Extracorporeal shockwave lithotripsy in infants

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Introduction: *Pediatric urolithiasis is relatively uncommon and limited information is available on the application of minimally invasive management modalities in young children. We present a single centre experience with extracorporeal shockwave lithotripsy (ESWL) for infants with upper urinary tract calculi.*

Material and methods: *A total of 74 infants aged 3 months to 24 months with upper urinary tract calculi were treated with ESWL under general anesthesia using the Wolf 2500 and the 2501 Piezolith lithotriptors over a 14 and a half-year period. Patient and stone characteristics, risk factors for urolithiasis, treatment parameters, clinical outcomes and long-term follow-up were assessed and recorded.*

Results: *The mean patient age was 14.5 (range 3 to 24) months. The mean renal stone size was 18.2 (range 7 to 32) mm while the mean ureteral stone size was 9.4 (range 5 to 14) mm. Metabolic abnormalities, structural anomalies and urinary tract infections were identified as contributory factors for stone formation in 34% of the infants. At the 3-month follow-up there was an overall successful outcome in 72 infants (97%) that included 65 (88%) who were rendered stone-free and 7 (9%) who had clinically insignificant stone fragments. Retreatment was required in 27 (35%) patients, auxiliary procedures after ESWL were needed in 5 (7%) and secondary operative procedures were required in 2 (3%). Major complications were encountered in 5 (7%) patients that included complete ureteral obstruction with sepsis in 2, partial ureteral obstruction in 1 and febrile urinary tract infection in 2 other children. Long-term follow-up was recorded in 39 infants: 8 developed recurrent stones, 2 had stone regrowth and 1 developed mild hypertension but none had significant deterioration of renal function.*

Conclusions: *ESWL is an effective treatment for upper urinary tract calculi in infants. In the short-term, complications are minimal but long term follow up is needed.*

Key Words: children, lithotripsy, pediatric, renal calculi, ureteral calculi, urolithiasis

Introduction

The management of children with urinary tract calculi is a challenging proposition. Traditionally, open surgical techniques were employed in children due to the unavailability of appropriately sized endoscopes and lithotriptors. During the last two decades, owing to the continuing advances in technology, stone management in children has evolved from open surgery into less invasive modalities such as extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) and ureteroscopy.[1-4] Since its introduction by Chaussy et al in 1980, ESWL has revolutionized urinary stone treatment and numerous reports have documented the efficacy of ESWL in adults as well as older children.[1,2,5] There is, however, limited information available in regard to the effectiveness and safety profile of ESWL in infants.

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Conventionally, infants with urinary calculi have been grouped with older children even though they present several unique treatment challenges. Due to the anatomical proximity of the lower lung to the kidney, the potential for pulmonary injury after ESWL in infants is greater than in older children.[6] Because of the smaller anatomy with a larger part of the kidney exposed to the zone of highest shock wave energy, theoretically the risk of renal damage is higher in infants. Positioning infants on lithotriptor tables basically designed to treat adults, represents a difficult task. In addition, the treatment parameters with regard to ESWL are well defined in adults and older children, however, they have not been clearly established in infants. Furthermore, owing to the narrow caliber of the infantile urethra and ureter, endourological manipulation, when required, is both technically demanding and potentially hazardous.

We present a comprehensive single centre experience with the use of ESWL in infants with upper urinary tract calculi.

TABLE 1. **Risk factors for urolithiasis**

	No. of patients
Metabolic abnormality	
Hyperuricosuria	5
Hypocitraturia	3
Hypercalciuria	1
Hyperuricemia	1
Total	**10**
Structural anomaly	
Duplex system	2
Vesicoureteral reflux	2
Solitary kidney	2
Neurogenic bladder	1
Ureterocele	1
Horseshoe kidney	1
Total	**9**
Infection	
Proteus	4
Pseudomonas	2
Total	**6**
Total	**25 (34%)**

Materials and methods

Between September 1991 and February 2006, a total of 514 children with upper urinary tract calculi underwent ESWL using the Wolf 2500 and the 2501 Piezolith lithotriptors (Richard Wolf GmbH, Knittlingen, Germany) at our tertiary referral centre. Of these, 74 (14%) were very young children aged 2 years or younger.

