

Insulin Resistance in Patients with Metabolic Syndrome

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Keywords: Metabolic syndrome, Insulin resistance, HOMA-IR

Abstract: MS (Metabolic Syndrome), which is a combination of obesity, hypertension, hyperglycemia and abnormal blood lipid levels, has increased the morbidity and mortality of cardiovascular and cerebrovascular diseases, and has become a chronic disease and public health problem seriously endangering human health. The occurrence of MS is closely related to various unhealthy lifestyles. If this is not intervened, the metabolic syndrome is bound to be a global epidemic, causing a huge burden to society. Insulin resistance mainly refers to the decrease of the sensitivity of the body to insulin regulating glucose metabolism, and will affect the metabolism of lipids, proteins, water and electrolytes. Therefore, this study intends to measure the insulin resistance index (HOMA-IR and a series of indicators) of a group of patients with metabolic syndrome and compare them with the normal control group. To investigate the relationship between serum leptin, IL-18, serum amyloid A and insulin resistance in patients with metabolic syndrome, so as to observe the improvement of insulin resistance.

1. Introduction

With the improvement of people's living standards and the increasingly westernized lifestyle, the number of people with metabolic syndrome is increasing [1]. MS is a pathological state formed by abnormal aggregation of various metabolic components in patients. Insulin resistance is the basis of type 2 diabetes, impaired glucose tolerance, obesity, and dyslipidemia [2]. The main manifestations are hypertension, dyslipidemia, hyperglycemia and insulin resistance [3]. A large number of epidemiological data show that metabolic syndrome is closely related to the incidence of cardiovascular disease and diabetes, and has become a serious public health problem [4]. Relevant research results in the United States show that the prevalence of MS in women is higher than that in men, and the prevalence of MS in adults is increasing with age [5]. The prevalence of MS among the 50 year olds is more than 30%, and 40% among the 60 year olds. ChubbS, HydeZ, AlmeidaOP, etc. found that the prevalence rates obtained by applying WHO, CDS and ATP definitions were 614%, 618% and 482% respectively in patients with type 2 diabetes [6]. From a global perspective, the prevalence and growth trend of MS is not optimistic [7]. Recent studies suggest that adipokines and IR (insulin resistance) are important pathogenic links in the pathogenesis of MS. Insulin resistance promotes the increase of sympathetic nerve activity, and the vagus nerve function of diabetic patients has been impaired in the early stage, indicating that insulin resistance will cause changes in neural function [8].

2. About Metabolic Syndrome

2.1. Diagnostic Criteria

Comparing the standards of WHO and NCEP~ATPl, the main difference between the two standards is that WHO standards emphasize the aggregation of multiple risk factors based on the disorder of glucose metabolism, and take abnormal glucose metabolism as the premise of diagnosing MS [9]. At the same time, more than two other abnormalities were combined, and insulin resistance and microalbuminuria were also included [10]. The NCEP~ATPl standard only requires that MS can be diagnosed when at least three of the four conditions are met, and does not require detection of microalbumin in urine and insulin resistance [11]. In 1998, the World Health Organization recommended the use of metabolic syndrome to name it. Its components mainly include impaired glucose tolerance (diabetes, impaired glucose tolerance), lipid metabolism disorder, hypertension, obesity or central obesity, microalbuminuria and other metabolic abnormalities. So far, a consensus has been reached on the name of metabolic syndrome (Table 1).

Table 1: MS work definition of WHO (1999)

In addition to diabetes, impaired glucose tolerance or increased fasting glucose, insulin resistance. The following 2 or more ingredients are required.	
1	Increased blood pressure $\geq 140/90$ mmHg
2	Triglyceride ≥ 1.70 mmol/L and/or low HDL-C: < 0.9 mmol/L for males and < 1.0 mmol/L for females
3	Central obesity: WHR (waist hip ratio): male ≥ 0.90 , female ≥ 0.85 and/or BMI ≥ 30
4	Microalbuminuria: urinary albumin excretion rate ≥ 20 μ G/min or albumin/creatinine ≥ 30

The main consequence of MS is cardiovascular damage. The harm of coronary heart disease, stroke, renal insufficiency and peripheral atherosclerosis caused by MS is obviously greater than that of simple hypertension and abnormal glucose and lipid metabolism, and its control is more difficult. The long-term and chronic increase of FFA (Free fatty acids) will cause neutral lipids to settle in pancreatic islet tissue, which will not only reduce the release of insulin, but also damage the transformation of proinsulin to insulin, leading to increased blood sugar. Therefore, early diagnosis and prevention of MS and avoidance of serious cardiovascular events have become the consensus of cardiovascular and metabolic endocrinologists at home and abroad. For example, more and more attention has been paid to insulin sensitizing agents such as glipizides and dimethyl double muscle drugs, which can improve insulin sensitivity. However, whether it can effectively interfere with cardiovascular risk factors, especially in patients with insulin resistance combined with elevation, remains to be further studied.

