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Urology Research

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The Effect of Lidan Huashi Pills on the Glutathione Peroxidase Activity and Growth of Calcium Oxalate Crystals in the Kidneys of Rats

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Abstract: *Objective:* To explore the effects of Lidan Huashi Pills on the glutathione peroxidase (GSH-Px) activity and growth of calcium oxalate crystals in the kidneys of rats. *Methods:* 30 rats were randomly divided into a blank group, a model group, and an experimental group, with 10 rats in each group. The blank group was free to eat and drink water for 8 weeks; the ethylene glycol method was used for the standard calcium oxalate crystal modeling in the control group and experimental group for 4 weeks. The model group was given free feeding and physiological saline (2 ml/d) by continuous gavage for 4 weeks; the experimental group was given free feeding and Lidan Huashi Pills (450 mg/kg, 2 ml/d) by continuous gavage for 4 weeks. After 4 weeks, all rats were euthanized, and the left kidney was taken for GSH-Px level detection. The right kidney was stained with hematoxylin and eosin (H&E) to observe the formation of calcium oxalate crystals. *Results:* After 4 weeks of modeling, the urinary calcium levels in the model group and experimental group significantly increased compared to the blank group (868.00 ± 39.29 vs 929.40 ± 33.61 , $P < 0.05$), indicating successful modeling. The urine calcium ion concentration in the experimental group after modeling was significantly lower than that in the model group (929.40 ± 33.61 vs 888.60 ± 25.92 , $P < 0.05$). The grading score of calcium oxalate crystals in the model group was significantly higher than that in the blank group ($P < 0.05$); the grading score of calcium oxalate crystals in the experimental group was lower than that in the model group, and the difference was not statistically significant ($P > 0.05$). The GSH-Px activity in the left kidney of the model group was significantly lower than that of the blank group [203.49 (208.21, 144.22) vs 494.91 (431.32, 538.18), $P < 0.05$]; the GSH-Px activity in the left kidney of the experimental group was significantly higher than that of the model group [433.60 (383.86, 504.49) vs 203.49 (208.21, 144.22), $P < 0.05$). Morphological observation and H&E staining suggest that the formation of right kidney crystals and inflammation in the experimental group are between the blank group and the model group. *Conclusion:* Lidan Huashi Pills can enhance the serum GSH-Px activity in rats and inhibit the growth of calcium oxalate crystals and inflammatory response in the kidneys, thus playing a role in preventing and treating urinary tract stones.

Keywords: Calcium oxalate; Kidney stones; Oxidative stress; Lidan Huashi Pills; Rats

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1. Introduction

Urinary tract stones are a high-risk disease of the urinary system. However, the mechanism of stone formation is not yet clear^[1]. Calcium oxalate stones are the most common component in urinary tract stones. Currently, there are numerous theories about explaining the formation of calcium oxalate stones, among which the oxidative stress theory is a research hotspot in this field^[2]. Based on the theory of “pathogen and heat invading the kidneys”^[3], traditional medicine has achieved ideal therapeutic effects in treating urinary tract stones using Lidan Huashi Pills^[4]. Therefore, this study will explore the effects of Lidan Huashi Pills on calcium oxalate crystals and oxidative stress indicators in rat kidneys, elucidate their potential mechanisms of action, and provide a new theoretical basis for the prevention and treatment of urinary tract stones with Lidan Huashi Pills.

2. Materials and methods

2.1. Animal information

30 1-month-old specific-pathogen free (SPF) Sprague Dawley male rats with a body weight of 200 ± 20 g, sourced from Nanjing Kales Biotechnology Co., Ltd. [Production license number: SCXK (Zhejiang) 2019-0001]. The feeding environment provided was 12 hours of alternating light and dark, temperature maintained at $22 \pm 2^\circ\text{C}$, humidity maintained at 45% to 55%, free diet, and adaptive feeding for one week.

2.2. Reagents and instruments

The materials used were 1% ethylene glycol and 2% ammonium chloride (analytical purity, provided by the low-value consumables procurement platform of Nanjing University of Traditional Chinese Medicine), Lidan Huashi Pills (LDHSP, internal preparation of Jiangsu Provincial Hospital of Traditional Chinese Medicine, provided by the pharmacy of Jiangsu Provincial Hospital of Traditional Chinese Medicine).

The instruments used included fully automated blood analyzer (SYSMEX pocH-100i, Nanjing Huaren Biotechnology Co., Ltd., Jiangsu Provincial Hospital of Traditional Chinese Medicine Laboratory), fully automated urine analyzer (iChemVelocity, Shanghai Haier Shi Medical Equipment Co., Ltd., Jiangsu Provincial Hospital of Traditional Chinese Medicine Laboratory).

Other reagents and instruments were glutathione peroxidase (GSH-Px) test kits, micropipette, vortex mixer, centrifuge, 37°C constant temperature water bath, and visible spectrophotometer (wavelength 412 nm) (provided by Nanjing Jiancheng Biotechnology Research Institute).

2.3. Modeling methods

The ethylene glycol method was used for the standard calcium oxalate crystal modeling: free feeding, 1% ethylene glycol free drinking water, 2% ammonium chloride gavage every other day (2 ml/animal), and the modeling time was 4 weeks^[5]. In the fourth week of modeling, the urine calcium ion levels of rats were detected and compared. The urine calcium ion levels of the model group were significantly higher than those of the blank group. In addition, the pathological examination of the kidney tissue in the model group showed crystalline substances in the renal tubules, indicating successful modeling^[6].

