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Mini Review

The Role of the Gut in Chronic Kidney Disease: The Effect of Microbiota

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Abstract

Chronic Kidney Disease (CKD) is a globally prevalent public health issue that significantly affects quality of life and increases morbidity and mortality rates. Recent studies have highlighted the important role of the gut in CKD progression, demonstrating a bidirectional relationship between gut microbiota and kidney health. In patients with CKD, the accumulation of uremic toxins leads to dysbiosis of the gut microbiota, disruption of the intestinal barrier, and systemic inflammation. These factors contribute to disease progression by exacerbating kidney damage. As CKD progresses, the dysregulation of the gut microbiota becomes more pronounced, creating a vicious cycle that accelerates the disease's progression.

Traditional medical approaches, including medications and dialysis, play a fundamental role in slowing CKD progression and managing symptoms. However, microbiota-based approaches may be beneficial in improving patient outcomes. Regulating gut microbiota has become an important strategy in CKD management alongside traditional treatments. Potential interventions include probiotics, prebiotics, dietary modifications, and even fecal transplantation. These strategies show promising results in reducing the impact of CKD by restoring a balanced gut microbiota and reducing systemic inflammation and uremic toxins.

This review examines the complex relationship between gut microbiota and CKD and emphasizes the potential of microbiota-based therapies as an adjunct to traditional CKD treatments. By focusing on gut health, new therapeutic approaches may offer significant benefits in slowing CKD progression and improving patient quality of life.

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Introduction

Chronic Kidney Disease (CKD) is an increasing global health problem, associated with various etiological factors, primarily uncontrolled diabetes mellitus, hypertension, and other chronic diseases [1]. CKD is a multifaceted condition that not only involves impaired kidney function but also affects multiple organs and systems due to the accumulation of uremic toxins. CKD significantly impairs patients' quality of life, is a major cause of mortality, and increases treatment costs. One of the systems affected by CKD is the gut [2]. Gut microbiota plays an important role in human health, and recent studies have shown that imbalances in the microbiota significantly influence the progression of CKD [3].

In CKD patients, the disruption of gut microbiota is primarily caused by increased inflammation and the effects of uremic toxins. The accumulation of uremic toxins leads to increased intestinal permeability. This exacerbates the imbalance in the gut microbiota and triggers dysbiosis. The disruption of the intestinal barrier allows bacterial endotoxins to enter the systemic circulation. Endotoxins stimulate the immune system, increase inflammation, and promote kidney inflammation, accelerating the deterioration of kidney function. As CKD progresses, this vicious cycle becomes more pronounced, as the interaction between gut microbiota and kidney function becomes increasingly complex [3].

As a result, regulating gut microbiota is crucial in CKD treatment. Microbiota-based therapeutic approaches can slow the progression of the disease, reduce the impact of uremic toxins, and decrease inflammation. These approaches include probiotics, prebiotics, dietary modifications, and fecal transplantation. Such treatments could reduce the need for more invasive options like kidney transplantation or dialysis. This, in turn, could improve the quality of life for CKD patients and lower healthcare costs. This review explores the intricate relationship between CKD and gut microbiota, discussing microbiota-focused therapeutic strategies. These innovative treatment approaches could offer new hope in the management of CKD.

Alterations in gut microbiota in chronic kidney disease

Numerous studies on animal models and human subjects have shown the presence of dysbiosis in CKD [4,5]. The main causes include the accumulation of uremic toxins, reduced dietary fiber intake, impaired intestinal permeability, metabolic acidosis, medications, and slowed intestinal motility [5,6].

Dysbiosis

There are several causes of dysbiosis in CKD patients. One of them is dietary restriction of fiber-rich foods. Additionally, patients are often advised to limit foods such as milk, yogurt, and cheese due to their high phosphorus content. Since these foods have prebiotic and probiotic properties, their restriction can slow down intestinal motility, contributing to dysbiosis [6,7].

Furthermore, structural changes in the gut and the use of medications in CKD also contribute to dysbiosis [8,9].

Studies have shown that CKD patients experience a reduction in saccharolytic bacteria, which ferment carbohydrates, while proteolytic bacteria, which ferment proteins, increase. The bacteria that decrease in CKD include *Lactobacillus, Bifidobacterium, Roseburia,* and *Faecalibacterium,* whereas *Clostridium, Bacteroides,* and *Enterobacteriaceae* are reported to increase. These microbial alterations play a role in disrupting the intestinal barrier system [10,11].

All these changes contribute to the increased production of uremic toxins in the gut, which can accelerate CKD progression.

