N.A Mo’minova - Andijan State
Medical Institute
Assistant of the department of
clinical pharmacology, pharmacology and
medical biotechnology

DIABETIC NEPHROPATHY

Anotation: Hyperlipidemia - hyperlipidemia plays a huge role in the development of DN, which characterized increase content general cholesterol, lipoproteins low density (LDL) And lipoproteins Very low density (VLDL), reduction level lipoproteins high density (HDL) And Also leads to kidney pathology. For a long time this factor were not taken into account, only after research JF Moorhead And J Diamond hyperlipidemia began to be seen as quite serious nephrotoxic factor. So way, implementation damaging impact Togo or other factor a will depend from character interaction genetically conditioned activity this factor a And genetically conditioned receptivity To his influence.

Key words: Diabetic nephropathy, kidneys, diabetes mellitus, hyperglycemia, end products glycosylation.

Аннотация: Гиперлипидемия - огромную роль в развитии ДН играет гиперлипидемия, которая характеризуется повышением содержания общего холестерина, липопротеинов низкой плотности (ЛПНП) и липопротеинов очень низкой плотности (ЛПОНП), понижением уровня липопротеинов высокой плотности (ЛПВП) и также приводит к патологии почек. Долгое время этот фактор не брали во внимание, лишь после исследований J.F. Moorhead и J. Diamond гиперлипидемия стала рассматриваться как довольно серьезный нефротоксичный фактор. Таким образом, реализация повреждающего

воздействия того или иного фактора будет зависеть от характера взаимодействия генетически обусловленной активности этого фактора и генетически обусловленной восприимчивости к его воздействию.

Ключевые слова: Диабетическая нефропатия, почки, сахарный диабет, гипергликемия, гликозилирование конечных продуктов.

Despite the existing successes in the treatment of diabetes, currently, to a large extent Unfortunately, there is an increase in incidence both type 1 and type 2 diabetes. Greatest danger SD, undoubtedly, associated with complications that develop due to his damaging influence on vessels. An important place in this series is occupied by diabetic nephropathy (DN), which develops at approximately at 20.1% patients With SD 1st type And 6.3% patients With SD 2nd type. In patients with type 2 diabetes, diabetic nephropathy ranks third among the causes of death after diseases cardiovascular system and oncological pathologies. Diabetic nephropathy presented complex lesions arterioles, arteries, glomeruli And tubules kidney _ DN characterized defeat fabrics kidney at sugar diabetes, which leads To development diffuse or nodular glomerulosclerosis , which, in turn, leads to the development chronic renal insufficiency. Despite the existing successes in the treatment of diabetes, currently, to a large extent Unfortunately, there is an increase in incidence both type 1 and type 2 diabetes. Greatest danger SD, undoubtedly, associated with complications that develop due to his damaging influence on vessels. An important place in this series is occupied by diabetic e - Skye nephropathy (DN), which develops at- approximately at 20.1% patients With SD 1st type And 6.3% patients With SD 2nd type. In patients with type 2 diabetes, diabetic nephropathy ranks third among the causes of death after diseases cardiovascular system and oncological pathologies. Diabetic nephropathy presented complex lesions arterioles, arteries, glomeruli And tubules kidney _ DN characterized defeat fabrics kidney at sugar diabetes, which leads To development diffuse or nodular glomerulosclerosis , which, in turn, leads to the development chronic renal

insufficiency. Classically accepted highlight three stages Diabetic _ nephropathy: stage Nuria microalbums (UIA); stage proteinuria With safe renal function and the stage of chronic renal disease insufficiency (CRF). But the initial structural and functional changes are still starting to develop before moment increase excretion albumin With urine. Modern achievements in the fields of molecular medicine and experimental nephrology lead to a gradual increasing the amount of knowledge about more detailed mechanisms of development of MAU and PU. And it was proven home role V these processes podocytes are the main components of the slit diaphragm glomeruli. Exist work, which demonstrate the relationship between AC growth and functional disorders in podocytes . These changes have been shown to develop long ago before moment identifying UIA And can show up even at short during the course of diabetes. Thus, podocytes present yourself interest For development methods braking development DN. Myself the podocyte has a rather complex structural structure, which provides extensive a set of its functions and adaptive reactions under physiological conditions, but, in its own queue, does this cell Very sensitive to various damaging factors. As a result of exposure to pathogenic agents (metabolic, toxic, hemodynamic) podocytes are exposed structural and functional changes (this phenomenon is called "podocytopathy"). Explicit sign podocytopathy smoothing podocyte feet with impaired permeability slit diaphragm, as well as hypertrophy and cell death - apoptosis, podocyte detachment from glomerular basal membranes (GBM) with their desquamation into the urinary space And appearance V urine How whole cells (podocyturia), and its structural proteins, for example, nephrine. As a result of the processes described above, a decrease in the number of podocytes in the glomerulus occurs (podocytopenia). Podocytopenia leads To more more violation glomerular permeability. At the site where podocyte loss occurs, The GBM is exposed and fuses with the Shumlyansky-Bowman capsule. It has been proven What a loss 20-40% of podocytes in the glomerulus leads to the formation of synechiae with a capsule, with a loss of 40- 60% of podocytes develop glomerulosclerosis, a loss more 60% data