2.4. Experimental plan and observation indicators

Experimental plan: All rats were adaptively raised for one week and randomly divided into groups based on body weight, with 10 rats in each of the blank group, control group, and experimental group. In the second week, the blank group had a free diet, while the control group and experimental group were modeled using the ethylene glycol method for a period of 4 weeks. In the 6th week, the blank group had a free diet, while the

control group had free feeding and was given physiological saline by gavage (2 ml/d); the experimental group was free to feed and administered Lidan Huashi Pills by gavage (450 mg/kg, 2 ml/d) for 4 weeks. In the 10th week, all rats were euthanized by excessive inhalation of isoflurane (8 ml/min, 25–30 min). Blood samples were taken from the neck to detect serum GSH-Px levels, and bilateral kidneys were dissected for hematoxylin and eosin (H&E) staining to observe the formation of calcium oxalate crystals.

Observation indicators: (1) Urine calcium ion level: 24-hour urine was collected from rats using the “metabolic cage method” and the urine calcium ion level was measured to evaluate the modeling effect; (2) Morphological observation of the right kidney; (3) Observation of pathological changes under the microscope after H&E staining of the right kidney; (4) Right kidney calcium oxalate crystal grading score: The calcium oxalate crystal in renal tubules was observed under light microscopy and scored ^[7]; 0 level: No calcium oxalate crystal; Grade I: There are small crystals but not piles; Grade II: Calcium oxalate crystals grow larger and pile up, but are not connected to each other; Grade III: Interconnection between calcium oxalate crystals; Grade IV: Calcium oxalate crystals are widely stacked and connected in sheets. (5) Left kidney GSH-Px activity: Blood collection was after anesthesia. After centrifugation, the supernatant was taken and stored in a -20°C freezer. The specimen was sent to the laboratory of Jiangsu Provincial Hospital of Traditional Chinese Medicine for testing the activity of GSH-Px in the left kidney (**Figure 1**).

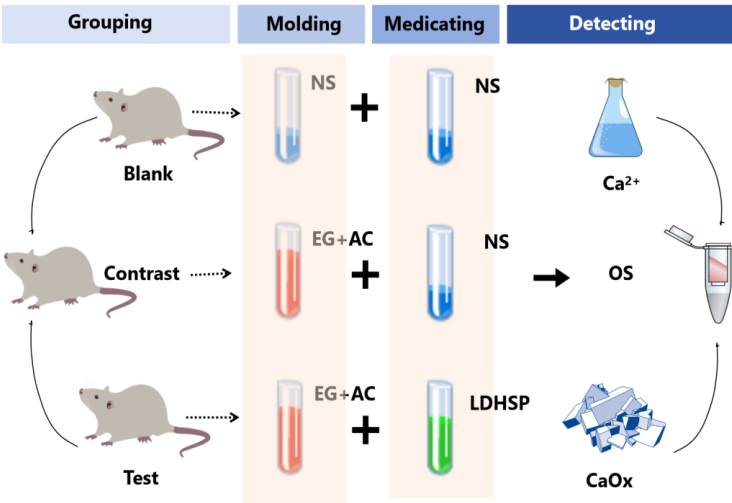


Figure 1. Experimental plan

2.5. Statistical processing

SPSS22.0 software was used to analyze the data. If the measurement data conformed to normality, they were represented by mean ± standard deviation (SD), non-normality was represented by M (P25~P75); count data were represented by [n (%)], when the distribution conforms to normality, independent sample *t*-test was used, and when deviating from normality, non-rank sum test was used. *P* < 0.05 indicated a statistically significant difference.

3. Results

3.1. Comparison of urinary calcium ion levels among three groups of rats

After treatment, there was a statistically significant difference in urinary calcium ion concentration among the three groups of rats (*t* = 3.476, *P* = 0.003 < 0.05). Further pairwise comparison showed that the urine

calcium ion concentration in the model group was higher than that in the blank group after modeling, and the difference was statistically significant ($t_a = 2.655$, $P_a = 0.019 < 0.05$). The urine calcium ion concentration in the experimental group after modeling was higher than that in the blank group, but the difference was not statistically significant ($t_b = 1.177$, $P_b = 0.260 > 0.05$). The urine calcium ion concentration in the experimental group after modeling was lower than that in the model group, and the difference was statistically significant ($t_c = 3.476$, $P_c = 0.003 < 0.05$) (**Table 1**).

Table 1. Comparison of urinary calcium ion concentrations among three groups

Groups	Calcium concentration (Mmol/L)	χ^2	P
Blank group ^{ab}	868.00 ± 39.29 ^{ab}	3.476	0.003
Model group ^{ac}	929.40 ± 33.61 ^{ac}		
Experimental group ^{bc}	888.60 ± 25.92 ^{bc}		

Note: Compared with the blank group, ^a $P < 0.05$, ^b $P > 0.05$; Compared with the model group, ^c $P < 0.05$

3.2. Comparison of right kidney calcium oxalate crystal grading scores among three groups of rats

After treatment, there was a statistically significant difference in the grading scores of calcium oxalate crystals among the three groups of rats ($\chi^2 = 17.843$, $P = 0.001 < 0.05$). Further pairwise comparison showed that the grading scores of calcium oxalate crystals in the model group of rats were higher than those in the blank group, and the difference was statistically significant ($\chi^2_a = -3.773$, $P_a = 0.000 < 0.05$), the grading score of calcium oxalate crystals in the experimental group rats was higher than that in the blank group, but the difference was not statistically significant ($\chi^2_b = -1.985$, $P_b = 0.141 > 0.05$), the grading score of calcium oxalate crystals in the experimental group of rats was lower than that in the model group, but the difference was not statistically significant ($\chi^2_c = -1.609$, $P_c = 0.323 > 0.05$) (**Table 2**).

