DOI: 10.53469/jcmp.2025.07(01).43

# Research Progress of Combination of Chinese and Western Medicine in the Treatment of CKD-MBD

**Yue Yang[1], Chunying Liu[2,*]**

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
**Correspondence Author*

**Abstract:** ***Chronic kidney disease mineral matter and abnormal bone metabolism syndrome, which can be manifested as renal bone disease also known as renal osteodystrophy, is one of the multiple complications in patients with chronic kidney disease. It is a special form of abnormal bone mineral metabolism syndrome, mainly caused by renal parenchymal dysfunction or renal parenchymal deficiency leading to bone softening and secondary hyperparathyroidism leading to impaired conversion of vitamin D to its active form, which is accompanied by the development of the disease, which can lead to severe bone damage, which seriously affects the quality of life of patients, greatly increases the risk of fracture, and even endangers their lives. And mineral metabolism disorders can lead to increased cardiovascular morbidity and mortality in CKD patients. With the rising incidence of chronic kidney disease, the incidence of this disease is also increasing, and timely and effective treatment is more important. At present, Western medicine treatment mainly consists of phosphorus binding agents, calcium agents, blood purification and other treatments, with a relatively single target of action, and there is a lack of experimental basis for the selection of drugs for different types of renal bone disease, which makes the selection of clinical drugs difficult. Chinese medicine, on the other hand, is characterized by individualization, multi-targeting and holistic treatment, and a large number of studies have shown that the combination of Chinese and Western medicine has achieved good therapeutic effects in the treatment of this disease. In this paper, the research progress of the combination of Chinese and Western medicine in the treatment of CKD-MBD syndrome is summarized in order to provide more ideas for clinical work.***

**Keywords:** CKD-MBD, Combination of Chinese and Western medicine, Research progress**.**

## 1. Introduction

Chronic kidney disease-mineral and bone metabolism syndrome (CKD-MBD), which can be manifested as renal osteodystrophy (ROD) also known as renal osteodystrophy, is the result of impaired calcium and phosphorus metabolism, vitamin D conversion, secondary to chronic renal failure (CRF). Hyperparathyroidism and acid-base balance disorders and other factors caused by a group of comprehensive manifestations. According to the survey, the global trend of kidney disease is still in high incidence, high cost of treatment and high impact on health. The prevalence of CKD in Chinese adults is 8.2% [1]; when the glomerular filtration rate (GFR) is <50%, about half of the patients will show pathological changes of renal bone disease. When the disease progresses to end-stage renal disease (ESRD), almost 100% of patients will develop renal bone disease. And the probability of fracture in patients with chronic kidney disease is three to four times higher than that in patients with non-chronic kidney disease [2]. As one of the common complications of CKD, along with the progression of the disease, patients may suffer from bone pain, arthralgia, bone deformation, muscle weakness, vascular calcification, and even spontaneous fracture, which may lead to a decline in the quality of life of the patients, an increase in the psychological and economic burden, and an increase in mortality. [3,4].

### 1.1 Western Medicine

CKD-MBD is one of the most common complications of chronic kidney disease, and the pathogenesis of this disease is complex, mainly involving: abnormal hormone regulation, kidney disease leads to 1,25-(OH)2D3 deficiency, which causes obstacles to intestinal calcium absorption and calcium release from the bones; imbalance of bone metabolism, kidney disease causes metabolic acidosis and hyperphosphatemia, which stimulates the excessive secretion of parathyroid hormone (PTH), and bone resorption increase [5]; imbalance of bone morphogenetic proteins (BMP) and bone morphogenetic protein antagonists (BMP-antagonists); and chronic kidney disease leading to oxidative stress, inflammatory response, and other factors, which promotes apoptosis of bone cells [6]. Its main target organs are bone, cardiovascular, and even make multiple organ damage [7]. Renal osteodystrophy is categorized into high-conversion type and low-conversion type according to the difference in the conversion status during bone reconstruction. The high-conversion type, also known as PTH-increased bone disease, accounts for 34.5% of cases and is mainly caused by increased osteoclast activity and increased bone resorption due to increased PTH in the blood [8]. The low-conversion type, also known as mineralization-imperfect bone disease, accounts for 23.5% of cases. During the development of renal bone disease, vascular calcification is mostly observed, which is caused by the process of localized bone formation induced by the development of resident cells into osteoblast-like cells in the vessel wall [9].