Preoperative evaluation

All infants were assessed by biochemical studies, urine culture, ultrasonography (USG) and excretory urography (IVU). Metabolic investigations including estimates of serum calcium, phosphorous and uric acid concentrations along with screening for cystinuria were routinely used; the 24-hour urinary calcium, phosphate, oxalate, citrate and urate excretions were evaluated in 47 of the 74 infants. From these results the risk factors for urolithiasis were identified, Table 1. In 23 infants the ^{99m}Tc dimercapto succinic acid (DMSA) renal scintigraphy was performed prior to ESWL.

Procedure

All patients underwent ESWL under general anesthesia. The patients were treated in the supine position for renal and upper ureteral calculi and in the prone position for mid and lower ureteral calculi. The Wolf 2500 Piezolith lithotriptor was used in the first 39 infants. The Wolf 2501 Piezolith lithotriptor replaced our 2500 Piezolithin 1997 and was used in the last 35 infants. All infants with renal calculi underwent ESWL without prophylactic ureteral stenting except those with staghorn calculi or a solitary kidney in whom a 4F, 8 cm to 10 cm double pigtail ureteral stent was inserted pre-operatively immediately before ESWL. Infants with a proven urinary tract infection received appropriate antibiotic treatment before and after ESWL. The patient was placed on the lithotriptor table that has a water-bath covered by a membrane; this allowed children of any size to be positioned without requiring modification. Renal stones were localized using ultrasound whenever possible, to reduce radiation exposure. Radiopaque ureteral calculi were localized using fluoroscopy, while in infants with radiolucent ureteral calculi, a ureteral catheter with contrast was utilized to facilitate localization. The treatment regime involved delivering a maximum of 3000 shocks per session with the shockwave intensity initially set at level 3 (35 MPa) and gradually increased to a maximum of level 5 (65 MPa.). In infants with staghorn calculi a fractionated disintegration technique was used wherein the pelvic component of the staghorn was initially fragmented, followed by sequential fragmentation of the upper, mid and lower caliceal components. This technique facilitated stone clearance and prevented steinstrasse. Patients were usually hospitalized for 48 hours after each ESWL session.

Follow-up evaluation

Infants with adequate stone fragmentation were followed with plain abdominal x-ray and USG at 3-week intervals until the fragments were completely cleared. If further ESWL sessions were required, they were scheduled at 3-week intervals. Plain abdominal x-ray, USG and limited IVU / non-contrast computerized tomography (IVU 51 infants, NCCT 23 infants) were routinely performed in all cases 3 months after the completion of treatment. The patients were categorized as 'stone-free', 'clinically insignificant residual fragments' (CIRFs) or 'failure'. Stone-free status was defined as the complete absence of residual stone fragments on radiological imaging 3 months after the last ESWL session. Asymptomatic, non-infectious and non-obstructive fragments smaller than 3 mm were considered CIRFs. ESWL was regarded as a failure if no fragmentation was noted after the second session. The ureteral stent was removed 3 weeks after the last ESWL session under general anesthesia. DMSA renal scans were repeated 6 months after ESWL in those infants who had them prior to ESWL. The infants were subsequently followed up 6-monthly with blood pressure evaluation, urine analysis, serum creatinine, blood glucose and USG. Appropriate medical therapy was instituted in infants with metabolic stones after the completion of ESWL.

Comparison of stone-free rates between infants with stones ≤ 2 cm in size and those with larger stones were made using the Pearson Chi-square test. A comparison of complication rates in the abovementioned groups was performed using the Fisher's Exact test. Values were considered significant at $p < 0.05$ for all statistical tests. All analyses were done using commercially available statistical software.

Results

Patient demographics

There were 51 boys and 23 girls with a mean age of 14.5 (range 3 to 24) months. Six infants were below 6 months of age, 23 were between 6 months and 12 months, 20 were between 13 months and 18 months and the remaining 25 patients were aged between 19 months and 24 months. The presenting symptoms were hematuria (gross or microscopic) in 29 infants (39%), recurrent urinary tract infection in 18 (24%), abdominal colic in 15 (20%), failure to thrive in 3 (4%) and anuria in 1 (2%). In the remaining 8 patients (11%) the calculi were asymptomatic and discovered accidentally. Fifty-seven patients (77%) had isolated renal calculi, 9 (12%) had isolated ureteral calculi while the remaining 8 (11%) had a combination of renal and ureteral calculi. The renal calculi varied in size from 7 to 32 (mean size 18.2) mm while the ureteral calculi varied in size from 5 to 14 (mean size 9.4) mm. A total of 55 infants were noted to have calculi ≤ 2 cm, while in the remaining 19 infants the calculi were larger. Of the 65 infants with renal calculi, 40 had calculi located in the renal pelvis, 21 had caliceal and 4 had staghorn calculi. Of the 17 infants with ureteral calculi, 9 had distal ureteral, 4 had mid ureteral, 3 had proximal ureteral calculi while 1 had both proximal and

