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Extracorporeal shock wave lithotripsy (ESWL) versus flexible ureteroscopy (F-URS) for management of renal stone burden less than 2 cm in children: A randomized comparative study

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Abstract
Objective: To compare the outcome of flexible ureteroscopy (F-URS) versus extracorporeal shock wave lithotripsy (ESWL) for the management of renal stone burden less than 2 cm in children.
Patients and methods: A randomized comparative study was conducted at our hospital between December 2013 and May 2015. Seventy two children with renal stone burden less than 2 cm were assessed for eligibility. Our primary outcome is to assess the stone free rate after the first session. The secondary goal is to assess the operative outcome and the associated postoperative complications.
Results: Finally, 57 children were completed the treatment and follow up; 27 patients in F-URS group and 30 patients in ESWL group. Patient's demographics and stone characteristics were comparable between both groups. F-URS group was associated with significantly longer operative time and hospital stay versus ESWL group. Overall complications occurred in 29.6% and 33.3% in F-URS groups and ESWL group, respectively (p value = 0.1) and most of them were of minor degree. F-URS was associated with significantly higher stone free rate after the first session which reached 81.4% versus 53.3% for ESWL group (p value = 0.00). The overall success was 92.5% and 90% in F-URS and ESWL group, respectively (p value = 0.5).

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Conclusion: Stone free rate after one session of F-URS is higher than ESWL with comparable rates of complications. F-URS could be offered to children who are less likely to respond completely after ESWL monotherapy.

Introduction

In 1986, Newman and his colleagues published the first report on management of pediatric renal calculi using ESWL [1] and since that time it has been the first choice for management of renal calculi less than 2 cm in children worldwide [2]. However, it still has some drawbacks; the success rate after the first session is low and more than half of the treated children would require an additional sessions [3,4].

Re-ESWL is considered a large burden on the child and his family as it requires anesthesia again with more stress on the child and parents and also multiple sessions may have a hazardous effect on the child's kidney [5]. With the evolution in the technology and miniaturization of the endoscopic instruments many minimal invasive procedures have been used as an alternatives to ESWL in many centers worldwide including mini-PCNL, micro PNL, ultra-mini PCNL and retrograde intrarenal surgery (RIRS) [6].

F-URS in association with holmium: YAG laser can fragment any stone irrespective of its size, composition and site in contrast to ESWL that has many limitations [7]. The safety and efficacy of F-URS have been proved in children in recent years [8], however only one randomized study compared it with ESWL in children [9]. We designed this randomized study to compare the efficacy and safety of ESWL and F-URS for treating renal calculi less than 2 cm in children.

Subjects and methods

A randomized controlled study was conducted at our hospital between December 2013 and May 2015. We included patients less than 18 years with renal stone burden less than 2 cm for whom treatment was indicated. We excluded those with acute urinary tract infection, renal insufficiency, renal congenital anomalies, distal obstruction, previous failed intervention, bleeding diathesis and unfit for general anesthesia. All patients were evaluated preoperatively by history taking, routine laboratory work-up and imaging. All patients underwent preoperative imaging with renal ultrasonography (US), plain X-ray and non contrast spiral computerized tomography (CT). Patient's demographics, stone characteristics (size, site, side, number, density) were collected. Eligible patients were randomized using sealed opaque envelopes between F-URS group and ESWL group. Randomization was done in the clinic. The study protocol was approved by the hospital ethics committee. Informed consents including the procedure and possible complications were taken from all parents.

Surgical procedures

1. F-URS group (27 patients).
   All patients underwent Double J (DJ) stent insertion 2–4 weeks preoperative to allow passive dilatation. The procedure was carried out under general anesthesia in the lithotomy position started with stent removal and insertion of 2 guide wires; one for safety and one working wire for flexible ureteroscopy entrance, we used FLEX-X^{C} (digital) 8.5 Fr. flexible ureterorenoscope (Karl Storz Endoskope, Tuttlingen, Germany) with laser disintegration of stones using holmium:YAG laser (Versa Pulse PowerSuit 20 W; Lumenis Inc., Dreieich-Dreieichenhain, Germany) at energy of 0.4–0.6 J and pulse rate of 10–15 Hz. Stones were fragmented into powder without extraction. Hydrodilatation was used and ureteral access sheath not used. All patients underwent postoperative ureteric catheter insertion for one day except in case of ureteric injury or with sizable residual fragments DJ stent insertion was done.

