THE RELATIONSHIP BETWEEN SERUM LEVELS OF FGF-21, ANGPTL 2 AND NESFATIN-1 AND INSULIN RESISTANCE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To analyse the relationship between the levels of serum fibroblast growth factor 21 (FGF-21), angiopoietin like protein 2 (ANGPTL 2), feeding inhibition factor (nesfatin-1) and insulin resistance (IR) in patients with type 2 diabetes.

Methods: Fifty-six patients with type 2 diabetes treated in the Endocrine Department of our hospital from April 2016 to September 2017 were selected as the observation group, and 56 healthy subjects in the same period were selected as the control group. Fasting blood glucose (FBG) and glycosylated haemoglobin (HbAlc) were measured by the glucose oxidase method. The levels of serum insulin resistance index (IR), fasting insulin (FINS) and blood lipid indexes (total cholesterol [TC], triglyceride [TG], low density lipoprotein [LDL] and high density lipoprotein [HDL]) were measured by enzyme-linked immunosorbent assay (ELISA). The levels of FGF-21, ANGPTL 2, nesfatin-1, FBG, HbAlc, TC, TG, IDL, HDL and IR were analysed.

Results: Compared with the control group, the levels of FBG, HbAlc, IR and FINS in the observation group were significantly higher, and the differences were statistically significant (P<0.05). The levels of TC, TG and LDL in the observation group were significantly higher than those in the control group, and the level of HDL was significantly lower than that in the control group (P<0.05). Compared with the control group, the levels of FGF-21, Angptl 2 and nesfatin-1 in the observation group were significantly higher, and the differences were statistically significant (P<0.05). Pearson correlation analysis revealed that IR was positively correlated with FBG, HbAlc, FGF-21, Angptl2, nesfatin-1, TC, TG and LDL (P<0.05), and negatively correlated with FINS and HDL (P<0.05).

Conclusion: The serum levels of FGF-21, nesfatin-1, FBG, HbAlc, TC, TG and IDL in patients with type 2 diabetes mellitus are significantly higher than those in healthy subjects, and the levels of Angptl 2 and HDL are significantly lower than those in healthy subjects; in addition, the above indexes have a certain correlation with IR.

Keywords: Type 2 diabetes, FGF-21, ANGPTL 2, nesfatin-1, insulin resistance, correlation.

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Introduction

Diabetes is a form of metabolic disease caused by the deficiency of insulin secretion or the impairment of its biological function; it has long been characterised by hyperglycaemia[1]. According to the different pathogenesis of diabetes, it can be divided into type 1 diabetes and type 2 diabetes. With the development of the global economy and the improvement in people's living standards, the incidence of type 2 diabetes is increasing annually, and the multi-ple age is after 35 years old. There is a lengthy treatment time for diabetes, which has a serious impact on people's quality of life[2]. Insulin resistance (IR) is the main treatment for type 2 diabetes. IR refers to the reduction of insulin's efficiency in promoting glucose intake and utilisation due to various reasons. The body produces hyperinsulinemia by secreting too much insulin to maintain the stability of blood glucose[3]. IR is an important factor leading to type 2 diabetes. Serum fibroblast growth factor 21 (FGF-21) is a peptide secreted by pituitary and hypothal-

amus, which can promote the mitosis of fibroblasts and the growth of mesoderm cells[4]. Some studies have shown that angiogenin like protein 2 (Angptl 2) is closely related to the generation and development of type 2 diabetes. Angptl 2 is a glycoprotein mainly secreted and expressed by visceral adipocytes, which has the function of regulating angiogenesis. It is a key factor linking the chronic inflammatory response of adipose tissue with systemic IR and is closely related to cardiovascular disease[5].

Nesfatin-1 is a type of Adipocyte Factor; it has been reported that nesfatin-1 can regulate glucose metabolism by activating a variety of energy metabolism signal pathways in the body, thus affecting the level of IR in the body[6]. In this study, the serum levels of FGF-21, Angptl2 and nesfatin-1 were measured in patients with type 2 diabetes mellitus, and the correlation between the above factors and IR was analysed.

Materials and methods

General information

Fifty-six patients with type 2 diabetes who were treated in the Endocrine Department of our hospital from April 2016 to September 2017 were selected as the observation group.

Inclusion criteria:

• All patients met the diagnostic criteria for type 2 diabetes set by the World Health Organization (WHO) and the International Diabetes Federation (IDF)[7]: they were over 30 years old;

• They had good mental symptoms and were able to cooperate with the treatment;

• All patients and their families were informed with the approval of the hospital ethics committee;

• They agreed to participate in this study and signed the informed consent.