Table 2. Comparison of grading scores for three groups of calcium oxalate crystals ($n = 30$)

Groups	0	I	II	III	IV	χ^2	P
Blank group ^{ab}	7	0	1	1	0	17.843	0.001
Model group ^{ac}	0	0	0	6	2		
Experimental group ^{bc}	1	1	1	4	0		

Note: Compared with the blank group, ^a $P < 0.05$, ^b $P > 0.05$; Compared with the model group, ^c $P > 0.05$

3.3. Comparison of GSH-Px activity in the left kidney of three groups of rats

After treatment, the activity of GSH-Px in the left kidney of the three groups of rats is detailed in **Figure 2**. The inter-group comparison showed a statistically significant difference in GSH-Px activity in the left kidney of the three groups of rats ($U = 82.739$, $P < 0.001$). Further pairwise comparison showed that the GSH-Px activity in the left kidney of the model group rats was lower than that of the blank group, and the difference was statistically significant ($Z_a = 6.933$, $P_a < 0.001$). The GSH-Px activity in the left kidney of the experimental group rats was lower than that of the blank group, but the difference was not statistically significant ($Z_b = -1.282$, $P_b = 0.20 > 0.05$). The GSH-Px activity in the left kidney of the experimental group rats was higher than that of the model group, and the difference was statistically significant ($Z_c = 8.056$, $P_c < 0.001$) (**Figure 2**).

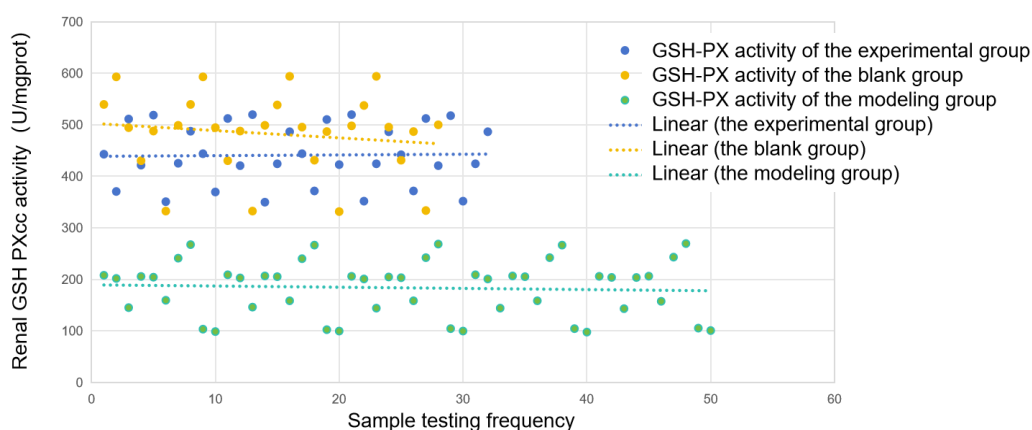


Figure 2. Comparison of GSH-Px activity in the left kidney of three groups of rats

3.4. Morphological observation and H&E staining comparison of the right kidney in three groups of rats

Morphological observation of the right kidney in the blank group of rats: The average weight of the right kidney was about 1.84 g, with a fava bean shape and a coordinated ratio of skin and marrow thickness. No stone and no friction sensation were found during the renal cortex and medulla cutting process (**Figure 3a**).

Pathological changes of H&E staining in the right kidney of blank group rats: The glomerulus volume was moderate, the renal tubules volume was moderate, the staining was light red, the epithelial cells of the proximal convoluted tubules were uniform and not protruding into the tubules, the lumen size was regular, and no crystals were seen. There were a small number of evenly distributed same-sized pink small particles in the cytoplasm, with clear nuclear structure (**Figure 3b, c, d**).

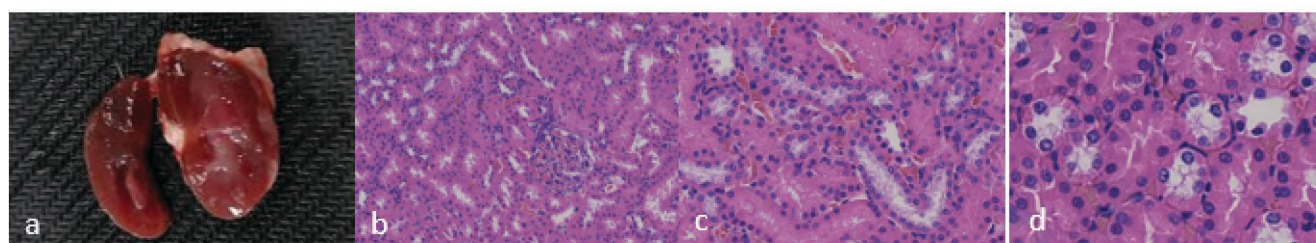


Figure 3. (a) Morphological observation of the blank group; (b) Blank group x20; (c) Blank group x40; (d) Blank group x80

Morphological observation of the right kidney in the model group of rats: The average weight of the right kidney was about 3.08 g, with a fava bean shape and granular protrusions on the surface. The thickness ratio of the cortex and medulla was not coordinated, and there was atrophy in the cortex. There was friction during the process of renal cortex and medulla cutting, and a large number of stones can be seen. Some large stones can be seen in the renal pelvis (**Figure 4a**).

