Recent Advances in the Characteristics of Gut Microbiota in Patients with Urinary Calculi and Their Clinical Significance

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Abstract: Urinary calculi are a common condition in urology, with a rising incidence in recent years. The intestinal microecosystem, a crucial component of the human microbiome, is closely linked to various diseases, including obesity, diabetes, and inflammatory bowel disease. Recent studies have shown that patients with urinary calculi exhibit a significant decrease in gut microbiome diversity, particularly in oxalate-metabolizing bacteria such as Oxalobacter formigenes, which is closely associated with the formation of calcium oxalate stones. Additionally, an increase in pro-inflammatory bacteria, such as Escherichia coli, further disrupts oxalate metabolism, raising the risk of stone formation. The use of antibiotics has been implicated in disturbing the gut microbiome, potentially increasing the recurrence of urinary calculi. This review summarizes the relationship between urinary calculi and the intestinal microecosystem, exploring the mechanisms by which gut microbiota contribute to stone formation and offering new insights into the prevention and treatment of urinary calculi.
***Keywords*:** urinary calculi; gut microbiota; oxalate metabolism; antibiotics; intestinal microecosystem

1. Introduction

Urinary calculi, commonly known as kidney stones, affect a significant portion of the global population, with an increasing incidence driven by factors such as metabolic syndrome and dietary habits[1]. Calcium oxalate stones are the most prevalent, accounting for over 80% of cases, and their formation is closely linked to metabolic disturbances, particularly those involving oxalate metabolism[2].

The gut microbiota, a complex community of microorganisms residing in the human digestive tract, plays a crucial role in maintaining metabolic homeostasis and overall health[3]. Dysbiosis, or the disruption of this microbial balance, has been implicated in a variety of diseases, including kidney stone disease. Notably, the gut microbiota influences oxalate metabolism, a key factor in calcium oxalate stone formation. Bacteria such as Oxalobacter formigenes degrade dietary oxalate, thereby reducing its absorption and subsequent excretion in urine[4]. However, studies have shown that patients with kidney stones often exhibit reduced levels of O. formigenes and other beneficial bacteria, increasing their susceptibility to stone formation[1][5].

In addition to gut microbiota, recent discoveries have highlighted the role of the urinary microbiome—previously thought to be sterile—in stone formation. The presence of certain bacterial species in the urinary tract may directly influence crystal formation and stone growth[1]. This dual influence of both intestinal and urinary microbiomes suggests that microbiota-targeted therapies could offer new avenues for the prevention and treatment of kidney stones.

Given the rising prevalence of kidney stones and the expanding knowledge of microbiome-related mechanisms, this review aims to explore the relationship between gut microbiota and urinary calculi. By focusing on the microbial and metabolic processes involved, this review seeks to provide insights into potential preventive and therapeutic strategies.

2. Gut Microbiota and Oxalate Metabolism

The gut microbiota plays a pivotal role in oxalate metabolism, which is critical in the formation of calcium oxalate kidney stones. Oxalobacter formigenes, a key bacterium in the gut, degrades oxalate, reducing its absorption and subsequent excretion in urine. This action lowers the risk of stone formation. Studies have shown that a lack of O. formigenes in the gut, often due to antibiotic use, leads to higher urinary oxalate levels and an increased risk of kidney stones[6]. Therapeutic reintroduction of O. formigenes has been proposed as a strategy to reduce this risk by restoring its population in the gut[6].

In addition to O. formigenes, probiotics like Lactiplantibacillus plantarum have shown potential in preventing calcium oxalate stones. L. plantarum J-15, for example, modulates the gut microbiota, enhances intestinal barrier function, and reduces inflammation, all of which contribute to lowering the risk of stone formation[7]. This strain also enriches beneficial bacteria linked to the production of short-chain fatty acids (SCFAs), which play a protective role against kidney stones[7].

Recent research has expanded the understanding of how the gut microbiome influences kidney stone formation. Beyond degrading oxalate, the microbiome affects immune responses and inflammation, both of which are crucial in the development of nephrolithiasis. These insights suggest that modulating the gut microbiota could be a promising strategy for preventing kidney stones[8].

3. Impact of Antibiotics on Gut Microbiota and Stone Formation

Antibiotics significantly disrupt the gut microbiota, which can increase the risk of kidney stone formation by altering the balance of oxalate-degrading bacteria like Oxalobacter formigenes. In a study with genetic hypercalciuric stone-forming (GHS) rats, antibiotics such as ciprofloxacin and Bactrim were shown to decrease microbial diversity, leading to higher urinary oxalate levels and increased kidney calcification[9]. This disruption in the gut microbiome directly impacts urine chemistry, elevating the risk of calcium oxalate stone formation.Further research on humans confirmed that antibiotic treatment suppresses O. formigenes colonization in the gut, altering urinary pH and overall microbiome structure. Although urinary oxalate levels remained unchanged, the loss of O. formigenes suggests a significant impact on the microbial ecosystem that influences stone formation[10].

