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THE POTENTIAL OF MICRO-CHINESE MEDICINE OSMOTHERAPY USING NANOPARTICLES AS A TREATMENT FOR CHRONIC KIDNEY DISEASE

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Abstract

The kidneys are the most important to excretory organs because they have function to remove waste products from the body has metabolism. In the excretory system, the damage that could occur is the kidney has decreased until finally unable to perform its function properly which is called Chronic Kidney Disease (CKD). Chronic Kidney Disease caused by age, gender, and a history of diseases such as diabetes. One of the nanoparticle therapies that could be given to patients with chronic kidney disease is Micro-Chinese Medicine Osmotherapy. The purpose of this paper is to determine: 1) structure and how they work of the kidney and its relation to the urinary system, 2) causes and effects of chronic kidney disease on the urinary system, 3) mechanism of the urinary system in conditions of chronic kidney disease, and 4) mechanism and results of Micro-Chinese Medicine Osmotherapy. The research method used is a literature review from various sources which helps in reviewing the four focus of the study. Kidney is divided into three major parts, namely cortex, medulla, and renal pelvis. The excretory system has three stages, including filtration, reabsorption, and augmentation. Chronic kidney disease can be caused by age, where older age has a risk of developing CKD. Kidney disease can be divided into several stages, including normal, at risk of damage, kidneys are damaged, kidneys are not functioning properly and kidneys are no longer functioning or chronic kidney disease (CKD). The mechanism of action of Micro-Chinese Medicine Osmotherapy is divided based on its function, named as anti-inflammatory, anti-coagulation, and degradation. The results of treatment for kidney disease is Micro Medicine Osmotherapy could make all renal arteries of patients with chronic kidney disease widen and increase perfusion.

Keywords*: Kidney disease; Kidney; Osmotherapy; Trigger; Excretory system*

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INTRODUCTION

The excretory system is a process of removing waste products of metabolism unused by the body. These metabolic wastes consist of compounds that are toxic (poisons) and will result in disruption of the function of the organs in the body if not removed. Organs that have a role in the process of the excretory system are the kidneys, lungs, skin, and liver (Legiawan & Agustina, 2021). Kidneys are the main and most important excretory organs because they remove the remains of the body's metabolism, including toxic substances that accidentally enter the body. This is the reason why the kidney is one of the main target organs for toxic effects. Urine has a function as the main route in the excretory system, causing the kidneys to have a high blood volume, concentrate toxicants in the filtrate, carry toxicants through tubular cells, and activate certain toxicants (Mayori *et al.,* 2013).

In the excretory system, damage can occur to the kidney organ. As a result, the kidneys may experience a decrease in performance and cannot function properly. This occurrence is known as Chronic Kidney Failure (CKD). CKD is one of the diseases that causes major problems worldwide (Belian *et al.,* 2017). Chronic Kidney Failure (CKD) is a pathophysiological process with various causes, such as a decrease or impairment in kidney function such as the inability to remove toxins which can later cause disturbances in the body's organs. For instance, increase in urea levels in the body can cause damage to all cells, including neuron cells. Kidney damage (renal damage) that occurs for more than 3 months can cause structural or functional abnormalities, with or without a decrease in the glomerular filtration rate (GFR) (Zasra *et al.,* 2018). In chronic renal failure where GFR is decreased until less than 60 ml/minute/1.73 m2 for 3 months, the disorder can be caused by many factors.

Kidney failure can be caused by gender, age, and diabetes, hypertension and other metabolic disorders (Pranandari & Supadmi, 2015). Diabetic nephropathy is one of the most common causes of kidney failure. This process begins with hyperglycemia, which causes non-enzymatic glycation of amino acids and proteins. Through the reaction that occurs between glucose and protein, AGEs (Advanced Glycosylation Products) are produced. The formation of AGEs and ROS (Reactive Oxygen Species) will result in metabolic and hemodynamic effects. Through the stimulation of the Renin Angiotensin Aldosterone system, it

hypertension will be triggered. This proves that one of the causes of hypertension is diabetic nephropathy that had been previously experienced by the patient. The continous and long-term accumulation of AGEs in the glomerulus or renal tubules will entirely damage the glomerulus and cause kidney failure (Rini *et al.,* 2016). In addition, abuse of the use of analgesic drugs and NSAIDs can trigger the risk of papillary necrosis and chronic kidney failure. Unhealthy behaviors such as smoking and consuming energy supplement drinks can also cause kidney failure (Pranandari & Supadmi, 2015).