2.2. Etiology and Pathogenesis

The pathogenesis of MS mainly involves the following three aspects:

(1) Insulin resistance. It is mainly manifested in the decreased ability of insulin stimulated adipose tissue and skeletal muscle to transport and metabolize glucose and insufficient inhibition of liver glucose output. At present, it is believed that insulin resistance is the main pathophysiological basis of MS, which is closely related to abnormal glucose and lipid metabolism and hypertension in MS patients. The dyslipidemia related to insulin resistance includes triglyceride, low high-density lipoprotein cholesterol and small and dense low-density lipoprotein, especially the increase of LDL3.

(2) Obesity and metabolic disorder of adipose tissue. Central obesity is an independent risk factor of cardiovascular disease. Obese people's fat tissue catabolism is enhanced, and the production of free fatty acids is increased. In the liver, high levels of FFA can affect many functions

of insulin, increase hepatic gluconeogenesis and glycogen decomposition, and inhibit the inactivation of insulin by liver cells. In skeletal muscle, it mainly inhibits glucose uptake and oxidation.

(3) Other related independent risk factors, such as chronic inflammatory state, vascular dysfunction, etc. It was previously believed that adipose tissue was only an organ for storing energy, but now it has been confirmed that adipose tissue is also an endocrine organ. Fatty acids are one of the main energy supplies of the body. Triglycerides in adipocytes are hydrolyzed into free fatty acids and glycerol under the action of various lipases and released into the blood, which are used by body tissues. Adiponectin levels in obese and type 2 diabetic patients decreased significantly, and were negatively correlated with body fat and fasting insulin levels, while positively correlated with insulin sensitivity.

3. Experiment and Preventive Measures

3.1. Treatment and Prevention

The main goal of prevention and treatment of MS is to prevent clinical cardiovascular disease and T2DM, and to prevent recurrence of cardiovascular events, disability and mortality in patients with existing cardiovascular diseases. Hyperinsulinemic euglycemic clamp technique is a classical method to comprehensively estimate the ability of tissue to dispose blood glucose. At present, many simple formulas for estimating insulin sensitivity have been developed based on the relationship between fasting and (or) post load blood glucose and insulin levels. These formulas are convenient for epidemiological and clinical research. Among them, the steady state model evaluation formula HOMA-IR (fasting blood glucose \times Fasting insulin/22.5).

The high-risk groups of MS recommended by Diabetes Branch of Chinese Medical Association are shown in Table 2. This group of people should reshape their lifestyles, treat the existing components of MS and its concomitant diseases, such as polycystic ovary syndrome and gout, and strengthen regular monitoring of the changes of diagnostic indicators of MS.

Table 2: High risk population of metabolic syndrome

1	≥ 50 years old
2	Those who have 1 or 2 components of MS but do not meet the diagnostic criteria
3	People with cardiovascular disease, non-alcoholic fatty liver disease, gout, polycystic ovary syndrome and various types of fat atrophy
4	People with obesity, T2DM, hypertension, dyslipidemia, especially multiple combinations or MS family history
5	Family history of cardiovascular disease

(1) Renew the concept and attach importance to primary prevention. The majority of medical workers, especially public health workers, must first understand and be familiar with the new concept of MS. Then, a new strategy for prevention and treatment of cardiovascular and cerebrovascular diseases is formed from the prevention of insulin resistance and its derived metabolic abnormalities and other risk factors. For patients with MS, aspirin should be used for primary prevention of cardiovascular disease.

(2) Focus on early detection and early intervention of MS high-risk groups with various factors that promote insulin resistance (old age, pregnancy, menopause, high-fat and high-sugar diet, obesity, smoking and lack of exercise, etc.). MS patients with hypertension and diabetes should be prevented and treated according to the guidelines for prevention and treatment of hypertension and diabetes. When choosing hypoglycemic agents, it should be determined according to the degree of IR and β cell functional defects and the relationship between them.

(3) In terms of diet, patients need to ensure a balanced diet, focusing on high-quality protein. At the same time, take more food rich in vitamins and trace elements. Keep away from fried, high-fat, high sugar and high calorie foods. In addition, exercise properly. Whether aerobic or anaerobic exercise is used, it is beneficial to prevent metabolic syndrome.

3.2. Experiments

In this experiment, 50 patients with metabolic syndrome diagnosed in hospital were selected as the study group, and all patients met the criteria of the International Diabetes Union on metabolic syndrome. 38 patients without autoimmune disease, heart disease, diabetes, hypertension and tumor were selected as the control group. There was no significant difference between the two groups in terms of gender and age ($P>0.05$), which was comparable. The upper quartile of the specific population under study can be used as the segmentation point of IR. Because the insulin determination methods are not consistent, the segmentation point must be confirmed with the background population data of the study sample. Evaluation of insulin resistance: HOMA-IR is calculated according to HOMA formula, $HOMA-IR = \text{fasting blood glucose} \times FINS / 22.5$, the data were converted into natural logarithms and then entered into statistical analysis.

