Molecular mechanism and therapeutic strategy of metabolic disorder in renal diseases

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Abstract: The molecular mechanism and therapeutic strategy of metabolic disorder in renal diseases are the focus of medical research at present. As an important excretory and regulatory organ of human body, the dysfunction of kidney will lead to electrolyte imbalance, acid-base balance disorder, abnormal blood lipid and blood sugar and other metabolic disorders. In this paper, the molecular mechanism of metabolic disorder in renal diseases is reviewed, and the targeted treatment strategies are discussed. Studies have shown that mechanisms such as gene mutation, abnormal signal pathway and inflammatory reaction play an important role in metabolic disorder. Gene editing techniques such as CRISPR-Cas9 provide new possibilities for gene therapy, while targeted therapy and the use of metabolic regulators provide effective means to correct metabolic disorders. In addition, this study also emphasizes the importance of paying attention to and correcting metabolic disorders in the treatment of renal diseases in order to improve the prognosis and quality of life of patients. Future research needs to further explore the molecular mechanism of metabolic disorders and develop more accurate and personalized treatment programs.

Keywords: metabolic disorder; Molecular mechanism; therapeutic strategy; renal diseases

1. Introduction

As a global health problem, kidney disease is getting more and more attention. As an important excretory organ of human body, kidney is not only responsible for filtering blood, eliminating waste and excess water, but also participating in regulating water and electrolyte balance and maintaining many important physiological functions. However, when the kidney is damaged, these functions may be seriously affected, leading to imbalance in the internal environment and further aggravating the disease.

Among the clinical manifestations of many kidney diseases, metabolic disorder is particularly prominent. This disorder involves not only electrolytes and acid-base balance, but also blood lipids and blood sugar. These metabolic abnormalities not only affect the health status of patients, but also accelerate the decline of renal function [1]. Therefore, it is very important to explore the molecular mechanism of metabolic disorder in renal diseases for developing more effective treatment strategies. In recent years, with the rapid development of molecular biology and clinical medicine, the molecular mechanism of metabolic disorder in kidney diseases has been deeply understood [2]. However, how to operate these mechanisms in complex human environment and how to intervene effectively through clinical means are still hot and difficult points in current research.

The purpose of this study is to explore the molecular mechanism of metabolic disorder in renal diseases through comprehensive analysis of existing clinical research data, and on this basis, put forward targeted treatment strategies. Through this study, we can provide new ideas and methods for the treatment of kidney diseases, improve the quality of life of patients and delay the progress of the disease.

2. Relationship between renal diseases and metabolic disorders

As an important excretory and regulatory organ of human body, kidney plays a vital role in maintaining the homeostasis of the internal environment. However, in the state of kidney disease, its normal function is damaged, which often leads to a series of complex metabolic disorders.
Electrolyte imbalance often occurs in patients with kidney disease. Because the kidney's reabsorption and excretion of electrolytes are impaired, patients may have electrolyte abnormalities such as hyperkalemia and hyponatremia [3]. These abnormalities not only affect the normal physiological function of cells, but also may lead to serious complications such as arrhythmia. Acid-base balance disorder is also one of the common metabolic disorders in kidney diseases. The kidney is the key organ to regulate the acid-base balance of the body, and it maintains the stability of blood pH value by expelling acid and preserving alkali. In the state of kidney disease, this regulatory function may be damaged, leading to acidosis or alkalosis, which in turn affects the normal function of the whole body organs.

In addition, kidney disease is closely related to dyslipidemia [4]. After kidney damage, lipid metabolism may change, leading to hyperlipidemia, especially hypertriglyceridemia and hypercholesterolemia. These dyslipidemia are important risk factors for cardiovascular diseases, which further increase the health risks of patients with kidney diseases.

There is a close relationship between renal diseases and metabolic disorders. These metabolic disorders not only affect the health status of patients, but also may accelerate the decline of renal function. Therefore, in the treatment of renal diseases, we should pay close attention to and correct these metabolic disorders in order to improve the prognosis and quality of life of patients.

3. Study on molecular mechanism of metabolic disorder

Kidney is one of the key organs to maintain metabolic balance in the body. Metabolic disorder is a common clinical manifestation in renal diseases, and its occurrence is related to various molecular mechanisms. In recent years, with the rapid development of molecular biology technology, it has been possible to deeply analyze these mechanisms, including core elements such as gene mutation and abnormal signal pathway.

Gene mutation plays an important role in metabolic disorders related to kidney diseases. Many studies have shown that the mutation of some genes will directly affect the electrolyte transport and reabsorption function of the kidney [5-6]. For example, gene mutation related to sodium and potassium ion channels or transporters may lead to abnormal treatment of these ions by the kidney, which may lead to electrolyte disorder. Similarly, genetic variation involved in lipid metabolism may also lead to dyslipidemia and increase the risk of cardiovascular diseases.