### 1.2 Traditional Chinese Medicine

Traditional Chinese medicine does not have the name of renal bone disease, but according to its main symptoms, it is categorized as “bone paralysis”, “bone impotence”, “deficiency labor” and so on. The disease is mainly located in the kidney, and is closely related to the liver and spleen. Suwen - six sections of the theory of hidden signs” cloud ‘the

kidney is the main bone, the birth of the marrow', Chinese medicine believes that the kidney is the foundation of the innate, the essence of the kidney for the growth of all parts of the body, the development of the fundamental. The growth, development and repair of bones depend on the marrow generated by kidney essence. If the kidney essence is sufficient, the bone marrow will have its source of production, the sea of marrow will be full, and the bones will be strong and healthy; on the contrary, if the kidney essence is insufficient, the sea of marrow will be empty, which will easily lead to abnormal bone development. Water and grain qi in the spleen and stomach into essence, nourish the whole body, maintain the shape of the bone, tendons and veins smooth, qi and blood run smoothly, so as to nourish and nourish the body; bones for the support of the human body's backbone, the muscle is like a wall, to protect the bones. Kidney is the main bone, spleen is the main muscle, kidney deficiency is not full of bone marrow, spleen deficiency is the lack of qi and blood biochemistry, muscle is not full, qi and blood flow is not conducive. The liver is the master of the fascia of the whole body and is related to the movement of the limbs. If the liver's qi and blood are abundant and the fascia is nourished, then the muscles will be strong and healthy, and the movement will be flexible. Liver and kidney are of the same origin, and essence and blood are mutualized. If the liver does not store enough blood, the kidney essence will be affected, which will lead to the lack of bone marrow, and the loss of nourishment of the sinews and bones, resulting in thinness and loss of use of the limbs.

## 2. Clinical Treatment

### 2.1 Western Medical Treatment

2.1.1 General treatment

The general treatment of CKD-MBD mainly refers to the change of life style including the adjustment of diet structure. Patients should strictly limit the intake of high-phosphorus foods, such as animal offal and foods with too many additives, and increase the intake of foods rich in vitamin D and calcium, in addition to ensuring the normal nutritional intake of the body.

2.1.2 Drug therapy

2.1.2.1 Phosphorus binding agents

Hyperphosphatemia is a common complication of CKD, with a high prevalence and a low rate of treatment attainment [10]. Currently common phosphorus binding agents include (1) calcium-containing phosphorus binding agents. By binding calcium ions to phosphate in the intestines to form insoluble phosphate deposits, they increase the rate of phosphorus excretion through the intestines and reduce blood phosphorus levels. (2) Aluminum-containing phosphorus binding agents. Aluminum ions combine with phosphorus in food to form insoluble phosphate deposits and inhibit phosphate absorption. (3) Calcium- and aluminum-free polymeric phosphorus binding agents. These polymers are ion-exchanged and hydrogenated to bind phosphate ions and reduce phosphorus absorption. Compared with other types of phosphorus binding agents, the toxic side effects and adverse reactions are relatively small, and the clinical efficacy is good, and it is now used as the main drug for the treatment of hyperphosphatemia in a large number of clinical applications [11]. (4) Iron-containing phosphorus binding agent. It can not only reduce phosphorus, but also provide the body with hematopoietic raw material iron, which can alleviate patients' anemia symptoms to a certain extent while reducing phosphorus [12].

2.1.2.2 Calcimimetics

Calcimimetics can activate calcium receptors in the parathyroid gland, thus reducing the secretion of parathyroid hormone, enhancing the sensitivity of parathyroid calcium receptors to calcium in the blood, and lowering the levels of parathyroid hormone, calcium, phosphorus and calcium-phosphorus complexes. At the same time, calcium mimetics can play a delaying role in complications such as bone disease, heart failure, and cardiovascular death caused by calcium and phosphorus metabolism disorders [13].

2.1.2.3 Vitamin D drugs

Such drugs can effectively supplement vitamin D in the body, help calcium absorption, improve muscle level and balance, and increase bone density [14]; reduce renal inflammatory response, delay renal fibrosis, reduce the risk of cardiovascular disease, and reduce mortality [15].

2.1.2.4 Exogenous recombinant Klotho and FGF23 monoclonal antibodies

FGF23 is one of the important hormones regulating calcium and phosphorus metabolism [16]. Klotho has an important role in regulating mineral metabolism homeostasis [17]. FGF23 specifically targets FGFR1 in renal tubular epithelial cells and forms a complex with Klotho. This complex in turn inhibits renal reabsorption of phosphorus, controlling circulating phosphorus homeostasis and indirectly affecting bone mineralization, and it also attenuates oxidative stress and inflammatory responses and delays renal fibrosis [18].

