



RESEARCH ARTICLE

RESEARCH PROGRESS IN WESTERN MEDICINE IN THE PREVENTION AND TREATMENT OF CHRONIC RENAL FAILURE

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ABSTRACT

Chronic renal failure (CRF) is a common and frequently-occurring disease in clinic. It develops from various kidney diseases and eventually leads to renal failure, which seriously endangers human health. Chronic renal failure is the end stage of various kidney diseases, which belongs to irreversible kidney damage. At present, the effective control method for chronic renal failure is alternative therapy. However, due to the lack of kidney source, immune rejection and high mortality after dialysis. Therefore, how to intervene before it develops into chronic renal failure? Pretreatment and treatment of chronic kidney disease, in order to delay or prevent further damage to the kidney is very important. This article reviews the pathological mechanism of chronic renal failure in western medicine and how to prevent and treat chronic renal failure in order to provide reference for clinical treatment and experimental study of chronic renal failure.

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INTRODUCTION

Chronic renal failure (CRF) is a common clinical syndrome. It occurs on the basis of various primary or secondary chronic kidney diseases, and slowly leads to renal failure (Chen H.Z., 2005). According to statistics, the incidence and mortality of chronic renal failure are increasing all over the world, which has caused serious harm to human health (Xue J.L., et al., 2010). With the change of medical environment, living environment and lifestyle, the proportion of secondary renal failure caused by diabetes, hypertension and drugs is gradually increasing (Koye D. N., et al., 2018; Chang Y.L., 2006). In 2001, the Guidelines for Clinical Practice of Chronic Kidney Disease and Dialysis (Liu Z.S., 2008), compiled by the K/DOQI Working Group of the American Kidney Foundation (NKF), proposed the concept of Chronic Kidney Disease (CKD), and recommended a scheme for delaying the progression of kidney disease and improving its prognosis at various stages. This guideline was accepted by most people. As can be seen from the guidelines, before the fifth phase, it is an important period for intervention and delaying the progress of kidney disease. Therefore, how to prevent and treat the first four stages of chronic kidney disease in clinic has become a hot issue for scholars. This article will sort out the pathogenesis and prevention methods of chronic renal failure in order to provide

reference for the prevention and treatment of chronic renal failure.

Pathological Mechanism of CRF

The pathogenesis of chronic renal failure is complex. Current studies can not fully elaborate the mechanism of CRF occurrence and development, but a full study of the pathogenesis of CRF can provide theoretical basis and guidance for clinical prevention and treatment of CRF. The current understanding of the pathogenesis of CRF can be summarized as follows.

Toxin Theory

If the toxins produced by metabolites or intestinal bacteria in vivo can not be eliminated in vitro in time, they will cause damage to the body. In vivo toxins can be divided into small molecular toxic substances and medium and macromolecule toxic substances, of which the study of small molecular toxic substances is the most.

Small Molecular Toxic Substances

In recent decades, studies on small molecular toxic substances (molecular weight < 500) have shown that guanidines (such as methyl guanidine, guanidine succinic acid), amines (such as dimethylamines, trimethylamines, aromatic amines, polyamines,

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etc.), phenols and indoles are toxic products of nitrogen metabolism (Qiu C.L.,1989). Among them, guanidine substances have been widely studied. Animal experiments have proved that guanidine-related products can induce gastrointestinal symptoms and symptoms of spasm, sleepiness, hemorrhage and hemolysis in animals. When patients are treated with hemodialysis solution containing more than 300 mg% urea during hemodialysis, sleepiness and fatigue will occur after dialysis; but if the above toxic small molecules does not reach a certain concentration, the body will not show poisoning symptoms (Qiu C.L.,1989). Therefore, whether the toxic products of nitrogen metabolism must lead to uremia symptoms remains to be further studied.