1. ESWL group (included 30 patients):
   The procedure was carried out using electromagnetic machine (Dornier Gemini lithotripter®) under general anesthesia in a supine position. ESWL session is usually started at E1 for firstly 250 shocks, and then moving to next level for the next 250 shocks and the voltage is then gradually increased up to a maximum of E5. The shock waves were delivered at a rate of 70 shocks/min. The number and energy of shock waves were modified until adequate fragmentation was achieved or the maximum number of shocks was reached. A maximum of 2600 shocks were planned for each session or 75 J energy of shock waves.

Outcome

All patients underwent initial follow up after 2 weeks then after 1 month with US and plain X-ray, patients with significant residuals more than 4 mm after one month were scheduled to another session. NCCT was carried out after 3 months for those who received only one session to ensure complete clearance of all fragments, finally stone free rate was defined by absence of any residuals after 3 months. The primary outcome is to assess the stone free rate after one session treatment then the overall success. The secondary outcome is to compare between both techniques as regard the mean number of sessions required to achieve complete clearance. Operative and postoperative parameters of the first session including operative time, intra and postoperative complications, fluoroscopy time, postoperative hospital stay. Complications were classified according to the modified Clavien–Dindo system.

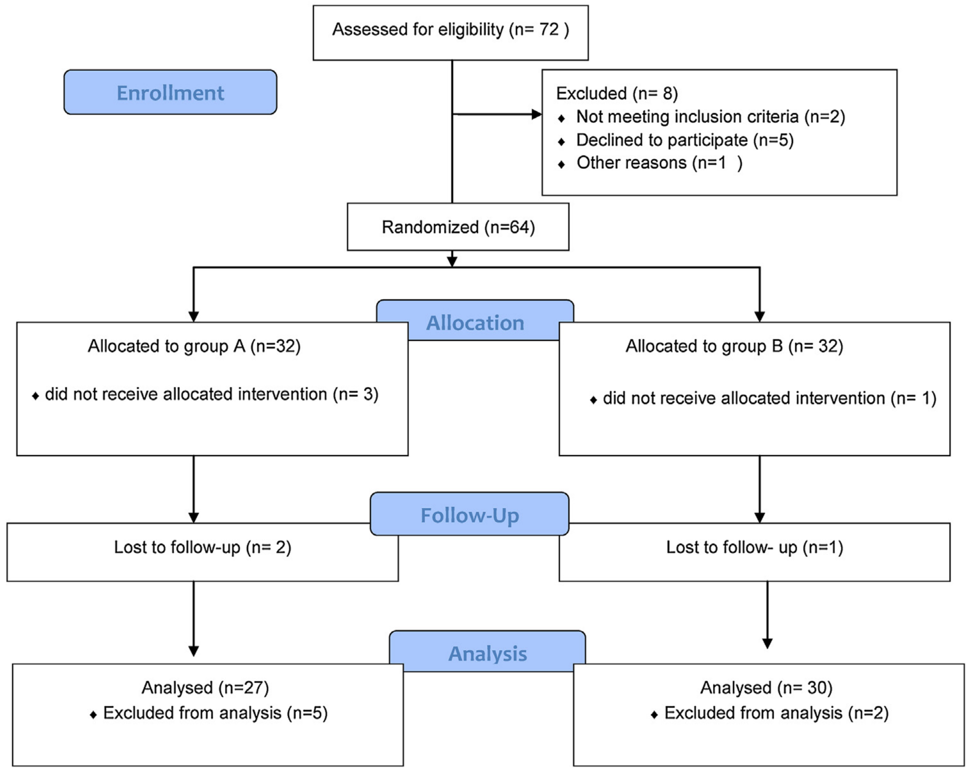

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) diagram for patients' flow through the study.

Statistical analysis

Continuous variables were recorded as means with SDs, categorical variables were recorded as frequencies. Differences between the groups were assessed using Student's *t*-test for continuous variables, and Chi square test for categorical variables with p value ≤ 0.05 indicate significance. All statistical analyses were performed using IBM statistical software version 16 (Chicago, IL, USA).