2.1.2.5 ActRIIA monoclonal antibody and some inflammatory factor inhibitors

Act A signaling plays an important role in chronic kidney disease-mineral bone disorder (CKD-MBD) and vascular calcification, and there is also experimental evidence that ActRIIA inhibition is effective in ameliorating and delaying CKD-MBD [19]. A large body of clinical and experimental evidence suggests that pro-inflammatory cytokines (TNF-α, IL-6, and IL-17) are associated with the development of osteoclasts [20], TNF -α inhibitors increase collagen synthesis in osteoblasts and inhibit osteoclast production, and IL-17 inhibitors reduce synovial inflammation and disruption of bone structure, delay bone loss, and reduce the potential for pathologic fractures [21].

2.1.3 Surgical treatment

Severe secondary hyperparathyroidism may increase the mortality rate of patients, and parathyroidectomy (PTX) is recommended for treatment when medication is not effective

[22].

2.1.4 Treatment of patients on renal replacement therapy

Patients may choose to reduce serum phosphorus levels by taking oral phosphate binders and using vitamin D analogs [23]. For HD patients, electrolyte levels need to be monitored regularly, and the need for additional oral drug therapy should be considered in the context of adequate dialysis [24]. Different concentrations of dialysate can be selected according to each patient. At the same time, no matter what kind of dialysis patients need to strictly monitor the serum calcium ion level, to prevent vascular calcification due to hypercalcemia, increasing the risk of patient death [25].

**2.2 Chinese Medicine Treatment**

Chinese medicine believes that insufficient kidney essence is the basis for the occurrence of renal bone disease, on which pathological products such as phlegm, blood stasis and turbid toxicity can appear. According to many studies, patients with renal bone disease are mainly characterized by deficiency of spleen and kidney, deficiency of liver and kidney, stasis and blood stagnation, internal stagnation of turbid toxicity, and stagnation of dampness and stagnation. Wang Shitao et al [26] believed that the treatment should be based on tonifying the kidney and bone, benefiting the kidney and blood, nourishing the liver and kidney, warming the kidney and spleen, and dispelling dampness and draining turbidity. Liu Mei et al [27] proposed the method of tonifying the kidney to strengthen the bones, tonifying the kidney to activate the blood to eliminate turbidity, and tonifying the kidney to strengthen the spleen to drain turbidity according to the theory of "the kidney is responsible for the bones and produces the marrow". Prof. He Liqun [28] believes that fire is the key factor leading to renal bone disease, and at the same time, patients with renal bone disease have damage to both yin and yang, so the treatment of renal bone disease should support the positive and eliminate the evil, specifically, clearing the heat and water to activate the blood to facilitate the watercourse, through the abdomen to diarrhea and fire to facilitate the intestinal tract, at the same time, replenish the kidneys and strengthen the spleen, and successive days of the same tonic. Prof. Li Yousheng [29], from the theory of "gallbladder is the main bone", proposed to strengthen the spleen and tonify the kidney, the successive days of the same tonic, tonifying the liver and kidney, E and K, warming the medulla oblongata to eliminate blood stasis, and dredge the gallbladder to elevate yang and drain turbidity to treat this disease. A large number of studies have shown that many traditional Chinese medicines that tonify kidney yang and nourish kidney yin can have certain therapeutic effects on osteoporosis [30,31].

## 3. Summary

In conclusion, the mechanism and treatment of CKD-MBD in modern medicine are still under research, and with the progress of research, there will be opportunities for more new therapeutic programs and drugs to provide efficient and safe treatment options to better serve the clinic and patients. In recent years, the role of the combination of Chinese and Western medicine in the treatment of this disease has been recognized by most scholars, but the pharmacological composition of traditional Chinese medicine is too complex, and there is a problem of difficulty in defining its pharmacological composition, and Chinese medicine focuses on individualized treatment plans, which makes it difficult to define the target point of drug action and the main components of the action of the drug. Currently, the research on the mechanism of Chinese medicine in treating this disease is gradually deepening and shows a broad research prospect. In the future, we need to more deeply explore the active ingredients of Chinese medicine and the mechanism of treatment and therapy of the disease, in order to let Chinese medicine play a greater role in bringing health and hope to more patients, and to provide a justified program for the treatment of this disease.