TABLE 2. **Results after ESWL for stones at various levels**

	Renal pelvis	Calix	Staghorn	Proximal ureter	Mid ureter	Distal ureter	Combined renal and ureteral	Total n (%)
No. of patients	35	19	3	2	2	5	8	74
Stone-free	31	18	2	2	2	4	6	65 (88)
CIRFs	4	1	-	-	-	-	2	7 (9)
Overall success, n (%)	35 (100)	19 (100)	2 (67)	2 (100)	2 (100)	4 (80)	8 (100)	72 (97)
Failure of fragmentation	-	-	1	-	1	-	-	2 (3)
Failure of clearance	-	-	-	-	-	-	-	-
Post-ESWL auxiliary procedures:								
a) PCN	2	-	-	-	-	-	-	2 (3)
b) Ureteroscopy	2	-	-	-	-	-	-	2 (3)
c) ESWL	-	1	-	-	-	-	-	1 (1)
Secondary operative procedures:								
a) Open surgery	-	-	1	-	-	-	-	1 (1)
b) Ureteroscopy	-	-	-	-	-	1	-	1 (1)

distal ureteral calculi. Overall 47 patients had radiopaque calculi, 21 had radiolucent calculi and in the remaining 6 the calculi were faintly opaque.

Outcome

A total of 91 calculi were treated in 74 infants. The mean number of shocks was 4750 (range 1700 to 12000), the mean duration per treatment session was 47 (range 25 to 72) minutes and the mean fluoroscopy time was 43 (range 26 to 71) seconds. Overall, 65 of the 74 infants (88%) were rendered stone-free, 7 (9%) had CIRFs and 2 (3%) were failures. The detailed results are illustrated in Table 2. To obtain success 47 patients (65%) required only 1 ESWL session; 21 (29%) needed 2; 3 (4%) required 3; and 1 (2%) required 4 ESWL sessions. Among the patients who required a single ESWL session was a 24-month-old infant who was referred to us with a nephrostomy tube in-situ that had previously been placed to relieve obstruction caused by a radiolucent upper ureteral calculus. Among those who required three ESWL sessions was an 18-month-old boy who had a combination of staghorn and distal ureteral calculi, Figure 1a, 1b, 1c. One complex case treated with ESWL deserves special emphasis. In this 11-month-old infant with hypercalciuria and bilateral duplex collecting system, several stones developed all over the upper urinary tract. The patient was rendered stone-free after four ESWL sessions.

ESWL failed to fragment stones in two infants, one of whom had a dense partial staghorn calculus associated with urinary tract infection (Proteus). This calculus was eventually removed by open surgery and stone analysis revealed struvite. The other had a distal ureteral, radiolucent calculus that was difficult to localize during the ESWL session despite the use of a ureteral catheter and contrast. He was subsequently rendered stone-free using ureteroscopy and Holmium: YAG (Ho: YAG) laser lithotripsy. Major complications were observed in five cases (7%). Two infants who had a 2.2 cm and a 1.4 cm renal calculus respectively developed steinstrasse and complete ureteral obstruction with sepsis after the first ESWL session;

Figure 1a. KUB shows a partial staghorn calculus and lower ureteral calculi.

Figure 1b. KUB after double-J-stent placement and one ESWL session reveals partial stone fragmentation.

