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INSULIN RESISTANCE IS THE MOST PRESSING PATHOLOGY OF OUR CENTURY

Asia International University
Temirova Dilnoza Olimjonovna

Annotasia.Insulin resistance is the loss of sensitivity of the body's cells to the hormone insulin. This is a pathological condition,

Insulin (Latin insula - islet) is a protein hormone of animal and human origin. It is produced in the islets of Langerhans of the pancreas. It was first isolated by Canadian scientists F. Banting and Ch. Best (1921-22). Mol. m. 6000. The insulin molecule is composed of two polypeptide chains connected by disulfide bonds and consists of 51 amino acid residues. The sequential arrangement of amino acid residues in insulin was determined by the English biochemist F. Sanger (1945-56). This made it possible to synthesize insulin chemically. Insulin was synthesized by chemical and genetic engineering. Insulin is the first protein whose amino acid sequence was determined.

Keywords: Insulin resistance, obesity, glucose, insulin, pancreas

Insulin reduces blood sugar levels by inhibiting glycogen breakdown and glucose synthesis in the liver. At the same time, it increases the permeability of cell membranes to glucose, which allows glucose to enter the tissues. Insulin deficiency in the body causes diabetes. Insulin preparations used to treat it (prepared from the pancreas of slaughtered cattle): amorphous zinc-insulin suspension, protamine-zinc-insulin solution, protamine-insulin suspension, and others have a longer effect than insulin. In some diseases, such as weakness, loss of appetite, etc., insulin injections are prescribed in small doses. It is also prescribed for the treatment of intoxications (for example, incessant vomiting in pregnant women), schizophrenia, and liver diseases. Insulin is injected subcutaneously or intramuscularly 30-60 minutes before eating. Since it is a protein, it is destroyed by the action of digestive juices, so drinking it is not beneficial. Repeat injection after 6-8 hours

Insulin resistance is a loss of insulin sensitivity at the cellular level. In this case, even if normal insulin concentrations are restored, the cellular response is significantly reduced. This process, which occurs mainly in hepatocytes in the muscles, adipose tissue and liver, disrupts the body's glucose homeostasis and leads to the development of compensatory hyperinsulinemia. The normal physiological effects of insulin consist of the following steps: glucose transport into the cell (via GLUT4), stimulation of gluconeogenesis, activation of lipogenesis, inhibition of gluconeogenesis and stimulation of protein synthesis. In the case of insulin resistance, all or part of these processes are disrupted.1.2 Pathogenesis at the Molecular LevelThe insulin signal is transmitted through an ATP-dependent signaling system. This process consists of the following steps: activation of the insulin receptor (autophosphorylation of tyrosine residues in the β-subunits), activation of IRS (Insulin Receptor Substrate), activation of Akt/PKB, inhibition of GSK-3β and activation of mTORC1. Disruption at any stage of this chain can lead to insulin resistance. Mitochondrial dysfunction, endoplasmic reticulum stress, and inflammasome activation are important components of these processes.

Usually, after the food we eat is processed in the intestines, it enters the blood in the form of glucose and spreads to all tissues and organs - it is considered a source of nutrition for cells. Glucose uptake by cells is carried out through a special key - insulin hormone.

This hormone is produced by the pancreas in response to increased blood sugar levels. Under the influence of insulin, the cells receive glucose and become saturated. When a person feels refreshed and full of energy, and the amount of glucose in the blood returns to the norm, the

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production of insulin stops. This process is repeated during the next meal. This is usually the case.

In insulin-resistant people, the cells in the body do not respond to the "switch" (insulin). That is, glucose is not absorbed through the cell membrane, and its amount in the blood increases as much as the pancreas produces insulin.

As a result, even if a person eats, his organs and tissues do not receive the necessary amount of nutrients, and the person has complaints such as relaxation, rapid fatigue, and a sharp decrease in work performance. Unabsorbed free glucose goes to the fat cells and causes them to grow and, as a result, fatten the body.

Insulin resistance is initially manifested by increased gluconeogenesis in the liver, decreased glucose utilization in muscle tissue, and increased lipolysis in adipose tissue. This leads to hyperinsulinemia and hyperglycemia in the body. At the initial stage, the beta cells of the pancreas try to produce more insulin to normalize this process, but over time, these compensatory capabilities are exhausted and hyperglycemia becomes chronic. In particular, insulin resistance is associated with overeating. Especially prone to this are those who love light carbohydrates (sweets: candy, cake, pie). Sweets not only increase the amount of sugar in the blood, but also increase the amount of free fatty acids in the blood, dramatically reducing the sensitivity of cells to insulin.

There are other causes of insulin resistance:

• Large waist circumference - more than 80 cm in women and more than 94 cm in men. This parameter indicates the accumulation of excess visceral fat around the internal organs in the abdomen, which secretes a special protein that reduces the sensitivity of cells to insulin.

• Sedentary lifestyle. Physical activity increases the sensitivity of cells to insulin, and vice versa.

• Chronic inflammatory processes in the body.

• Disruption of the intestinal microflora. Excess or deficiency of certain bacteria.

• Age. The older a person is, the less insulin resistance decreases. Insulin resistance develops in 40% of people over 50 years old.

• Heredity.

Some diseases: polycystic ovary syndrome in women, non-alcoholic fatty liver disease, sleep apnea.

• Smoking,

• Insomnia.

There are no specific symptoms. Only a doctor can suspect insulin resistance and refer you to blood tests. What can be seen in a blood test:

• High blood sugar on an empty stomach (at least 8 hours after eating);

• High triglycerides in the blood;

• Decreased "good" cholesterol in the blood and increased "bad" cholesterol.

The Mediterranean diet is the best choice for normalizing the diet: a large amount of fruits and vegetables, vegetable oils based on olive oil, reducing the amount of red meat, increasing fish and seafood. Calorie restriction: weight loss of 0.5-1 kg per week, reducing liver fat by 5-10%. Physical activity: aerobic exercise 150 min/week, resistance exercise 2-3 times/week. 3.2 Pharmacological Treatment First-line drugs: Metformin (500-1000 mg 2 times a day) - inhibits hepatic gluconeogenesis, increases weight loss and insulin sensitivity. Pioglitazone (15-30 mg per day) - PPAR-γ agonist, increases insulin sensitivity, reduces liver fat. Vitamin E (800 IU/day) - for NASH, has an antioxidant effect. Second-line drugs

: GLP-1 agonists (Liraglutide 0.6-1.8 mg/day, Semaglutide 0.25-1 mg/week) - weight loss, reduction of liver fat. SGLT2 inhibitors (Empagliflozin 10-25 mg/day) - glycemic control, weight loss.3.3 ConclusionInsulin resistance and metabolic fatty liver disease are one of the urgent problems of modern society. Due to the complexity of the pathogenesis of these diseases,

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the presence of many risk factors and various complications, their prevention and treatment is a difficult task. Although lifestyle changes play a key role, pharmacological treatment also plays an important role. Effective implementation of primary and secondary prevention measures is a key factor in reducing the prevalence of these diseases. In the future, it is necessary to further study the molecular mechanisms of insulin resistance and MAFLD and create effective treatment methods.

Conclusion. Insulin resistance is one of the most pressing problems of our time. Because this process causes the onset of diabetes. Insulin resistance is mainly caused by poor nutrition, that is, excessive consumption of carbohydrate-rich foods, sleep disorders, inactivity, and obesity. Of course, this condition can be prevented. It mainly consists of following a healthy lifestyle, rational nutrition, an active lifestyle, and following a sleep regimen.

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