Metabolic syndrome and insulin resistance

Metabolic syndrome and insulin resistance are diseases that are associated with obesity, high blood pressure, risk of atherosclerosis, hypercholesterolemia and dyslipidemia. This tends to result in serious damage to the organs.

Insulin resistance

Insulin resistance is characterized by a reduced ability of tissues to respond to insulin (for example reduced production of insulin receptors).

Primary causes of insulin resistance

Polymorphism of **gene IRS-1**(important for insulin receptor function), genes for **glycogen synthase** or **glucose transporters**. It leads to hyperglycemia and thus to insulin resistance.

Secondary causes of insulin resistance

Stress (sympathoadrenal system) or infections caused by inflammation that lead to **increased cortisol levels**. This can also be caused by a hormonal disorder.

Cortisol **increases blood glucose**, to which the pancreas responds with increased insulin production.

Frequent increases in cortisol cause insulin resistance. Decreased glucose uptake leads to hyperglycemia. This condition tries to compensate the β-cells of the islets of Langerhans by producing insulin. In the short term, this compensation has a positive effect. Later, the expression of insulin receptors decreases, resulting in insulin resistance. Muscle and adipose tissue lack glucose uptake. Fat mobilization and **lipolysis** (increased plasma fatty acid concentrations) occur. Fatty acids affect sugar metabolism by reducing glucose uptake in muscle tissue. The glucose deficiency in cells increases glucagon production and induces gluconeogenesis in the liver. This increase in blood glucose conditions the production of **additional insulin.** Gluconeogenesis is also supported by the degradation of AMK.

Insulin resistance is the basic pathological unit of the metabolic syndrome.

Metabolic syndrome (Reaven syndrome)

A combination of some diseases and risk factors that lead to a number of health complications. They increase the risk of atherosclerosis and its associated complications (ischemic heart disease, ischemic lower limb disease, stroke).

Definitions vary depending on the society for which they are defined. However, all definitions today contain the following criteria.

Metabolic syndrome

Dyslipidemia

Increased TAG (≥ 1.7 mmol/l), decreased HDL (males <0.9 mmol/l, females <1.1 mmol/l), increased LDL, increased total cholesterol, increased apolipoprotein and blood.

Abdominal obesity (especially visceral)

A critical factor for the development of **glucose metabolism disorders**, **hypertension**, **atherosclerosis** (vascular complications), but also other diseases (tumors, neurodegenerative diseases).

Adipose tissue is highly metabolically active, used to produce growth factors (suitable for cancer). Carcinogens can also be deposited in it. At the same time, it is highly endocrine active, thus stimulating an inflammatory response (chronic subclinical micro-inflammation).

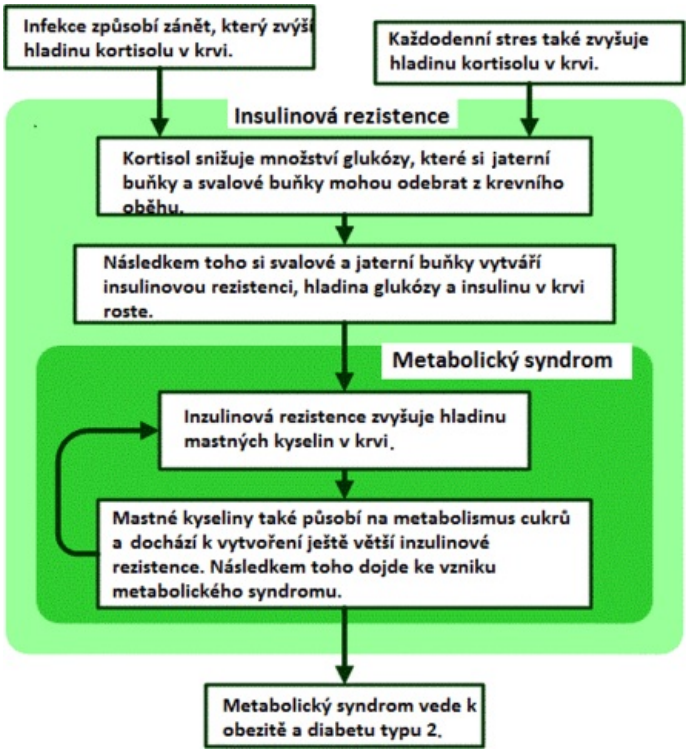
About 80% of patients with diabetes are also obese.

Disorder of glucose metabolism

Long-term hyperglycemia (IFG ≥ 5.6 mmol/l), impaired glucose tolerance, hyperinsulinemia, type 2 diabetes mellitus.