Pathological changes of H&E staining in the right kidney of the model group rats: Renal tubules were large in volume, with light red staining, obvious edema of epithelial cells in the proximal tubules, protruding into the tubules, enlarged lumens, and a large number of crystals visible (5 or more/40x field of view). Inflammatory cells infiltrated the distal tubules, crystals were found in the papillary ducts, and a large number of detached cells were found in the renal calyces (**Figure 4b, c, d**).

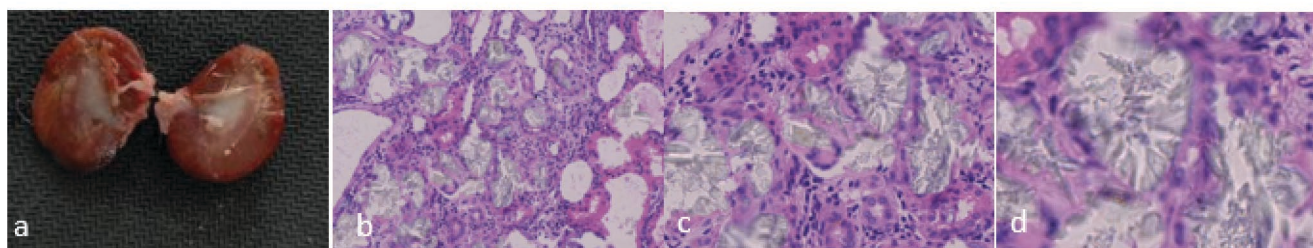


Figure 4. (a) Morphological observation of the model group; (b) Model group x20; (c) Model group x40; (d) Model group x80

Morphological observation of the right kidney of experimental group rats: The average weight of the right kidney was about 3.43 g, with a fava bean shape and granular protrusions on the surface. The thickness ratio of the cortex and medulla was not coordinated, and the cortex had atrophic changes. There was a mild friction sensation during the process of renal cortex and medulla cutting, and occasional stones were seen. Small stones are occasionally seen in the renal pelvis (**Figure 5a**).

Pathological changes of H&E staining in the right kidney of experimental group rats: Renal tubules were slightly larger in volume, with light red staining, mild edema of epithelial cells in the proximal tubules, not obvious protrusion into the tubules, enlargement of the lumen, and a small number of crystals visible (about 1/40x field of view). The amount of crystals was small, and there were more inflammatory cells infiltrating the distal tubules. A small number of crystals were found in the papillary ducts, and a small number of detached cells were found in the renal calyces (**Figure 5b, c, d**).

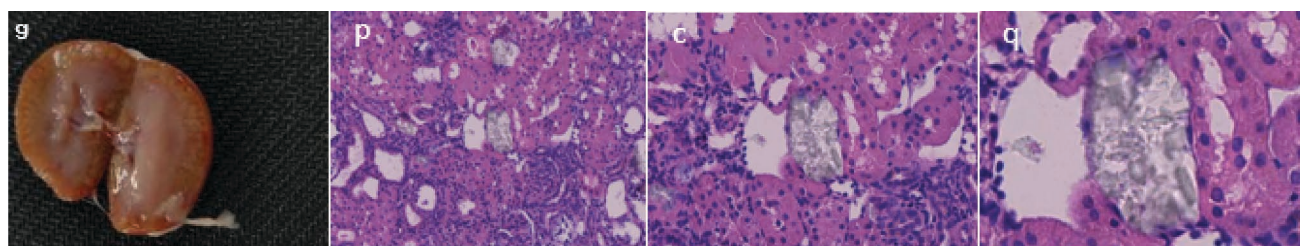


Figure 5. (a) Morphological observation of the experimental group; (b) Experimental group x20; (c) Experimental group x40; (d) Experimental group x80

4. Discussion

For thousands of years, traditional Chinese medicine has developed a unique understanding of the formation of stones through continuous clinical practice and exploration. According to *A Treatise on the Origins and Stages of Various Diseases*, “Pathogen and heat invading the kidneys and leading to gonorrhea syndrome as well as weak kidney cannot restrain the stones, so urinate profusely and drain the stones”^[3]. It is pointed out that one of the mechanisms for the formation of kidney stones is “the pathogen and heat invading the kidneys.” Based on this theory, this study verifies the anti-inflammatory and inhibitory effects of Lidan Huashi Pills on calcium oxalate kidney stones through animal experiments. It provides a new theoretical basis for the prevention and treatment of urinary tract stones with Lidan Huashi Pills.