Progressive chronic kidney disease can lead to several complications with a higher or lower prevalence and intensity. Complications that can occur include cardiovascular disease, hypertension, anemia, bone mineral abnormalities, electrolyte disturbances, diabetes mellitus, and metabolic acidosis (Karinda *et al.,* 2019). Complications are very influential on high morbidity and mortality and poor quality of life. The limited physical condition of patients with kidney failure can result in hampered productivity and activities, causing many patients to stop working and participating in social activities. (Priyanti & Farhana, 2016).

A nanoparticle therapy that chronic kidney patients can undergo is Micro-Chinese Medicine Osmotherapy. The application of Micro-Chinese Medicine is based on a combination of herbs in the form of small molecules and particles, which results in optimal effectiveness of the medicinal ingredients. The effective ingredients in these drug particles are mixed with penetration and used as a "medication bag" externally on the lower back of patients with kidney failure. a microwave assisted osmosis device will also be provided to help these drug particles enter the kidney directly. Through Micro-Chinese Medicine, osmotherapy can help treat patients with kidney failure by increasing blood circulation in the kidney area and throughout the body (Hadiwijaya & Manatar, 2014).

The purpose of this paper is to determine: 1) the structure and workings of the kidney and its relation to the urinary system, 2) the causes and effects of chronic kidney disease on the urinary system, 3) the mechanism of the urinary system in conditions of kidney failure, and 4) the mechanism and results of Micro-Chinese Medicine Osmotherapy.

RESEARCH METHODS

The research method used was a literature review by studying and discussing four main focuses, namely: 1) the structure and workings of the kidneys and their relation to the urinary system. 2) the causes and effects of chronic kidney disease on the urinary system, 3) the mechanism of the urinary system in conditions of kidney failure, and 4) mechanism and results of Micro-Chinese Medicine Osmotherapy technology.

RESULTS AND DISCUSSION

Structure and Mechanisms of the Liver along with Its Relation to the Urinary System

The urinary system is a canal consisting of the kidneys, urinary bladder, ureters, and urethra. Humans have a pair of kidneys located on the left and right side of the lumbar spine near the abdominal cavity. The adult kidney is ±12 cm long, ±6 cm wide, ±3 cm thick and weighs ±200 grams. Every minute the heart will pump ± 25% of blood to the kidneys. The kidneys are covered by two layers of fat, namely the pararenal fat and the perirenal layer. Both layers are bounded by the Gerota fascia (Siregar, 2020). Kidney function is very essential for the body, including regulating osmotic pressure in the body, regulating the concentration of compounds in blood plasma (Na^+, K^+, Ca^{2+}), filtering toxins from the acid-base balance in the body, and helping regulate arterial blood pressure by adjusting Na+ compounds (Ariyanto *et al.,* 2017). The structure of the functional and structural unit of the kidney is called the nephron. Each nephron is composed of a vascular component consisting of a glomerulus and peritubular and tubular capillaries (Sutresno *et al.,* 2020).

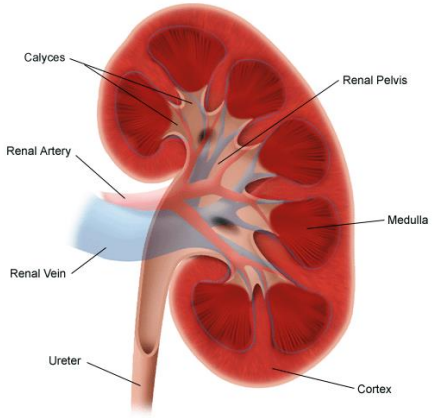

Figure 1. Structure of kidney
(John, 2014)

The kidneys are composed of the cortex (kidney skin), medulla (renal marrow) and renal pelvis (kidney cavity). The cortex functions to protect the kidneys from external damage, preventing the release of blood from cells or macromolecules such as protein and glucose (Nuari & Widawati, 2017). The medulla is where the urine process (reabsorption and augmentation) occurs

(Tanner *et al.,* 2018). In the medulla, there are renal columns consisting of thousands of vessels that continue into the Bowman's capsule. Through the Bowman's capsule, urine will be lifted from the results of filtering the blood through the Malpighian body. The renal pelvis is the link between the kidneys and the bladder and is located at the end of the ureter (Nandana & Justitia, 2013).