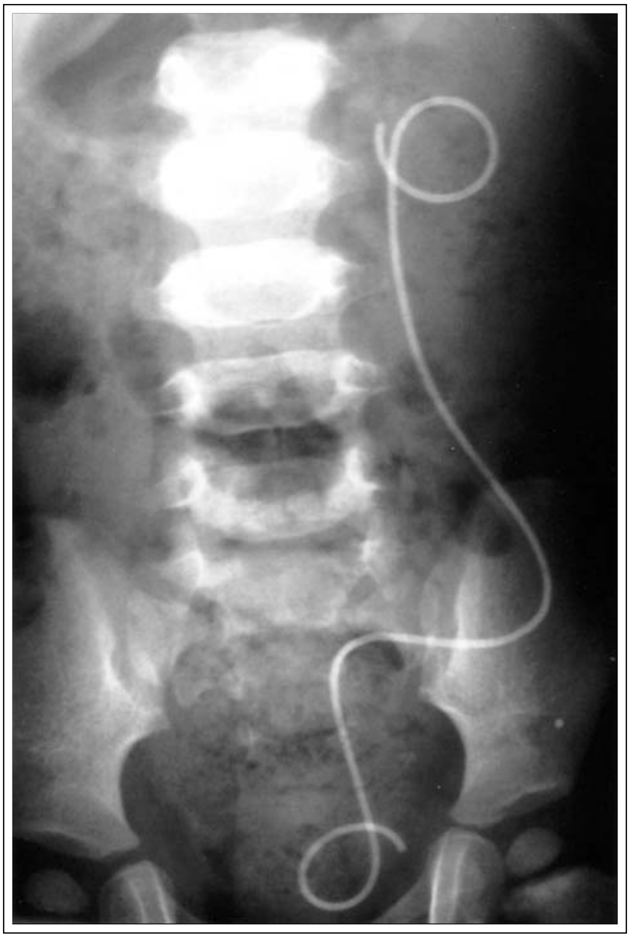

Figure 1c. KUB after three ESWL sessions demonstrates complete stone-free status.

they were rehospitalized and initially treated with nephrostomy drainage and parenteral antibiotics. They were eventually rendered stone-free by ureteroscopy with Ho: YAG laser lithotripsy and electrohydraulic lithotripsy respectively. Another patient with a 1.2 cm renal caliceal stone developed partial ureteral obstruction after ESWL caused by a distal ureteral fragment; this was completely fragmented and cleared with further ESWL. Two other infants developed persistent fever associated with urinary tract infection, necessitating readmission, intravenous antibiotics and antipyretics. Minor complications were encountered in 36 cases (49%) in the immediate post-ESWL period; they included transient and self-limiting hematuria in 16, entry site ecchymosis in 13, low grade fever in 4 and small perinephric hematomas (< 1 cm in size) in 3 infants. None of the patients with a ureteral stent had any stent-related morbidity that required treatment although the ureteral stents were left in-dwelling for 3 to 11 (mean 4.6) weeks. Fragments of calculi obtained from urine during the 48-hours after ESWL were available for analysis in 38 cases (51%). Stone composition was ammonium acid urate in 22, struvite in 9, calcium oxalate in 5 and calcium phosphate in 2.

The comparison of stone-free rates in infants with stones ≤ 2 cm and larger stones revealed no significant statistical difference ($p = 0.315$). Likewise, the comparison of complication rates of infants with stones ≤ 2 cm and larger stones also demonstrated no significant statistical difference ($p = 0.599$).

Long-term follow-up

Complete data was available in 39 infants who were followed up for a mean of 7.5 (range 5 to 13) years. Eight infants (21%) had recurrent stone formation after achieving stone-free status. Of these, 7 had recurrences in the kidney while 1 had a recurrent ureteral stone. From this group, 3 had an underlying metabolic lithogenic disorder in the form of hyperuricosuria in 2 and hypocitraturia in 1. All 8 patients with recurrent calculi were rendered stone-free by repeat ESWL. From the 7 patients with CIRFs, 3 had spontaneous clearance of the fragments within the first 6 months after ESWL, whereas 2 infants spontaneously passed the stone fragments in months 7 and 9 respectively. The episodes of stone passage were not associated with any additional morbidity such as pain, haematuria or hospitalization. In two cases the CIRFs showed regrowth up to 7 mm and 9 mm fragments respectively. Both were located in the lower calices and were rendered stone-free with further ESWL. A 14-month-old infant, who was treated for bilateral renal calculi with a total of 6000 shocks, developed mild hypertension 7 years after treatment and is presently being managed with antihypertensive medications. None developed diabetes mellitus. The DMSA renal scans were carefully reviewed in 17 infants and the results were classified as both normal (14 infants) and demonstrating pre-existing parenchymal lesions not altered by ESWL (3 infants). Neither renal scars nor significant deterioration in differential renal function attributable to ESWL were detected in the renal scans 6 months after treatment. Deterioration of renal function was defined as a change of split function greater than 10% of total value at follow-up compared to baseline.