For calculating the sample size, considering the following factors; type 1 statistical error less than 5% and type 2 statistical error less than 20%, possible drop-out rate of 10% and based on previous reports [10–12]; the difference in first session success rate between F-URS and ESWL is 35%. A total sample of 60 patients will be required, 30 patients in each group.

Results

From 72 patients who were tested for eligibility 64 were randomized into both groups. After allocation 3 patients in F-URS group didn't receive the treatment; 1 patient due to technical problems in the laser machine, in 2 patients stones were migrated to the ureter before the procedure and they were managed with ureteroscopic stone extraction using semigrid URS. In ESWL group 1 patient didn't attend at his appointment. Two patients in F-URS group and 1 patient in ESWL group didn't complete the follow-up regimen and there were excluded. Finally, 57 patients completed the treatment and follow up, 27 patients underwent F-URS and 30 underwent ESWL (Fig. 1).

The 2 groups were comparable as regard age, Sex and BMI (Table 1). All patients had irrelevant medical and surgical histories except for 3 patients; 1 patient in F-URS group underwent previously urteroscopic stone extraction for lower end ureteric stone at the same side of intervention, while in ESWL group 2 patients underwent ESWL previously on the contralateral side. Out of 57 patients, the main presentation was pain in 45 (79%) patients, incidentally discovered in 8 (14%) patients and hematuria in 4 (7%) patients. The mean (SD) stone size was 14 (3.6) mm and 12.4 (3.4) mm in groups 1 and 2, respectively with no significant difference (p value = 0.07). Both groups were comparable as regard stones number, side, site and density (Table 1).

1st session parameters

The operative time was significantly longer in F-URS group (Table 2). In F-URS group the procedures were aborted in 2 patients due to hematuria in one patient with difficulty to reach the stone and ureteric injury in the other one. In ESWL group all patients completed the treatment sessions without complications. In ESWL group, 17 (56.6%) patients underwent fluoroscopy guided ESWL and the radiation exposure time was comparable to F-URS group (p value = 0.09). For group 2 the mean (SD) number of delivered shocks and total received energy were 2101 (340) and 68.2 (16) Joules (j), respectively.

Postoperative complications were classified according to Clavian system. Overall 8 (29.6%) patients in F-URS group and 10 (33.3%) in ESWL group (p values = 0.1) developed complications. All complications were of minor degree except in 4 patients (2 per each group). In F-URS group 2 (7%) patients developed GIII complications that include ureteric wall injury required stent insertion in one patient, while the other patient admitted 1 week postoperatively with obstructed kidney and high grade fever due to lower end ureteric stone and he underwent also stent insertion. In ESWL group 2 (6.6%)

Table 1 Patients' demographics and stone characteristics.

	F-URS group ($n=27$)	ESWL group ($n=30$)	p value
Mean (±SD) age (Y.)	6.5 (3.3)	7.4 (2.9)	0.15
Gender, pat. no. (%)			0.1
Male	21 (77.8%)	18 (60%)	
Female	6 (22.2%)	12 (40%)	
Mean (±SD) BMI (kg/m^2)	16.2 (1.2)	16 (1.1)	0.6
Mean (±SD) stone size (mm)	14 (3.6)	12.4 (3.4)	0.07
Stones no. (%)			0.7
Single	19 (70.4%)	20 (66.7%)	
Multiple	8 (29.6%)	10 (33.3%)	
Laterality, pat. no. (%)			0.6
Right	15 (55.6%)	15 (50%)	
Left	12 (44.4%)	15 (50%)	
Stone site, pat. no. (%)			0.3
Renal pelvis	14 (51.9%)	13 (43.3%)	
Calyceal	7 (25.9%)	13 (43.3%)	
Pelvis + calyceal	6 (22.2%)	4 (13.3%)	
Mean (±SD) Hounsfield unit (HU)	613 (223)	665 (214)	0.4
Stone opacity, pat. no. (%)			0.4
Radio-opaque	10 (37%)	16 (53.3%)	
Faint radio-opaque	6 (22.2%)	4 (13.3%)	
Radiolucent	11 (40.7%)	10 (33.3%)	

Table 2 Operative and post operative outcome.

