Sports Science, Human Performance, and Health Journal
ISSN 3064-7533
Volume 12 Issue 2
April – June 2024
Impact Factor: 7.71
Enquiry: contact@continentalpub.online
Published by Continental Publication | http:// https://continentalpub.online/index.php/sshphj

THE INTERPLAY BETWEEN CHRONIC RENAL FAILURE AND HYPOTHYROIDISM: EXPLORING A COMPLEX MEDICAL RELATIONSHIP

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Abstract: *Chronic renal failure (CRF) is a complex condition characterized by metabolic disruptions, fluid and electrolyte imbalances, and systemic symptoms stemming from renal dysfunction caused by various primary or secondary chronic renal diseases. It progressively evolves into end-stage renal disease (ESRD), a common outcome of various chronic renal conditions. The long and generally ineffective treatment course for CRF, coupled with the high cost and potential complications associated with alternative therapies such as dialysis or renal transplantation, places substantial burdens on patients and society. These therapies can significantly impact disease prognosis and diminish the quality of life for affected individuals, underscoring the urgency of early and effective interventions.*

Recent years have witnessed a growing focus on the link between thyroid-related disorders and kidney-related diseases. Understanding this connection holds promise for advancing the management and treatment of CRF. This study explores the intricate relationship between thyroid-related conditions and chronic renal failure, shedding light on potential avenues for more effective therapeutic approaches.

Keywords: *Chronic renal failure, end-stage renal disease, thyroid-related diseases, treatment, metabolic disruptions*

Introduction

Chronic renal failure is a series of metabolite retention, water, electrolyte and acid-base metabolism disorders, and systemic symptoms including some endocrine function abnormalities that occur as a result of renal impairment caused by various primary or secondary chronic renal diseases, and progressively develops to end-stage renal disease (ESRD), which is a common outcome of the continuous progression of various chronic renal diseases [1~2]. The treatment cycle of chronic renal failure is long and the efficacy is general, once the disease develops to the end stage, patients can only use alternative therapies such as dialysis or renal transplantation[3] , the cost of alternative therapies is high, which brings huge pressure to patients and society, and the alternative therapies are prone to cause a variety of serious complications, which seriously affects the prognosis of the disease as well as the quality of patients' survival, so early and effective treatment is particularly important for the control of the disease. Therefore, early and effective treatment is particularly important for disease control. In recent years, the relationship between thyroid-related diseases and kidney-related diseases has received increasing attention.

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DOI: https//doi.org/10.5281/zenodo.14179

1. Effects of hypothyroidism on the kidneys

1.1 Effects on water electrolytes and acid-base balance

Kidney [4] has the functions of metabolizing wastes, excreting urine, maintaining the balance of water, acid-base and electrolytes in the body, and also has endocrine functions. Damage to the renal organs is the main cause of chronic renal failure, therefore, kidney damage to a certain extent will cause endocrine disorders.

Hypothyroidism leads to insufficient secretion of thyroid hormones, which play an important role in regulating human metabolism and promoting human growth and development, especially in promoting renal growth and development, increasing renal tubular reabsorption of calcium and sodium ions, stimulating renin secretion, and maintaining water, acid-base, and electrolyte balance, which has an impact on renal hemodynamics[6] .

The kidneys regulate water by altering the degree of concentration and dilution of urine [7], and regulate electrolyte balance by altering glomerular filtration and tubular absorption. Thyroid hormones can alter renal regulation of water-electrolyte and acid-base homeostasis by affecting the above mechanisms. Thyroid hormone deficiency severely affects renal blood flow, glomerular filtration rate, blood creatinine, blood urea nitrogen and creatinine clearance. It has been reported in the literature[8-9] that hypothyroidism can directly lead to renal ischemia with elevated creatinine. Patients with chronic renal failure already show signs of renal insufficiency, and when the thyroid hormone is insufficient, it further aggravates the damage to the kidneys, which is greatly detrimental to the patient.

1.2 Effects on lipid metabolism, cardiovascular

Total cholesterol (total cholesterol, TC), low-density lipoprotein (10w density lipoprotein, LDL), glycerol triglyceride (triglyceride, TG) and apolipoprotein B (apolipoprotein B, ApoB) levels will be significantly higher in patients with hypothyroidism. Abnormal lipid metabolism leads to thickening and hardening of the arterial wall, narrowing of the blood vessel lumen, and the development of atherosclerosis. Atherosclerosis-induced renal vascular stenosis and hyperlipidemia synergistically promote renal injury [10-11] .

Cardiovascular disease [12-13] is the leading cause of death in patients with chronic kidney disease, especially end-stage renal disease, and the most important factor affecting the survival and disability of patients with chronic renal failure toward end-stage. Water and sodium retention and increased reninangiotensin caused by renal failure increase the incidence of hypertension, and long-term hypertension leads to overloading of the left ventricle, myocardial hypertrophy, decreased myocardial contractility, and ultimately heart failure. The heart is one of the most important target organs of thyroid hormone, thyroid hormone has the effect of increasing myocardial contraction and diastolic function, reducing peripheral vascular resistance, lowering the cardiac load, and increasing cardiac output. Abnormal thyroid function can lead to myocardial hypertrophy and ventricular remodeling through the genetic and nongenetic effects of cardiomyocytes and vascular smooth muscle cells. Some findings suggest that thyroid metabolic disorders are involved in left ventricular hypertrophy and dysfunction. When both renal failure and hypothyroidism occur, the damage to the heart is exacerbated, which is extremely detrimental to patient survival.