Bacterial endotoxins and gut-derived uremic toxins

Among the gut-derived products detected in the systemic circulation of CKD patients, one of the most studied is the lipopolysaccharide (LPS) toxin from Gram-negative bacteria. LPS activates the immune system and contributes to the development of atherosclerosis [12].

In CKD, especially in dialysis patients, increased levels of circulating endotoxins have been demonstrated [13]. Gut bacteria in CKD contribute to the production of uremic toxins through proteolytic fermentation. The major uremic toxins that increase in CKD include *p-Cresyl Sulfate (p-CS), Indoxyl Sulfate (IS), Indole-3-Acetic Acid (IAA),* and *Trimethylamine N-Oxide (TMAO)* [14].

Among these, TMAO has been shown to accelerate CKD progression and serve as an independent risk factor for cardiovascular events and mortality in CKD patients [15,16].

Disruption of the intestinal barrier

In CKD, dietary restrictions and dysbiosis lead to impaired intestinal motility. The accumulation of uremic toxins in circulation, combined with the effects of metabolic acidosis, disrupts the intestinal barrier and increases gut permeability in CKD patients [17]. As a result, gut-derived toxins enter the systemic circulation, triggering chronic inflammation [18].

Therapeutic approaches to regulate gut microbiota

As the impact of microbiota in CKD has become evident, therapeutic strategies aiming to improve microbiota balance have gained attention [19].

Prebiotics, probiotics, and synbiotics

The use of prebiotics, probiotics, and synbiotics as dietary supplements has emerged as a novel treatment strategy for CKD patients. Prebiotics are indigestible carbohydrates that support gut health, while probiotics are live microorganisms that contain beneficial gut bacteria.

Probiotic intake, in particular, has been shown to reduce uremic toxins and play a role in maintaining the integrity of the intestinal barrier [20]. The combined use of prebiotics and probiotics is crucial for balancing gut microbiota.

Dietary interventions

A plant-based diet is known to regulate gut microbiota and reduce the risk of cardiovascular disease. Increasing insoluble fiber intake supports gut integrity. These effects may have a positive impact on CKD progression [21].

Fecal Microbiota Transplantation (FMT)

Fecal Microbiota Transplantation (FMT) involves transferring stool from a healthy donor to a patient's gut [22]. It has been applied in conditions such as inflammatory bowel disease and Parkinson's disease. FMT may help restore gut microbiota in CKD patients, potentially slowing disease progression and offering a promising therapeutic approach [23,24].

Discussion

The relationship between gut microbiota and chronic kidney disease has become increasingly significant in recent years. Numerous studies have provided evidence suggesting that gut dysbiosis plays a crucial role in the development and progression of CKD. A study conducted by Jiang et al. demonstrated that kidney dysfunction leads to an accumulation of uremic toxins, which subsequently alter the composition of the gut microbiota, causing dysbiosis and increasing inflammation [5]. Similarly, Tang et al. showed that changes in the microbiota of CKD patients result in increased toxin levels that disrupt the gut barrier, facilitating the translocation of bacterial endotoxins into the systemic circulation [16]. This, in turn, exacerbates inflammation and accelerates disease progression [25]. The interaction between gut microbiota and CKD follows a complex mechanism in which changes in the gut microbiota contribute to kidney dysfunction and vice versa.

Microbiome-based approaches in CKD patients should be personalized. Additionally, gut microbiota can be improved through the use of probiotics, prebiotics, synbiotics, and dietary modifications [26].

Further research is needed to develop new strategies for improving gut microbiota in CKD patients. Personalized dietary modifications, prebiotic, probiotic, and synbiotic interventions, along with fecal microbiota transplantation, may enhance patient outcomes. The integration of microbiome-based therapies with conventional treatments such as pharmacological therapy and dialysis presents a promising approach.

In conclusion, gut microbiota represents a promising therapeutic target in CKD management. However, more clinical evidence is required to establish definitive treatment protocols.

Conclusion

The relationship between gut microbiota and chronic kidney disease plays an important role in the progression and management of the disease. Gut microbiota significantly influences systemic inflammation, metabolic functions, and immune responses, all of which are crucial in CKD. As a result, maintaining a healthy gut microbiota has become important in CKD management.

Microbiome-based treatments, such as probiotics, prebiotics, and synbiotics, have emerged as promising adjunct therapies in the management of CKD. The widespread adoption of personalized microbiome-based nutrition approaches could offer substantial benefits in improving patient outcomes. Additionally, probiotics can help restore a healthy gut microbiota balance, while fecal microbiota transplantation may slow CKD progression by rebalancing the gut ecosystem. As research continues to evolve, microbiota-based therapies may become a new hope in the treatment approach for CKD.

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