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Primary hyperoxaluria type 1: urologic and therapeutic management

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ABSTRACT

While the surgical approaches available in primary hyperoxaluria (PH) are common to all patients requiring intervention for urolithiasis, the indications for treatment and their corresponding toxicities are unique. Being a rare disease, we are guided by case series. This review summarizes the available literature highlighting the important disease-specific considerations. Shockwave lithotripsy (SWL) is of particular interest. It is generally the first-line treatment for stones in children, but here the stones produced will be relatively resistant to fragmentation. In addition, there are concerning reports in children of sudden unilateral decline in function in the treated kidney as measured by nuclear renography. Percutaneous nephrostolithotomy might intuitively seem favorable given the shortest drain duration and the ability to treat larger stones efficiently but, similar to SWL, rapid chronic kidney disease (CKD) progression has been seen postoperatively. Ureteroscopy is therefore generally the safest option, but considerations regarding stent encrustation, the growth of residual fragments and the large volume of stone often faced may limit this approach. The surgeon must balance the above with consideration of the patient's CKD status when considering a plan of monitoring and treating stones in PH.

Keywords: hyperoxaluria, percutaneous nephrolithotomy, shockwave lithotripsy, urolithiasis, ureteroscopy

The urologist managing urolithiasis in a patient with primary hyperoxaluria (PH) faces a considerable challenge. While the surgical approaches available are common to all children with stones, namely shock wave lithotripsy (SWL), ureteroscopy (URS) with lithotripsy, percutaneous nephrolithotomy (PCNL), and laparoscopic or open stone procedures, the toxicity and risk of each procedure have special considerations in PH. We will review the literature regarding outcomes from each' modality.

Open or laparoscopic approaches are seldom used, especially trans parenchymal approaches, due to their greater invasiveness. Several series exist for robot-assisted laparoscopic approaches to stones in children in the non-PH population [1, 2]. This may work well for selected patients as a one-time treatment. We caution that while there is no literature specific to revision pediatric laparoscopic renal surgery for stones, both experience and extrapolation from similar cases show clearly that reoperative renal surgery in children carries additional risk. Reoperative robotic pyeloplasty in children takes longer and has a longer associated length-of-stay [3, 4], as well as a higher rate of complications than comparable series of primary cases [4, 5]. Similarly, the stone procedures reported are largely in older children and teens [1, 2]; patients with PH often present as infants and toddlers, creating additional surgical challenge and risk.

SWL is a non-invasive treatment modality for nephrolithiasis that was first introduced in 1980 [6]. Since the first reported use of SWL in a pediatric patient in 1986 [7], it has remained a mainstay of treatment of pediatric nephrolithiasis. High efficacy and low complication rates have established SWL as a first-line treatment modality in many cases [8]. However, stone-free rates are variable and are likely affected by stone composition [9].

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Additionally, while SWL has low rates of complications in general, there are concerns regarding effects on renal function when used in PH. Therefore, use of SWL in PH remains controversial.

Boddy *et al*. described the first use of SWL in two pediatric patients with PH in 1988 [10]. Both of these patients experienced a significant decline in renal function following SWL as measured by postoperative DMSA scan, with ipsilateral function dropping by ∼25%. It is unclear, however, whether deterioration in renal function is a direct result of treatment with SWL, or is coincidental and due to natural progression of the disease. Subsequent reports have demonstrated varying success in treatment of calculi in patients with PH without effect on renal function [11–13]. Al-Abadi and Hulton reported 23 stones in 10 PH patients who underwent SWL, and while no deterioration in renal function was noted, only 20% of PH type 1 (PH1) stones showed improvement [13].

Treatment success is another important consideration in the use of SWL in management of calculi in PH and is primarily affected by stone composition. Calculi formed in PH are calcium oxalate monohydrate stones, which have been shown to be difficult to fragment with SWL [14, 15]. Additionally, incomplete stone clearance may lead to rapid enlargement. *In vitro* studies have demonstrated enlargement of post-SWL residual fragments composed of calcium oxalate monohydrate within 24 h [16]. Repeat treatment has been required in up to 61% of patients [13, 17]. Last, interpretation of pre- and postoperative imaging to plan for and evaluate stone clearance is complicated in PH by nephrocalcinosis. For all of the aforementioned reasons, treatment with direct visualization, either with URS and laser lithotripsy, or PCNL, is generally the preferable approach in PH.