Exclusion criteria:

• Exclusion of type 1 diabetes or other diabetes; serious liver and kidney function, heart function insufficiency;

• Serious drug allergy;

• Serious infectious diseases;

• Pregnancy or lactation patients.

Of these, 31 were male and 25 were female, aged 36-71 years, with an average age of 56.87±5.41 years, and the body mass index (BMI) was 25.26±3.25kg/m². At the same time, 56 healthy subjects in the same period were selected as the control group, including 29 males and 27 females, aged 36-71 years, with an average age of 57.29±4.73 years and a BMI

of 23.27±2.96 kg/m². The BMI of the observation group was significantly higher than that of the control group; the difference was statistically significant (P<0.01) but there was no significant difference in age and gender between the two groups (P>0.05). See Table 1.

Group	n	Age (years)	Gender (cases)		Body mass index (kg/m²)
			male	female	
Control group	56	57.29±4.73	29	27	23.27±2.96
Observation group	56	56.87±5.41	31	25	25.26±3.25
t/χ²		0.437	0.144		3.388
P		0.663	0.705		0.001

Table 1: Comparison of general data between two groups.

Observation indicators

Five millilitres of fasting venous blood was collected from all patients in the morning and stored in anticoagulant tubes. The serum and blood cells were separated at 3000r / min. The serum was stored in a refrigerator.

Blood glucose

the changes of fasting blood glucose (FBG) and HbAlc were measured by glucose oxidase method.

IR, FGF-21, ANGPTL 2, nesfatin-1 and blood lipid index levels

The IR levels of the two groups were detected by enzyme linked immunosorbent analysis (ELISA) [IR=(FBG×FINS)/22.5], fasting plasma insulin (FINS), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels.

Statistical methods

Spss22.0 software package was used for statistical data analysis, an independent sample t test was used for the comparison of measurement data, and an χ² test was used for the comparison of count data. The Pearson correlation test was used for correlation analysis. Statistical results showed that P<0.05 was statistically significant, and P>0.05 was not statistically significant.

Results

Comparison of blood glucose index, IR and FINS between the two groups

Compared with the control group, the FBG, HbAlc and IR levels of the observation group were

significantly higher, and the FINS levels were significantly lower. The difference was statistically significant (P<0.05). See Table 2.

Group	n	FBG (mmol/L)	HbAlc (%)	IR	FINS (mU/L)
Control group	56	5.14±0.46	5.79±0.42	3.73±1.07	16.42±4.68
Observation group	56	12.21±4.52	9.55±2.81	7.25±5.12	12.57±7.31
T value		11.645	9.903	5.036	3.319
P value		<0.001	<0.001	<0.001	0.001

Table 2: Comparison of blood glucose index, IR and FINS between the two groups (x̄±s).

Comparison of blood lipid indexes between the two groups

The levels of TC, TG and LDL in the observation group were significantly higher than those of the control group, and the level of HDL was significantly lower than that of the control group (P<0.05). See Table 3.

Group	n	TC (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
Control group	56	4.88±0.88	1.27±0.65	1.62±0.38	2.78±1.05
Observation group	56	5.81±1.76	2.97±2.69	0.25±0.27	3.32±1.29
T value		3.537	4.597	12.142	2.429
P value		<0.001	<0.001	<0.001	0.017

Table 3: Comparison of blood lipid indexes between the two groups (x̄±s).

Comparison of FGF-21, Angptl 2 and nesfatin-1 levels between the two groups

Compared with the control group, the levels of FGF-21, ANGPTL 2 and nesfatin-1 in the observation group were significantly higher, and the differences were statistically significant (P<0.05). See Table 4.

Group	n	FGF-21 (µg/L)	Angptl 2 (µg/L)	nesfatin-1 (µg/L)	LDL (mmol/L)
Control group	56	221.74±11.87	1.16±0.19	5.82±1.03	2.78±1.05
Observation group	56	316.42±24.75	3.97±0.63	9.41±1.36	3.32±1.29
T value		25.812	31.956	15.747	2.429
P value		<0.001	<0.001	<0.001	0.017

Table 4: Comparison of FGF-21, Angptl 2 and nesfatin-1 levels between the two groups (x̄±s).