2. Diagnosis of chronic renal failure with hypothyroidism

Because endocrine, water-electrolyte, acid-base and lipid metabolism disorders caused by hypothyroidism will aggravate the renal damage in chronic renal failure, as well as increase the possibility of complications. On the contrary, endocrine disorders occurring in chronic renal failure will lead to a decrease in thyroid hormone secretion, which is not conducive to the mitigation of renal failure. In the process of treating chronic renal failure, especially when the therapeutic efficacy is fair, it should be considered whether there are other diseases, especially hypothyroidism, affecting the therapeutic efficacy of chronic renal failure. In addition, some manifestations of chronic renal failure often hide the symptoms of hypothyroidism, so that doctors are easy to miss the diagnosis in clinical diagnosis, and chronic renal failure can also cause low T3, T4 syndrome, which makes the two easy to

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be confused, and easy to be ignored in the clinic, so it is crucial to identify whether a kidney disease patient is accompanied by hypothyroidism in the clinical treatment. (1) If chronic renal failure with plasma membrane cavity effusion, diuretic treatment by symptomatic treatment is not obvious effect should pay attention to the measurement of T3, T4 and TSH, such as T3, T4 are low, TSH increased can be diagnosed as hypothyroidism. (2) Chronic renal failure appears obvious pericardial effusion, but the heart rate is slow, and there is no pericardial tamponade symptoms, especially at the same time with ventricular or septal hypertrophy, heart failure on diuretics, digitalis treatment effect is not good, blood cholesterol increased significantly is also suspected of combining with hypothyroidism possibility[14]. (3) Detection of TSH level in serum (more than 2 above normal) can be a reliable diagnosis of hypothyroidism in combination with chronic renal failure[5].

3. Progress in Chinese medicine treatment

3.1 Treatment of chronic renal failure

Chronic renal failure patients clinical manifestations of oedema, fatigue, pale, low voice, urine long or nocturnal urination, fear of cold limbs cold, tongue pale, pulse is thin and so a faction of the cold phenomenon; but also because of the deficiency of the internal organs, spleen and kidney yang deficiency, qi stagnation, the loss of the water and grain essence of the transmission of the chemical, is bound to the increasing gradual decline of the positive, the disease is constantly worsening. Therefore, in terms of the disease process[15] , for chronic renal failure is the early stage, but relative to the original disease is already the advanced stage of disease progression, so the deficiency of visceral functions will inevitably become the main aspect of the contradiction of the disease mechanism. In addition, Western medicine in the treatment of chronic kidney disease treatment process for a long time using antibiotics, immunosuppressants and other drugs. From the perspective of Chinese medicine flavor analysis, these drugs are in fact bitter cold, clearing heat and detoxification products, long time use easy to damage and yuanyang. Hormones are also commonly used in the treatment of kidney disease. From the point of view of the flavor of Chinese medicine, hormones are dry and hot products, which consume kidney yin, and the long-term use of yin damage and yang, and ultimately lead to yang deficiency. Therefore, in the use of traditional Chinese medicine in the treatment of chronic renal failure, most doctors have taken the warming of yang [3][15-18] as the main method, dialectical treatment, and achieved good results.

3.2 Treatment of hypothyroidism

Hypothyroidism [19] is a common chronic disease of the endocrine system, mainly caused by the thyroid gland pathology, resulting in a reduction of thyroid hormone synthesis and secretion, or physiological effects of insufficient and lead to the body's physiological metabolism to reduce the syndrome. Most of the patients show symptoms such as pale or yellowish color, tiredness, indifference, cold expression, dizziness, drowsiness, etc., presenting the phenomenon of yang deficiency and qi weakness, and most of the patients are accompanied by edema, which manifests itself in a non-sagittal manner.

Many modern reports have shown that warming the kidney yang [20-24] method is effective in treating subclinical hypothyroidism, thus proving that the pathogenesis of the disease is based on kidney yang deficiency. Prof. Fang Zhaohui[25] has accumulated some experience in the treatment of hypothyroidism in Chinese medicine. He believes that the disease is located in the kidney and ultimately attributed to yang deficiency, which causes impaired production, secretion, and action of thyroid hormones, resulting in a series of typical symptoms of hypothyroidism. Prof. Fang Zhaohui, based on the cause and effect theory of Chinese medicine, suggested that the first principle of treatment for this disease should be warming and tonifying kidney yang. Many doctors also use warm acupuncture[26] and moxibustion[27] as adjunctive treatments for hypothyroidism, to regulate the whole body and treat both symptoms and root causes, so as to achieve the effect of supporting the right and dispelling the evil, warming the yang and benefiting the qi, tonifying the kidneys and strengthening the spleen, and regulating the qi and blood.

