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Correlation between diabetes mellitus insulin resistance and cardiovascular endocrine hormones in the elderly

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Abstract: The objective of this study was to analyze the correlation between insulin resistance (IR) in diabetes mellitus (DM) and cardiovascular endocrine hormone (CEH) in the elderly population. In our research methodology, we selected 58 elderly DM patients from the endocrinology department of our hospital as the observation group (OG) and compared them to 58 healthy individuals, who served as the control group (CG). By retrospectively analyzing the IR index of all 116 participants, we measured indicators such as insulin and C peptide (CP) using radioimmunoassay. Furthermore, we conducted a glucose tolerance test (OG-TT). Cardiovascular endocrine hormones like atrial natriuretic peptide (ANP), endothelin (ET), angiotensin I, II (AI, AII), insulin, and CP were determined through radioimmunoassay, while catechol aminophenol (CA), epinephrine (E), and norepinephrine (NE) were ascertained using fluorescence analysis. Our results indicated that the levels of ANP, ET, A Ⅱ, CA, EN, and E in OG patients were significantly higher than those in the CG group ($P < 0.05$). During the insulin release experiment for DMIR patients, the insulin levels recorded at intervals of 0h, 2h, and 4h differed notably from those of the healthy individuals ($P < 0.05$). However, there was no significant variation in CP levels between DMIR patients and the healthy group ($P > 0.05$). A multiple linear regression analysis highlighted that ANP, ET, AII, CA, 2h glucose tolerance, and insulin release at 1h post meal consumption are the primary factors influencing the IR index. In conclusion, the study reveals that IR in elderly DM patients has a relationship with CEH disorders. Monitoring CEH levels can therefore be instrumental in offering evidence-based treatments.

1. Introduction

Diabetes mellitus(DM) is a complex disease composed of both genetic and environmental factors. It is characterized by multiple metabolic abnormalities with hyperglycemia, and vascular and neuropathy may occur in the course of the disease, resulting in disability and death. DM is a common chronic disease in clinic, and most patients are accompanied by insulin resistance(IR). The sensitivity of muscle, fat, liver and other tissues and organs to insulin decreases, and the blood sugar level of patients increases significantly. There are many and serious clinical complications in DM patients, which have an important impact on patients' life and health. Controlling blood sugar

stability and preventing related complications as soon as possible are the keys to improve the prognosis of DM patients. In recent years, due to the rapid development of interventional therapy and drug therapy for cardiovascular diseases, the mortality rate of cardiovascular diseases without DM has decreased significantly [1-2]. The incidence and mortality of diabetes mellitus type 2(T2DM) are associated with coronary heart disease, congestive heart failure and sudden death. Many characteristics of IR often appear before blood sugar rises [3].

The risk of cardiovascular disease in DM population is 2-3 times that in non-DM population. Some studies have found that controlling glycosylated hemoglobin level can not effectively reduce the occurrence of cardiovascular events. Studies have shown that hypoglycemia is related to impaired cardiovascular autonomic nervous function and increased risk of arrhythmia, especially nocturnal arrhythmia [4-5]. Because it is closely related to glucose metabolism, IR leads to the decrease of glucose uptake by skeletal muscle, white adipose tissue and liver, and the decrease of the ability to inhibit endogenous glucose production (mainly in liver). IR is not only closely related to sugar metabolism, but also other nutrients actually participate in the formation of IR [6]. It was found in the study [7-8] that there was a significant correlation between fasting free fatty acids and the production of liver sugar, suggesting that free fatty acids (FFA) may lead to the formation of liver IR. Some studies have also observed that increasing fetal insulin concentration can inhibit FFA concentration, inhibit fat decomposition, and finally increase fetal fat deposition [9].

In recent years, the related research between IR and cardiovascular endocrinology has become a hot spot in cardiovascular and endocrinology research. There is widespread IR in elderly patients with DM, and whether it is related to cardiovascular endocrine hormone (CEH) is seldom reported in the literature. This paper intends to discuss the correlation between IR and CEH in elderly DM patients.

