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The Role of the Probiotics in Urolithiasis

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Mr. R. A. Patil*, Dr. S. C. Burali

Tatyasaheb Kore College Pharmacy Warananagar, Maharashtra, India.

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ABSTRACT

Kidney stone is a complex disease of worldwide prevalence that is influenced by both genetic and environmental factors. About 80% of kidney stones are predominantly composed of calcium oxalate and urinary oxalate. Bacteria may have a role in the pathogenesis and prevention of kidney stones and the involvement of the intestinal microbiome in this renal disease have been investigated. Oxylobacter formigenes is a gram-negative bacteria that degrades oxalate in the gut decreasing urinary oxalate excretion. In this review, collection of the data is collected to study the role of probiotic Oxylobacter formigenes in kidney stone disease in humans and animals.

INTRODUCTION

Kidney stone is a complex disease influenced by genetic and environmental factors. Studies have revealed that implicated factors include diet, exercise, work environment and geography [1]. The huge numbers of bacteria that colonize the human body and form complex communities are referred to as the microbiome. It involves in communicates with host human cells and performs various biological processes. There is increasing concern that the change in human lifestyle affects the genetic composition and metabolic activity of the intestinal microbiome. The effects of these changes in bacterial populations have been associated with the increasing incidence of diseases such as obesity, coronary vascular disease, allergies, and metabolic syndrome [2]. These effects make tenable the possibility that the gut microbiome also affects the absorption and secretion of solutes relevant to kidney stone formation. A recent study has identified distinct differences in the gut microbiome of kidney stone patients compared to patients without stones [3]. Broad characterizations of the microbiome will need more extensive investigations to link to specific solutes that compose kidney stones and specific agents affecting the crystallization process.

Microbiota of lumen

Oxylobacter formigenes

The discovery of an oxalate-degrading bacteria, Oxylobacter formigenes (Oxf), by Allison and coworkers in 1985 has attracted considerable attention regarding its involvement in calcium oxalate stone disease [4]. Clinical findings have suggested that there is a direct correlation between the organism’s absence and hyperoxaluria and oxalate stone formation. Oxf is a Gram-negative, obligate anaerobic bacterium that is part of the normal bacterial flora in the large intestine of humans and other mammalian species. It is unique in that it requires oxalate both as a carbon source and for ATP generation, which it finds in the intestinal lumen [5,6]. It has been found in the gut of humans, rodents, dogs, pigs, and cattle. If present, it could degrade ingested oxalate reduce intestinal absorption, and stimulate oxalate secretion from the colon, offering protection from hyperoxaluria.

Bifidobacterium lactis

Recently, Hatch et al. demonstrated that Bifidobacterium lactis colonization decreases urinary oxalate by degrading dietary oxalate and reducing its intestinal absorption in a mouse model [7, 8].

Lactobacillus species

Studies have reported an extensive variation in the degree to which Lactobacillus species colonize the normal human gut. In contrast, abundance of the organism decreased with increasing calcium intake, which would bind oxalate and reduce its availability [9].

Association of microbiota and kidney stones

There are multiple epidemiological studies suggesting a protective role for microbiota. Human studies have also shown a strong inverse association between microbiota colonization and recurrent calcium oxalate renal stones. A case-control study of 247 patients with recurrent episodes of calcium oxalate stones and 259 subjects without stone disease matched by age, gender and region found a strong inverse association between colonization with microbiota and recurrent calcium oxalate stones with a 70% risk reduction [10]. Duncan et al. showed that the oral ingestion of a single dose of Oxf, followed by a dietary oxalate load, resulted in reduced urinary oxalate excretion, recovery of oxalate-degrading activity in feces, and prolonged colonization in 3 of 3 participants.

Antibiotic effect on O. formigenes in humans and mice

The hypothesis that antibiotic use could be responsible for the decrease in the prevalence of microbiota in adults has been investigated in recent studies. The effect of antibiotics on Oxf colonization was evaluated in patients receiving oral antibiotic treatment for Helicobacter pylori (HP) [11]. Microbiota strains are susceptible to multiple antibiotics including quinolones, macrolides, tetracycline, and metronidazole. In a prospective study, the prevalence of microbiota colonization was compared between an HP-positive group who was treated with either clarithromycin or metronidazole and an HP-negative control group who did not receive antibiotics. 92% of the control group of 12 patients who were positive for microbiota on initial stool testing and were not administered antibiotics remained positive for microbiota on stool tests at 1 month and 6 months.

Animal studies

Multiple experiments have investigated the role of microbiota in reducing urinary oxalate excretion in animal models. Sidhu et al. showed that in rats, colonization with O. formigenes resulted in a reduction of urinary oxalate excretion [12]. Likewise, in a mouse model of primary hyperoxaluria, a genetic disorder causing increased endogenous oxalate production,

O. formigenes induces enteric oxalate secretion, ultimately reducing net urinary oxalate excretion [13]. The urinary oxalate was similarly reduced when lysate of the bacterium was used in lieu of the whole bacterium [14]. Chen et al. transfected mouse stem cells with oxc and frc genes, encoding the oxalate decarboxylase and the formyl Co-A transferase, and demonstrated reduction in oxalate levels in the media [15]. An alternative hypothesis is that microbiota possesses a unique characteristic that allows it to reduce urinary oxalate excretion not only by reducing intestinal absorption but also by enhancing enteric oxalate secretion. Hatch et al. reported that microbiota interacts with colonic epithelium by inducing distal colonic secretion with a net secretive flux of oxalate from serosa to mucosa, leading to reduced urinary excretion [14]. This was shown by the studies on mice using two strains of microbiota, a human and rat strain.