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To summarize, when both diseases occur as independent diseases, both are based on tonifying the Kidneys and warming the Yang in the application of Chinese medicine; and when both coexist, tonifying the Kidneys and warming the Yang is also an important method of treating them.

3.3 Treatment of chronic renal failure with hypothyroidism

Yu Yaping[28] et al. studied the relationship between the severity of chronic renal failure and endocrine disruption, and found that the use of warming yang yiqi method can improve the immune status of patients with chronic renal failure, and regulate the level of endocrine thyroid hormones. By warming the spleen and kidneys and helping the positive qi, the body's yin and yang are balanced, the qi and blood are sufficient, and the metabolism of water and fluid is restored to normal, so as to improve the state of oneself and the immunity of the body, and then achieve a good therapeutic effect in the treatment of chronic renal failure. Some scholars also pointed out that when chronic renal failure combined with hypothyroidism patients, the appropriate application of supplemental thyroid hormone replacement therapy[29] , on the reversal and delay the progression of renal function is beneficial.

In clinical treatment, doctors often give oral eugenol to supplement the lack of thyroid hormone in patients with hypothyroidism. Therefore, when patients with chronic renal failure are clinically diagnosed with hypothyroidism, in addition to focusing on the treatment of tonifying the kidney and warming up the yang in traditional Chinese medicine, they are also given small-dose eugenol for diagnostic treatment.

4. Selenium research

With the progress of research, some scholars have found that among the tissues and organs of the whole body, selenium concentration in the kidney is the highest, and the main way of free selenium loss is through the kidney, so the kidney plays an important role in maintaining the dynamic balance of selenium. Selenium, as an essential trace element for mammals, participates in a variety of metabolic activities in the body, has antioxidant and anti-inflammatory effects, and is directly involved in the synthesis of thyroid hormones, which has a close relationship with the human body's immunity, metabolism, nutrition, and so on, and also influences the onset, development and regression of autoimmune diseases, and also prevents cardiovascular diseases, especially in reducing the degree of atherosclerosis.

Most of selenium does not exist in free state in the organism, it mainly binds with plasma proteins to form selenoproteins. Hypoproteinemia caused by chronic renal failure makes the trace element selenium binding with proteins less, and the selenoproteins content in the body decreases. Therefore, for patients with chronic kidney disease, the selenium content in plasma and whole blood of the patients is decreased compared with the normal control, and the worse the renal function, the lower the selenium content in their bodies. Meanwhile, plasma selenium level was negatively correlated with blood urea nitrogen and blood creatinine levels, indicating that the selenium deficiency state in the organism becomes more serious with the progression of chronic kidney disease, and low selenium promotes the progression of chronic kidney disease. Chronic renal failure is already an advanced stage of disease progression relative to the primary disease such as chronic kidney disease, therefore, the blood selenium level of patients with chronic renal failure is significantly lower than that of normal people, and insufficient selenium in the organism is even more unfavorable to the prognosis of patients with renal failure. In addition, the selenium content of the thyroid gland is second only to the liver and kidney. It is particularly sensitive to selenium deficiency. When hypothyroidism occurs, selenium deficiency should not be ignored.

When the body has abnormal kidney function and thyroid function, the content of the trace element selenium in the body will be less than the normal selenium content in the body, which will make the body's oxidative stress response enhancement, inflammatory response enhancement, or may aggravate the severity of cardiovascular disease, which is the most important complication that leads to death of patients with chronic renal failure, and may also aggravate the series of symptoms brought about by

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DOI: https//doi.org/10.5281/zenodo.14179
chronic renal failure and hypothyroidism. Renal failure and hypothyroidism bring a series of symptoms.[30-33]
Therefore, supplementation with the trace element selenium in the treatment of chronic renal failure combined with hypothyroidism may be effective in slowing down renal damage and reducing the risk of complications. This treatment method is not supported by a large number of samples and studies, and further research is needed.

5. Summary

In this paper, through a large amount of literature, from the hypothyroidism caused by renal injury to elaborate, we found that, in the treatment of chronic renal failure, in addition to renal injury and a series of endocrine disorders caused by acid-base metabolism, lipid metabolism disorders, renal failure caused by the low T4, high TSH manifestation of hypothyroidism, will exacerbate the progression of renal function as well as a series of acid-base metabolism, lipid metabolism disorders and a series of complications, but Because the symptoms of the two are relatively similar, it makes clinical identification difficult. Therefore, in clinical treatment, it is necessary to analyze and identify whether renal failure is accompanied by hypothyroidism, and medical doctors have summarized the treatment of tonifying the kidney and warming the yang, and also proposed the diagnostic treatment of eugenol, and scholars have pointed out the importance of selenium, but all of them lack of a large number of studies to confirm. Therefore, in the follow-up treatment, the treatment of chronic renal failure with hypothyroidism using traditional Chinese medicine to tonify the kidney and warm the yang as the main method, supplemented by oral eugenol and selenium (XIVEL) has certain clinical research significance.

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