Medium and macromolecule toxic substances

Medium molecular toxic substances (molecular weight 500-5000) in vivo include many high concentration normal metabolites, hormones with normal structure and high concentration, polypeptides produced by disordered cell metabolism and cell or bacterial lysates. According to research, high concentration of medium molecular substances can cause peripheral neuropathy, uremic encephalopathy, inhibit erythropoiesis, insulin and lipoprotein lipase activity and antibody production, resulting in platelet dysfunction, low cellular immune function, sexual dysfunction, etc. (Qian T.S.,1984). However, the nature of the toxic substances is still unclear, but it is believed that the toxic effect on the nervous system is greater (Qian T.S.,1984; Zhong B.T., 1994). With the further deterioration of renal function, the levels of macromolecule substances such as parathyroid hormone, growth hormone, adrenocorticotrophic hormone and other polypeptide hormones in the body increase, which will cause greater damage to the body. among which the toxicity of parathyroid hormone is the most significant, so that some scholars believe that parathyroid hormone is one of the main uremic toxic substances.

Survival nephron theory

Bricker put forward the theory of surviving nephron in 1960. He believed that a considerable number of nephrons were destroyed and lost their function in renal parenchymal lesions, and the surviving nephron had to do more work to maintain the body's fluid, electrolyte and acid-base balance. Therefore, compensatory hypertrophy occurs in the surviving nephron, and the filtering function and the ability to process filtrate are enhanced to adapt to the above changes. This is the theory of surviving nephron(Zhong B.T., et al,1994).

On this basis, the following theories have been derived: renal tubular hypermetabolism, glomerular hyperfiltration, glomerular hypertension, hyperperfusion and hyperfiltration. Experiments have proved(Qian T.S.,1984) that when the GFR of the affected kidney decreases, the GFR of the healthy kidney increases correspondingly. Therefore, the changes of GFR can be seen that the kidney has strong adaptability and energy-saving ability in the occurrence of pathological changes. However, with the gradual decrease of the nephron, when the metabolites produced by the body exceed the regulation range of the residual nephron, There will be different pathological symptoms in the whole body, which is chronic renal failure.

Theory of Correcting Imbalance

In the early 1970s, Bricker put forward the theory of correcting the disequilibrium on the basis of the theory of surviving nephron to supplement the deficiency of the theory of surviving nephron. He believed that there was imbalance in the body when the renal function was insufficient in chronic kidney disease. In order to rectify the imbalance, some compensatory changes in the body caused some substances to increase, so as to rectify it. However, these compensatory changes lead to new imbalances and clinical symptoms, which are called "correction imbalance", among which parathyroid hormone and natriuretic hormone have been studied more. The electrolyte disturbance in chronic renal failure leads to the increase of parathyroid hormone and natriuretic hormone secretion in vivo to correct the electrolyte imbalance, but at the same time, the increase of the two hormones also has some side effects in vivo, such as When uremia occurs, the secretion of natriuretic hormone increases, which promotes the excretion of sodium from kidney, at the same time, it also causes abnormal sodium pump in tissue cells, intracellular retention of water and sodium, and symptoms such as hypertension and brain edema.

Disturbance of lipid metabolism

The results show that(Wu S.W., et al.,2010) blood fat changes play an important role in the progress of CRF. Hyperlipidemia, especially elevated LDL and cholesterol, can activate mononuclear macrophages, promote their migration and aggregation to the subendothelium, and release bioactive mediators; LDL and oxidized LDL can bind to receptors on mesangial cell membrane to produce direct toxicity, reduce cell membrane fluidity, stimulate macrophages to release polypeptide growth factor and prostaglandin and other mediators.

In addition, hyperlipidemia increases blood viscosity, abnormal circulation dynamics and hypertension, promotes coagulation, thrombosis and inflammatory reaction, and aggravates glomerular damage and sclerosis(Jiang J.J., 1994). In animal experiments, the progressive destruction of nephron was aggravated by high cholesterol diet; low fat and unsaturated fatty acids could inhibit glomerulosclerosis and matrix expansion (Wu S.W., et al.,2010). Studies have shown that the main mechanisms of kidney damage caused by dyslipidemia are oxidative stress, endoplasmic reticulum stress and inflammatory stress (Ruan X.Z.,2018).