Correlation analysis of serum levels of FGF-21, Angptl 2, nesfatin-1, FBG, HbAlc, TC, TG, IDL, HDL and IR in the observation group

Pearson correlation analysis showed that IR was positively correlated with FBG, HbAlc, FGF-21, Angptl2, nesfatin-1, TC, TG and LDL (P<0.05), and negatively correlated with FINS and HDL (P<0.05). See Table 5.

index	IR	
	r	P
FBG	0.426	<0.05
HbAlc	0.617	<0.05
FINS	-0.586	<0.05
FGF-21	0.263	<0.05
Angptl 2	0.457	<0.05
nesfatin-1	0.448	<0.05
TC	0.714	<0.05
TG	0.186	<0.05
HDL	-0.312	<0.05
LDL	0.216	<0.05

Table 5: Correlation Analysis of serum levels of FGF-21, Angptl2, nesfatin-1, FBG, HbAlc, TC, TG, IDL, HDL and IR in the observation group.

Discussion

The pathogenesis of diabetes is the decrease of the efficiency of insulin intake and utilisation of glucose, which results in a series of metabolic abnormalities mainly due to the increase of blood glucose. Type 2 diabetes accounts for more than 90% of diabetic patients. The ability of insulin production in type 2 diabetes patients is not completely absent, but there is a state of relative lack of insulin[8]. The incidence of diabetic complications is high, and once the complications occur, they are difficult to reverse, which seriously affects people's quality of life. The purpose of this study is to explore the expression of serum FGF-21, ANGPTL and nesfatin-1 in patients with type 2 diabetes and their correlation with IR so as to provide a more accurate theoretical basis for the treatment of diabetes.

FGF-21 is a newly discovered endogenous metabolic regulator, which is mainly secreted by the liver and has the functions of angiogenesis, repair of tissue damage and metabolic regulation[9]. Serum FGF-21 can directly affect the islet cells and promote the secretion of insulin. It has been reported that the level of serum FGF-21 in patients with type 2 diabetes is significantly higher than that of healthy people. Lukaszuk et al[10] showed that the increase

of serum FGF-21 level may be related to IR. FGF-21 can promote the metabolism of glucose and lipid and the sensitivity of insulin, which can be used as an important index to detect diabetes.

In recent years, many studies have shown that obesity is an important cause of diabetes and hypertension, and also an important cause of IR. In the study of diabetic mice, Koren et al.[11] found that the occurrence and development of diabetes-related hyperlipidaemia was closely related to the level of Angptl2. Angptl 2 can inhibit the activity of lipoprotein lipase and increase the TG level significantly[12]. Angptl 2 is a glycoprotein mainly derived from vascular endothelium, which is a kind of angiogenesis stimulating factor. It has been found that Angptl 2 can promote the activity of vascular endothelial cells and promote angiogenesis. According to Hu et al.[13], Angptl 2 can not only cause fatty tissue lesions but also other organ tissue lesions, and can activate the inflammatory response through multiple signalling pathways, thus significantly increasing the risk of endothelial dysfunction. The level of Angptl 2 was significantly increased in type 2 diabetic patients.

Nesfatin-1 is a new neuropeptide found in hypothalamus and brain stem, which is widely distributed in the central and peripheral nervous system. Nesfatin-1 can increase glucose utilisation in peripheral tissues through AMPK/TORC2AKT signalling pathway, thus increasing insulin sensitivity[14].

Mirakhor Samani et al.[15] showed that nesfatin-1 plays an important role in the development of anti-obesity and IR, which can regulate the energy balance of the body and participate in the body's glucose metabolism. This study's results show that the levels of FBG, HbAlc, TC, TG, LDL, IR, FGF-21, ANGPTL 2 and nesfatin-1 were significantly higher in type 2 diabetic patients than in healthy subjects, and the levels of FINS and HDL were significantly lower than those in healthy subjects (P<0.05). IR was positively correlated with FBG, HbAlc, TC, TG, LDL, FGF-21, Angptl2 and nesfatin-1, and negatively correlated with FINS and HDL (P<0.05). This suggests that the above indicators may be involved in the occurrence and development of type 2 diabetes, which is consistent with the results of Hayoz et al.[16]. In conclusion, the levels of IR, FGF-21, Angptl 2 and nesfatin-1 in patients with type 2 diabetes were significantly increased, and the levels of FGF-21, ANGPTL 2 and nesfatin-1 in patients with type 2 diabetes were correlated with IR to a certain extent, meaning the above indexes can be used as objective indexes of IR.

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