Moreover, a case-control study found that exposure to certain antibiotics, particularly sulfa drugs and fluoroquinolones, significantly increased the risk of nephrolithiasis, especially when administered at younger ages or shortly before diagnosis[11]. These findings emphasize the importance of antibiotic stewardship to mitigate the rising incidence of kidney stones linked to gut microbiota disruption.

4. Gut Microbiota and Diet in Stone Formation

The gut microbiota plays a key role in calcium oxalate kidney stone formation, with diet being a critical factor in modulating this relationship. Patients with calcium oxalate nephrolithiasis often exhibit gut dysbiosis beyond just a reduction in Oxalobacter formigenes, with broader microbial imbalances that are influenced by diet[12]. High salt intake, low fruit and vegetable consumption, and high animal protein intake exacerbate these imbalances, increasing the risk of stone formation. For instance, while high oxalate foods like tea can raise the risk of kidney stones, the presence of beneficial bacteria such as Lactobacillus spp. can counteract this effect by degrading oxalates in the gut. Certain gut bacteria like Phascolarctobacterium and Faecalibacterium, which produce short-chain fatty acids (SCFAs), have also been linked to reduced stone risk, emphasizing the importance of a diet that supports beneficial microbial populations[13].

5. Predictive Models for Kidney Stone Risk

Recent advances have led to predictive models that integrate gut microbiota data with clinical information to better assess the risk of kidney stones. These models, particularly those using machine learning techniques like random forest, have shown high accuracy in predicting stone formation by analyzing gut microbiota profiles alongside patient data. For instance, a study from West China Hospital achieved an AUC of 0.94 in predicting kidney stone occurrence, underscoring the potential of personalized medicine in nephrolithiasis management[14].

Meta-analyses also reveal that specific gut bacteria, such as increased Bacteroides and Escherichia-Shigella and decreased Prevotella_9, are consistently associated with higher stone risk, further supporting the use of microbiota profiles in predictive models[5]. These insights pave the way for individualized prevention strategies based on gut microbiota assessments.

6. Therapeutic Implications and Future Directions

Microbiota-based interventions hold significant promise in the prevention and management of urinary calculi. Strategies such as the use of probiotics and prebiotics aim to restore beneficial bacteria like Oxalobacter formigenes and Lactobacillus spp., which play key roles in oxalate degradation and maintaining gut health[12][13]. Dietary modifications, including increased intake of fruits, vegetables, and fiber, can support a balanced gut microbiota, potentially reducing the risk of stone formation.

Personalized medicine approaches offer a tailored strategy for managing kidney stones, where treatment plans are developed based on an individual's gut microbiota profile. By identifying specific microbial imbalances, clinicians can design interventions that target the root causes of stone formation, improving patient outcomes and reducing recurrence rates[14].

Future research should focus on exploring the gut-kidney axis in greater detail, particularly the role of specific microbial metabolites in stone formation. Additionally, long-term studies on the effects of microbiota-targeted therapies will be crucial

in understanding their effectiveness and safety in preventing kidney stones. These insights could pave the way for more effective, personalized treatments that leverage the gut microbiome's potential in urological health.

7. Conclusion

In summary, the gut microbiota plays a crucial role in the development and prevention of urinary calculi, particularly calcium oxalate stones. Disruptions in the gut microbiome, such as reduced levels of oxalate-degrading bacteria like Oxalobacter formigenes and increased pro-inflammatory species, significantly contribute to the formation of kidney stones. The use of antibiotics, which can disturb the balance of these important microbes, further exacerbates the risk of stone formation by altering the gut's metabolic processes[6][9][10].

The integration of microbiota research into clinical practice is essential for improving the management and prevention of kidney stones. Personalized medicine approaches, which consider an individual's unique gut microbiota profile, offer a promising strategy to tailor interventions, reduce stone recurrence, and enhance patient outcomes[12][13]. Dietary modifications, alongside probiotics and prebiotics, can help restore beneficial microbial populations and mitigate the risk of stone formation[7][14].

Looking ahead, future research should focus on deepening our understanding of the gut-kidney axis and the specific microbial metabolites involved in stone formation. Long-term studies on microbiota-targeted therapies will be critical in developing more effective and personalized treatments for urinary calculi, potentially revolutionizing the approach to kidney stone prevention and management[5][11].

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