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Electromagnetic and Electrohydraulic Shock Wave Lithotripsy-Induced Urothelial Damage: Is There a Difference?

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Abstract

Purpose: To evaluate and compare the acute effect of electromagnetic and electrohydraulic extracorporeal shockwave lithotripsy (SWL) on the urothelial layers of kidney and ureter.

Materials and Methods: Fifty patients, 29 males (58%) and 21 females (42%), with an average age of 51.68 years (range: 37–70) who underwent SWL application in two different centers were included. Twenty-eight patients (56%) were treated with electrohydraulic and 22 (44%) were treated with electromagnetic lithotripsy. Urinary cytologic examinations were done immediately before and after SWL therapy and 10 days later. The average numbers of epithelial cells, red blood cells (RBC), and myocytes were counted under $40\times$ magnification.

Results: There were significant differences in the number of epithelial cells and RBC before and after immediate application of SWL: 1.66 and 14.9 cells/field, ($p=0.001$), 5.44 and 113.45 cells/field, respectively ($p=0.001$). The number of RBC was significantly higher in patients treated with electromagnetic lithotripsy than those treated with electrohydraulic: 141.9 and 93.4 cells/field, respectively ($p=0.02$). No myocyte or basement membrane elements were detected in any of the cytologic examinations. Cytologic examinations done after 10 days of SWL therapy revealed recovery of all abnormal cytologic findings.

Conclusions: The acute increments in the number of epithelial cells and RBC after SWL were statistically significant but it was not permanent. SWL-induced urinary urothelial lesion is limited to the mucosal layer and there was no evidence of damage to the basal membrane or muscle layer. Electromagnetic lithotripsy caused high numbers of RBC than the electrohydraulic device on the postimmediate urine cytologic examination.

Keywords: urolithiasis, SWL, ureter

Introduction

Extracorporeal shockwave lithotripsy (SWL) represents the corner stone in the urologist's armamentarium for the treatment of renal and upper ureteral stones. It is the least invasive treatment modality for urinary calculi; however, its established efficacy has been associated with a number of side effects and complications. Several reports in the literature are present regarding the possible harmful effect of extracorporeal SWL on the kidneys and adjacent organs: the lungs, liver, pancreas, and intestine.[1–5] Perirenal hematoma with or without hematuria is the most common acute complication. Transient increase in intrarenal vascular resistance, diastolic blood pressure, and markers of tubular damage was reported after SWL.[6–9] Long-term complication of SWL is rare and controversial. Development of hypertension as a late complication was reported in some studies[7,9–11] but could not be confirmed by others.[12,13] Diabetes mellitus was reported as a late complication after SWL due to acute necrotizing pancreatitis.[2,11] The majority of the studies about the side effects of SWL investigated the parenchymal damage and renal function, however, only few studies investigated the possible effect of SWL on the peristaltic movement of the ureter.[14,15] Recently, we have published a study where the effect of electrohydraulic lithotripter on the urothelial and muscle layer of the ureter and kidney was investigated.[16] The injury on the mucosal layer was limited to the epithelial and it was temporary. A lot of prospective randomized trials compared electrohydraulic with electromagnetic lithotripters for stone disintegration and induced renal trauma.[17,18] These studies showed that Dornier electrohydraulic lithotripters are still the gold standard in disintegration of the pelvicaliceal stones with less

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renal-induced trauma and postoperative complications.[17,18] To our knowledge, there is no study that compared the two lithotripters in terms of damage on the urothelial layer. In this study, we sought to evaluate and compare the urothelial damage caused by electromagnetic and hydraulic lithotripters in patients who underwent SWL application due to kidney or ureteral stones.