Discussion

Urolithiasis in childhood is relatively uncommon in the developed world with a prevalence rate of 1% to 5%.[7] However, pediatric urolithiasis remains endemic in developing countries, affecting children younger than 1 year to adolescence with a relatively high prevalence rate of 5% to 15%.[8,9] The etiology of stone formation in children is largely unknown. The most common causes are metabolic risk factors, structural urinary tract anomalies and infection.[8]

The introduction of ESWL in 1980 revolutionized the management of urolithiasis; 6 years later Newman et al were the first to report the efficacy of ESWL in the pediatric population.[5,10] Since then, numerous investigators have documented successful results in the treatment of renal and ureteral calculi in children using ESWL although most reports describe experience with relatively older children.[1,2,11-13] In 2000 Lottmann and associates specifically addressed the issue of efficacy of ESWL in infants.[14] They treated 19 patients aged 5 months to 24 months using the Sonolith 3000 / Nova lithotriptors and reported a 100% stone-free rate after two ESWL sessions. A year later Shukla et al subjected eight infants aged 9 months to 15 months to ESWL with the Dornier HM3 lithotriptor and obtained a 100% stone-free rate after a single ESWL session.[15] More recently, McLorie and colleagues described the effectiveness of ESWL in a multi-centre study involving 34 infants using the Dornier MFL 5000 / HM3 lithotriptors.[6] They documented single and multiple treatment success rates of 66% and 86% respectively. In the current study, which is to our knowledge the largest reported single centre experience involving the use of ESWL in infants, we attained comparable results with an overall stone-free rate of 88% at the 3-month follow-up. Interestingly, our stone-free rates for calculi ≥ 2 cm were comparable to the stone-free rates for smaller calculi. The excellent outcome achieved by ESWL in fragmenting and clearing urinary tract calculi in infants, irrespective of stone size, could be explained by certain factors. The smaller body volume of infants facilitates more effective shockwave transmission with minimal loss of energy.[16] Chemical composition of stones and comparable shorter duration of the existing pathology in infants may also have a role in the results. In addition, the pediatric ureter is shorter, more elastic and distensible and, thus, permits easier transmission of stone fragments and prevents ureteral impaction.[17] Furthermore, the density of the bony pelvis is less in infants resulting in less energy loss during passage; this fact probably accounts for satisfactory stone-free rates even for the calculi located in the mid ureter where traditionally the results after ESWL are comparatively inferior.[11]

The Wolf 2500 and 2501 Piezolith lithotriptors offer certain advantages for the treatment of urinary calculi in younger children and infants. These lithotriptors have relatively small focal zones (11 mm x 3 mm) reducing the risk of trauma to the adjacent organs and obviates the need for shielding of the lungs and gonads. In contrast, infants treated with the Dormier HM3 lithotriptor require gantry modification with a wooden platform and polystyrene foam positioning for lung and visceral protection.[15] Also, the flat table of Piezolith lithotriptors have a waterbath covered by a membrane that permits easy positioning of infants regardless of their size. No special restraints are required during the treatment session even in the smaller infants; in the present study the smallest child was 3-months-old. In addition, these lithotriptors have a dual imaging system comprised of real time ultrasound and fluoroscopy that facilitates excellent stone localization, irrespective of stone location. Another advantage of piezoelectric shock wave generation is the relatively long life span of the generator and of each piezoelectric element up to 1,000,000 impulses. Several investigators have documented the comparative clinical efficacy of different lithotriptors in the pediatric age group.[2,18] Our overall stone-free rates using the Wolf Piezolith compare favorably with the results obtained using other lithotriptors. A major disadvantage of piezoelectric elements is that the amount of shock wave energy per pulse is small leading to a considerable retreatment rate. In the present study the retreatment rate was 35%.

Metabolic abnormalities have been reported to contribute to stone formation in as many as 16% to 83% of children with stones.[19,20] In a recent study by McLorie and colleagues, metabolic disorders were documented in 40% of infants, with hypercalciuria being the commonest abnormality.[6] Shukla et al observed that nearly 50% of their infants with stones had an underlying metabolic condition.[15] In the present study, an underlying metabolic disorder was uncovered in 10 infants (21%); hyperuricosuria and hypocitraturia were the most common metabolic disorders. Uric acid is a weak acid that exists in its relatively insoluble non-ionized form below the pH of 5.5.[21] Its propensity to stone formation increases significantly in acidic urine. Uric acid over-production may result from an inborn error of purine metabolism wherein phosphoribosyl pyrophosphate accumulates due to partial or complete hypoxanthine-guanine phosphoribosyltransferase deficiency. The accumulation of phosphoribosyl pyrophosphate leads to the over-production and over-excretion of uric acid.[22] Urinary alkalinization and allopurinol forms the backbone of therapy for hyperuricosuria.[23]