	F-URS group ($n=27$)	ESWL group ($n=30$)	p value
Mean (SD) operative time (min)	60.8 (11.5)	39.5 (9)	0.03
Mean (SD) fluoroscopy exposure (sec.)	65 (21)	97 (50)	0.09
Mean (SD) postoperative hospital stay (days)	1.3 (0.45)	0	.00
Post operative complications	8 (29.6%)	10 (33.3%)	0.1
Minor Clavian (I–II) complications	6 (22.2%)	8 (26.6%)	
Major Clavian (III–IV) complications	2 (7%)	2 (6.6%)	

patients developed GIII complications, both patients presented with obstructed kidney by steinstrasse and recurrent attacks of fever; they were managed stent insertion (Table 2).

Stone free rate

The first session was successful in 22 (81. 4%) patients in F-URS group and 16 (53.3%) in ESWL group (p value = 0.00). In F-URS group 3 patients required an additional 1 session to achieve an overall 92.5% success rate, while 2 patients were shifted to ESWL. In ESWL group 11 patients required an additional sessions (1 session in 6 patients, 2 sessions for 3 patients and 3 sessions for 2 patients) to achieve an overall success of 93.3% while 3 patients had a persistent significant lower calyceal residuals and they were managed conservatively (Table 3).

Discussion

Pediatric urolithiasis represents a large problem in the developing countries where it is considered as an endemic disease [13]. Children are considered a high risk group for stone recurrence even in absence of residual fragments or anatomical factors [14]. Tasian et al. found recently that nearly 1/4 of children usually develop stone recurrence half of them at 3 years [14]. Moreover, presence of small residual fragments in children post intervention is clinically significant and associated with high risk of symptoms recurrence and stone growth [15]. This means that these patients would require many procedures in their pediatric age. This consumes many resources and represents a large burden on the family as well as the health care system; therefore, children should receive treatment that achieve high success rate with less morbidity and minimum number of treatment sessions.

It is well known that ESWL is safe and effective option for management of pediatric renal stones less than 2 cm, but the problem is the crucial need to achieve complete clearance that is to prevent the adverse clinical outcome of residual fragments [15]. The overall success of ESWL in the literature is high and it varies between 71% and 90%, however the success rate after one session is low and mean number of sessions required to achieve stone free varies between 1.5 and 1.9 [3,10,11]. In a large series that included 408 renal calculi the success rate after one session was 44.1% [3], El-Nahas et al. investigated 207 patients with mean stone size 11.6 mm (range 5–25) and the success rate after one session was 39% [10]. Habib et al. treated 186 stones with mean stone size 1.35 ± 0.8 cm and only 50.5% of the stones cleared after one session [11]. Therefore, ESWL has an important drawback that half of children would require at least 2 sessions to achieve clearance, also after multiple sessions the failure is expected in about 10–30% and this triggered the urologists to search for other minimal invasive procedures like PNL and retrograde intrarenal surgery (RIRS).

Table 3 Success rate.

	F-URS group ($n = 27$)	ESWL group ($n = 30$)	p value
Mean (SD) sessions no.	1.1 (0.3)	1.5 (0.6)	0.01
1st session success, pat. no. (%)	22 (81.4%)	16 (53.3%)	0.00
Overall success	25 (92.5%)	27 (90%)	0.5

The efficacy and safety of flexible ureterosopy in children have been proved previously and it's used currently in many centers worldwide [8,16]. The success rate is higher than 80% after one session; Kim et al. performed 170 ureteroscopic procedures with mean stone burden of 6.1 mm (range 3–24), they reported a success rate of 100% for stone burden ≤1 cm and 97% for >1 cm [8]. Erkurt et al. treated 65 patients with mean (range) stone size 14.66 (7–30) mm and 83% become stone free after one session [17]. Corcoran et al. reported 94% success rate for a mean stone size 8.8 mm (1.5–25) [12]. Resorlu et al. treated 95 patients with mean stone size 14.3 mm (10–30) and the success rate was 84.2% [18]. The literature is still lacks randomized studies comparing flexible URS with ESWL in children. Our study is the second randomized one to compare ESWL versus RIRS in children after Mokhless et al. in 2014 [9].