Lidan Huashi Pills are mainly used to treat kidney stones and gallstones, and has achieved satisfactory therapeutic effects in clinical practice for many years. Lidan Huashi Pills are composed of *Lysimachia christinae*, *Plantago asiatica*, *Artemisia scoparia*, dandelion, *Verbena*, rhubarb, *Polygonum cuspidatum*, *Scutellaria baicalensis*, *Paeonia lactiflora*, *Corydalis yanhusuo*, elecampane, citron, *Rhizoma sparganii*, and

Curcuma zedoaria. The whole prescription has a cold and cool nature, fully reflecting the treatment method of “clearing heat.” Among them, *Lysimachia christinae* and *Plantago asiatica* have a clear heat and diuretic effect; *Dandelion*, *Verbena*, rhubarb, *Artemisia scoparia*, *Scutellaria baicalensis* clear heat and dampness; *Paeonia lactiflora* softens liver and relieves pain; *Corydalis yanhusuo*, *Rhizoma sparganii*, citron, and *Curcuma zedoaria* all have the effects of relieving stones, promoting blood circulation and removing stasis, and promoting qi and relieving pain. In this study, compared with the model group, the H&E pathological staining of the kidneys in the experimental group showed a reduction in the degree of edema in the epithelial cells of the proximal tubules, and a decrease in the number of inflammatory cells and detached cells in the distal tubules, indicating that Lidan Huashi Pills have a good anti-inflammatory effect. The study by Zhang *et al.* shows that Lidan Huashi Pills can significantly inhibit egg white-induced plantar swelling and acute inflammatory response in the ear caused by xylene, and it has significant sustained analgesic and antibacterial activity^[8]. In this article, the urine calcium ion concentration and renal calcium oxalate crystal grading score of the model group were higher than those of the blank group after modeling, indicating the successful modeling of calcium oxalate kidney stones in rats. After treatment, the urine calcium ion concentration in the experimental group was lower than that in the model group, indicating that Lidan Huashi Pills can inhibit the formation of calcium oxalate crystals in the urinary system by reducing the urine calcium ion concentration in rats with calcium oxalate kidney stones. Compared with the model group, the H&E pathological staining of the kidneys in the experimental group showed a decrease in crystal distribution density and crystal quantity, which was consistent with the results of urine metabolomics. The grading score of calcium oxalate crystals in the experimental group was lower than that in the model group, and the difference was not statistically significant. However, the experimental group did not show any advantages in improving the grading score of calcium oxalate crystals in rats, this is likely due to the short study time not reflecting the expected positive results and the lack of quantitative analysis of crystal fluorescence staining.

When the body’s oxidative and antioxidant systems are imbalanced, it can lead to oxidative stress (OS), and the theory of oxidative stress is currently a hot topic in the study of the causes of urinary tract stones. This theory suggests that calcium oxalate crystals (CaOx) can induce the release of reactive oxygen species (ROS) in HK-2 cells, and the generated ROS can mediate related signaling pathways to induce the production of inflammatory factors in the kidneys again, and induce chemotactic inflammatory cells to enter the inflammatory tissue, thereby damaging HK-2 cells, promoting CaOx crystal aggregation, and ultimately leading to stone formation^[9]. The endogenous or exogenous production of ROS in cells destroys HK-2 cells by attacking lipids, proteins, nucleic acids, or mitochondria. OS and inflammation are important factors in the formation of CaOx stones. The study by Cakir *et al.*^[10] provided evidence that OS is related to CaOx formation, that is, the serum antioxidant enzyme levels in CaOx stone patients decrease. Oxalate-mediated red blood cell OS can activate free radical oxidation, which may lead to the interaction between CaOx crystals and HK-2 cells in patients with hyperoxaluria, ultimately leading to the accumulation of stones. Khan’s research^[11] found that renal tissue deposited with CaOx crystals has accumulated ROS. CaOx crystals stimulate HK-2 cells to produce ROS-mediated inflammatory responses, which release a large amount of inflammatory factors and interact with OS, triggering an inflammatory cascade reaction that promotes the aggregation, nucleation, and growth process of calcium salt crystals, ultimately leading to crystal aggregation and even the formation of stones^[12].

In this article, the GSH-Px activity in the kidneys of rats in the model group was lower than that in the blank group after treatment, while the GSH-Px activity in the kidneys of rats in the experimental group was higher than that in the model group. This indicates that the antioxidant enzyme system of kidney stone model rats is inhibited and enters the OS state under the stimulation of CaOx, and Lidan Huashi Pills can effectively

counteract ROS production and oxidative stress response by upregulating GSH-Px activity. Glutathione peroxidase is a selenium-containing antioxidant enzyme that clears ROS during oxidative stress in mammalian cells. It has antioxidant effects and can eliminate oxygen free radicals in the body, reducing lipid oxidation^[13]. Among them, glutathione peroxidase 1 (GPx1) can use glutathione (GSH) as a reducing substrate, not only catalyzing toxic H₂O₂ to non-toxic water, but also catalyzing other water-soluble hydroperoxides. Glutathione peroxidase 4 (GPx4) can not only catalyze H₂O₂, but also directly reduce phospholipid hydroperoxides on biofilms, thereby inhibiting cellular lipid peroxidation^[14]. However, the sample size of this study is relatively small, and there is a lack of detection of changes in the activity of other urinary metabolomics and oxidative stress-related indicators for various reasons. Therefore, future prospective large-scale studies with more detailed data on Lidan Huashi Pills are necessary.

5. Conclusion

In summary, Lidan Huashi Pills can inhibit the growth of calcium oxalate crystals and inflammatory response in rat kidneys, thereby playing a role in preventing and treating urinary tract stones, and is worthy of clinical promotion and application.

Disclosure statement

The authors declare no conflict of interest.