Materials and Methods

Fifty patients, 29 males (58%) and 21 females (42%), with an average age of 51.68 years (range: 37–70) who underwent SWL application in two different centers between July 2015–November 2015 and July 2009–October 2009 were included. Thirty-three (66%) patients had renal pelvic stones and 17 (34%) of them had upper ureteral stones. The average size of renal pelvic stones and ureteral stones was 13.12 mm (range: 9–19) and 10.06 mm (range: 5–15), respectively. The demographic characteristics of the patients are shown in Table 1. Twenty-eight patients (56%) underwent electrohydraulic lithotripsy (ELMED, Turkey) and 22 (44%) underwent electromagnetic lithotripsy (MODULITH SLX-F2; Storz Medical, Switzerland). Urinary cytologic examinations were done immediately before and after SWL therapy and 10 days after SWL application. Urine sample was more than 20 mL to a certain sufficient cytologic evaluation. The average numbers of epithelial cells, red blood cells (RBC), and myocytes were counted under 40 × magnification. Triocular light microscopes were used (model BX51TF; Olympus BX51, Tokyo, Japan) and centrifuge machine (ROTOFIX32A, Germany and Shandon Cytospin 4, Germany). The change in the number of RBC was used as an indicator for the degree of urothelial damage on the superficial layer, however, the number of muscle cell or basement membrane element was used to detect any deep damage to the submucosal, basement membrane and muscle layer. Cytologic examination done after 10 days of SWL therapy was used to detect the recovery of urine cytology abnormalities. Any patient with history of renal or ureteral surgery, patient with a stenting, and patient with previous application of SWL were excluded. The number of shock waves applied for each patient was 2000 per session for all patients. All patients had effective fragmentation of the stone. No anesthesia was given, only nonsteroidal anti-inflammatory drugs were administered when needed. In electrohydraulic lithotripter, the treatment was started at 12 kV and the energy was increased step by step up to 19 kV. In electromagnetic lithotripter, the energy level was changed from 1 to 7 kV. The rate of shock wave delivery was identical in both groups, 60 SW/min. The settings of the device in each group in terms of focal zone (–6 dB), peak pressure (MPa), and energy density (mJ/mm^2) were standard for all patients in the same group.

Statistical analysis

Student's two-tailed paired test was done to compare the number of cells before and after immediate SWL cytologic examination in both lithotripters. The Pearson correlation test was used to determine the factors that influence the increment of cell number after SWL.

Results

There was a significant difference in the number of RBC before and after immediate SWL: 5.44 and 113.45 cells/field, respectively ($p = 0.001$). Similarly, the average numbers of epithelial cells before and after immediate SWL were 1.66 and 14.9 cells/field, respectively ($p = 0.001$). There was significant difference between patients with renal or ureteral stones in terms of numbers of RBC in the postimmediate SWL: 150 and 42.58 cells/field, respectively ($p = 0.001$). Also, there was significant difference between patients with renal or ureteral stone in terms of epithelial cells: 18.72 and 6.59 cells/field, respectively ($p = 0.001$) (Table 1). The number of RBC after immediate SWL was significantly higher in patients who underwent stone fragmentation using the electromagnetic lithotripter device than those who used the electrohydraulic device: 141.9 and 93.4 cells/field, respectively ($p = 0.022$). Table 2 shows the comparison between the findings of both lithotripters. No myocyte or basement membrane elements were detected in any of the cytologic examinations. The controlled cytologic examinations, which were done after 10 days of SWL therapy, revealed recovery of all cytologic findings with abnormalities and the findings became similar to that of pre-SWL cytologic examination.

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE STUDY GROUP

	Patients with renal stone	*Patients with ureteral stone,* n *(%)*	*Total*
Patients (*n*, %)[a]	33 (66)	17 (34)	50 (100)
Sex (male, female)	20	9	29
	13	8	21
Age (year, average, range)	51 (27–75)	55 (45–70)	53 (27–75)
Stone size (average range, mm)	13.12 (9–19)	10.06 (5–15)	11.98 (5–19)
Transitional cell at pre-SWL cytologic examination (average, cells/field)	2.03 (0–6)	1.29 (0–4)	1.66 (0–6)
Transitional cell at postimmediate SWL (average, cells/field)	18.72 (3–40)	6.59 (3–6)	14.90 (3–40)
Transitional cell at post-10 days SWL (average, cells/field)	1.03 (0–30)	1.82 (0–6)	4.56 (0–30)
RBC before SWL (average, cells/field)	7.30 (0–30)	1.82 (0–6)	5.44 (0–30)
RBC after SWL (average, cells/field) range	150 (40–350)	42.58 < 50 (31–70)	113.45 (31–350)
RBC after SWL (average, cells/field) 10 days	2.77 (0–25)	3.88 (0–20)	3.4 (0–25)
Shock wave (*n*)	2000	2000	2000

[a]*n* = number; RBC = red blood cells; SWL = extracorporeal shockwave lithotripsy.