Peptide Growth Factor and Cytokines

Recent advances in cell and molecular biology have shown that polypeptide growth factors produced by mesangial cells, macrophages, platelets and endothelial cells, such as transforming growth factor, epidermal growth factor, insulin-like growth factor and platelet-derived growth factor, etc. and cytokines such as interleukin, tumor necrosis factor, etc. these will lead to self-regulatory systems that initiate cell-cell, cell-matrix interactions and produce a series of chain amplification effects that cause progressive kidney damage.

They have similar mitotic effects on mesangial cells and fibroblasts, promote proliferation and metabolism, and then produce more polypeptide factors. It can also induce excessive oxygen free radicals and inflammatory mediators, promote

intraglomerular coagulation, platelet aggregation and fibrin deposition.

To sum up, although the current research on the pathological mechanism of CRF is not comprehensive, the results of the study have important practical value and guiding significance for clinical prevention and treatment of CRF.

Prevention and Treatment Methods

All the causes, inducements and harmful substances that can aggravate renal function damage are the main treatment targets and directions for preventing and treating CRF. Reducing or even eliminating these factors will effectively protect renal function, delay the occurrence of CRF, and reduce the morbidity and mortality of CRF. At present, there are different opinions about the prevention and treatment of delaying the occurrence of CRF, but there are also some consensus parts. In view of the above pathological mechanism of CRF, the author will sort out the prevention and treatment of CRF from the following aspects.

Active Control of Risk Factors

Chronic renal failure develops from various chronic kidney diseases. At present, the incidence of secondary CRF is higher than that of primary CRF (Koye D. N., *et al.*,2018; Chang Y.L.,2006). Common diseases include diabetes, hypertension, glomerulonephritis and so on. Therefore, active treatment or control of primary diseases will prevent the occurrence of CRF from the source.

Control of Blood Sugar

Diabetic nephropathy is a serious complication of diabetes mellitus. Kidney damage exists in the early stage of diabetes mellitus. In the process of CKD, the level of blood sugar affects the progress of chronic renal failure. According to the domestic research and expert consensus (Chen H.Y.,2018), it was suggested that fasting blood glucose in non-dialysis patients should be 7.8-10 mmol/L and 1.8-13.9 mmol/L 2 hours after meal; 8.25-11.1 mmol/L on fasting and 11.1-16.5 mmol/L 2 hours after meal are safer for hemodialysis patients. For patients with CKD combined with hyperglycemia, the dosage reduction or discontinuation should be considered according to the use of drugs.

Controlling Blood Pressure

In 2018, experts in blood pressure management of patients with CKD and hypertension have reached a consensus (Shao F.M.,2018): after the diagnosis of hypertension has been established (i.e., blood pressure > 140/90 mmHg), it is recommended that patients with CKD, regardless of whether they have diabetes mellitus or not, should start antihypertensive drugs at the same time as lifestyle adjustment; blood pressure > 150/90 mmHg of 60-79 years old people should start antihypertensive drugs treatment; \geq 80 years old elderly blood pressure > 150/90 mmHg, can start antihypertensive drugs. Treatment methods include non-drug therapy and antihypertensive drugs, emphasizing individualized treatment. At present, ACEI and ARB are commonly used antihypertensive drugs in patients with CKD. Studies have shown that (Radcliff K, *et al.*,2012.): ACEI can inhibit the systemic and intrarenal effects of angiotensin II and improve