Kidney diseases are often accompanied by local or systemic inflammatory responses. Inflammatory mediators such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and C-reactive protein (CRP) can affect the function of renal cells, leading to metabolic disorders [7]. TNF-α can inhibit the reabsorption of glucose by renal tubular cells, thereby affecting glucose metabolism. Oxidative stress refers to the imbalance between the production of Reactive Oxygen Species (ROS) and the antioxidant defense system [8]. In kidney diseases, excessive production of ROS can lead to lipid peroxidation, protein modification, and DNA damage, which can interfere with normal metabolic pathways. For example, oxidative stress can damage mitochondrial function, affecting energy metabolism.

Abnormal signal pathway is also an important factor leading to metabolic disorder in renal diseases. The signal transduction network in the kidney is fine and complex, involving multiple pathways and intermolecular interactions. In some cases, these signal pathways may be disturbed or blocked, resulting in the out-of-control regulation of electrolytes, acid-base balance and lipid metabolism by the kidney [9]. Abnormal expression or activity change of some signal molecules may directly affect the function of renal epithelial cells, and then cause metabolic disorder.

The progression of kidney disease is often accompanied by changes in energy metabolism. Mitochondrial dysfunction is an important factor leading to abnormal energy metabolism. Mitochondria are the energy factories of cells, and their dysfunction can lead to a decrease in ATP production, affecting the normal operation of sodium/potassium pumps and other ion channels, thereby impacting renal filtration and reabsorption functions. Kidney disease can affect the synthesis and secretion of hormones, such as antidiuretic hormone (ADH), the renin-angiotensin-aldosterone system (RAAS), and vitamin D metabolism [10]. The imbalance of these hormones can further exacerbate metabolic disorders. The activation of the RAAS system can lead to elevated blood pressure and sodium and water retention, while vitamin D deficiency can affect calcium and phosphorus metabolism.

Gene mutation and abnormal signal pathway are important molecular mechanisms leading to
metabolic disorder in renal diseases. In-depth study of these mechanisms not only helps to understand the pathophysiological process of renal diseases more comprehensively, but also provides a theoretical basis for developing targeted treatment strategies. Correcting these molecular abnormalities is expected to provide more accurate and effective treatment for patients with renal diseases.

4. Clinical research progress

Chronic kidney disease (CKD) is a global public health problem, and its pathogenesis is complex, involving a variety of molecular and cellular processes. Metabolic disorder is an important aspect in the pathogenesis of CKD, including the integration disorder of energy metabolism, innate immunity and neuroendocrine function.

In recent years, researchers have made significant progress in understanding the molecular mechanisms of metabolic disorders in kidney disease. Studies have shown that renal tubular damage is associated with mitochondrial dysfunction, especially in acute kidney injury (AKI) [11]. The dysregulation of mitochondrial biogenesis and autophagy flux is considered a key link in the repair of renal tubular damage [12].

The latest research reveals that renal tubular injury stress leads to lipid metabolism disorder, in which ceramide synthesis pathway is over-activated, and AMPK is dephosphorylated by activating protein phosphatase PP2A, thus mediating mitochondrial autophagy injury and renal tubular cell apoptosis [13]. Intestines and lungs have been found to be important mediators in the interaction between the kidney and the outside world, participating in the occurrence and development of cardiovascular diseases and other systemic complications [14]. The application of omics technology is helpful to deeply understand the pathophysiological mechanism related to CKD, so as to formulate corresponding treatment measures [15].

Based on the understanding of the molecular mechanism of metabolic disorder, researchers are developing new therapeutic strategies. Studies have shown that targeting AMPK can improve renal tubular injury and apoptosis caused by ischemia-reperfusion and provide potential drug targets for the prevention and treatment of AKI [16]. Research and development of mitochondrial protective agents to improve mitochondrial homeostasis and improve mitochondrial quality control [17]. Metabolic regulators are used to correct metabolic disorders, such as regulating fatty acid oxidation and sugar metabolism [18].

In the aspect of electrolyte disorder, many clinical studies have focused on the mechanism of kidney's treatment of electrolyte. For example, some studies have found gene mutations related to renal sodium and potassium ion transport through gene detection, which directly affect the renal electrolyte reabsorption and excretion function [19]. These findings provide a new idea for individualized treatment of electrolyte disorders. Aiming at the disorder of acid-base balance, clinical research began to pay attention to the mechanism of acid-base regulation in kidney. Through in-depth analysis of patients' blood and tissue samples, researchers found that some signaling pathways played a key role in acid-base balance regulation [20]. These studies provide potential targets for developing drugs for acid-base balance disorders. In the aspect of dyslipidemia, clinical research reveals the complex relationship between renal diseases and lipid metabolism. By comparing the blood lipid levels of patients with different kidney diseases, the researchers found that there is a close relationship between renal dysfunction and dyslipidemia [21]. These findings emphasize the importance of kidney in lipid metabolism and provide a new perspective for the prevention and treatment of cardiovascular diseases related to kidney diseases.

