

Advances in the study of hyperuricemia and chronic kidney disease

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ABSTRACT. *At present, hyperuricemia is becoming an increasingly serious problem after hypertension, hyperglycemia, and hyperlipidemia. It has also become a hot topic in recent years. Uric acid passes through the glomerular filtration and is then reabsorbed or excreted by the URATI transporter in the renal tubules. Hyperuricemia affects the functional status of the glomerulus and renal tubules, and high uric acid indirectly leads to renal insufficiency through vascular sclerosis. This article reviews the development of chronic kidney disease caused by high uric acid, including glomerular damage, renal tubule damage and vascular sclerosis.*

KEYWORDS: *Uric acid, Hyperuricemia, Chronic kidney disease, Renal tubule, Glomerular, Vascular sclerosis.*

1. Introduction

With the improvement of people's living standards, the prevalence of hyperuric acidemia is getting higher and younger, and chronic kidney disease caused by high uric acid has also brought a great burden to the family and society. Kidney function is an important organ of the human body, maintaining the stability of the body environment by regulating body fluids, blood pressure, regulating blood composition and removing organic waste. Chronic kidney disease refers to a series of pathophysiological changes such as disturbances in the body's environment after renal function is impaired [1]. Under normal circumstances, there are two ways of excretion of uric acid, two-thirds of which are excreted mainly through the kidneys and one-third excreted with feces through the intestines [2]. The classic quartet of kidney excretion of uric acid is glomerular filtration, reabsorption of kidney tubes, re-secretion of kidney tubes, reabsorption after secretion. The normal excretion of uric acid depends on the full functional state of the glomerular and renal tubes, but if any part of it is damaged, can lead to urea excretion disorders, which in turn leads to kidney disease, cardiovascular, diabetes, gout and a series of other diseases. Therefore, it is particularly important to reduce uric acid, improve vascular sclerosis, and protect the normal function of the glomerular and renal tubule. This article reviews the effects of the metabolic pathway of uric acid on the kidney, and reviews

the progress of glomerular injury, tubular injury, and vascular sclerosis caused by high uric acid.

2. Renal tubules damaged by high uric acid

Uric acid is an important metabolite of the body and micro-soluble in water, it is the product of purine metabolism, which finally released into the blood. Only small molecular substances such as uric acid, urea, water and inorganic salt can enter the kidney tube through the glomerular, most of which uric acid is reabsorbed on the wall of the near-end tube, other urine is expelled from the body [3]. Uric acid as a selective antioxidant, can form urea, oxalate and other products of free reaction against hypochloric acid and hydroxyl, the uric acid with appropriate level helps inhibit cell dissolution and apoptosis to protect cell DNA and kidneys [4]. The kidney tube is composed of a variety of epithelial cells with high differentiation, morphology and function, connected with the lining layer of the kidney sac, consisting of a near-end tube, a remote tube, a fine section, a connecting tube, and a different transport protein on the side of the tube cavity and the side of the substrate film to maintain the dynamic balance of body fluids [5]. The reabsorption of uric acid in the kidneys mainly depends on the transporter protein URAT1 mediated [6]. The top membrane is a small tube cell located on the inside of the tube, which is between the kidney tube and the collection tube and the epithelial cell. The substrate film faces the blood side and is the membrane between epithelial cells and the fluid between the tissues. The apical membrane is the tubule cell located inside the tubule, which is the membrane between the renal tubule and the collecting duct and the epithelial cell. Facing the blood side, the basement membrane is the membrane between epithelial cells and tissues. Transporters URAT1 help uric acid through the renal tubule cells at the top of the membrane, and mediated the absorption of uric acid in the top of the membrane, as anion exchange, through the across the top of the membrane Na + coupling transfer or through the basement membrane of organic anion by OAT protein into cells, keep the balance of ion, uric acid is the last to leave cells through unknown channel through the basement membrane [3]. Therefore, the impaired regulatory function of the transporter URAT1 will directly affect the reabsorption function of the renal ducts, leading to uric acid metabolism disorders.

There are three types of uric acid excretion: reduced excretion type, increased production type, and mixed type. The reabsorption of uric acid in the renal duct depends on the URAT1 transporter, which reduces uric acid excretion by inhibiting URAT1, thereby reducing uric acid reabsorption and increasing excretion. Verinurad has been shown to be an effective transport protein URAT1 inhibitor, which is currently widely used in clinical trials of asymptomatic hyperuric acidemia [7].

Physiological concentration of uric acid is beneficial to human body and can prolong survival [3]. However, the level of hematuriatric acid is influenced by many factors such as eating habits, race, geographical location, age, weight, etc. Increasing uric acid concentration can lead to increased superoxide anion production, NADPH enzyme protein levels, and renal tubular epithelial cell apoptosis in renal tubular

epithelial cells [8]. On the comparison of the two dimensions of uric acid dose and duration, the effects of Na-K-ATP enzyme (NKA) on renal tube damage were analyzed in rats with high uric acidemia, and the results showed that the activity of NKA decreased with the increase of uric acid concentration, and the activity of NKA increased in 24 hours. After more than 48 hours, the activity began to decline. It can be seen that high uric acid affects the NKA pathway of proximal renal tubular epithelial cells, eventually leading to renal tubular damage. [9]. High concentrations of uric acid not only cause damage to NKA signaling pathways, but also cause apoptosis of oxygen free radical-induced renal tube cells by activating NADPH oxidase NOX4 [10]. The concentration of uric acid in the normal range is essential to maintain the functional state of the renal tubule.

