying diseases.

On the day of examination, the early morning fasting venous blood (5 mL) was collected from each subject as blood test sample and stored in a special vacuum anticoagulant tube for blood test. After the blood sample was centrifuged at 3000 rpm and 10 cm radius for 10 min continuously, the serum was collected. Later, the serum 25-(OH)D3 level was determined by high-performance liquid chromatography-tandem mass spectrometry, fasting blood glucose (FBG) was measured by glucose oxidase method, glycosylated hemoglobin (HbA1c) was detected by high-performance liquid chromatography and fasting insulin (FI) was determined by immunochromatography. IR index and insulin secretion index were calculated as follows: IR index=FI×FBG/22.5, insulin secretion index=20×FI/(FBG-3.5). Serum 25-(OH)D3, FBG, HbA1c, FI, IR index and insulin secretion index were compared between observation group and control group. According to insulin secretion index, patients in observation group were divided into normal insulin secretion group (insulin secretion index ≥ 50) and abnormal insulin secretion group (insulin secretion index < 50) and serum 25-(OH)D3, FBG, HbA1c, FI and IR index were compared between the two groups. Based on the serum 25-(OH)D3 level, patients in observation group were divided into serum 25-(OH)D3 positive group ($< 7.37 \mu\text{g/L}$) and serum 25-(OH)D3 negative group ($\geq 7.37 \mu\text{g/L}$) and FBG, HbA1c, FI, IR index and insulin secretion index were compared between the two groups. Moreover, the correlations

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of serum 25-(OH)D3 with FBG, HbA1c, FI, IR index and insulin secretion index were analyzed in T2DM patients. SPSS 26.0 software was utilized for statistical analysis. The χ^2 test was performed for numerical data (n) and the t-test was used to examine the measurement data ($\bar{x}\pm s$). $p < 0.05$ suggested that a difference was statistically significant. Spearman's test was employed to analyze the correlations and $p < 0.05$ suggested a linear correlation. $r > 0$ indicated a positive correlation and $r < 0$ implied a negative correlation. Observation group had lower serum 25-(OH)D3 level and insulin secretion index and higher FBG, HbA1c, FI and IR index than those of control group ($p < 0.05$) (Table 1). Among the 80 T2DM patients, 59 had abnormal insulin secretion and 21 had normal insulin secretion. Abnormal insulin secretion group had a lower serum 25-(OH)D3 level and higher FBG, HbA1c, FI and IR index than normal insulin secretion group ($p < 0.05$) (Table 2). Among the 80 T2DM patients, 54 were positive for serum 25-(OH)D3 and 26 were negative for serum 25-(OH)D3. Serum 25-(OH)D3 positive group had higher FBG, HbA1c, FI and IR index and lower insulin secretion index than serum 25-(OH)D3 negative group ($p < 0.05$) (Table 3). Serum 25-(OH)D3 was negatively correlated with FBG, HbA1c, FI and IR index, but positively correlated with insulin secretion index in T2DM patients (Table 4). T2DM, a chronic disease with a long disease course, is clinically manifested as abnormal increase of blood glucose level. Patients with T2DM are often accompanied by symptoms such as thirst, polyuria and fatigue, seriously affecting their physical and mental

health^[6-8]. T2DM is more common in the elderly patients. In recent years, with the increase in the elderly population, the incidence rate of T2DM has shown an upward trend, and this disease has become a public health problem endangering people's health^[9]. The pathogenesis of T2DM has not been fully elucidated and there is still a lack of means to cure T2DM, so the major treatment goal is to control blood glucose^[10]. Insulin is the major means of clinical treatment of T2DM and it suppresses the secretion of insulin in the body mainly through exogenous supplement of insulin, so as to reduce insulin and IR in the body, thereby controlling the blood glucose level^[11]. Prior to treatment of T2DM, it is necessary to clarify the condition of T2DM patients and whether they have abnormal insulin secretion. Vitamin D is the main substance which regulates calcium and phosphorus metabolism in the body clinically. After entering the human blood, vitamin D can be converted into 25-(OH)D3 by 25-hydroxylase in the liver and stored in the human body in the form of 25-(OH)D3, which is then converted into active 1, 25-(OH)D3 by 1-hydroxylase in the kidney. After binding to pancreatic vitamin D receptor, 1,25-(OH)D3 can effectively activate calcium channels in human β cells and release insulin, promoting tyrosine phosphorylation of insulin receptor substrate, stimulating insulin signal transduction and thus improving insulin secretion^[12,13]. In recent years, there have been increasing reports on the correlation between 25-(OH)D3 and T2DM. In this study, the association between 25-(OH)D3 and T2DM was investigated and it was found that: Observation