We observed a comparable overall success between both techniques, however after the first session only F-URS showed a significant higher efficacy which reached 81.4% versus 53.3% for ESWL (p value = 0.00). These results are comparable with that we previously mentioned. Also there is another advantage of F-URS which is the less radiation exposure which represents a higher risk on the children. The problems of F-URS were the longer operative time and hospital stay in addition to the higher cost.

One of the limitations in our study is in that we used a preliminary DJ stent insertion for all patients to allow passive dilatation. Accessing the upper tract using flexible uretrosocpy is difficult in children without ureteral dilatation. Erkurt et al. succeeded to introduce the flexible URS over a guide wire without dilatation in 20 out of 65 patients (30.8%) [17], while Kim et al. succeeded in 75 (44%) out of 170 patients [8]. Therefore, more than half of the children would require either passive or active ureteral dilatation for accessing the upper tact. Active ureteral dilatation can be done using serial ureteral dilator, balloon dilatation, access sheath or by usage of semi rigid URS, but also the active dilatation was not successful in about 40% of patients in 2 previous reports [12,17]. Corcoran et al. tried to predict those patients for whom successful upper tract access can be achieved from first session without need of preoperative stent by doing active ureteral dilatation up to the iliac vessels and they failed in 40% and unfortunately they couldn't identify the predictors and they recommended finally an initial attempt with ureteroscopy and if it failed stent insertion for passive dilatation is the correct choice [12].

We preferred to use passive dilatation for many reasons; initially we use a larger size flexible URS (Karl Storz FLEX-XC (digital) 8.5 Fr) than all the previous studies which is the first time to be used in children. We tried to minimize the problems associated with active dilatation (failure and complications) and also to standardize the technique in all patients to avoid the affection on the outcome by using different methods.

Both groups were comparable as regard to the minor and major complications, we reported 29.6% overall complications following F-URS, but only 2 were of major degree that required only stent insertion, our results are in harmony with the literature Most of the complications reported in the literature were of minor degree and the only reported major complications was ureteral perforation and all these patients were managed with stent insertion only. Corcoran et al. and Erkurt et al. reported 2 cases of ureteral perforation in their series representing 6.6% and 3% respectively [12,17]. We reported only one case (3.7%) of ureteric injury.

Although the higher initial success of F-URS in association with less radiation exposure and comparable complications rate to ESWL, we think that ESWL is still the first choice in well selected patients. Identification of patients who will respond to ESWL after one session was difficult in our study due to small sample size. Many previous studies tried to identify these factors using multivariate analysis. Stone size was an important determinant of ESWL success in most of these studies [4,19], El-Assmy et al. found that stone attenuation ≤600 Hounsfield unit (HU) was an independent predictor of success [4], McAdams et al. concluded that only attenuation in HU was a significant predictor of success when patients were stratified into 2 groups (less than 1000 and 1000 HU or greater) [20]. El-Nahas et al. found that calyceal location adversely affect the success rate in children, it was the only study that found a correlation between the site and success in children [10].

Finally we acknowledge that our study has some limitations, initially the small sample size prevented us from performing subgroup analysis, and then we didn't estimate the cost which is the major disadvantage of using F-URS.

Conclusion

F-URS is a safe and effective option for treating renal stones in children and it could be offered to children who are less likely to respond completely after ESWL monotherapy.

Informed consent

Informed consents including the procedure and possible complications were taken from all parents.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest

The authors declare that there is no conflict of interest.

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Ethical Committee Approval

The study was approved by Faculty of Medicine, South Valley University ethical committee under number 00231.

Authors' contributions

Gamal A. Alsagheer: principle investigator.

Atef Fathi: data collection.

Mohamed Sayed Abdel-Kader: manuscript revision.

Ahmed M. Hasan: data collection and writing.

Omar Mohamed: data collection and writing.

Osama Mahmoud: data collection and writing.

Mostafa Abdel Razek: data collection and writing.

Ahmad Abolyosr: manuscript revision.

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