Kidney Conditions

**OVERVIEW**

The intestinal microbiome has been linked with kidney dysfunction, including kidney stones and chronic kidney disease (CKD). Alterations in gut microbiota and subsequent host responses may play a role in the development and progression of kidney disease, and may also present novel areas for treatment.

**KIDNEY STONES**

Kidney stones are common, affecting 1 in 11 people in the United States [1]. The most common form of the condition is the calcium oxalate stone. Current treatments include dietary modification, medications, and surgical treatment. Medications may be used to reduce calcium in the urine or to reduce uric acid levels.

Studies suggest that the gut microbiome may play a role in calcium stone formation, and may therefore present a novel treatment approach. A low level of Oxalobacter formigenes has been identified as a risk factor for calcium oxalate stone formation [2,3]. O. formigenes breaks down oxalates in the gut; if O. formigenes levels are low, oxalate levels can accumulate in the kidneys and potentially form calcium oxalate stones. The presence of O. formigenes is associated with a 70% reduction in the risk of recurrent kidney stones [4].

**CHRONIC KIDNEY DISEASE**

Chronic kidney disease (CKD) is a condition characterized by gradual loss of kidney function over time, and may be caused by any disorder that affects kidney structure and function. Current international guidelines classify CKD by glomerular filtration rate (GFR) and albuminuria [5,6]. In recent decades, CKD has become an increasingly relevant health issue in the United States, with a 6.9% prevalence in 2012 [7].
Hypertension and diabetes are responsible for the majority of cases of CKD, but other conditions may play a role, including congenital malformations, autoimmune disease, and polycystic kidney disease. Chronic kidney disease is also associated with an increased risk for systemic complications, including mineral and bone deficiency and increased cardiovascular disease risk [8].

Other studies have suggested that CKD is also associated with changes in gastrointestinal (GI) tract microbiota, identifying butyrate (a product of microbiota metabolism) as a possible component in ameliorating CKD-associated inflammation and CKD progression [9,10].

**INDICATIONS FOR SMARTGUT TESTING**

- History of chronic kidney disease, hypertension or diabetes
- Associated symptoms: nausea, vomiting, loss of appetite, edema, fatigue, changes in urination, weight loss, muscle cramps, chest pain, shortness of breath, persistent itching
- Personal or family history of calcium oxalate kidney stones

**RELEVANT SMARTGUT RESULTS**

**Kidney Stones**
- High levels of: *Bacteroides* [11]
- Low levels of: *O. formigenes* [3], and *Prevotella* [11]

**Chronic Kidney Disease**
- Low levels of: *Bacteroides fragilis* [9], *Bifidobacterium* [9], *Prevotella* [9], and *Roseburia* [9]

**CLINICAL TREATMENT SUGGESTIONS**

**Kidney Stones - Interventions to Consider:**
- Avoid calcium in supplement form: Calcium supplementation has been found to increase kidney stone risk. However, normal calcium intake through dietary sources can help bind oxalates in the digestive tract [12,13].
- Recommend a low-fat diet: A low-fat diet may help limit the effects of bile acids on oxalate absorption in the colon [13].
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CLINICAL TREATMENT SUGGESTIONS (CONT.)

Kidney Stones - Interventions to Consider (Cont.):

• Prescribe a probiotic with *O. formigenes*: This is not yet commercially available in the United States and studies do not demonstrate sustained colonization [14-16]. This may be an area for future intervention.

• Avoid antibiotics to which *O. formigenes* is known to be sensitive [17], including the following:
  - Azithromycin
  - Ciprofloxacin
  - Clarithromycin
  - Clindamycin
  - Doxycycline
  - Gentamicin
  - Levoflaxacin
  - Metronidazole
  - Tetracycline

• Check a bone density scan: Low levels of *O. formigenes* in the gut of patients with calcium oxalate stones are associated with decreased bone mineral density [18].

• Consider probiotics: Studies have shown that several probiotic strains have the capability to degrade oxalate, suggesting a potential role in the management of kidney stones [19]:
  - Ingesting a probiotic containing *L. acidophilus*, *L. brevis*, *L. plantarum*, *S. thermophilus*, and *B. infantis* (formerly available as OxadropTM) may reduce urinary oxalate excretion [20,21].
  - A mixture of *Lactobacillus*, *Bifidobacterium*, and *Streptococcus thermophilus* (VSL#3) may significantly decrease gastrointestinal oxalate absorption in healthy subjects [22].
CLINICAL TREATMENT SUGGESTIONS (CONT.)

Chronic Kidney Disease - Interventions to Consider:

- Treat the cause of the CKD: If identified, treating the underlying cause of kidney disease can potentially lead to improved outcomes and slow progression toward more severe complications of disease. See the Metabolic Conditions Treatment Guide for related suggestions.

- Consume probiotics or synbiotics: If clinically appropriate, certain combinations of probiotics and synbiotics (mixtures of pro- and prebiotics) may improve physiologic markers associated with CKD [23]:
  
  - A combination probiotic twice daily containing B. infantis, L. acidophilus, and E. faecalis (Lebenin™) may significantly decrease indole and p-cresol (uremic toxins) plasma levels, decrease Enterobacteria levels in stool samples, and decrease indican levels in plasma [24].
  
  - A combination synbiotic containing 5×10⁹ L. plantarum, 2×10⁹ L. casei subsp. rhamnosus, 2×10⁹ L. gasseri, 1×10⁹ B. infantis, 1×10⁹ B. longum, 1×10⁹ L. acidophilus, 1×10⁹ L. salivarius, 1×10⁹ L. sporogenes and 5×10⁹ S. thermophilus as well as prebiotic inulin and resistant starch (Probinul-neutro®) may significantly decrease total plasma p-cresol (an uremic toxin) in CKD patients [25].
  
  - A combination probiotic taken six times daily containing S. thermophilus, L. acidophilus, and B. longum total 1.5 x 10¹⁰ CFU (Renadyl®) appears to decrease blood urea nitrogen (BUN) and uric acid in comparison with placebo [26].
  
  - A daily dose of 1.6 x 10¹⁰ CFU Lactobacillus casei sp. shirota may decrease blood levels of urea in patients with patients with chronic renal failure [27].

- Consider probiotics for dialysis patients: If clinically appropriate, patients on peritoneal dialysis (PD) treatment may benefit from a daily dose of probiotics containing 10⁹ B. bifidum A218, 10⁹ B. catenulatum A302, 10⁹ B. longum A101, and 10⁹ L. plantarum A87 to improve cytokine response. Probiotics may also preserve residual renal function in PD patients [28].

POTENTIAL OUTCOMES

- Improved kidney function and reduced risk of kidney-related comorbidities
- Decreased need for dialysis or renal transplant
- Reduced rates of calcium oxalate stones
- Decreased need for medications and/or surgical intervention for calcium stones
REFERENCES