TABLE 1: DETECTION INDICES OF OBSERVATION AND CONTROL GROUPS ($\bar{x}\pm s$)

Group	25-(OH)D3 ($\mu\text{g/L}$)	FBG (mmol/L)	HbA1c (%)	FI (mU/L)	IR index	Insulin secretion index
Observation (n=80)	6.57 \pm 2.14	8.69 \pm 1.58	7.36 \pm 1.89	30.41 \pm 9.94	3.05 \pm 0.76	46.25 \pm 9.36
Control (n=80)	15.73 \pm 4.85	5.02 \pm 1.07	5.19 \pm 1.30	18.56 \pm 5.27	2.30 \pm 0.61	59.74 \pm 12.08
t	15.455	17.202	8.461	9.421	6.884	7.896
p	0.000	0.000	0.000	0.000	0.000	0.000

TABLE 2: DETECTION INDICES OF NORMAL AND ABNORMAL INSULIN SECRETION GROUPS ($\bar{x}\pm s$)

Group	25-(OH)D3 ($\mu\text{g/L}$)	FBG (mmol/L)	HbA1c (%)	FI (mU/L)	IR index
Abnormal insulin secretion (n=59)	5.95 \pm 1.03	9.23 \pm 0.98	7.89 \pm 1.02	32.97 \pm 4.76	3.24 \pm 0.39
Normal insulin secretion (n=21)	7.18 \pm 1.20	8.14 \pm 0.87	6.81 \pm 0.94	28.03 \pm 4.15	2.85 \pm 0.36
t	4.498	4.501	4.250	4.216	4.012
p	0.000	0.000	0.000	0.000	0.000

TABLE 3: DETECTION INDICES OF SERUM 25-(OH)D3 POSITIVE AND NEGATIVE GROUPS ($\bar{x}\pm s$)

Group	FBG (mmol/L)	HbA1c (%)	FI (mU/L)	IR index	Insulin secretion index
Serum 25-(OH)D3 positive (n=54)	9.16 \pm 0.95	7.78 \pm 0.89	32.73 \pm 4.20	3.21 \pm 0.34	44.37 \pm 3.18
Serum 25-(OH)D3 negative (n=26)	8.21 \pm 0.84	6.90 \pm 0.75	28.25 \pm 3.51	2.87 \pm 0.31	48.09 \pm 3.60
t	4.344	4.349	4.702	4.307	4.693
p	0.000	0.000	0.000	0.000	0.000

TABLE 4: CORRELATION ANALYSIS RESULTS

Index	25-(OH)D3	
	r	p
FBG	-0.790	0.006
HbA1c	-0.802	0.005
FI	0.879	0.002
IR index	-0.797	0.006
Insulin secretion index	0.854	0.003

group had lower serum 25-(OH)D3 level and insulin secretion index and higher FBG, HbA1c, FI and IR index than control group ($p < 0.05$); Abnormal insulin secretion group had a lower serum 25-(OH)D3 level and higher FBG, FI and IR index than normal insulin secretion group ($p < 0.05$); Serum 25-(OH)D3 positive group had higher FBG, HbA1c, FI and IR index and lower insulin secretion index than serum 25-(OH)D3 negative group ($p < 0.05$); Serum 25-(OH)D3 was negatively correlated with FBG, HbA1c, FI and IR index, but positively correlated with insulin secretion index in T2DM patients. The above results suggest that there is a positive correlation between serum 25-(OH)D3 and insulin secretion index in T2DM patients. The down regulated serum 25-(OH)D3 level indicates that the insulin secretion may be abnormal and IR may occur in T2DM patients, so it is necessary to monitor their blood glucose level so as to strengthen blood glucose control. In summary, the expression of serum 25-(OH)D3 is generally down regulated in T2DM patients, which is closely related to abnormal insulin secretion. In clinic, serum 25-(OH)D3 can be detected to judge the insulin secretion function of T2DM patients.

Authors' contributions:

Yuhu Cheng and Xiaofen Guo contributed equally to this study.

Conflicts of interest:

The authors declared no conflicts of interest.

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