Potential role of probiotics and whole microbial communities

The recent microbial transplants of oxalate-degrading bacteria from the mammalian herbivore Neotoma Caligula into a laboratory rat resulted in a significant increase and persistent colonization of oxalate-degrading bacteria. This result may represent a new target for therapeutic intervention to confer persistent oxalate degradation across species [15]. Attempts to introduce oxalate-degrading microbes through oral probiotic formulations into the human or rat gut have temporarily resulted in a decrease in urinary oxalate excretion. These oral probiotic preparations include different combinations of Oxf, Lactobacillus, Bifidobacterium, Enterococcus, and other oxalate degraders. With all formulations, the probiotics tested in both humans and rodents initially lead to a reduction in urinary oxalate excretion.

Conclusion

The research establishing a direct causal relationship between alterations in the gut microbiome and the incidence of kidney stones is lacking, the reviewed literature is highly suggestive. While research in this field is still in its early stages, the advancement of sequencing technologies and analytical tools offers a unique opportunity to explore previously unanswered questions on the role of gut and urine bacteria in stone pathophysiology. A few limitations in previous studies can be identified and considered in developing further studies. All the animal studies manipulated rodents' microbiome with the addition of microbiota and changes in diet. We know that the human microbiome and diet are significantly different from the rodent's, so finding a more representative model might be necessary to translate this work to humans. In addition, the understanding of the gut

microbiome as a network of bacterial species performing a function, e.g. oxalate degradation, instead of as a single species, will likely be of important therapeutic implications.

References

1. Goldfarb DS, Fischer ME, Keich Y, et al. A twin study of genetic and dietary influences on nephrolithiasis: a report from the Vietnam Era Twin (VET) Registry. Kidney Int. 2005; 67:1053. [PubMed: 15698445]
2. Blaser MJ, Falkow S. What are the consequences of the disappearing human microbiota? Nat Rev Microbiol. 2009; 7:887. [PubMed: 19898491]
3. Stern JM, Moazami S, Qiu Y, et al. Evidence for a distinct gut microbiome in kidney stone formers compared to non-stone formers. Urolithiasis. 2016; 44:399. [PubMed: 27115405]
4. Allison MJ, Dawson KA, Mayberry WR, et al. Oxalobacter formigenes gen. nov., sp. nov.: oxalate degrading anaerobes that inhabit the gastrointestinal tract. Arch Microbiol. 1985; 141:1. [PubMed: 3994481]
5. Allison MJ, Cook HM, Milne DB, et al. Oxalate degradation by gastrointestinal bacteria from humans. J Nutr. 1986; 116:455. [PubMed: 3950772]
6. Anantharam V, Allison MJ, Maloney PC. Oxalate:formate exchange. The basis for energy coupling in Oxalobacter. J Biol Chem. 1989; 264:7244. [PubMed: 2708365]
7. Abratt VR, Reid SJ. Oxalate-degrading bacteria of the human gut as probiotics in the management of kidney stone disease. Adv Appl Microbiol. 2010; 72:63. [PubMed: 20602988]
8. Klimesova K, Whittamore JM, Hatch M. Bifidobacterium animalis subsp. lactis decreases urinary oxalate excretion in a mouse model of primary hyperoxaluria. Urolithiasis. 2015; 43:107. [PubMed: 25269440]
9. Jiang J, Knight J, Easter LH, et al. Impact of dietary calcium and oxalate, and Oxalobacter formigenes colonization on urinary oxalate excretion. J Urol. 2011; 186:135. [PubMed: 21575973]
10. Kelly JP, Curhan GC, Cave DR, et al. Factors related to colonization with Oxalobacter formigenes in U.S. adults. J Endourol. 2011; 25:673. [PubMed: 21381959]
11. Kharlamb V, Schelker J, Francois F, et al. Oral antibiotic treatment of Helicobacter pylori leads to persistently reduced intestinal colonization rates with Oxalobacter formigenes. J Endourol. 2011; 25:1781. [PubMed: 22017284]
12. Sidhu H, Allison MJ, Chow JM, et al. Rapid reversal of hyperoxaluria in a rat model after probiotic administration of Oxalobacter formigenes. J Urol. 2001; 166:1487. [PubMed: 11547118]
13. Hatch M, Gjymishka A, Salido EC, et al. Enteric oxalate elimination is induced and oxalate is normalized in a mouse model of Primary Hyperoxaluria following intestinal colonization with Oxalobacter. Am J Physiol Gastrointest Liver Physiol. 2010; 300:G461. [PubMed: 21163900]
14. Hatch M, Cornelius J, Allison M, et al. Oxalobacter sp. reduces urinary oxalate excretion by promoting enteric oxalate secretion. Kidney Int. 2006; 69:691. [PubMed: 16518326]
15. Chen Z, Liu G, Ye Z, et al. The construction of an oxalate-degrading intestinal stem cell population in mice: a potential new treatment option for patients with calcium oxalate calculus. Urol Res. 2012; 40:131. [PubMed: 21892601]
16. Miller AW, Oakeson KF, Dale C, et al. Microbial community transplant results in increased and long-term oxalate degradation. Microb Ecol. 2016; 72:470. [PubMed: 27312892]