renal function by reducing systemic blood pressure, dilating renal vessels and reducing proteinuria. In addition, ACEI selectively dilates the glomerulus and has a small glomerular output. The arteries are more obvious than the small arteries entering the globe. Therefore, in the early stage of application, the GFR can be significantly decreased, and the serum creatinine (SCr) and blood urea nitrogen (BUN) increase temporarily. We should pay attention to the changes of SCr and BUN. ARB can specifically antagonize angiotensin converting enzyme receptor I (ATI), inhibit vasoconstriction and aldosterone release by selectively blocking the binding of angiotensin II to ATI, and increase GFR and blood flow through reducing intraglomerular pressure, thereby delaying glomerular flow. Sclerosis can protect kidney (TonneijckLennart,*et al.*,2014.). The combination of ACEI and ARB can significantly reduce urinary protein and renal hypertension, and has better renal protection effect (Wang S.Q.,2018).

Active Treatment of Urinary Diseases

Urinary system diseases such as glomerulonephritis, urinary tract infection, calculi, obstruction and drug poisoning are all risk factors for CKD. Therefore, urinary system diseases should be treated actively and nephrotoxic drugs should be avoided.

Diet

The diet of CKD patients is closely related to the severity of the disease. In the process of renal function damage, nutrition deficiency or excessive will lead to the decline of renal function. Therefore, reasonable diet should be formulated according to the condition and prognosis of CKD patients. If the patient has diabetes or hypertension, the intake of carbohydrates, sugar and sodium should be reduced. At present, the diet of CKD patients approved by many scholars is mainly low protein diet.

Low-protein diet is an important prevention and treatment method to delay the occurrence and development of CKD patients to CRF. It can prevent metabolic acidosis caused by accumulation of organic acids, hydrogen ions and phosphates by restricting protein intake, alleviating clinical symptoms of acidosis and alleviating renal excretion. The burden of metabolic waste can delay the progress of renal function and improve complications in CKD 3-5 patients (Huang Y.Y., *et al.*, 2018; Shah BV, *et al.*,2016; Rizzetto F, *et al.*,2017; Kalantar-Zadeh K, *et al.*,2016; Piccoli GB, Deagostini Mc, *et al.*,2014).

At present, it is considered that the control target of (Ko GJ, *et al.*,2017) CKD patients should be: diet protein intake (DPI) of patients in stage 3-5 is 0.8-0.3 g/kg; DPI of patients in stage 3 is at least 0.8 g/kg; DPI target of patients in stage 3-4 is 0.6 g/kg; DPI target of patients in stage 5 is 0.6-0.3 g/kg, while ensure adequate calorie intake at the same time. The requirement of CKD low protein diet quality is at least 70% high biological value protein, which is mainly obtained from animal protein. When the total protein intake is close to the minimum value necessary for human survival, there is little room for the body to choose the protein provided by food. Therefore, the low protein diet of CKD patients needs high biological value and high quality protein. The energy intake requirement is at least 30 kcal/(kg.d) (1 cal = 4.184 J) (Watanabe S.,2017; Chan M.,2016). However, in a low-protein diet, attention should be paid to protein energy consumption, adequate energy intake and

intake should be gradually (Huang Y.Y., 2018). Therefore, low-protein diet has a positive effect on CKD in non-dialysis stage, and is safe in nutrition and metabolism; however, more well-controlled studies are needed to explore the optimal starting time and low-protein diet quantity of low-protein diet, and to provide more reliable evidence for the role of low-protein diet (Wang Y., et al,2018).

Regulating Blood Fat

It can be seen from pathogenesis 1.4 that blood fat play an important role in CKD injury. Because the pathogenesis of blood fat in CKD is complex, and the blood fat has its own characteristics in each period of CKD (Yuan W.J., et al,2012). Therefore, for different patients, blood fat therapy should be carried out according to each individual's condition, rather than just referring to the guidelines. For example, Yuan W.J.,et al.(2012) analyzed the choice of drugs from the aspects of safety, reducing the occurrence of cardiovascular events and the choice of specific drugs:①Statins are used in patients with CKD1-2, and their drug safety has been affirmed; however, patients with CKD3-4 have impaired renal excretion function, which will affect the blood of statins, drug concentration needs to be adjusted in drug dosage;②Statins can significantly reduce the incidence of CVD in patients with mild to moderate CKD; ③High TG is the characteristic of blood fat metabolism in patients with CKD, in addition to statins, beta drugs can significantly reduce the incidence of TG.