Metabolic disorder in renal diseases is a complex pathological process involving multiple molecular and cellular pathways. Through in-depth study of these mechanisms, we can better understand the pathophysiology of CKD and develop more effective treatment strategies. Future research needs to further explore these mechanisms and verify the clinical application potential of new therapeutic targets.

5. Exploration and practice of treatment strategy

5.1. Gene therapy

Gene therapy is a kind of treatment method which uses gene transfer technology to introduce
foreign genes into patients to correct or compensate abnormal genes. In renal diseases, the goal of gene therapy is to restore the normal metabolic process and renal function by replacing, repairing or regulating the expression of pathogenic genes.

In recent years, gene therapy has shown potential in the treatment of kidney diseases, especially in dealing with the molecular mechanisms related to metabolic disorders. For hereditary kidney diseases caused by specific gene mutations, such as polycystic kidney disease and Alport syndrome, gene therapy can directly treat the defective genes [22]. By regulating the key genes that affect metabolism, such as those that regulate fatty acid oxidation, sugar metabolism and amino acid metabolism, the metabolic state of kidney can be improved. Gene therapy can be used to inhibit inflammatory reaction and fibrosis in kidney diseases, for example, by down-regulating the expression of proinflammatory cytokines.

The development of gene editing technology such as CRISPR-Cas9 provides new possibilities for gene therapy of kidney diseases [23]. These technologies allow precise modification of the genome, thus correcting the mutation of pathogenic genes or regulating gene expression. Through CRISPR-Cas9 technology, researchers can increase the efficiency of homologous directional repair mediated by Cas9, which is of great significance for repairing gene mutation in kidney diseases.

Gene therapy provides an innovative therapeutic strategy for the molecular mechanism of metabolic disorder in renal diseases. With the progress of gene editing technology and the in-depth understanding of the molecular mechanism of kidney diseases, gene therapy is expected to become an important means to treat kidney diseases in the future. However, to achieve this goal, we need to overcome technical and ethical challenges and conduct a lot of pre-clinical and clinical research.

5.2. **Targeted therapy**

Targeted therapy is a modern treatment method, which achieves therapeutic effect by specifically acting on the molecular targets of diseases. In renal diseases, targeted therapy aims at correcting the molecular mechanism of metabolic disorder, thus improving renal function and slowing down the disease process.

Because mitochondria play a central role in energy metabolism and cell death, mitochondrial targeted therapy has become a new field of CKD therapy. This includes the use of mitochondrial cardiolipin protectants, mitochondrial synthesis agonists, mitochondrial antioxidants and mitochondrial acid 5 to improve mitochondrial dysfunction [24]. Renal immune cells, such as dendritic cells and macrophages, play an important role in renal diseases. Targeting metabolic pathways of these cells, such as fatty acid oxidation and glycolysis, may help to regulate immune response and alleviate renal inflammation. Targeting key signal pathways in renal diseases, such as mTOR, AMPK and NF-κB, can regulate cell growth, proliferation and survival, thus affecting the progress of renal diseases.

The main advantage of targeted therapy is that it can accurately act on the key molecules of diseases, thus reducing the toxic effects on normal cells [25]. However, targeted therapy also faces challenges, including the development of drug resistance, the side effects of targeted drugs, and the differences in curative effects caused by individual differences. The effectiveness and safety of these treatments still need further clinical research to verify. Future research should focus on discovering more potential molecular targets and developing more accurate and personalized treatment programs.

In addition to the above-mentioned emerging treatment strategies, traditional treatment methods are constantly improving and optimizing. For patients with dyslipidemia, in addition to diet control and exercise therapy, doctors will prescribe lipid-lowering drugs according to the specific conditions of patients. These drugs reduce blood lipid levels through different mechanisms, thus reducing the risk of cardiovascular diseases. However, the efficacy and safety of traditional treatment methods vary from individual to individual, so it is necessary to closely monitor the patient's response and adjust the treatment plan in time.

6. **Conclusion**

The molecular mechanism of metabolic disorder in kidney diseases is complex and diverse, involving inflammatory mediators, oxidative stress, abnormal signal pathway, gene mutation and many other aspects. Inflammatory mediators, such as TNF-α, IL-6 and CRP, lead to metabolic disorder by affecting the function of renal cells. Excessive production of ROS under oxidative stress damages
mitochondrial function and interferes with normal metabolic pathway. The abnormality or interruption of signal transduction network in kidney will affect the regulation of electrolyte, acid-base balance and lipid metabolism in kidney. Gene mutation directly affects the transport and reabsorption of electrolytes and lipids in the kidney, leading to electrolyte imbalance and dyslipidemia. In view of these molecular mechanisms, therapeutic strategies should focus on alleviating inflammatory reaction, reducing oxidative stress, correcting abnormal signal pathways and gene defects. This requires the comprehensive application of drug intervention, gene therapy, nutritional support and comprehensive management to improve the quality of life of patients with kidney disease and delay the progress of the disease. With the continuous development of molecular biology technology and the deepening of clinical research, it is expected to provide more accurate and effective strategies for the treatment of metabolic disorders in kidney diseases in the future.

References


