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Research Progress on the Correlation between Oral Diseases and Chronic Kidney Diseases

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Abstract: *Objective:* To review the research progress on the correlation between oral diseases and chronic kidney diseases. *Methods:* Recent Chinese literature on the treatment, analysis, and correlation studies of oral diseases and chronic kidney diseases was collected. A comprehensive review, analysis, induction, and organization of the literature were conducted. *Results:* A high correlation exists between oral diseases and chronic kidney diseases, which mutually reinforce each other. *Conclusion:* A deep-level association exists between oral diseases and chronic kidney diseases. Persistent inflammatory symptoms can promote the elevation of C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, thereby exacerbating the development of chronic kidney diseases. Therefore, clinicians should comprehend the mechanism of interaction between oral diseases and chronic kidney diseases to foster diverse clinical thinking, improve the treatment efficacy of chronic kidney diseases, and effectively shorten disease duration.

Keywords: Oral diseases; Periodontitis; Chronic kidney diseases; Correlation; Interleukin-6 (IL-6)

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1. Introduction

The correlation between oral diseases and chronic kidney disease (CKD) is a significant area of medical research with implications for improving patient outcomes. Poor oral health, particularly periodontal disease, is often directly linked to systemic inflammatory responses. This inflammation can potentially exacerbate the progression of CKD through various factors and pathways. Conversely, patients with CKD exhibit suppressed immune function, rendering them highly susceptible to oral infections, which can further deteriorate their overall health. By improving oral hygiene, the risk of bacteremia is significantly reduced, thereby slowing the progression of CKD. In conclusion, understanding the correlation between these two conditions and analyzing previous scholarly research on both diseases is crucial for developing more comprehensive treatment strategies for CKD and mitigating the risk of complications.

2. Nephropathy and chronic kidney disease

In the clinical field, nephropathy typically refers to diseases diagnosed as related to kidney organs, such as glomerulonephritis, pyelonephritis, lupus nephritis, and similar conditions. Generally, nephropathy is difficult to cure once it manifests, and if the disease duration exceeds three months, abnormalities in urine and related blood indicators, as well as abnormalities in renal pathology and imaging, or a glomerular filtration rate (GFR) less than 60%, may indicate CKD. Failure to receive timely and effective treatment for CKD can lead to further disease progression, potentially culminating in chronic renal failure, renal insufficiency, and ultimately, uremia. According to statistics from medical departments, the most common type of CKD currently is chronic renal insufficiency, characterized by elevated levels of urea nitrogen and creatinine, kidney volume atrophy, and potential anemia or elevated parathyroid hormone (PTH) levels [1].

CKD is typically characterized by the "three highs" and "three lows." The "three highs" refer to a high incidence rate, high fatality rate, and a high probability of concomitant cardiovascular diseases. The "three lows" indicate low awareness of kidney disease, low rates of prevention and treatment, and low awareness of concomitant cardiovascular diseases. Surveys show that the prevalence of CKD among the Chinese population aged 40 and above exceeds 10%, but the awareness rate remains below 5% [2].

3. Correlation between oral diseases and chronic kidney diseases

3.1. Factors influencing chronic kidney diseases from oral diseases

Numerous scholars have conducted in-depth studies on the correlation between oral diseases and chronic kidney diseases based on clinical experience.

Some scholars have indicated that inflammation, a critical risk factor, can lead to the progression of CKD to end-stage renal disease (ESRD), subsequently triggering uremia. The inflammatory response generated by CKD and ESRD often serves as a key factor leading to cardiovascular disease (CVD). Additionally, patients with CKD frequently experience a significant burden of periodontal inflammation, typically characterized by persistent inflammatory symptoms. Levels of C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) may exhibit varying degrees of elevation [3].