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Analysis of the Effect and Value of Combined Chinese and Western Medicine in the Treatment of Uremic Pruritus

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Abstract: *Objective:* To analyze the effect of combined Chinese and Western medicine therapy in patients with uremic pruritus. *Methods:* 80 cases were randomly selected from uremic pruritus patients from January 2022 to October 2023, and were divided into Group A (40 cases, pure Western medicine therapy) and Group B (40 cases, combined Chinese and Western medicine therapy) by the numerical envelope method to compare the treatment effects of the two groups. *Results:* The levels of clinical symptom scores (itching degree, itching area, dry skin, secondary lesions) and test indexes (high-sensitivity C-reactive protein, tumor necrosis factor- α , interleukin-6, 5-hydroxytryptamine, blood phosphorus, parathyroid hormone) in Group B were lower than those in Group A after treatment ($P < 0.05$). *Conclusion:* Uremic pruritus patients can rapidly improve their clinical symptoms by using combined Chinese and Western medicine therapy.

Keywords: Combined Chinese and Western medicine therapy; Pruritus; Clinical symptoms

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1. Introduction

Pruritus is a common skin complication in patients with uremia, with many and varied triggering causes, both endogenous and exogenous. Uremia is the main endogenous cause, in addition to other common endogenous causes such as skin morphology changes, such as skin keratinization, erythroplasia, ichthyosis, etc.; common exogenous causes are temperature and humidity, the use of strong alkaline bathing products, direct contact with chemicals, and improper diet, etc. ^[1]. The main factors triggering pruritus in uremic patients are the massive secretion of histamine, amines such as 5-hydroxytryptamine (5-HT), protein polypeptides such as vasopressin, and inflammatory factors such as interleukin-6 (IL-6) by tissue cells ^[2]. Itching is a complex sensation transmitted through multiple neural pathways in the human body. The receptors for itching sensations are densely distributed on the unmyelinated free nerve endings in the dermal papillae and on the skin surface. These receptors specifically bind to pruritogens, substances that cause itching. Anti-itch factors stimulate the receptors to generate nerve impulses, which are ultimately conducted to the signal-receiving nerve cells in the cerebral cortex, thereby inducing the sensation of itching ^[3]. Pruritus causes patients to scratch the affected local skin

violently, resulting in scratches, scabs, hyperpigmentation, etc., and even inducing eczema-like lesions, mossy lesions, inflammation, etc. [4]. At present, the commonly used drugs for the treatment of uremic pruritus patients include antihistamine drugs such as loratadine tablets, which can antagonize peripheral histamine H receptors after oral administration, and can effectively improve the clinical symptoms of patients. In addition, patients with uremic pruritus can be treated with topical tacrolimus ointment, which belongs to the immunomodulators with small molecular weight, and after applying in the itchy area, it can reduce the activity of T cells, which has a good effect of improving the local skin immunity and inflammation [5]. However, clinical practice has confirmed that the use of Western medicine therapy alone in uremic pruritus patients can improve itching symptoms to a certain extent, but the overall efficacy does not meet expectations [6]. In Chinese medicine, itchy skin is included in “itchy wind,” and it is believed that the main factor triggering this disease is the invasion of external pathogenic factors (blood deficiency, blood heat, wind, etc.) into the skin locally, and the basic principle of treatment is to nourish the blood, dispel the wind, and stop the itch. This study analyzes the effect of combined Chinese and Western medicine therapy in patients with uremic pruritus.

2. Information and methods

2.1. General information

80 cases were randomly selected from uremic pruritus patients from January 2022 to October 2023 and grouped by numerical envelope method into Group A and Group B. Group A (40 cases): aged 35–82 (58.62 ± 5.23) years, weight 45.53–87.92 (65.49 ± 6.71) kg, duration of disease 1–20 (7.86 ± 1.23) months, and male to female ratio 26:14; Group B (40 cases): aged 38–85 (58.92 ± 5.43) years, body weight 45.68–87.56 (64.89 ± 6.53) kg, duration of the disease 2–18 (7.62 ± 1.31) months, and male to female ratio 24:16. The general information of the two groups was comparable ($P > 0.05$).

Inclusion criteria: A comprehensive understanding of the content of the study and consent to participate in the study; clinical data to meet the clinical needs; able to cooperate with the completion of all examinations and assessments.

Exclusion criteria: Combined with organic diseases of major organs, schizophrenia, cognitive dysfunction, severe infections, and so on.

2.2. Methods

2.2.1. Group A

Group A was given Western medical therapy. The frequency of hemodialysis was 2–3 times/week, hemoperfusion combined with hemodialysis once in a fortnight, and water-electrolyte and acid-base balance treatments were given to correct anemia and control diet. Oral loratadine tablets (Xi'an Janssen Pharmaceutical Co., Ltd, State Pharmaceutical License: H20070030, specification: 10 mg*6s) (10 mg/times, 1 time/d); oral pregabalin [Qilu Pharmaceutical (Hainan) Co., Ltd, State Pharmaceutical License: H20203040, specification: 75 mg × 8 capsules × 4 boards] (75 mg/times, 2 times/d); oral vitamin C tablets (Huazhong Pharmaceutical Co., Ltd, State Pharmaceutical License: H42020614, specification: 0.1g*100s) (0.1 g/dose, 1 time/d); tacrolimus ointment [Sinopharma, State Pharmaceutical License: J20140148, specification: 0.1% (10 g:10 ml)] (2 times/d). Treatment was done for 1 month.