## References

[1] Wang L, Xu X, Zhang M, Hu C, Zhang X, Li C, Nie S, Huang Z, Zhao Z, Hou FF, Zhou M. Prevalence of Chronic Kidney Disease in China: Results from the Sixth China Chronic Disease and Risk Factor Surveillance. JAMA Intern Med. 2023 Apr 1; 183(4): 298-310.

[2] Dooley AC, Weiss NS, Kestenbaum B. Increased risk of hip fracture among men with CKD. Am J Kidney Dis. 2008 Jan;51(1):38-44.

[3] Fu R, Meng K, Zhang R, Du X, Jiao J. Bone marrow-derived exosomes promote inflammation and osteoclast differentiation in high-turnover renal osteodystrophy. Ren Fail. 2023;45(2):2264396.

[4] Li C, Chen XM, Li Y, Zhou YL, Yan JN, Du XG. Factors and Outcome of Renal Osteodystrophy - Associated Initial Fragility Fracture in End-Stage Renal Disease Patients. Kidney Dis (Basel). 2019 Mar; 5(2): 118-125.

[5] Cunningham J, Locatelli F, Rodriguez M. Secondary hyperparathyroidism: pathogenesis, disease progression, and therapeutic options. Clin J Am Soc Nephrol. 2011 Apr;6(4):913-921.

[6] Kemper MJ, van Husen M. Renal osteodystrophy in children: pathogenesis, diagnosis and treatment. Curr Opin Pediatr. 2014 Apr;26(2):180-186.

[7] Chen Z, Zhang X, Han F, Xie X, Hua Z, Huang X, Lindholm B, Haarhaus M, Stenvinkel P, Qureshi AR, Chen J. High alkaline phosphatase and low intact parathyroid hormone associate with worse clinical outcome in peritoneal dialysis patients. Perit Dial Int. 2021 Mar;41(2):236-243.

[8] Chen X, Wang Z, Duan N, Zhu G, Schwarz EM, Xie C. Osteoblast-osteoclast interactions. Connect Tissue Res. 2018 Mar;59(2):99-107.

[9] Arcidiacono T, Paloschi V, Rainone F, Terranegra A, Dogliotti E, Aloia A, Soldati L, Vezzoli G. Renal osteodystrophy and vascular calcification. J Endocrinol Invest. 2009;32(4 Suppl):21-26.

[10] Vervloet MG, van Ballegooijen AJ. Prevention and treatment of hyperphosphatemia in chronic kidney disease. Kidney Int. 2018 May;93(5):1060-1072.

[11] Zheng Y. Analysis of the effectiveness and safety of sevelamer carbonate on hyperphosphatemia in patients on maintenance dialysis [J]. Chinese Journal of Modern Drug Application,2024,18(14):133-136.