2. Research objects and methods

2.1. Research objects

58 elderly patients with DM who were hospitalized in the endocrinology department of our hospital were selected as the observation group (OG), including 31 males and 27 females, with an average age of 67. 8 ±7. 6 years and an average body mass index (BMI) of (22. 3 ± 2.7) kg/m^2.

58 healthy people were taken as control group (CG), including 33 males and 25 females, with an average age of 68. 1 ± 7.2 years, and the average body mass index (BMI) was (23. 8 ±2.5) kg/m^2. The two groups of data can be compared ($P > 0.05$).

2.2. Methods

The IR index of 116 elderly patients with DM was analyzed retrospectively. Five ml of blood from the right elbow vein were collected as samples, which were anticoagulated with heparin, stored at 4°C, centrifuged at 3000 r/min, and serum or plasma were extracted. The indexes such as insulin and C-peptide (CP) were determined by radioimmunoassay. Glucose tolerance test (OG-TT) was performed.

Atrial natriuretic peptide (ANP), endothelin (ET), angiotensin I, II (A I, A II), insulin and CP were determined by radioimmunoassay. Catechol aminophenol (CA), epinephrine (E) and norepinephrine (NE) were determined by fluorescence analysis. After the determination, record the results, compare the two groups and analyze the CEH level.

2.3. Statistical treatment

SPSS26. 0 software was used for analysis. The measurement data were represented by $\bar{x} \pm s$, and the counting data were analyzed by χ^2 test. The comparison between the two groups was conducted by t test, and the influencing factors were screened by multiple linear regression.

3. Result

3.1. Comparison of CEH level between two groups

The ANP, ET, AII, CA, EN and e in OG patients were higher than those in CG ($p < 0.05$). See Table 1.

Table 1: Comparison of CEH level between two groups

index	OG	CG
ANP(pg/ml)	65.869±19.552*	36.449±14.399
ET(pg/ml)	98.262±20.535*	63.79±19.162
AI(ng ml^{-1} h^{-1})	0.76±0.494	0.791±0.22
AII(pg/ml)	181.835±75.08*	125.248±86.929
CA(nmol/L)	44.429±13.788*	24.153±10.391
E(nmol/L)	37.197±18.892*	26.054±17.394
NE(nmol/L)	56.535±23.859*	37.159±19.556

Note: *P <0. 05.

3.2. Comparison of insulin and CP levels

In order to further clarify the relationship between DMIR and CEH, insulin release experiments were carried out in this study. The results showed that there were significant differences between DMIR patients and healthy people in insulin release experiment at 0 h, 2 h and 4h ($P < 0.05$). There was no significant difference in CP between DMIR patients and healthy people ($P > 0.05$). See Table 2.

Table 2: Comparison of insulin and CP levels

index	period of time	OG	CG
insulin(pmol/L)	0 h	115.031±10.743	89.507±1.411
	2 h	312.787±6.966	278.902±3.43
	4h	302.671±3.261	179.455±2.322
CP(nmol/L)	0 h	0.887±0.174	0.547±0.337
	2 h	1.09±0.135	1.727±0.47
	4h	1.268±0.314	1.454±0.169

3.3. Correlation between IR and CEH in elderly DM patients

Multiple linear regression showed that ANP, ET, AII, CA, 2 h glucose tolerance and insulin release at 1 h after meal were the main factors affecting IR index. See table 3.