2.2.2. Group B

Group B was treated with Wushe Zhiyang Pills (Guangzhou Baiyunshan Zhongyi Pharmaceutical Co., Ltd, State Pharmaceutical Standard: Z44020044, specification: 30 g/bottle) on the basis of Group A, 2.5 g/times

orally, 3 times/d. Traditional Chinese medicine external cleansing formula: 30 g (*Bassia scoparia*, *Sophora flavescens*, *Angelica sinensis*, *Spatholobus suberectus*), 15 g (*Xanthium sibiricum*, *Portulaca oleracea*, *Dictamnus dasycarpus*). It was taken one dose per day. 2000 mL of water was added and brought to a boil. Once the water temperature was comfortably warm, it was used to wash the areas of itchy skin. Treatment was done for 1 month.

2.3. Observation indicators

2.3.1. Clinical symptoms score after treatment

Our self-made scale evaluated the patients' clinical symptoms from the aspects of itching degree, itching area, skin dryness, secondary skin lesions, etc. The maximum score of 4 points for each item indicated that the clinical symptoms are very serious.

2.3.2. Test indicators

2 ml of fasting venous blood was collected, centrifuged, and processed; automated blood biochemical analyzer was used to detect high-sensitivity C-reactive protein (hs-CRP); enzyme-linked immunosorbent assay was used to detect tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6); high-performance liquid chromatography-ultraviolet detection method was used to detect 5-HT.

2.4. Statistical analysis

SPSS25.0 software was used to process the data, mean \pm standard deviation (SD) and % expressed the measurement and count data, respectively, using *t* value and χ^2 test; *P* < 0.05 was statistically significant.

3. Results

3.1. Comparison of clinical symptom scores after treatment

The clinical symptom scores of Group B were lower than those of Group A (*P* < 0.05), as shown in **Table 1**.

Table 1. Clinical symptom scores after comparative treatment [mean \pm SD (points)]

Groups	<i>n</i>	Degree of itching	Itchy area	Dry skin	Secondary lesions
Group B	40	1.15 \pm 0.38	1.24 \pm 0.35	1.21 \pm 0.37	1.19 \pm 0.36
Group A	40	1.86 \pm 0.53	1.94 \pm 0.58	1.93 \pm 0.56	1.81 \pm 0.56
<i>t</i>	-	6.885	6.535	6.784	5.890
<i>P</i>	-	0.000	0.000	0.000	0.000

3.2. Comparison of post-treatment test indexes

The post-treatment test indexes of Group B were lower than those of Group A (*P* < 0.05), as presented in **Table 2**.

Table 2. Comparison of post-treatment test indexes (mean \pm SD)

Groups	<i>n</i>	hs-CRP (mg/L)	TNF- α (ng/L)	IL-6 (ng/L)	5-HT (μ g/L)	Serum phosphorus (mmol/L)	Parathyroid hormone (pg/ml)
Group B	40	11.64 \pm 1.53	4.75 \pm 0.67	14.86 \pm 1.68	395.48 \pm 40.37	82.26 \pm 7.84	61.48 \pm 5.12
Group A	40	14.25 \pm 2.14	5.69 \pm 0.81	18.54 \pm 2.57	461.53 \pm 43.95	82.94 \pm 7.72	68.75 \pm 5.67
<i>t</i>	-	6.274	5.655	7.580	6.999	0.390	6.018
<i>P</i>	-	0.000	0.000	0.000	0.000	0.697	0.000

4. Discussion

Pruritus is a common symptom that can occur in any person at any time, and the elderly are more prone to pruritus due to the progressive decline of body functions^[7,8]. Clinically, it is classified into six categories according to the causes of itching: neurological itching, psychiatric itching, itching due to skin and systemic diseases, and itching due to multifactorial and unknown factors. If the presence of a primary lesion causing pruritus can be determined by relevant examinations, it may be due to diseases such as uremia, and if the cause of itching cannot be determined, it may be idiopathic itching, which is also known as senile skin pruritus^[9,10]. As the specific cause of uremic pruritus cannot be clearly articulated in the clinic at present, some scholars believe that it is due to dry skin, plasma histamine levels, mast cells, hyperthyroidism, inflammation, immune abnormalities, etc.^[11]. Patients with uremic pruritus commonly suffer from varying degrees of sleep disorders due to itchy skin, thus leading to anxiety, depression, and other adverse emotions^[12]. Patients with uremic pruritus taking Western medicines can temporarily improve itching symptoms, but not only is it easy to recur after stopping the medication, but with the prolongation of the medication time, it is also prone to adverse reactions such as dry mouth, drowsiness, etc., which reduces the quality of life of the patients. Although it is possible to increase the number of dialysis and hemofiltration to improve the itching symptoms, the treatment cost is higher. Traditional Chinese Medicine (TCM) has a long history of treating skin diseases. By differentiating the eight principles of yin and yang, sequentially exploring the six channels, defensive qi, nutrient blood, and the Sanjiao, TCM applies syndrome differentiation and treatment. This approach not only effectively improves clinical symptoms but also reduces the risk of adverse reactions.^[13] The use of a combination of traditional Chinese and Western medicine in patients with uremic pruritus improves the efficacy and safety of the treatment regimen.