Two groups of subjects were given oral 75g glucose tolerance test and 12 samples of FSIGTT. The two tests were carried out successively, with an interval of more than 3 days. Give up smoking for 1 week before the test, and keep a relatively stable diet intake 3 days before the test, and the carbohydrate intake is maintained above 250g/d. The blood glucose and insulin values measured in FSIGTT in each phase are input into BergmanMINIMOD computer software package, and SI and SG are calculated. See Table 3 for the comparison of blood pressure, blood glucose, insulin, blood lipid and uric acid between the two groups.

Table 3: Comparison of insulin sensitivity and β cell function

Group	Numberofcases	SI $\times 10^{1/4}$	SG $\times 10^{1/2}$	AIRg	DI
ResearchGroup	50	7.1 ± 2.0	2.5 ± 1.5	2.41 ± 0.6	3.25 ± 0.18
Controlgroup	38	1.2 ± 0.8	1.3 ± 0.2	0.9 ± 0.1	1.47 ± 0.2

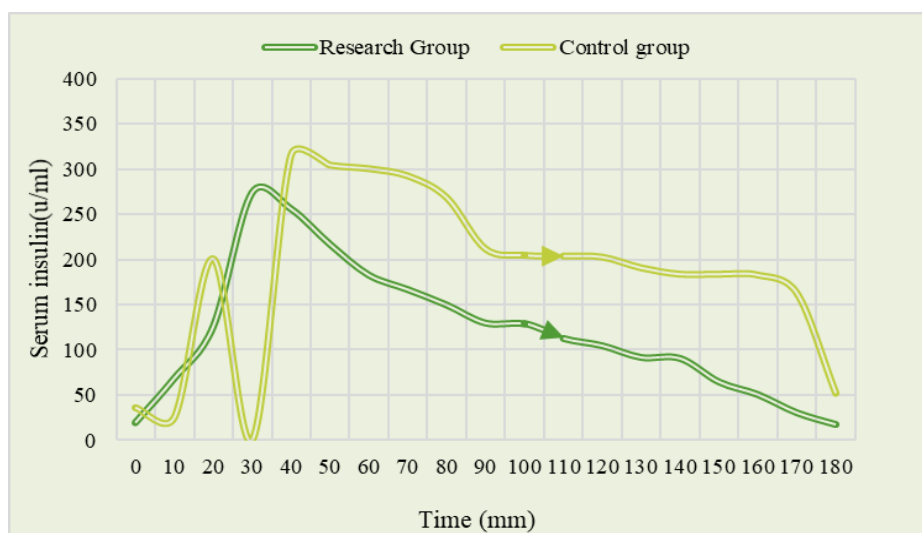


Figure 1: Dynamic changes of insulin in each group

It can be seen from Figure 1 that, compared with the control group, the acute insulin secretion response AIRg after glucose load in FSIGTT was significantly increased in the study group ($P<0.01$), and significantly decreased in T2DM group, while there was no significant difference in

IGT group. It is generally believed that insulin resistance (IR), overweight and centripetal obesity are the basis of dyslipidemia, hypertension and hyperglycemia, and are important links in the pathogenesis of MS. Scholars generally believe that obesity, as the main initiating factor of MS, induces the occurrence of insulin resistance, and IR is the core link in the pathophysiological development of MS. We aim to understand the changes of serum FFA level in MS patients and analyze the relationship between serum FFA and insulin resistance. Thereby providing a basis for treating and preventing the occurrence of MS.

4. Conclusions

The research of MS related fields has become a significant subject, and we should also realize that MS is preventable. Several cohort studies abroad have shown that controlling weight and active and moderate physical activity can delay the occurrence of MS. This is of great practical significance to the improvement of the people's physical quality and the development of the national economy. Although the situation of MS prevention and control is severe, as long as we actively respond, make full use of existing resources and research results, and constantly strive to explore new prevention and control strategies, we will certainly achieve good results in MS prevention and control. Therefore, this paper will explore the pathogenesis of metabolic syndrome and carry out early intervention to develop a comprehensive prevention and treatment strategy. The prevention and treatment of MS emphasizes an all-round and individualized treatment centered on improving insulin resistance. At the same time of intervention on the patients' unhealthy lifestyle, the possible abnormalities of glucose and lipid metabolism, hypertension and blood coagulation should be comprehensively corrected. Relevant measures are of great significance to fundamentally reduce the incidence and mortality of cardiovascular diseases and other metabolic diseases.

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