[12] Choi YJ, Noh Y, Shin S. Ferric citrate in the management of hyperphosphataemia and iron deficiency anaemia: A meta-analysis in patients with chronic kidney disease. Br J Clin Pharmacol. 2021 Feb; 87(2): 414-426.
[13] Tsai SH, Kan WC, Jhen RN, Chang YM, Kao JL, Lai HY, Liou HH, Shiao CC. Secondary Hyperparathyroidism in Chronic Kidney Disease: A Narrative Review Focus on Therapeutic Strategy. Clin Med (Lond). 2024 Aug 27:100238.
[14] Martínez-Arias L, Panizo S, Alonso-Montes C, Martín-Vírgala J, Martín-Carro B, Fernández-Villabrille S, García Gil-Albert C, Palomo-Antequera C, Fernández-Martín JL, Ruiz-Torres MP, Dusso AS, Carrillo-López N, Cannata-Andía JB, Naves-Díaz M. Effects of calcitriol and paricalcitol on renal fibrosis in CKD. Nephrol Dial Transplant. 2021 Apr 26; 36(5): 793-803.
[15] Cirilo MAS, Ribeiro FPB, Lima NKDS, Silva JK, Gomes JADS, Albuquerque JSS, Siqueira LCDS, Santos VBS, Carvalho JM, Tenorio FDCAM, Vieira LD. PARICALCITOL PREVENTS RENAL TUBULAR INJURY INDUCED BY ISCHEMIA-REPERFUSION: ROLE OF OXIDATIVE STRESS, INFLAMMATION AND AT1R. Mol Cell Endocrinol. 2024 Sep 2:112349.
[16] Grigore TV, Zuidscherwoude M, Olauson H, Hoenderop JG. Lessons from Klotho mouse models to understand mineral homeostasis. Acta Physiol (Oxf). 2024 Aug 23: e14220.
[17] Jia M, Han S, Wang Y. Systemic immunoinflammatory indexes in albuminuric adults are negatively associated with α-klotho: evidence from NHANES 2007-2016. Ren Fail. 2024 Dec;46(2):2385059.
[18] Milovanova LY, Nezhdanov KS, Milovanova SY, Lebedeva MV, Beketov VD, Volkov AV, Kamyshova ES, Suvorov AY, Moiseev SV. α-Klotho is associated with cardiovascular and all-cause mortality in patients with stage 3b and 4 chronic kidney disease (CKD): a long-term prospective cohort study. J Nephrol. 2024 Sep 2.
[19] Kundra S, Kaur R, Pasricha C, Kumari P, Gurjeet Singh T, Singh R. Pathological insights into activin A: Molecular underpinnings and therapeutic prospects in various diseases. Int Immunopharmacol. 2024 Sep 30; 139:112709.
[20] Koo BS, Oh JS, Park SY, Shin JH, Ahn GY, Lee S, Joo KB, Kim TH. Tumour necrosis factor inhibitors slow radiographic progression in patients with ankylosing spondylitis: 18-year real-world evidence. Ann Rheum Dis. 2020 Oct;79(10):1327-1332.
[21] Kampylafka E, d'Oliveira I, Linz C, Lerchen V, Stemmler F, Simon D, Englbrecht M, Sticherling M, Rech J, Kleyer A, Schett G, Hueber AJ. Resolution of synovitis and arrest of catabolic and anabolic bone changes in patients with psoriatic arthritis by IL-17A blockade with secukinumab: results from the prospective PSARTROS study. Arthritis Res Ther. 2018 Jul 27;20(1):153.
[22] Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant. 2009 Nov;9 Suppl 3:S1-155.
[23] Maranduca MA, Cozma CT, Clim A, Pinzariu AC, Tudorancea I, Popa IP, Lazar CI, Moscalu R, Filip N, Moscalu M, Constantin M, Scripcariu DV, Serban DN, Serban IL. The Molecular Mechanisms Underlying the Systemic Effects Mediated by Parathormone in the Context of Chronic Kidney Disease. Curr Issues Mol Biol. 2024 Apr 25;46(5):3877-3905.
[24] Rodriguez-Benot A, Martin-Malo A, Alvarez-Lara MA, Rodriguez M, Aljama P. Mild hyperphosphatemia and mortality in hemodialysis patients. Am J Kidney Dis. 2005 Jul;46(1):68-77.
[25] You M, Tang B, Wang ZJ, Wang KL, Wang H. Radiological manifestations of renal osteodystrophy in the orofacial region: a case report and literature review. Oral Radiol. 2018 Sep;34(3):262-266.
[26] Wang Shitao,Zhang Farong. Progress of traditional Chinese medicine treatment of renal bone disease[J]. Chinese Journal of Integrated Traditional and Western Nephrology,2023,24(04):368-370.
[27] Liu Mei, Ruan Taoren, Xing Mao, et al. Research progress on the treatment of CKD-MBD based on the theory of “the kidney governs bone and produces marrow” [J]. Chinese Journal of Integrated Traditional and Western Nephrology,2023,24(10):925-927.
[28] Chen Xian, Li Xiangwei, He Liqun. Prof. He Liqun's experience of treating renal bone disease in a collection of shells[J]. Chinese Journal of Integrated Traditional and Western Nephrology,2015,16(06):477-478.
[29] Zhao Yifang, LIAO Yao, Zhu Huizheng, et al. Li Yousheng treats renal osteodystrophy from “gallbladder” [J]. Shaanxi Journal of Traditional Chinese Medicine, 2022, 43(08):1091-1094+1098.
[30] Cui J, Lin L, Hao F, Shi Z, Gao Y, Yang T, Yang C, Wu X, Gao R, Ru Y, Li F, Xiao C, Gao Y, Wang Y. Comprehensive review of the traditional uses and the potential benefits of epimedium folium. Front Pharmacol. 2024 Sep 11; 15:1415265.
[31] Lin JY, Kuang HM, Rong K, Peng L, Kuang JJ, Yan X. Correction: Effectiveness of desertliving cistanche in managing hyperlipidemic osteoporosis in ovariectomized rats through the PI3K/AKT signaling pathway. J Orthop Surg Res. 2024 Aug 31;19(1):528.