Table 2. Comparison Between Electrohydraulic and Electromagnetic Lithotripters in Terms of Clinical Variables

Variable	*Electrohydraulic lithotripter*	*Electromagnetic lithotripter*	p
Patient (*n*)	28	22	
Sex (male/female) (*n*)	14/14	15/7	
Renal stones (*n*)	16	17	
Ureteral stones (*n*)	12	5	
Age (year, average, range)	52.7 (27–75)	51.68 (37–70)	
Stone size (mm, average, range)	11.7 (5–18)	12.86 (5–19)	
Pre-SWL transitional cell (average, cells/field)	1.5 (0–7)	1.3 (0–6)	
Pre-SWL RBC (average, cells/field)	5.28 (0–28)	6.22 (0–30)	
Postimmediate SWL transitional cell (average, cells/field)	12.8 (3–34)	17.11 (4–40)	0.16
Postimmediate SWL RBC (average, cells/field)	93.28 (31–320)	142.06 (34–350)	0.02
Postimmediate SWL transitional cell (average, cells/field) in patients with renal stones	17.95	19.47	0.34
Postimmediate SWL RBC (average, cells/field) in patients with renal stones	128	171	0.01
Postimmediate SWL transitional cell (average, cells/field) in patients with ureteral stones	5.5	9.2	0.12
Postimmediate SWL RBC (average, cells/field) in patients with ureteral stones	47	41	0.15

n = number of patients.

Discussion

It is well known that extracorporeal SWL is a safe procedure and has no significant long-term effects on renal function regardless of the type of machine used. However, SWL does cause pathologic changes in various organs, but little is known about its effects on the ureter and its peristaltic movement. In this study, we sought to investigate and compare the acute effects of SWL on the urothelial mucosa caused by two different types of lithotripters. Few studies have investigated the effect of shock waves on the ureteral muscle and peristaltic movement and no study detected any difference between the types of shock waves applied in the lithotripter machines.[14,15,19] There are three different mechanisms for shock wave generation: electrohydraulic shock waves are generated via the spark-gap technology where high-voltage electrical current passes across the spark-gap electrode located within a water-filled container, an ellipsoidal metallic reflector is used to focus the shock waves in electromagnetic lithotripter: high voltage is applied to an electromagnetic coil to induce high-frequency vibration in an adjacent metallic membrane. This vibration is then transferred to a wave-propagating medium (i.e., water) to produce shock waves. The MODULITH SLX-F2 cylindrical shockwave generator and paraboloid reflector represent the most important elements. The piezoelectric lithotripsy creates ultrasonic vibrations, resulting in the production of a shock wave.

The mechanism of the damage caused by shock waves is expected to be caused by membrane permeability changes or cavitation-related effect.[20,21] To exclude any factor that may aggregate the effect of urothelial damage, any patient with previous surgery, severe hydronephrosis, stenting, or urinary tract infection was excluded. Previous surgery may cause fibrosis in the urothelial mucosa and thus the shock wave effect is underestimated; similarly, the presence of double J stent (DJS) may interfere with the pathway of shock waves, infection also makes the mucosa more fragile and thus overestimation of the shock wave damage is expected. Severe hydronephrosis leads to the movement of the stone during SWL application and thus may alter the mucosal injury. There was significant increment in the numbers of RBC and epithelial cells on the postimmediate urine cytologic evaluation. This increment was higher in patients with kidney stones. This indicates that there is injury to the urothelial layer and to the parenchymal kidney as the degree of RBC was higher in patients with kidney stones. This may be due to the passage of the shock waves through the kidney parenchyma. The last urine cytologic examination done after 10 days showed complete recovery of all abdominal findings in patients with kidney or ureteral stones. This means that the damage on the urothelial layer of the kidney and ureter is temporary and healing of the urothelial injury is established. However, this does not exactly exclude that there are no negative consequences on the kidney and ureteral function.

There was no element of the basement membrane or muscle cells in any of the urine cytology examination. This is an important issue because any damage on the muscle layer of the ureter will affect the peristaltic movement of the ureter or formation of the stricture of the ureter. The ureteral wall is not protected like that of kidney pelvis layer by the parenchyma of the kidney, so we expected more a harmful effect on the ureteral layer. Kirkali and colleagues investigated the ureteral layer damage after SWL on rabbits and found that there are obvious microscopic and functional findings that showed cellular and subcellular changes, which may lead to the reduction in the ureteral contraction.[14] These changes were reversible but repeating of the same application for SWL with higher energy may have some clinical impact on the ureteral contraction.[14] Horgan and colleagues reported increase in the contractility of the ureter and justified this by the increment of thromboxane B2 and prostaglandin F1 and x03AC.[19] Boybeyi and colleagues evaluated in an experimental trial the effect of electrohydraulic shock wave lithotripsy on the distribution of interstitial cells of Cajal (ICCs) in rabbit renal pelvis and proximal ureter.[15] They concluded that SWL may cause histopathologic alterations in the renal pelvis and ureter and reduced contractility of the ureter after SWL may not be attributed to altered distribution of ICCs in the renal pelvis and ureter.[15] It is clear that the ureteral muscle layer seems to be a possible target of the shock wave lithotripters and should be investigated in human and animal models. Any change in the contractility of the ureter leads to a significant effect on kidney function. This issue is supported by our finding that the electromagnetic lithotripter caused more RBC than the electrohydraulic lithotripter in the postimmediate SWL urine cytology. We believe that the nature and source of the shock waves may have different harmful effects on the urothelial mucosa, and this ascertains the claim of the author Zia Kirikali that different machines or high energy may have significant effects on the ureteral urothelial and ureteral muscle layer.[14] This also is supported by many reports in the literature that showed more efficacy for hydraulic lithotripters with less side effect and low renal damage.[17,18] Therefore, we may conclude that the electrohydraulic lithotripter causes less injury to the urothelial layer than electromagnetic lithotripter. The absence of the myocyte at cytologic evaluation shows that there is no acute damage to the muscle layer of the ureteral wall, but this finding alone is not enough to conclude that the peristaltic movement will not be negatively affected. We do recommend further studies to be carried out to investigate the effect of various types of SWL especially electromagnetic lithotripters with different voltage and different shock waves on the ureteral muscle layers and peristaltic movement. We also recommend that such studies should be carried out without timing gap as we have in our present study, and thus, the comparison between both lithotripters could be more objective.

