Findings

Oxalate Excretion Linked to Risk of CKD Progression

Higher urinary oxalate excretion is linked to an increased risk of progressive chronic kidney disease (CKD), reports a study in *JAMA Internal Medicine*.

The analysis included 3123 patients with stage 2 to 4 CKD, drawn from the Chronic Renal Insufficiency Study. Twenty-four-hour urinary oxalate excretion was measured at enrollment in 2003-08. Median oxalate excretion was 18.6 mg/24 hours; this value was inversely correlated with estimated glomerular filtration rate (eGFR) and positively correlated with 24-hour proteinuria.

Progression of CKD was evaluated in 2003-08, with a total follow-up of 22,318 person-years. At follow-up, 752 patients had developed end stage renal disease (ESRD), while 940 patients had reached the composite endpoint of a 50% decline in eGFR or ESRD. Both risks were significantly elevated for patients with higher oxalate excretion. From the highest to the lowest quintile (27.8 versus 11.5 mg/24 hours), hazard ratios were 1.33 for CKD progression and 1.45 for ESRD.

The association was nonlinear, with a threshold effect for patients in the third to fifth quintiles. Using the 40th percentile of oxalate excretion as a cutoff point, hazard ratios were 1.32 for CKD progression and 1.37 for ESRD.

High levels of urinary oxalate—a potentially toxic terminal metabolite—are known to be associated with acute kidney injury and CKD in certain disease states. This prospective cohort study reports that higher urinary oxalate excretion is an independent risk factor for CKD progression and ESRD. If confirmed, the findings may point to future studies evaluating the benefit of treatments to lower oxalate excretion in CKD patients [Waikar SS, et al. Association of urinary oxalate excretion with the risk of chronic kidney disease progression. *JAMA Intern Med* 2019; DOI: 10.1001/jamainternmed.2018.7980].

In Dialysis Patients, Spironolactone Doesn’t Reduce LV Mass

Spironolactone does not reduce left ventricular mass (LVM) in hemodialysis patients, concludes a randomized trial in *Kidney International*.

The Mineralocorticoid Receptor Antagonists in End-Stage Renal Disease (MiRENDa) trial included 97 adults receiving maintenance hemodialysis: 75 men and 22 women, mean age 60 years. They were assigned to treatment with spironolactone, 50 mg once daily, or placebo. At 40 weeks, cardiac MRI was performed to assess change in LVM index. Secondary outcomes included the incidence and severity of hyperkalemia and change in residual renal function.

Change in LVM index was not significantly different between treatment groups: 2.86 with spironolactone and 0.41 g/m² with placebo. Neither were there any significant changes in left ventricular ejection fraction, blood pressure, or functional capacity.

There were 155 episodes of moderate hyperkalemia (pre-dialysis potassium 6.0 to 6.5 mmol/L) in the spironolactone group versus 80 in the placebo group. However, the incidence of severe hyperkalemia was similar between groups: 14 and 24 events, respectively. There was no significant difference in residual urine volume or measured glomerular filtration rate.

Left ventricular hypertrophy is a key risk factor for sudden cardiac death and all-cause mortality in hemodialysis patients. Mineralocorticoid receptor antagonists such as spironolactone can favorably affect left ventricular remodeling in patients with heart failure, but there are few data on their safety and efficacy in dialysis patients.

The placebo-controlled MiRENDa trial finds no change in LVM index for hemodialysis patients assigned to spironolactone 50 mg/d. Spironolactone is associated with a higher rate of moderate but not severe hyperkalemia. The study finds no significant effect on surrogate cardiovascular end-points; the authors note that two trials are underway to evaluate the cardiovascular and survival benefits of spironolactone 25 mg in dialysis patients [Hammer F, et al. A randomized controlled trial of the effect of spironolactone on left ventricular mass in hemodialysis patients. *Kidney Int* 2019; https://doi.org/10.1016/j.kint.2018.11.025].

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: AURYXIA® (ferric citrate) is contraindicated in patients with iron overload syndromes.

WARNINGS AND PRECAUTIONS:

- **Iron Overload:** Monitor ferritin and transferrin saturation (TSAT). Patients may require a reduction in dose or discontinuation of concomitant intravenous (IV) iron

- **Risk of Overdose in Children Due to Accidental Ingestion:** Accidental ingestion and resulting overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Advise patients to keep AURYXIA out of the reach of children.

PREGNANCY AND LACTATION: Overdosing of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes and fetal malformation. Rat studies have shown the transfer of iron into milk. There is possible infant exposure when AURYXIA is taken by a nursing woman.

ADVERSE REACTIONS: The most common adverse reactions reported with AURYXIA in clinical trials were:

- **Iron Deficiency Anemia in CKD Not on Dialysis:** Discolored feces (22%), diarrhea (21%), constipation (18%), nausea (10%), abdominal pain (5%) and hyperkalemia (5%)

To report suspected adverse reactions, contact Akebia Therapeutics at 1-844-445-3799.

FOR MORE INFORMATION, VISIT AURYXIA.COM

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