Some scholars have conducted a meta-analysis on the influencing factors of periodontal basic treatment for patients with chronic kidney diseases. During the research phase, scholars provided the same duration of nephrology treatment to two groups of patients (experimental group and control group), with the experimental group receiving additional periodontal basic treatment. Meta-analysis revealed that patients who underwent periodontal basic treatment exhibited decreased levels of CRP and IL-6, although the underlying mechanism remains unclear. The analysis suggests that lipopolysaccharides and other bacterial components within periodontal pathogens may activate inflammatory factors or induce acute reactions in hepatocytes. Periodontal basic treatment can effectively eliminate these pathogens, thereby reducing the extent of inflammation. Furthermore, scholars noted that CRP, IL-6, and TNF-α can enter the bloodstream through periodontal pocket ulcers and spread to distant organs [4].

Scholars have pointed out that signaling pathways are key factors in the development of CKD influenced by periodontitis. During the research phase, scholars have suggested that latent membrane protein 1 encoded by the Epstein-Barr virus (EB virus) may generate a series of inflammatory factors, such as interleukin-8 (IL-8), through these signaling pathways. These factors are believed to be involved in the progression of chronic periodontitis (CP). While there is currently no research confirming that CP can directly cause CKD through signaling pathways,

studies have demonstrated that the activation of these pathways may be involved in the process linking CP to CKD. Typically, high expression of certain factors in these pathways may induce the expression of inflammatory markers such as CRP and IL-6, which can contribute to the progression of CKD [5]. Additionally, an increase in these factors can lead to elevated levels of TNF-α and interleukin-1 beta (IL-1β) in the serum, resulting in damage to renal tubules, glomeruli, and interstitial tissue. Based on an experimental study involving 80 rats, it has been proven that CP can enhance the levels of TNF-α and IL-1β through activated signaling pathways, thus promoting the occurrence of CKD. However, scholars have also noted that the research conclusions are based on animal experiments, and further confirmation is needed in human studies [6].

In 2020, some scholars conducted an analysis of the impact of periodontitis on renal interstitial fibrosis. They utilized a mouse model combining periodontitis and renal interstitial fibrosis for experimentation. Their findings suggested that periodontitis may be a potential risk factor for renal interstitial fibrosis. It promotes the expression of inflammatory factors such as matrix metalloproteinase-9 (MMP9), TNF-α, IL-1β, and interleukin-17A (IL-17A) in kidney tissues, while also facilitating the infiltration of neutrophils, thereby exacerbating the inflammatory response in kidney tissues. As the most common oral disease, periodontitis can lead to a systemic micro-inflammatory state. A series of toxic products, including lipopolysaccharides from periodontal pathogens, can induce host cells to secrete cytokines. These bacteria can aggravate the systemic inflammation level as the inflammation progresses. Through periodontal pathogen inoculation experiments in mouse mouths, it was found that pathogenic bacteria can significantly affect kidney function and histopathological changes in mice [7]. Within the category of periodontal pathogens, such as *Porphyromonas gingivalis* and *Prevotella intermedia*, they can trigger local inflammation by producing various toxic substances and enzymes. This local inflammation can transform into systemic inflammation via the bloodstream, intensifying chronic systemic inflammation, which is particularly detrimental to patients with CKD [8].

In this process, serum CRP serves as an important inflammatory marker. The continuous action of periodontal pathogens increases the stimulation of CRP synthesis in the patient's liver, resulting in elevated CRP levels. The specific mechanism may involve the release of bacterial lipopolysaccharides and other inflammatory mediators like interleukin-6, which further activate the body's immune response [9].

Compared to patients with other diseases, CKD patients are more prone to overreact to these microorganism-related inflammations. Their immune response is often disrupted due to decreased renal function. This enhanced inflammatory state not only exacerbates the destruction of periodontal tissues in CKD patients but may also accelerate the progression of CKD. By increasing the patient's systemic CRP level, it rapidly increases the risk of cardiovascular complications. Therefore, periodontal disease is not just a simple localized oral health issue for CKD patients; it is a critical factor affecting their overall health [10].