Arterial hypertension

Pressure values ≥ 130/80 mmHg.



Consequences

Hyperglycemia and insulinemia

Decreased glucose uptake by muscle tissue leads to lack of energy and fatigue. As already mentioned, hyperglycemia occurs due to insufficient glucose utilization. Lack of glucose in the cells conditions gluconeogenesis in the liver. An increase in blood glucose results in an increase in the amount of insulin in the blood (insulinemia).

Elevated insulin levels increase the **risk of developing cancer**.

Dyslipidemia

Dyslipidemia occurs, which is caused by increased **hydrolysis of TAG**. This increases the amount of fatty acids in the blood. Fat accumulates viscerally (around organs). This leads to an increase in the production of inflammatory cytokines (**chronic subclinical micro-inflammation**). This inflammatory reaction leads to **damage to the vessel wall** (endothelium).

At the same time, **cholesterol** rises.

Cardiovascular disease

Imbalance of endothelial NO synthase (eNOS) production causes vasodilation disorders. It also causes dysregulation of RAAS (increased angiotensin II production), which causes vasoconstriction disorders. Excess angiotensin II leads to proliferation of vascular and myocardial smooth muscle cells, leading to cardiovascular disease.

Plasminogen inhibitor is overexpressed. These disorders lead to endothelial dysfunction and increased coagulation. The result is ischemia of the competent organ.

Prevention

The preventive measure against the metabolic syndrome is primarily the control of the weight and amount of **abdominal fat** (waist circumference should not exceed 94 cm in men and 85 cm in women). In the case of obesity, weight reduction is appropriate, which includes **physical activity** and **dietary modification**.

Also important is a family history (diabetes, essential hypertension) as well as borderline or higher TAG values, increased insulinemia and hyperglycemia.

Last but not least, it is important to monitor the patient's mental state and observe the possible psychological consequences, closely related to physiological as well as psychosocial changes.

Therapy

Treatment of insulin resistance

PPARγ *(Peroxisome proliferator-activated receptor gamma)*

A nuclear receptor that serves as a transcriptional mediator for adipogenesis, lipid metabolism, insulin sensitivity, and glucose homeostasis. Its effect is to increase insulin sensitivity (lower blood glucose). It also reduces the level of free fatty acids and TAG. This leads to a reduction in blood pressure, microinflammation and atherogenesis.

In addition, there is apoptosis of vascular smooth muscle cells and reduced accumulation of oxidized LDL in macrophages.

Biguanides

Oral antidiabetics. They increase the sensitivity of tissues (liver, muscles) to insulin, thereby lowering blood glucose. They induce glycolysis, suppress gluconeogenesis and reduce the absorption of glucose from food.

Inhibitors of DPP-4 (dipeptidyl peptidase 4)

It breaks down proteins that promote insulin resistance.

RAAS inhibition

ACE inhibitors

They prevent the conversion of angiotensin I to angiotensin II (suppress vasoconstriction).

AT1-receptor blockers

They block the angiotensin II receptor (similar to ACE inhibitors).

Both of these lower blood pressure and have an antiproliferative effect on vascular smooth muscle cells, fibroblasts and cardiomyocytes.

Statins

HMG-CoA reductase inhibitors lead to a reduction in hypercholesterolemia, improving dyslipidemia. It has an antiproliferative effect on fibroblasts, vascular smooth muscle cells and cardiomyocytes.

Links

Related articles

- Inzulinoterapie
- Obezita
- Poruchy lipidového metabolizmu
- Hypolipidemická léčba
- Diabetes mellitus 2. typu

External links

- Insulin resistance (https://en.wikipedia.org/wiki/Insulin_resistance)
- WebMD - Insulin Resistance and Diabetes (https://www.webmd.com/diabetes/type-2-diabetes-guide/insulin-resistance-syndrome)
- Metabolic syndrome (http://www.potbellysyndrome.com/documents/0BB67A0E2FF9D485D5AA735C421011260860F067.html)
- Template:Mefanet
- Český institut metabolického syndromu (http://www.cims-ops.cz/cz/uvod)

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Source

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Recommended literature

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- GUPTA, Abhishek a Vani GUPTA. Metabolic syndrome: what are the risks for humans?. *Biosci Trends* [online]. 2010, vol. 4, no. 5, s. 204-12, dostupné také z <http://www.biosciencetrends.com/action/downloaddoc.php?docid=343>. ISSN 1881-7815 (print), 1881-7823.