Table 3: Correlation between IR and CEH in elderly DM patients

index	coefficient of regression	Standard error	F value	P value
OGTT 2 h	0.076	0.0042	4.053	0.036
IN 1 h	0.041	0.0041	2.372	0.046
CA	0.047	0.0035	2.845	0.034
ET	0.043	0.0009	3.03	0.036
ANP	-0.032	0.032	7.294	0.005
AII	0.832	0.034	2.969	0.036

4. Discussion

Compared with patients without DM, the risk of cardiovascular disease in patients with DM is significantly increased. Similarly, among the patients who have been diagnosed with cardiovascular diseases, the incidence of cardiovascular events in patients with DM is significantly higher than that in patients without DM [10-11]. Because IR may play a major pathophysiological role in these metabolic abnormalities, drugs like thiazolidinediones (such as rosiglitazone) can directly improve insulin sensitivity, improve IR status, and also improve other abnormalities of IR syndrome and treat hyperglycemia. A follow-up study showed [12] that metformin treatment and lifestyle improvement (weight loss of 7% and weekly exercise of 150m in) could reduce the incidence of DM in non-DM patients with elevated fasting blood glucose and post-load blood glucose levels by 31% and 58% respectively. However, the compliance of patients with this non-drug treatment is very poor, and most patients still have to be treated with drugs in the end.

IR refers to that under the action of a certain amount of insulin, the body's glucose intake and processing ability is reduced, muscle cells and fat cells can't use sugar, and liver cells can't effectively inhibit glycogen decomposition and gluconeogenesis, but release too much glucose into the blood, which leads to an increase in blood glucose concentration. IR, DM and hypertension: Hypertension is common in DM patients, and its incidence rate is 20% ~ 60%, which is 1.5 ~ 3 times that of non-DM. Exogenous insulin can restore the normal vascular response and block the vasoconstriction effect of catecholamine, but it needs a large dose of insulin to play its role. Possible mechanisms of hypertension caused by IR: exciting sympathetic nervous system, increasing plasma norepinephrine level, increasing responsiveness to pressor substances, increasing heart rate and cardiac output; Renal tubular sodium reabsorption increases, the overall sodium content increases, the blood volume increases, and the venous reflux volume (preload) increases.

Clinical research also found that compared with young people, older people have a higher risk of developing DM, and patients are often complicated with diseases such as hypertension and hyperlipidemia [13]. In recent years, with the deepening of related research, the relationship between the above diseases has been gradually discovered. Some scholars believe that insulin in the human body can play a role through the sympathetic nervous system and the secretion of vascular endothelial cells [14]. Patients with hyperinsulinemia are often accompanied by abnormal adrenaline secretion. It has been suggested that insulin can exert its influence through renal sodium retention, vascular baroreflex, renin-angiotensin system, sympathetic nervous system, CA, ANP, ET, bradykinin and transmembrane ion transport. The ANP and ET in DM patients increased, but the biological reactivity of cardiovascular system to ANP decreased. ANP can delay insulin decomposition.

We found that ANP, ET, AII, CA, EN and e in OG patients were higher than those in CG ($P < 0.05$). In order to further clarify the relationship between DMIR and CEH, insulin release experiments were carried out in this study. The results showed that there were significant differences between DMIR patients and healthy people in insulin release experiment at 0 h, 2 h and

4h ($P < 0.05$). There was no significant difference in CP between DMIR patients and healthy people ($P > 0.05$). Because CP can reflect the function of β cells, it can be considered that the reason of its IR may be the hypersecretion of β cells of islet, but there is no obstacle to insulin clearance. High TG interferes with the binding of insulin to receptors in surrounding tissues through free fatty acids, which weakens the effect of insulin. It can also compete with sugar to enter the cell, aggravating the function decline of IR and β cells under long-term IR load and causing DM.

This study suggests that there may be a causal relationship between IR and increased sympathetic activity, and IR and EA in DM patients are one of the important reasons for their susceptibility to hypertension. In addition, the phenomenon that insulin is high but CP is not high enough and the insulin /CP value may be caused by the decline of insulin degradation function of the liver. This study suggests that the main mechanism of IR-induced MS and EH may include the synergistic effect of CEH, which may also be one of the reasons why essential hypertension and T2DM often coexist in the elderly.

5. Conclusions

To sum up, CEH can reduce the sensitivity of patients to insulin, which may be one of the important mechanisms of senile DM. DM and cardiovascular diseases can be mutually causal and promote each other. Monitoring the level of CEH is helpful to provide evidence for treatment.

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