The number of shock waves has a positive correlation with the number of RBC and transitional cells at postimmediate urine cytologic examination.[16] Connors and colleagues reported that treatment at a firing rate of 60 SWs/min produces less morphologic injury and causes less alteration in renal hemodynamics than treatment at 120 SWs/min in the pig model of SWL-induced renal injury.[22] However, in our present study, we applied the same number of shock waves for all patients in both centers, so we cannot comment on this parameter but it is logical that as the number of shock waves increases the expected effect on the urothelial layer should be aggregated.[16] The rate of shock wave administration was identical in both lithotripters 60 SWs/min, thus we could minimize the harmful effect of the shock waves. The voltage also should have a significant effect on the urothelial layers and renal parenchyma. Optimal voltage treatment protocol ensuring effective stone comminution while minimizing tissue injury is not well established. It was reported that escalating voltage treatment strategy produces better stone comminution than a fixed strategy and there may be a protective effect against damage caused by SWL with an escalating treatment strategy.[23] In our study, the energy was started at 13 kV and increased up to 17 kV in electrohydraulic lithotripter, however, in electromagnetic lithotripter, the energy level ranged from 1 to 7 kV. Focal size (–6 dB) (mm), peak pressure (MPa), and energy density (mJ/mm^2) were reported to have significant effects on the outcomes of SWL in terms of efficacy and safety.[24] Rassweiler and colleagues concluded that new theories for stone disintegration favor the use of slow shock wave sources with larger focal zones.[24] The use of slower pulse rates, ramping strategies, and adequate coupling of the shock wave head can significantly increase the efficacy and safety of SWL.[24] Electromagnetic lithotripter with clinical dose of shock waves delivered at a slow rate (27 SWs/min) using a novel wide focal zone (18 mm) and low acoustic pressure (<20 MPa) provided better stone breakage with less tissue injury.[25] In our study, the standard settings of electromagnetic lithotripter, high peak pressure (MPa90) and narrow focal zone (9 mm), may justify the high RBC number at postimmediate SWL urine cytologic examination in comparison to less energy density, large focal zone (16 mm), and low peak pressure (MPa40) in electrohydraulic lithotripter. These facts may lead us to conclude that adjustment of focal zone, peak pressure, and shock wave delivery rate may be beneficial in electromagnetic lithotripter especially for patients with ureteral stones to minimize the urothelial injury.

Conclusion

The acute increments in the number of epithelial cells and RBC after SWL were statistically significant without clinical importance. SWL-induced urinary urothelial lesion is superficial and there is no evidence of damage to the basal membrane or muscle layer. Electromagnetic lithotripsy caused high numbers of RBC than electrohydraulic device on the postimmediate urine cytologic examination especially in patients with renal stones. Electromagnetic lithotripsy seems to have a more acute harmful renal effect than electrohydraulic lithotripters. Further studies with a larger number of patients, including human and animal models using electron microscopic evaluation of the ureter, are needed to confirm our findings and evaluate possible effects on the peristaltic movement of the ureter.

Compliance with Ethical Standards

Informed consent: The patients were informed about the operation and consent was obtained from the patients. Researches involving human participants/animals: Certificate from the National Institute of Health (NIH), Number: 1720774.

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

ICC = interstitial cells of Cajal
RBC = red blood cells
SWL = extracorporeal shockwave lithotripsy