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FEATURES OF THE COURSE OF GOUTY KIDNEY DISEASE IN PATIENTS WITH OBESITY

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ABSTRACT

Involvement of the kidneys in many common diseases in the population, including those initially not considered to be renal, has recently attracted close attention of clinicians. The study of the relationship between chronic kidney disease and the metabolic syndrome suggests that the high prevalence of GFR decline in the general population is determined mainly by metabolic nephropathies — gouty nephropaty, diabetic nephropaty, obesity-associated, and also by hypertensive nephroangiosclerosis.

Kidney damage in gout is provoked by metabolic abnormalities typical for this disease. Gouty kidney damage develops in 30-70% of patients with gout. Refers to the category of collective concepts, unites all types of renal pathology of gouty origin. The most common form of the disease is chronic interstitial nephritis, which in 17% of patients at the initial stages is characterized by episodes of acute renal ureteric obstruction and in 52% of cases is combined with nephrolithiasis.

In recent years, it has become evident that in the general population, obesity is a significant risk factor for impaired renal function. With a 10% increase in BMI, there is almost a 1.3-fold increase in the likelihood of a decrease in GFR to the level that would allow a diagnosis of chronic kidney disease. Kidney damage in obesity is commonly associated primarily with the effect of associated metabolic disorders - insulin resistance or type 2 diabetes mellitus, hyperuricemia, and arterial hypertension. In this regard, it is natural to increase the frequency of diabetic nephropathy, hypertensive nephroangiosclerosis and urate nephropathy described in obese patients [5].

The fact that increasing proteinuria and renal failure can form in obesity and in the absence of carbohydrate metabolism disorders, AH and hyperuricemia, suggests the participation of factors not directly related to metabolic disorders in the development of renal damage in this category of patients [5]. It is obesity that is considered as the initial component of the pathogenesis of metabolic syndrome and its complications. There is no doubt that obesity predisposes to the formation of

lipoprotein metabolism disorders, arterial hypertension, hyperuricemia. The problem of pathological metabolic consequences of obesity is of particular relevance due to the steady increase in its prevalence, starting from childhood, both in developed and developing countries. Currently, the number of established pathological consequences of abdominal obesity continues to grow steadily: along with cardiovascular complications, they also include calculous cholecystitis and nonalcoholic fatty liver disease, some malignant tumors (cancer of the colon, prostate, uterine body, breast). Abdominal obesity is particularly unfavorable prognostically and in terms of renal complications. Arguments in favor of the existence of a link between obesity, including abdominal obesity, microalbuminuria and renal failure now have a convincing clinical and pathogenetic justification.

The first ideas about obesity-associated nephropathy began to form based on the observation of small groups of obese patients without type 2 diabetes mellitus in whom proteinuria was recorded. Morphological examination of kidney tissue obtained by biopsy revealed signs of focal segmental glomerulosclerosis (FSGS). Significant increase of glomerular capillary loops and, as a consequence, glomerulomegaly are considered to be a characteristic morphological feature [2]. The clinical features of FSGS in obesity are the absence of signs of nephrotic syndrome (edema, hypoalbuminemia) even with a very large protein excretion with urine, as well as a favorable long-term renal prognosis. In obesity-associated FSGS, BP often remains normal or increases slightly. Obesity-associated FSGS patients often present with myocardial hypertrophy or left ventricular cavity dilatation, and obstructive sleep apnea syndrome is possible.

The formation and progression of obesity-associated nephropathy is determined primarily by the damaging effect on renal tissue structures of adipokines - mediators actively produced and secreted by adipocytes, predominantly brown, whose pool prevails in abdominal obesity. Leptin is of particular importance in the lesion of target organs in obesity. Leptin is a hormone of peptide nature that plays a key role in energy homeostasis by signaling to the brain about adipose tissue stores. Leptin is a satiety hormone. It stimulates the synthesis of several appetite-suppressing factors [3]. Obese patients develop resistance to leptin, accompanied by its hyperproduction. Excess leptin, in turn, begins to have a damaging effect on the myocardium, the vascular wall, and the renal tissue. Leptin induces renal fibrogenesis primarily by activating the expression of transforming growth factor-β (TGF-β) and its receptors on the membranes of mesangiocytes and endotheliocytes. The ability of the latter to express (TGF-β) is one of the components of leptin-induced endothelial dysfunction, which is generalized in obese patients and is of significant importance in the pathogenesis of renal damage [2]. The increased production of endothelin-1 and angiotensin-II by these cells, combined with the depression of endothelium-dependent vasodilation cascades, is also considered to be an important component of endotheliocyte dysfunction developing in hyperleptinemia. Microalbuminuria is considered as a marker of endothelial dysfunction, which is an early sign of a

potentially reversible stage of obesity-associated nephropathy. A consequence of renal glomerular endotheliocyte dysfunction is also impaired intrarenal hemodynamics, manifested by depletion of renal functional reserve. Thus, decreased renal functional reserve and microalbuminuria can be considered as signs of an early, preceding FSGS, stage of obesity-associated nephropathy.

Along with leptin, endothelial function can be impaired by the hormone resistin, which is produced in excess in obesity. Stimulation of endotheliocytes by resistin is accompanied by a significant decrease in their expression of endothelial NO synthase. Blockade of NO synthesis in turn leads to a decrease in adiponectin-mediator production by adipose tissue cells, which has a protective effect on the vascular wall. In chronic kidney disease, an increase in plasma resistin concentration is clearly associated with a decrease in GFR. Both hyperleptinemia and elevated plasma resistin levels in obese patients are combined with an increase in serum levels of soluble receptors to α-tumor necrosis factor and interleukin-6. These markers of inflammatory response are also produced by brown adipocytes. Expression of α- TNF and its receptor genes, as well as interleukin-6 transducer and leptin receptors in obesity-associated nephropathy at the proteinuria stage was proved by the results of analysis of kidney tissue samples obtained by biopsy.

Nephropathy in patients with very large body weight has now acquired the status of a general population problem. This fact has predetermined an intensive search of approaches to its treatment.

Lifestyle changes, including caloric restriction, moderate physical activity and optimization of work and rest mode, contribute to the effectiveness of medications used for the treatment of obesity. The effect of drugs effective in the treatment of obesity on the clinical signs and course of obesity-associated nephropathy has not been specifically

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