Scavenging Oxygen Free Radicals and Anti-inflammation

In the course of CKD, whether abnormal blood fat or polypeptide growth factors and cytokines, can lead to the production of oxygen free radicals and inflammatory cells; therefore, active scavenging of oxygen free radicals and anti-inflammatory treatment in CKD can not only protect renal function, but also avoid other serious complications to the body. Shrikant R. and Mulay (2019) analyzed the role of NLRP3 inflammation corpuscle in chronic kidney disease, which provided a new way for NLRP3 receptor antagonist to treat CKD.Liu X.Y.(2009) found that oxidative stress is particularly serious in kidney diseases, and oxidative stress gradually aggravates with the decrease of renal function, low molecular weight heparin has definite antioxidant effect and can improve oxidative stress in patients with chronic renal failure to a certain extent, which deserves great attention of clinicians. YanN.W.,et al.(2014)experimental studies showed that laccase 281 exopolysaccharide mono-component (LEP-1b) could improve the histopathological status of kidney and significantly reduce the pathological index of kidney. Serum creatinine (SCR) and urea nitrogen (BUN) increased, while total protein and albumin increased. It can also increase the activities of SOD, GSH-PX, CAT and GSH, and decrease the content of malondialdehyde in kidney and liver. Moreover, at the same dose, CLEP-1b has a more significant effect on LEP-1b,therefore, LEP-1B and CLEP-1B can alleviate chronic renal failure in mouse, and their effects are closely related to antioxidant activity.

Pay Attention to the Use of Drugs

Wang L.J.,et al.(2019)found that there are many unreasonable drug use situations in the clinical treatment of CKD, such as

unsuitable drug selection, unsuitable usage and dosage, unsuitable solvent selection, unsuitable drug dosage form or route of administration, unsuitable combination of drugs, and contraindication of drug use.Zheng W.C.et al.,(2018). believes that in the anti-infective treatment of chronic renal insufficiency complicated with infection, the pathophysiological changes of patients should be taken into account firstly; secondly, the PK/PD characteristics of antibiotics and the changes of patients'renal function should be combined to adjust the drug regimen so as to improve the clinical therapeutic effect and promote the rational use of antibiotics; this is in line with Xu X.L.et al.,(2018)., it is believed that when using antibiotics, doctors should select the type and dosage of antibiotics according to the individual condition of patients, closely monitor the adverse reactions of patients, so as to fully achieve the therapeutic effect without serious adverse reactions. Furthermore, nephrotoxic drugs should be avoided clinically. Drug use for CKD patients should be individualized, and rational drug use should be closely combined with the patient's condition.

Discuss

CRF is the end stage of the development of various kidney diseases, its clinical manifestations are diverse. In the late stage, dialysis and kidney transplantation can only be used as alternative treatment, but the long-term effect is not ideal, and the quality of life of patients is poor. Therefore, active prevention and treatment of CRF non-dialysis period for delaying chronic renal failure is the focus of prevention and treatment at present. However, due to the complexity of the pathogenesis, the current research on the pathogenesis of CRF has not fully elaborated the whole process of CRF, but is generally based on several theories that have been put forward; but the hypothesis has important value for clinical application; therefore, in the future, we should strengthen the etiology and pathogenesis of CRF to clarify the pathogenesis. Only after the system can we better guide the clinical medication. Furthermore, in the process of prevention and treatment of CRF, we should insist on individualized treatment, specific analysis of the disease, and avoid blindly using the guideline standards, so as to provide effective prevention and control measures for delaying or preventing the occurrence of CRF.

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