Hypocitraturia was the other common metabolic disorder seen in our group of infants. Urinary citrate acts as a stone inhibitor by forming a soluble complex with calcium.[21] Hypocitraturia is usually treated with citrate supplementation.[23] Hypocitraturia may have a role in the etiology of recurrent calculi since two of the three patients with hypocitraturia in the present series had more than one stone episode. A similar observation was made by Sternberg and associates from their report of 123 children wherein three patients had hypocitraturia and all had recurrent stone formation.[19] Other metabolic disorders such as cystinuria are reportedly rare and this was also our experience. Many urologists do not routinely perform metabolic evaluation after an initial stone event in adults. However, the relatively high incidence of metabolic abnormalities in the pediatric population necessitates a complete metabolic work-up after the initial stone event. The efficacy of medical management in preventing stone recurrence following ESWL has been established in adults but to date very few studies have demonstrated such an effect in children.[24] Therefore, further studies on metabolic risk factors in children undergoing ESWL and the efficacy of metaphylaxis are needed.

The subject of long-term detrimental effects of shockwaves on the growing kidneys is still being debated. The main concerns have been the impairment of renal function, hyperfiltration and the long-term risk of hypertension. Picramenos and colleagues compared DMSA scans before and at 1 and 3 months after ESWL in a group of 12 children treated with the Dornier HM4 lithotriptor; no significant variation in differential function was observed.[25] A 9-year follow-up study by Traxer et al also demonstrated lack of parenchymal damage in 39 children who underwent ESWL with the Sonolith 3000 lithotriptor.[26] Similarly, Lottmann and associates found ESWL to be a safe technique in their series of 19 infants aged 5 to 24 months treated with Sonolith 3000 / Nova lithotriptors; neither renal parenchymal scars nor significant changes in differential function attributable to ESWL were detected in the infants 6 months after treatment.[14] Likewise, in the present study, we did not observe any detrimental change in the differential renal function after ESWL in any of the 17 infants, although new onset hypertension was noted in one child at a mean follow-up of 7.5 years. On the other hand, experimental work in immature rats submitted to shockwave therapy have demonstrated long-term effects on renal function and permanent histological damage.[27] Similarly, a study on 29 children with a mean follow-up of 9 years revealed significant alterations of renal growth, although the authors could not determine whether these alterations were secondary to the ESWL treatment effect or to some underlying conditions intrinsic to pediatric kidneys with urolithiasis.[28] Thus, the long-term effects of ESWL on the growing kidneys has not been well established, indicating that further studies with long-term follow-up are required to resolve the major concerns about the potential hazards of ESWL in infants and young children.

The optimal treatment of upper urinary tract calculi in infants remains a matter of debate. Apart from ESWL, the other treatment options include the 'mini-perc', ureteroscopy and open surgery. The 'mini-perc' is a minimally invasive technique pioneered by Jackman and associates in 1998, wherein using a 11F peel-away vascular access sheath percutaneous nephrolithotomy is performed utilizing pediatric instruments and electrohydraulic lithotripsy.[29] From a group of seven infants, they obtained a stone-free rate of 85% without any major procedure-related complications or blood transfusion requirements. However, the 'mini-perc' is a technically demanding procedure and has a significant 'learning curve' even with an experienced endourologist. Recently ureteroscopy employing slender endoscopes has been used to treat urinary tract calculi in infants and small children.[30] Thomas and colleagues managed 29 pre-pubertal children including three infants with ureteroscopy and lasertripsy and obtained an 85% stone-free rate after a single endoscopic session.[30] However, urinary extravasation was encountered in one child and, furthermore, all children with proximal ureteral calculi required a secondary procedure to achieve stone-free status. Another more traditional form of treatment for upper urinary tract calculi in small children has been open pyelolithotomy/ureterolithotomy. The major disadvantages of open surgery are that it is invasive and is prone to significant morbidity; it should therefore be reserved for certain clinical situations such as large stone burden, failed ESWL/endoscopy and the presence of underlying structural abnormalities. Thus, when one compares the efficacy and safety of the various treatment options, ESWL appears to be the more favorable management modality for upper urinary tract calculi in infants.

Conclusion

Infants who have urolithiasis present unique challenges. In our experience ESWL can be used successfully for the treatment of upper urinary tract calculi in infants. This minimally invasive modality is suitable for stones at all levels in the upper urinary tract, irrespective of stone size. The efficacy of this treatment modality is enhanced by the almost negligible complication rate and it should be considered as a safer alternative to open surgery or endoscopic techniques. Long-term follow-up and metabolic evaluation are essential components of the overall treatment strategy. ☐

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