cells leads to irreversible damage to the glomerular filter with impaired renal function. It has now been established that this is so called phenomenon smoothing pedunculated processes – This product impact pathogenic factor on epithelial cells. As a result of this influence, a violation occurs actin cytoskeleton podocyte With transforming it into a dense network, which leads to an increase in the permeability of the glomerular filter behind check offsets slit-like aperture And mergers filtration cracks. The the phenomenon has been experimentally studied, a direct relationship between the severity of the data has been established changes with the degree of AC. According to modern ideas, the main barrier glomerular filter For plasma proteins is interpodocyte slit diaphragm. The complex molecular organization pedunculated processes podocytes. It was found that filtration cracks educated special adhesive compounds, the main component of which is the transmembrane protein nephrin. It is involved in binding to actin cytoskeleton podocytes, and also participates in the formation interpodocytic slotted diaphragm. At development of DN, even before the appearance of PU, areas of destruction of the slit-like diaphragm, relevant areas smoothed processes podocytes And reduced expression nephrine _ Pathogenesis diabetic nephropathy. Diabetic nephropathy develops under due to a huge number of reasons. But of all diversity mechanisms development DN most studied And proven are: metabolic (hyperglycemia, hyperlipidemia) And hemodynamic (intraglomerular hypertension, arterial hypertension (AG)).

Hyperglycemia

Undoubtedly, one from the most important metabolic factors, initiating kidney damage is hyperglycemia. There are several ways that ultimately in the end lead To death cells. IN conditions hyperglycemia are formed stable products glycosylation (or glycoxidation, _ advanced glycation end product _ AGE, CNG). IN body Maybe take place their autoxidation or interaction with cellular receptors. Restorative Sahara (glucose, mannose, G-6-P, fructose), containing structure aldehyde groups interact With amino groups, which provided, For example, proteins, And lead To education

reasons Schiffa. Further chemical transformation known as rearrangement Amadori (Hodge, 1955), reasons leads To formation glycosylated products. IN as a result the structure changes and protein functions, which in turn leads to To development sustainable damage cells. Final products glycosylation lead to changes in the metabolism of essential proteins body (collagen, myelin, DNA). IN result glycosylation structural proteins basal membranes glomeruli And mesangia there is a violation of their configuration, loss charge and size selectivity basal membranes glomeruli, A Also inhibition of the metabolism of the main protein components of the renal structures, which is accompanied an increase in the volume of the mesangial matrix and thickening of vascular basement membranes . Also in the kidney, AGEs formed in the basal membrane glomeruli, fix on her albumin, IgG, which leads to its thickening, deposition of immune complexes in it, which entail a change in properties and structure components glomerular matrix. Glycosylated proteins or cytokines (TNFα, interleukin-1, etc.) affect endothelial cells in such a way What They intensely produce various factors growth, which accelerate processes cell proliferation, which leads to even greater development DN. More one mechanism damaging action of hyperglycemia is to reduce activity enzymes, which accept participation V sulfation heparan sulfate (GS). GS of the vascular wall is involved in the creation negative charge endothelium, while providing anticoagulant properties vascular wall, and also regulates the proliferation of smooth muscle cells. Incompletely sulfated GS chains, being embedded in the glomerular basement membrane (GBM), do not provide sufficient negative charge, which leads to the loss of charge-selective properties of the waste filter and the development UIA. IN my queue inferior sulfated HS chains on the endothelium of others vessels also lead to increased membrane permeability and generalized endothelial dysfunction. Circulating in the blood, irreversible glycosylation products also affect lipid exchange. On the one hand, they glycosylate lipids, A With another – cause peroxide their oxidation. As a result, a violation occurs biological lipid activity, their transport and breakdown as a result of their

glycosylation . This leads To to that What LDL continues to enter the cells, despite on glut cells cholesterol. Except Togo, glycosylated collagen vessels acquires the ability to bind three times more LDL-C than collagen of healthy people. Walcher D. Et al found that when AGE binds to a specific receptor For AGE (RAGE) proinflammatory mediators are released in various types of vascular cells, which causes various microvascular And macrovascular complications. Systemic damage endothelium at DN final products glycation leads To increasing the permeability of the endothelial barrier For low molecular weight substances A Also release procoagulant factors, What provokes thrombotic occlusion capillaries and the development of coagulopathies. Products Amadori thus disrupt intrarenal hemodynamics, helping to maintain hyperfiltration. Hyperglycemia leads to an increase conversion of glucose through the glycolysis pathway, What, V my queue, increases synthesis diacylglycerol (DAG), key activator PKC in physiology. As a result of activation RKS are happening changes endothelial permeability, expression of *vascular endot e - lyal growth factor (VEGF)* in tissue, as well as activation and adhesion of leukocytes. *Transforming growth factor β1 (TGF-β1)* also plays a role in the pathogenesis of DN. Was It has been proven that the formation of this cytokine increases in affected kidneys. Various factors such as hyperglycemia, AT II, AGEs, activate the formation of TGF-β1 by podocytes. At stimulation receptors starts cascade reactions, which V final in the end pr i- leads to activation of the enzyme caspase, which entails the destruction of nuclear material podocytes and their subsequent death. TGF-β1 Also promotes expression podocytes α3(IV) collagen, resulting in GBM thickening and glomerulosclerosis develops, VEGF expression in podocytes also increases, which autocrine increases my activity And leads To damage kidney.

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