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TYPE 2 DIABETES MELLITUS PATHOGENESIS AND ITS COMPLICATIONS

[1]Kholikov Kahramon,
[2]Kholmatova Yokutkhan,
[3]Saidumarova Marguba
[1,2,3]Fergana Medical Institute of Public Health.
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ABSTRACT

Diabetes mellitus is characterized by impaired insulin secretion and varying degrees of insulin resistance, causing hyperglycemia. Early symptoms are associated with hyperglycemia and include polydipsia, polyphagia, polyuria, and visual field constriction. Late complications include angiopathy, peripheral neuropathy, nephropathy, and predisposition to infectious diseases. Diagnosis is based on the measurement of plasma glucose levels. Treatment includes diet, exercise, and glucose-lowering agents, including insulin, oral antidiabetic drugs, and non-insulin injectables. Complications can be delayed or prevented by proper glycemic control; Cardiac disease remains the leading cause of death in diabetes mellitus.

Diabetes mellitus (DM) is a disease caused by an absolute or relative deficiency of insulin in the body. Disturbances in insulin secretion in type 2 diabetes are quantitative and qualitative. An early indicator of impaired β-cell secretory function is the loss of the early phase of insulin release, which plays an important role in glucose (GL) metabolism. The peak of insulin secretion causes an immediate suppression of GL production by the liver, controlling the level of glycemia; inhibits lipolysis and secretion of glucagon; increases insulin sensitivity of tissues, contributing to the utilization of GL by them. The loss of the early phase of insulin secretion leads to excess production of the hormone at a later time, deterioration in glycemic control, hyperinsulinemia (GI), which is clinically manifested by an increase in body weight. This is accompanied by an increase in insulin resistance (IR), an increase in gluconeogenesis, and a decrease in the utilization of GL by tissues, which together leads to glycemia. At the same time, there is a decrease in insulin secretion induced by GL; violation of the biphasic secretion of this hormone and the conversion of proinsulin to insulin.

Another reason for the development of type 2 diabetes is the occurrence of IR, a decrease in the number or affinity of receptors in cells of insulin-sensitive tissues. The accumulation of GL and lipids leads to a decrease in the density of insulin

receptors and the development of IR in adipose tissue. This contributes to the development of GI, which inhibits the breakdown of fats and progresses obesity. A vicious circle develops: IR → GI → obesity → IR. GI depletes the secretory apparatus of β-cells, which leads to impaired tolerance to GL. DM can be characterized as a combination of syndromes of hyperglycemia, microangiopathy and polyneuropathy.

The pathophysiology of diabetic angiopathy consists in damage to the endothelium, which is accompanied by platelet adhesion to the structures of the vascular wall. The inflammatory mediators released at the same time contribute to vasoconstriction and an increase in their permeability. Hyperglycemia causes endothelial dysfunction, a decrease in the synthesis of vasodilators with a simultaneous increase in the release of vasoconstrictors and procoagulants, which contributes to the development of late complications of diabetes.

It was found that in patients with diabetes, the content of glycosylated hemoglobin increases. Increased incorporation of GL into blood serum proteins, cell membranes, LDL, nerve proteins, collagen, elastin, and the lens of the eye was found in most patients with DM. These changes disrupt the function of cells, promote the formation of antibodies to altered proteins of the vascular wall, which are involved in the pathogenesis of diabetic microangiopathies. In DM, an increase in platelet aggregation activity and an increase in the metabolism of arachidonic acid were revealed. A decrease in fibrinolytic activity and an increase in the level of von Willebrand factor were noted, which enhances the formation of microthrombi in the vessels.

It has been established that in patients with DM, capillary blood flow increases in many organs and tissues. This is accompanied by an increase in glomerular filtration in the kidneys with an increase in the transglomerular pressure gradient. This process can cause the flow of protein through the capillary membrane, its accumulation in the mesangium with the proliferation of the latter and the development of intercapillary glomerulosclerosis. Clinically, this is manifested by transient microalbuminuria, followed by permanent macroalbuminuria.

It has been shown that hypoglycemia is the cause of an increase in the concentration of free radicals in the blood, which cause the development of angiopathy as a result of oxidative stress. The oxidative load of the intima in DM dramatically accelerates the endothelial transport of LDL to the subendothelial layer of the vascular wall, where they are oxidized by free radicals with the formation of xanthoma cells, an increase in the influx of macrophages into the intima, and the formation of fatty streaks.

At the heart of neuropathies is the defeat of the myelin sheath and axon, which leads to a violation of the conduction of excitation along the nerve fibers. The main mechanisms of damage to the nervous tissue are a violation of energy metabolism and increased oxidation by free radicals. The pathogenesis of diabetic neuropathy consists in an excessive supply of GL to neurons with an increase in the production of sorbitol and fructose. Hypeglycemia can disrupt metabolism in the nervous tissue in various ways: glycosylation of intracellular proteins, increased intracellular

osmolarity, development of oxidative stress, activation of the polyol GL oxidation pathway, and reduced blood supply due to microangiopathy. These phenomena contribute to a decrease in nerve conduction, axonal transport, disruption of EBV cells and cause structural nerve tissue changes.

Thus, the basis of the pathogenesis of DM is hyperglycemia, which protein glycosylation, oxidative stress, development of atherosclerosis, impaired phosphoinositide metabolism leading to disruption of cellular functions. Wherein hemostasis plays an important role microcirculation. Therefore, treatment patients with diabetes should be complex with focus on correcting metabolic processes.

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