URS is an endoscopic treatment modality first used in the pediatric population in 1988 [18]. Since then, advances in surgical technique and equipment have allowed for stone-free rates as high as 85–90% to be attainable in the pediatric population [18, 19]. While complication rates of URS range between 12.4% and 20.5% in reviews of URS in pediatric patients [19, 20], which is higher than complication rates with SWL, the majority of these complications are minor and serious complications are rare. Reviews of URS in pediatric patients have demonstrated no significant difference between stone clearance rates when stratified by stone composition [20].

For these reasons, URS may be preferable as first-line treatment modality for stone burden <20–30 mm [19, 21] in the PH1 population. However, given the difficulty in estimation of total stone burden in some PH1 patients due to nephrocalcinosis, it may be advisable to perform an initial URS in all PH1 patients to assess the true total stone burden within the collecting system under direct visualization [19]. If a large stone burden is present, the procedure can be converted to PCNL under the same anesthetic. This can potentially spare some PH1 patients undergoing a more invasive treatment modality unnecessarily, without increasing the total number of procedures and anesthetics. It should be noted that URS may require stenting before or after the procedure, and PH patients have several risk factors for stent encrustation [22]. Minimizing use or dwell time of stents is advised.

PCNL involves treatment of calculi through a small incision in the kidney. This treatment modality was first used in adults in 1976, however it did not gain popularity in treating the pediatric population until the first reported series of patients treated between 1987 and 1995 [21]. Its use was initially limited due to the more invasive nature compared with SWL and URS, risks of major complications and longer hospital stays [23]. More recently, however, smaller tracts with or without dilation have been used. These techniques have been developed to help reduce the risk of complications and prevent more serious complications such as bleeding or organ injury. Furthermore, mini-PCNL has the theoretical advantage of less nephron injury [24]. PCNL is generally considered to result in insignificant renal scar formation and impairment of renal function [25]. Although reports of PH1 patients treated with PCNL are limited, there does not appear to be an association with adverse effects on renal function in these cases [13, 19]. In one of the largest series of PH patients who underwent surgical management of urolithiasis, Carrasco *et al*. reported an overall complication rate of 11%, similar to reported rates in endoscopic treatment of all types of stone formers [19]. In their experience, 3 of 14 patients progressed to end-stage renal disease (ESRD) within 30 days of stone treatment. Notably, however, these three patients had pre-existing stage 3 CKD and two of these patients experienced obstructive stone episodes with acutely decreased glomerular filtration rates (GFRs) just prior to progression to ESRD.

Stone-free rates of PCNL are similar to URS and even open surgery, and can be as high as >90% [19, 21]. This excellent rate of stone clearance holds true even in cases with a large total stone burden. Additionally, stone-free rates have been reported to be similar between larger traditional access and mini-PCNL techniques in patients up to 16 years old [26]. Because of the implications of residual fragments and stone enlargement, stone clearance is particularly important in the PH1 patient population and is best achieved through direct visualization with URS or PCNL, or combination of both.

When considering timing of stone treatment, there must be balance. While on one hand any surgical intervention may not render patients durably stone-free, obstructive stone episodes in all forms of PH patients can cause acute impairment in GFR and disturb the homeostasis of oxalate, which may lead to even further excessive excretion of oxalate [27]. This disruption can put all types of PH patients at risk for further deterioration in renal function. It remains unclear whether preemptive treatment has any effect on the risk of progression of chronic kidney disease to end-stage disease as there is a lack of high-quality data [28]. Clinicians should take into account the distinct differences between the PH1 patient population and other types of stone formers when considering urological therapeutic management.

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CONFLICT OF INTEREST STATEMENT

None declared.

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