Calyces are part of the renal pelvis. Shape of calycesis similar to that of the calyx which has a small space and serves to collect fluid before it is transferred to the bladder (Nandana & Justitia, 2013). Kidney arteries play a role to accommodate oxygen-rich blood. Kidney have two renal arteries for one each kidney. The right renal artery connects to the right kidney. The left renal artery connects to the left kidney. Oxygenated blood comes to the kidneys from the right and left renal arteries off the abdominal aorta (Sutresno *et al.,* 2020). The cortex provides a space for arterioles and venules from the renal artery and vein, as well as the glomerular capillaries. Medulla have a function to regulate concentration of the urine (Dwyer *et al.,* 2016).

Kidneys play a role in the process called excretion by transporting and filtering blood through arteries. The product of renal excretion is urine. Urine production is carried out in three stages. Substances in the body that are still useful will be filtered and flowed into the ureter before being stored in the bladder. Once the bladder is full, the bladder wall will be compressed to expel urine through the urethra. With the formation of urine, the kidneys have an essential function in the body. The resulting excretion is useful for maintaining balance in the body (Kallo *et al.,* 2017).

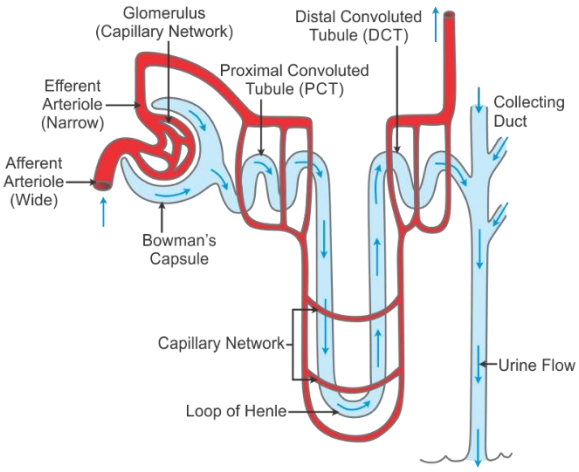

Figure 2. Process of urine production (Reyner *et al.,* 2016)

Nephrons play a role in the process of urine formation (Dwyer *et al.,* 2016). The kidneys regulate the composition of fluids in the body, excrete toxins and produce hormones such as erythropoietin renin and vitamin D. There are three stages in the formation of urine, namely filtration, reabsorption (absorption) and

augmentation (secretion) (Setyawan *et al.,* 2018). Filtration is the process of moving the glomerulus into the Bowman's capsule by filtering the fluid. The result of glomerular filtration is primary urine containing water, potassium, sodium chloride, and glucose but not blood cells (Mangan *et al.,* 2018). Reabsorption is the transfer of fluid from the renal tubules to the peritubular capillaries. Renal tubules will select substances that can be reabsorbed according to needs. The renal tubule is divided into three parts, namely the proximal convoluted tubule which transports water, glucose and sodium, the loop of Henle which transports potassium, sodium and chloride, and the end of the tubule which contains urea. Nutrients in primary urine will be reabsorbed as a whole while salt reabsorption depends on inorganic salts in blood plasma. The process of reabsorption occurs in the proximal convoluted tubule which produces secondary urine that will become increasingly concentrated due to lack of water. Augmentation results from the proximal convoluted tubule and loop of Henle to the distal convoluted tubule. Through blood capillaries, urine will release all substances that are not needed by the body, forming actual urine (Nuari & Widawati, 2017).

Causes and Effects of Chronic Kidney Disorder on The Urinary System

Damage to the kidneys results in the dependence of electrolytes in the body. CKD is a multifactorial disease that can be caused by risk factors that cause the disease, such as diabetes mellitus, hypertension, increasing age, or a family history of CKD (Siagian & Damayanty, 2018). Older age contributes to greater risk of CKD as compared to younger age. A decrease in estimated Glomerular Filtration Rate (eGFR), which is a decrease in glomerular filtration rate as a “normal aging” process is one of the criteria for diagnosing CKD (Eva & Sri, 2015).