The results of this paper showed that the clinical symptom scores (itching degree, itching area, skin dryness, secondary skin lesions) and test indicators (hs-CRP, TNF- α , IL-6, 5-HT) levels of Group B were lower than those of Group A after treatment ($P < 0.05$), confirming the feasibility and effectiveness of the combination of Chinese and Western medicines for uremic pruritus patients. The main Chinese herbs used in the manufacture of Wushe Zhiyang Pills are Wushe and Fangfeng, etc. Chinese medicine believes that the invasion of wind and other pathogenic factors is the main cause of uremic pruritus, and that effective measures to dispel wind can improve the symptoms of itching. Wushe has the effects of dispelling wind and relieving itching, clearing collaterals, and stopping spasms, and modern pharmacology has confirmed that its main components, such as amino acids and fatty acids, have the effects of anti-inflammatory, sedative, and analgesic and regulating immunity; Fangfeng has the effects of dispelling wind and eliminating dampness, modern pharmacology has confirmed that its main components of volatile oil, chromogenic ketone, etc., with antipyretic, analgesic, anti-inflammatory, antibacterial, and other effects, Wushe and Fangfeng are commonly used in traditional Chinese medicine to relieve itching. The adjuvants in Wushe Zhiyang Pills, Danggui and red ginseng, align with the traditional Chinese medicine principle of “treating wind by first treating the blood, as wind dissipates when blood flows properly.” Danggui nourishes and invigorates the blood, with modern pharmacology confirming its main components, such as volatile oils and flavonoids, have analgesic, anti-inflammatory, immune-boosting, and anti-aging effects. Red ginseng enhances qi and strengthens the spleen, and modern pharmacology verifies its main components, saponins and polysaccharides, possess immune-boosting, antioxidant, and anti-allergic properties. Together, Danggui and red ginseng play a fundamental role in the Wushe Zhiyang Pills. The auxiliary ingredients in Wushe Zhiyang Pills include *Phellodendron* bark, *Atractylodes*, tree peony bark, *Sophora flavescens*, artificial bezoar, snake bile, and *Cnidium monnieri*. *Phellodendron* bark clears heat and dries dampness, expels fire, and detoxifies sores, with modern pharmacology confirming its main components,

flavonoids and alkaloids, exhibit anti-inflammatory, antibacterial, antioxidant, and neuroprotective properties. *Atractylodes* dries dampness and strengthens the spleen, dispels wind and cold, with modern pharmacology verifying its main components, atractylodin and atractylenolide, have anti-inflammatory, antioxidant, edema-improving, and anti-itch properties. Tree peony bark activates blood circulation and clears heat, with modern pharmacology confirming its main component, paeonol, has anti-inflammatory, sedative, analgesic, and antipyretic effects. *Sophora flavescens* clears heat and dries dampness, with modern pharmacology verifying its main components, alkaloids and flavonoids, have antiviral and immune-regulating properties. Artificial bezoar clears heat and detoxifies, with modern pharmacology confirming its main components, ox bile powder, cholic acid, and taurine, exhibit anti-inflammatory, analgesic, and antipyretic effects. Snake bile clears heat and detoxifies, dispels wind, and dries dampness, with modern pharmacology confirming its main components, cholic acids and mucoproteins, have anti-inflammatory and anti-itch properties. *Cnidium monnieri* dispels wind, dries dampness, kills parasites, and stops itching, with modern pharmacology verifying its main components, coumarins and chromones, have antifungal, anti-allergic, sedative, and hypnotic effects. All these herbs are meticulously combined to treat patients with pruritus, exhibiting blood-nourishing, wind-dispelling, dampness-drying, and itch-relieving effects. In this study, the external wash formula used for traditional Chinese medicine includes *Xanthium*, which dispels wind-dampness and expels wind-cold, with modern pharmacology confirming its main component, tannins, reduce the activity of inflammatory factors like IL-6, lower histamine levels, and have anti-allergic effects. *Bassia scoparia* clears wind and stops itching, clears heat, and drains dampness, with modern pharmacology verifying its main components, terpenoids, saponins, and volatile oils, exhibit antifungal effects against pathogens like *Trichophyton mentagrophytes* and *Trichophyton rubrum*, are anti-allergic, and alleviate skin itching. *Dictamnus* root bark clears wind and detoxifies, clears heat, and dries dampness, with modern pharmacology confirming its main components, alkaloids, limonoids, and flavonoids, have anti-parasitic and antibacterial effects. Combining traditional Chinese and Western medicine for uremic pruritus patients, utilizing both internal and external treatments, can shorten the time needed to improve clinical symptoms and inflammatory responses, thereby enhancing patients' quality of life.

5. Conclusion

In conclusion, the use of combined Chinese and Western medicine therapy in patients with uremic pruritus can rapidly improve clinical symptoms.

Disclosure statement

The author declares no conflict of interest.

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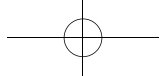
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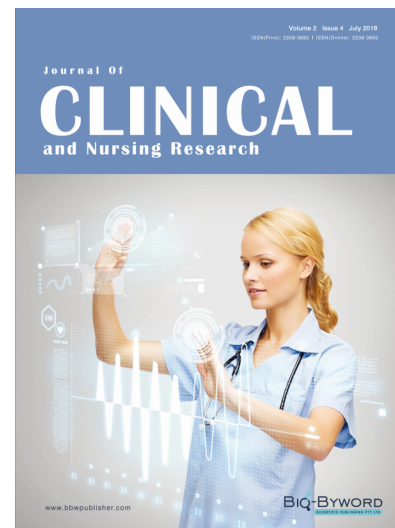
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