Regarding the role of *Porphyromonas gingivalis* in the development of chronic kidney disease, research has shown that as the primary periodontal pathogen, its interaction with the immune system is the main cause of increased serum CRP levels [11]. When *Porphyromonas gingivalis* invades periodontal tissue, the body produces IgG antibodies targeting its antigens. The IgG antibody-antigen reaction activates the complement system, releasing various inflammatory mediators, including cytokines such as the common IL-6 and TNF-α. The release of these cytokines promotes the synthesis of CRP in the patient's liver, with IL-6 playing a dominant role. IL-6 directly stimulates CRP synthesis by binding to hepatocyte receptors. Additionally, *Porphyromonas gingivalis* and its metabolic products, such as lipopolysaccharide (LPS), can directly trigger the activation of monocytes and macrophages, further amplifying the inflammatory response in patients and exacerbating the increase in CRP

levels. This mechanism indicates that *Porphyromonas gingivalis* is not just a simple local oral infection. The systemic inflammatory response it triggers plays a crucial role in the elevation of CRP levels [12].

3.2. Factors influencing chronic kidney disease on oral diseases

Scholars have specifically investigated the mutual promotion mechanism between periodontitis and CKD among elderly patients. The findings reveal that patients with CKD, due to the dysfunction of their immune system, are more susceptible to infection by periodontal pathogenic bacteria. Elderly patients with CKD often exhibit characteristics of decreased cellular and bodily immune function, such as reduced cell count, dysfunctional neutrophils, and suppressed neutrophil activity. These immune system abnormalities hinder the body's ability to effectively recognize and eliminate invading pathogenic microorganisms. Major periodontal pathogenic bacteria, including *Porphyromonas gingivalis*, can proliferate easily in a state of immunocompromise, subsequently triggering and exacerbating periodontitis [13]. Simultaneously, the accumulation of urea nitrogen and other metabolic waste products in the blood of CKD patients can also influence changes in the oral environment, such as reduced salivary flow and altered pH levels. These alterations provide favorable conditions for the growth of pathogenic microorganisms. Furthermore, the chronic inflammatory state induced by CKD, primarily manifested by elevated levels of inflammatory mediators, including IL-6 and TNF-α, can intensify the periodontal inflammatory response. Therefore, compared to individuals with a healthy constitution, patients with CKD are more susceptible to developing systemic inflammation from local periodontal infections. This further increases the burden on the body's immune system, leading to a vicious cycle of disease progression [14].

Additionally, scholars have pointed out that patients with chronic kidney disease, affected by decreased renal function, can experience loss and retention of trace elements in their serum. This, in turn, affects bone structure and contributes to a higher incidence of oral diseases. Research indicates that the impact of chronic kidney disease on the body's bone structure originates from metabolic disorders of trace elements caused by decreased renal function. CKD patients often exhibit characteristics of hyperphosphatemia and hypocalcemia. These metabolic disorders stimulate increased secretion of PTH, leading to renal osteodystrophy, which manifests as osteomalacia, osteoporosis, and other conditions. These bone metabolism disorders directly affect the health and stability of the body's alveolar bone, making it more prone to resorption and loss, and increasing the risk of tooth loosening and falling out. Typically, patients with CKD experience dysfunction in vitamin D metabolism, resulting in a continuous decline in active vitamin D levels. This exacerbates calcium absorption disorders and osteoporosis [15].

4. Conclusion

Based on a comprehensive analysis of numerous past scholarly research findings, a profound and mutually influential relationship exists between oral diseases and CKD. Oral diseases have the potential to elevate levels of CRP, IL-6, and TNF-α, thereby exacerbating the progression of CKD. Conversely, patients with chronic kidney diseases, due to the dysregulation of their immune systems, face a higher risk of developing oral diseases. Furthermore, in the context of impaired renal function, patients may experience changes in bone structure, leading to an increased risk of oral health issues such as tooth loss.

However, numerous aspects of the underlying mechanisms linking oral diseases to chronic kidney diseases remain to be further elucidated and confirmed. Most scholars have conducted their experiments using animal models. Therefore, it is imperative to continuously accumulate clinical experience and conduct further validations based on in-depth research to corroborate these findings.

Disclosure statement

The author declares no conflict of interest.

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