3. Damage of High Uric Acid to the Glomerulus

Glomerulus play an important role in the transport mechanism of uric acid, the metabolites in the blood are first filtered through the glomerular, and then excreted into the kidney tube or reabsorbed through the cell wall. Study finds uric acid is closely related to glomerular filtration rate. Rudolf P. Obermayr et al. confirmed that uric acid is an independent risk factor for renal insufficiency by studying the leaching rate [11]. Therefore, the functional state of the glomerular affects the excretion ability of uric acid, and the excretion of uric acid has a negative effect on the glomerular. The experiment showed that COX-2 expression, direct pro-inflammatory effect of PGE2 synthesis and oxidation caused damage to the glomerular by observing the glomerular membrane cells at high concentrations of 8-50 mg/dl for 24 hours [12]. There have also been experiments that have studied the kidneys of rats with hyperuric acidemia and found that glomerular hypertrophy is widespread, while angiotensin-conversion enzyme inhibitors can prevent the progression of glomerular hypertrophy to some extent [13]. If the glomerular hypertrophy is allowed to develop, it may turn into glomerular sclerosis [14].

A large number of clinical experiments have shown that uric acid plays an important role in promoting inflammation, inducing cyclooxygenase expression, and PGE2 synthesis. The appropriate concentration of uric acid acts as a scavenger in the case of infection, improving cell viability and inducing higher Concentration of reactive oxygen species and apoptosis, which in turn causes glomerulosclerosis in high concentrations of uric acid [12]. Hyperuric acid and uric acid crystals, especially in renal diseases, can easily lead to glomerulosclerosis, renal arteriosclerosis, and interstitial fibrosis. [15]. Uric acid deposition can directly lead to inflammation of the intertubal softos of the kidneys, while uiric acid causes the formation of uric acid stones to aggravate the obstructive kidneys [16]. High uric acid plays an important role in the development of glomerular sclerosis, reducing the deposition of uric acid can improve glomerular sclerosis and protect the kidneys. Reducing high uric acid concentrations is essential for maintaining the function of glomerular cells.

4. Effect of high uric acid on vascular sclerosis

Vascular sclerosis refers to a series of pathological changes caused by vascular diffuse atherosclerosis, stenosis of the tube cavity and the reduction of blood supply of organs due to small vascular closure. Atherosclerosis is a chronic inflammatory reaction caused by the regulation of the body after damage to the endothelial organs of the blood vessels [17]. Clinical data show that atherosclerosis is often accompanied by the emergence of avascular calcification [18]. Smooth myocyte phenotypes are one of the main causes of atherosclerosis plaque calcification [19].

Vascular calcification is common in a variety of conditions, including not limited to chronic kidney disease, atherosclerosis, diabetes, atherosclerosis development will always lead to the appearance of vascular calcification. Calcification lesions in patients with renal insufficiency are more complex than in normal people [20]. Hyperuric acidemia has always been a risk factor for cardiovascular disease in the heart and brain, tapan Mehta et al. experimental studies have shown that uric acid is positively correlated with the pulse wave velocity of the carotid artery-stoyric artery and the pulse wave velocity of the cervical artery-femoral artery, thereby increasing the rate of vascular sclerosis [21]. Uric acid plays a vital role in the progression of kidney disease [22]. Annayya R. Aroor et al. found that jaundice oxidase inhibitors can effectively control uric acid in rats by comparing the feeding of rats with hyperuric acidemia, and prevent the aortic EC cortex and vascular smooth muscle cells and extracellular sclerosis [23]. Uric acid causes changes in hemodynamics in the kidneys and ischemic hypoxia is associated with the decrease or disappearance of vascular elasticity. At the same time, Sanaz Sedaghat et al. through continuous observation of cervical artery stiffness, pulse pressure and so on in the experimental population, it is concluded that vascular sclerosis also leads to decreased kidney function [24]. Acid reduction is beneficial to improve vascular sclerosis, can protect kidney function and delay the progression of CKD.

5. Conclusion

The understanding of the harmful effects of high uric acid has gradually deepened. Increased uric acid concentration may cause symptoms such as kidney damage, gouty arthritis, and urinary stones [25]. But more and more studies show that high uric acid is also associated with cardiovascular disease, chronic kidney disease and so on. The renal tubules and glomeruli are important roles in the catheter pathway. This article reviews the effects of hyperuricemia on the renal tubules and glomeruli, as well as the vascular sclerosis caused by chronic renal insufficiency. In contrast, high concentrations of uric acid will not only affect the function of the renal tubules and glomeruli, but also cause vascular sclerosis, damage the kidney, and cause a series of health problems. The physiological concentration of uric acid has a protective effect on the human body, can resist oxidation, scavenge oxygen free radicals, and prolong survival. Therefore, it is very important to maintain the dynamic balance of uric acid. Although the effects of high uric acid on the kidneys have been studied extensively, the potential pathological mechanisms still need

further exploration, and it is necessary to carry out some experiments to quantitatively analyze the effects of uric acid concentration on the kidneys. Based on the metabolic pathways and excretion methods of uric acid, the research on the corresponding inhibition of production and promotion of excretion drugs can ultimately benefit the patients. Further research is needed on the application of uric acid lowering drugs in different diseases, while reducing their toxic and side effects.

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