The kidneys cannot regenerate new nephrons, resulting in kidney damage or a decrease in the number of nephrons. At the age of 40, the number of functioning nephrons decreases by about 10% every 10 years and at the age of 80 years, only 40% of the nephrons can still function (Nasution *et al.,* 2020). Diabetes mellitus is a high level of sugar in the blood due to impaired insulin secretion, insulin resistance or both (Lufthian *et al.,* 2020). Hypertension or increased blood pressure is a risk factor for impaired kidney function (Gustia *et al.,* 2019). This is because high blood sugar levels will affect the structure of the kidneys and damage the fine blood vessels

in the kidneys (nodular and diffuse glomerulosclerosis).

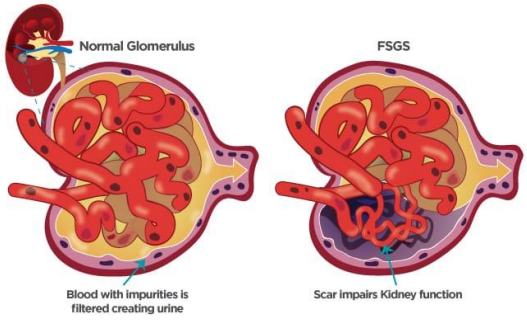

Figure 3. Glomerulus damage in kidneys (Alicic, Rooney & Tuttle, 2017)

Damage to blood vessels causes damage to the glomerulus which functions as a blood filter. The relationship between CKD and hypertension is cyclic, i.e. kidney disease can cause blood pressure to rise and conversely hypertension for a long time can cause kidney disorders (Karinda *et al.,* 2019). The effect of hypertension on the kidneys depends on the height and duration of hypertension. Uncontrolled hypertension in the long-term results in high intraglomerular pressure and affects glomerular filtration. In the urinary system, kidney infections can lead to chronic kidney disease. Kidney infection or commonly referred to as pyelonephritis is an infection that occurs in the urinary tract and can spread to the kidneys (Azhar *et al.,* 2016). Kidney infection or pyelonephritis is a disease caused by Escherichia coli bacteria that attack the ureters and kidneys (Black & Hawks, 2021).

Chronic kidney failure can lead to complications such as cardiovascular disease, hypertension, anemia, bone mineral abnormalities, electrolyte disturbances, diabetes mellitus, and metabolic acidosis (Karinda *et al.,* 2019). These complications lead to high morbidity and mortality as well as poor quality of life. Anemia, mineral and bone disorders in patients begin at stage 3, while hypertension in patients begin to worsen at stages 3-5. Chronic kidney disease can cause various complex manifestations such as fluid accumulation, pulmonary edema, peripheral edema, and uremic toxic overload which is responsible for pericarditis and irritation along the gastrointestinal tract from mouth to anus. Disorders of biochemical balance (hyperkalemia, hyponatremia, metabolic acidosis). Disturbance in the balance of calcium phosphate results in bone demineralization, peripheral neuropathy, pruritus, shallow breathing, anorexia, nausea, vomiting, weakness and fatigue (Wikadanda & Hasetidyatami, 2019).

Mechanisms of The Urinary System in Diseased Kidneys

Kidney failure is caused by progressive damage to the nephrons that leads to the inability to maintain metabolism and fluid balance in the body (Wikananda & Hasetidyatami, 2019). Indication of kidney failure is the functioning of only 70-75% of the normal ability of nephrons (Kallo *et al.,* 2017). The condition of kidney failure is determined by stage.

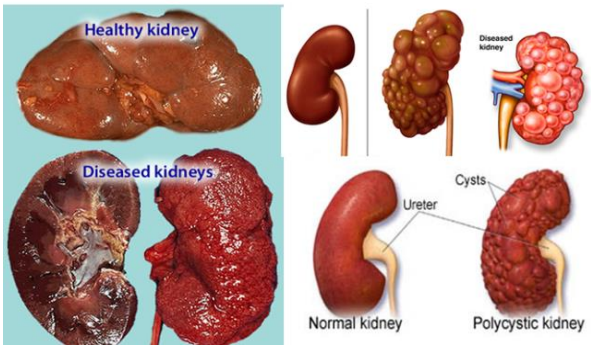

Figure 4. Condition of a normal kidney and diseased kidney (Nurbadriyah & Kep, 2021)

