Primary Hyperoxaluria
The Patient and Caregiver Perspective

Jennifer E. Lawrence and Debra J. Wattenberg


Introduction
Living with primary hyperoxaluria—a rare genetic disease with excess oxalate production leading to frequent kidney stones, kidney impairment, and oxalosis—presents many challenges to patients, caregivers, and their families. Although the progression and severity of primary hyperoxaluria is variable, care for any child or adult with primary hyperoxaluria is an unusual strain to the family due to intensity of required medical care and associated financial hardship. To identify the concerns of the primary hyperoxaluria community, multiple in-person meetings were convened and a web-based survey was developed by families, the Oxalosis and Hyperoxaluria Foundation (OHF), the Kidney Health Initiative (KHI), and the American Institutes for Research. The patient and caregiver perspectives listed in this paper as well as the survey findings (Figure 1) were derived from the respondents from the survey and meetings and highlight the daily challenges and the great need for new therapies. The companion paper, “Endpoints for Clinical Trials in Primary Hyperoxaluria” by Milliner et al. presents a systematic analysis of available data to identify appropriate end points to assess the efficacy of potential therapies in clinical trials.

Patient Survey Statistics
Among the 42 respondents, 17 were patients and 25 were parents/caregivers. The survey responses represented all types of primary hyperoxaluria (60% type 1, 29% type 2, 9% type 3, 2% unknown). Half of the patients were <17 years old, 26% were 18–34, and 24% were >35 years. All stages of the disease were represented, with 24% having experienced dialysis and 19% transplantation.

Current Therapies To Maintain Kidney Function
For patients with preserved kidney function, treatments are directed at reducing stone formation and preventing further kidney injury with significant fluid intake and multiple daily doses of medications. The amount of water required is burdensome and overwhelming. Young children may require a gastrostomy tube to maintain sufficient fluid intake, whereas older children and adults experience interruptions in school and work, and loss of sleep.

“It is a daily challenge to make sure our son is drinking constantly throughout the day. He visits the school nurse every day who gives him one of his four daily doses of medication through his (gastrostomy) mickey button. As a 12-year-old, he misses sleepovers, sleep away camp, and overnight school trips.”

Kidney Stones
The number of procedures patients may face is staggering. Patients consistently ranked kidney-stone attacks and urologic interventions as a top concern. Patients typically experience kidney stones during childhood and continue to suffer frequent, unpredictable, lifelong recurrences. Stones can require ureteral stent placement, ureteroscopic stone removal, ureteroscopic lithotripsy, extracorporeal lithotripsy, or open nephrolithotomy.

“My son has had multiple surgical procedures beginning at 6 months old. These procedures were very traumatic both physically and emotionally.”

“Kidney stones, procedures and hospitalizations interrupt school, work and require parents to miss work, creating financial burden on the family.”

Kidney Failure
Almost half (47%) of survey respondents listed anxiety associated with the potential for kidney failure. The decline in kidney function is variable, ranging from months to years, and can occur abruptly after an acute episode of dehydration, a stone obstruction, or stone surgery. The consequences of kidney failure can be particularly grave in primary hyperoxaluria because plasma oxalate levels rise rapidly, leading to oxalosis. For this reason, dialysis is often initiated earlier, at a higher eGFR in primary hyperoxaluria than would be initiated in other causes of kidney failure. Because dialysis is only partially effective in handling the oxalate load, hemodialysis 6 days per week in addition to daily peritoneal dialysis may be required.
”I’ve often thought back about what we did for the first 2 years of her life. Daily dialysis... sometimes up to 15 hours a day almost seems unthinkable!”

“Our schedule began every morning at 3:30 AM when I would awaken to prepare the daily medicines for our son. We would leave town at 5 AM to start our commute, have a 4 hour session on the machine and get home by 2 PM. I would put him to bed at 8 PM and begin sterilizing every thing to start four 1 hour ‘dwells’ of peritoneal dialysis once he was asleep. I would turn on his feeding pump and finally climb into bed next to him around midnight for 3 hours of sleep.”

Systemic Oxalosis
Patients fear progression to oxalosis and worry about the associated bone fractures, anemia, heart failure, joint damage, skin ulceration, severe weakness, vision impairment, and neuropathy.

“My brother experienced such intense nerve pain that he was unable to wear gloves during the winter. I ordered special gloves made of light but warm material for him. Unfortunately, he died before they were delivered.”

“When I first heard the crack, I was just convinced (or in denial) that anything serious had happened. Who breaks their leg playing ring around the rosie?”

Transplantation
Fear of organ transplantation was the greatest concern of the survey respondents. Transplantation can be life-saving, although complicated by features specific to primary hyperoxaluria. Because a transplanted kidney is at risk of oxalate injury, kidney transplantation alone is not satisfactory for most patients with primary hyperoxaluria. Whereas liver transplantation can replace the defective enzyme and restore oxalate production to normal levels, there are risks in transplantation. Further, the transplanted kidney remains at risk due to mobilization of calcium oxalate tissue stores.

“After much hesitation, (he) received two livers and one kidney which finally gave him a few short weeks of calm before horrific complications set in. The transplants failed and on that cold day in December, (he) was gone.”

“I didn’t fully understand the effects it would have on my life. You can never fully prepare for the emotional, mental, physical toll of dialysis and liver/kidney transplantation.”

The Psychologic Effect of Living with an Unknown Future
The psychologic effect and emotional stress resulting from diagnosis and disease management is a common theme expressed by patients. Many mention the fear and stress of not knowing when a painful kidney stone might occur or if kidney failure is imminent. Several children from the same family may have varying degrees of the condition, which can affect the dynamics between family members. This disease may cause considerable medical and financial burdens from lost work.

“Because (our son’s) care was so intense, our other two children had to move in with my parents.”

“As a child, I viewed myself as a fragile bomb that could blow up at any time. With that type of mentality, it is difficult to dream about the future and be excited for what is to come.”

“I feel like we are declining in health before trials can begin.”

Facilitating New Treatments
Congruent with these feared and serious outcomes, patient risk tolerance for therapeutics was high. The survey demonstrated that 94% of patients desired new therapies that would prevent dialysis, kidney or liver transplant, avoid oxalosis, and/or improve chances of a normal life span.

“We would be willing to take more risks for better quality of life, given the likelihood of kidney failure resulting
from this disease. We would like to see advances in therapies for patients across the disease spectrum. We need better medications which would reduce oxalate levels and methods to preserve current kidney function.”

In summary, living with primary hyperoxaluria presents many physical, emotional and financial challenges to patients, caregivers, and their families. Their voices express the profound effect of this disease on quality of life. Families desperately seek new treatment options to reduce the frequency of kidney stones, the need for organ transplantation, kidney failure, and oxalosis.

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