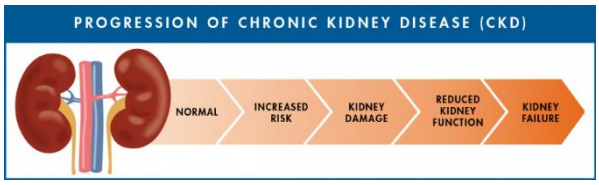

Figure 5. Progression of Chronic Kidney Disease (Susanti & Bistara, 2021)

Figure 3 shows that the physical state of a normal kidney with kidney failure is very different. Normal kidneys have a red bean-like shape and are smooth (Satriono *et al.,* 2018). Meanwhile, patients with kidney failure have damaged kidneys, indicated by changes in the shape of the kidneys and the appearance of circles on the external surface. Kidney failure can be divided into several progressive stages including normal, at risk of damage, kidney damage, reduced kidney function, and kidney failure (CKD) (Kurniawati & Asikin, 2018).

Any progression of kidney failure can be determined according to the (stage) experienced. Figure 4 shows the level of progression of the kidney according to stages that have been divided into 3 parts, starting from the mild stage to failure where the kidney is no longer able to function properly. Stage I is a mild decrease in kidney. The patient can still work without feeling excessive pain. Stage II is renal insufficiency. The kidney condition is 75% damaged and the BUN (Blood Urea Nitrogen) urea level has been disrupted, resulting in a 3:1 ratio of the amount of urine produced in one day. Stage III is chronic kidney failure. Nephrons are 90% damaged and the GFR value is only up to 50 while the normal GFR is 90 (Aisara *et al.,* 2015). Kidney failure causes disruption to the urinary system by decreasing the GFR and increasing BUN, causing the kidneys to lose their ability to concentrate urine. The kidneys can only produce urine with a

concentration of 150 mg/dl. This causes metabolic processes regulated in the organ system to be disrupted. The mechanism of the urinary system against kidney failure starts from the disruption of fluid balance to the accumulation of substances that are not filtered to the increase in speed of the nephrons in processing urine. This cycle requires the nephron to reabsorb protein in the middle of its shrinking process, resulting in a reduced formation of blood flow (Pearce, 2012).

Mechanism and Results of Micro-Chinese Medicine Osmotherapy

Micro-Chinese Medicine Osmotherapy is an herbal treatment therapy from China that can be applied to patients with chronic kidney failure (Lakshmi *et al.,* 2017). This therapy is carried out by utilizing the principle of herbal micronization and using an osmoscope electronic impulse. The herbs used in the treatment of Micro-Chinese Medicine Osmotherapy are Leonurus, Couch grass root, selfheal, Corn stigma, Astragalus mongolicus, Desmodium plantain, Honeysuckle, Dandelion, Tuckahoe, and Job's tears (Hadiwijaya & Manatar, 2014). These herbs can be used because they contain active anti-inflammatory and anticoagulant compounds that can inhibit kidney damage. The instrument used for treatment with Micro-Chinese Medicine Osmotherapy is an osmoscope with electrotherapy mode. In addition, there are also medicine packages and steam boils (Hadiwijaya & Manatar, 2014). The steps for its use are osmotic medicine soaked with penetrant in a container, one bag of the osmotic medicine for one bag of penetrant. Next, the medicine package that has been soaked is heated using a heater. After that, electrotherapy was carried out by placing a sanitary cloth on the bed so as not to contaminate the sheets when the medicine was spilled, then the two electrode plates were placed on a sanitary cloth, and finally, a heated medicine bag was placed on top. The next step is to lay the patient on top of the two bags right on top of the kidney area. After lying down, connect the osmoscope to the mains and select the electrotherapy mode.For example, Astragalus contains anti-inflammatory compounds, such as saponins, flavonoids, and others (Wikadanda & Hasetidyatami, 2019).

In this condition, Micro-Chinese Medicine Osmotherapy works by inhibiting the activation of inflammatory mediators so that the intrinsic damage to kidney cells can be inhibited and kidney metabolic function can return to normal. Inhibition of

the activation of inflammatory mediators can occur after the cessation of prostaglandin synthesis (Nasution *et al*., 2021). This causes IL-1 or TNF-α can not be expressed so that the inflammatory reaction does not occur.Osmosis is the transfer of a substance from a solution with a low concentration to a solution with a high concentration through a semipermeable membrane (Yahya, 2015), while nanoparticle technology is a technology that works by modifying or controlling the release of active compounds to increase drug efficacy and minimize side effects from a drug compound. With this technology, the active compound can be administered at high concentrations because the particle in small in size and equipped with a large surface area (Aspadiah *et al.,* 2020).

According to Hadiwijaya & Manatar (2014), the working mechanisms of Micro-Chinese Medicine Osmotherapy can be categorized based on its function, namely as anti-inflammatory, anti-coagulation, or degradation.

a) Anti-inflammatory

Inflammation arises as a response to harmful stimuli, such as pathogens, damaged cells, irradiation, or toxic compounds (Bare *et al.,* 2019). When the intrinsic cells of the kidney are damaged, an inflammatory reaction occurs, leading to the induction of renal fibrosis. In this condition, Micro-Chinese Medicine Osmotherapy works by inhibiting the activation of inflammatory mediators so that the intrinsic damage to kidney cells can be inhibited and kidney metabolic function can return to normal.

b) Anti-coagulation

Anticoagulation is generally used to inhibit blood clotting. With Micro-Chinese Medicine Osmotherapy, blood circulation can be improved and obstruction in the ducts disappears. This therapy causes vasodilation, increases blood flow in the kidneys, prevents the release of TAX2 and PDGF, and inhibits platelet reactivity and thrombopoiesis. Thus, this therapy can also prevent thrombus formation and overcome anoxia and ischemia (Rushwan, 2017).

c) Degradation

Degradation is a change that leads to a decline. Degradation can also occur in various parts of the kidney. When the intrinsic kidney cells turn into fibroblasts, then fibrin (extracellular matrix) will be secreted by these fibroblasts. The extracellular matrix cannot be degraded easily, affecting the work of the kidneys. Through Micro-Chinese Medicine Osmotherapy, fibroblast apoptosis can be enhanced, and extracellular matrix

synthesis can be prevented by breaking down the extracellular matrix, thereby inhibiting fibrosis in the kidney. In addition, Micro-Chinese Medicine Osmotherapy can also repair damaged kidney tissue, increase DNA synthesis, improve protein synthesis, and replenish vitamins and microelements needed by the body (Hadiwijaya & Manatar, 2014).

Gambar 6. Application of Micro-Chinese Medicine Osmotherapy (Lakshmi *et al.*, 2017)

Nanoparticle technology used in Micro-Chinese Medicine Osmotherapy allows herbs to be in the form of molecules and small particles so that the effective ingredients in the drug can be optimally released. In its application to treat chronic renal failure, the effective ingredients in the drug particles will be mixed with penetration and used as a "medication bag" placed on the patient's lower back. With the help of the microwave osmosis device, the drug particles will enter the kidney directly. As a result, all renal arteries will widen, then increase perfusion and reverse the anaerobic condition of the damaged kidney. All of these factors increase circulation throughout the body and relieve toxic symptoms (Hadiwijaya & Manatar, 2014). Thus, Micro-Chinese Medicine Osmotherapy can be said to be an effective method to treat chronic kidney failure.

CONCLUSION

Based on the discussion above, it can be concluded that the kidney is divided into three major parts, namely the cortex, medulla and renal pelvis. The product of renal excretion is urine. The kidneys produce urine by undergoing three stages which are filtration (filtering), reabsorption (absorption), and augmentation (secretion). The relationship between the kidneys and the urinary system is the excretory system that produces urine. Chronic kidney disease can be caused by age as the risk of developing CKD increases with age. Hypertension can also cause kidney problems, resulting in high blood sugar that will affect the structure of the kidneys and damage the fine blood vessels in the kidneys. Kidney failure can be divided into several stages, including normal, at risk of damage, kidney

damage, reduced kidney function, and chronic kidney failure (CKD).

The working mechanisms of Micro-Chinese Medicine Osmotherapy are divided into three categories, namely inflammation, anticoagulation, and degradation. The aim of this therapy is to dilate all the renal arteries and increase perfusion in CKD patients. Moreover, this therapy reverses the anaerobic condition of the damaged kidney. All these factors improve circulation throughout the body and relieve toxic symptoms. Suggestions that can be given by researchers are to further study literature and previous research related to the excretory system and Micro-Chinese Medicine Osmotherapy from various sources in efforts to create a more in-depth study.

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