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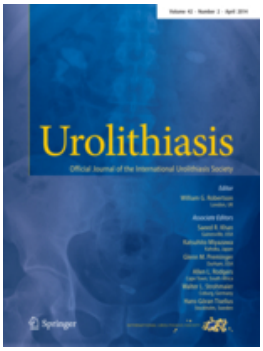

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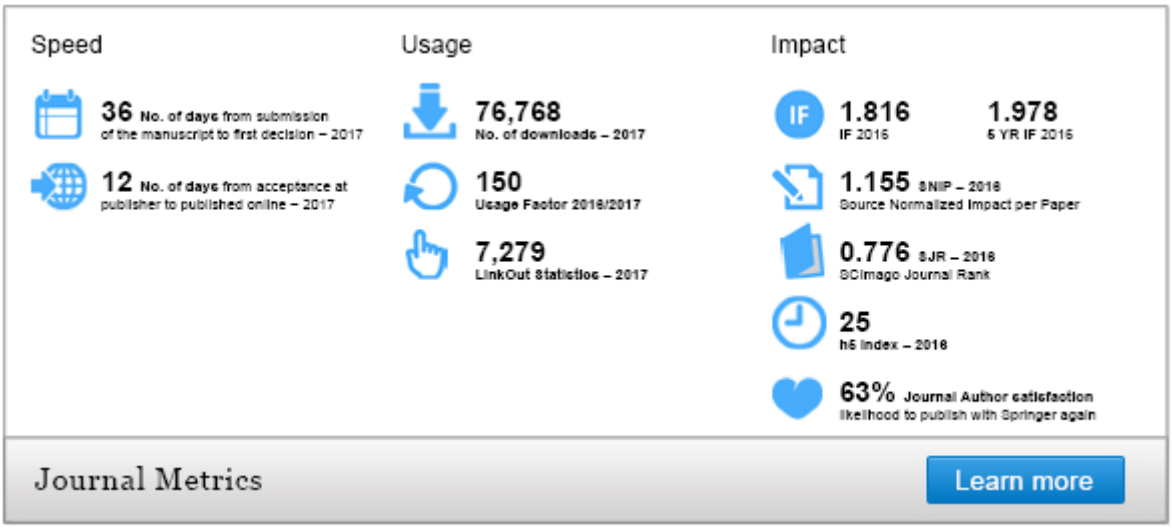

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ORIGINAL PAPER

Tissue effects of intracorporeal lithotripsy techniques during percutaneous nephrolithotomy: comparison of pneumatic and ultrasonic lithotripters on rat bladder

Akif Diri · Berkan Resorlu · Muzeyyen Astarci · Ali Unsal · Cankon Germiyonoglu

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Abstract The objectives of this study were to determine the tissue effects of ultrasonic and pneumatic lithotripsy on the rat urothelium. The rats were divided into three groups. Groups I and II consisted of ten rats each that underwent intracorporeal lithotripsy (pneumatic and ultrasonic lithotripsy, respectively). Group III contained ten control rats and no lithotripsy method was used, they served as references for absence of injury. The light microscopy findings were evaluated as follows: squamous metaplasia, papillary projection, inflammation, increased stratification, and stone formation. In five (71.4%) animals of group II, bladders were edematous and hemorrhagic, macroscopically. Histologically, the bladder wall was normal in four rats of group I and in one of group II. There was a significant increase in inflammation (31.5%), squamous metaplasia (85.7%), papillary projection (71.4%), increased stratification (71.4%), and microscopic or macroscopic stone formation (85.7%) in the bladder wall of group II rats in comparison with group I and control group. In the rat model, we noted that ultrasonic devices have a potential risk for tissue injury. In turn, this was associated with a markedly increased deposition of CaOx stones in the kidney. When confronted with harder stones, pneumatic lithotripsy can be more effective while also minimizing tissue injury.

Keywords Lithotripsy · Percutaneous nephrolithotomy · Tissue effects · Urothelium

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Introduction

Percutaneous nephrolithotomy (PCNL) was introduced in 1976 by Fernström and Johannson [1]. Since then, efforts have been made to reduce its morbidity and mortality to the current status by development of fine instruments, nephroscopes, fluoroscopes, and stone fragmentation techniques. Today, PCNL is the treatment modality of choice for renal calculus disease.

Intracorporeal lithotripsy is an integral part of percutaneous stone treatment. Ultrasonic and pneumatic devices are the most commonly used intracorporeal lithotripters during PCNL [2]. Pneumatic lithotripters are effective and economic devices for fragmenting even the hardest of stones, but subsequent extraction of the stone fragments is required. Ultrasonic energy devices fragment calculi into small pieces and have the ability to aspirate these small particles through the hollow bore of the transducer, which eliminates manual stone extraction [3]. These two techniques have been extensively evaluated and compared in terms of their therapeutic efficacy; however, the potential tissue effects of these devices have not been thoroughly investigated in an animal model.

In this study, we examined and compared the possible tissue effects of pneumatic and ultrasonic lithotripters on the bladder wall, using the rats as our animal model.

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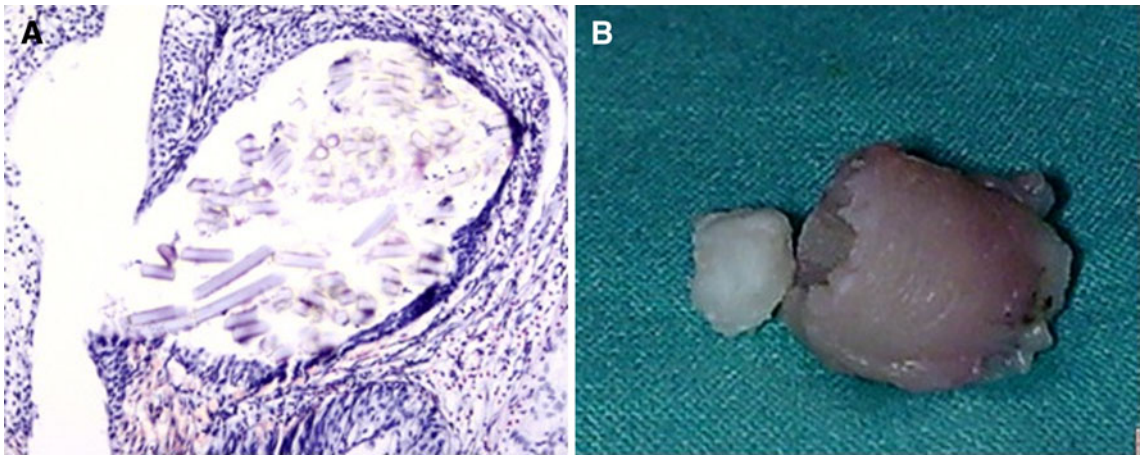

Fig. 1 Crystal deposition (**a**) and macroscopic stone formation (**b**) on rat bladder following lithotripsy (20 × 10 H&E)

Materials and methods

This study was approved by the institutional ethical board of Ankara Training and Research Hospital and was performed under institutional guidelines for the care and use of animals in research. Thirty Wistar rats weighing between 180 and 220 g were included in the study. The rats were divided into three groups. Groups I and II consisted of ten rats each that underwent intracorporeal lithotripsy (pneumatic and ultrasonic lithotripsy, respectively). Group III contained ten control rats and no lithotripsy method was used, they served as references for absence of injury.

All animals received intramuscular cefozoline sodium 20 mg/kg preoperatively for antibiotic prophylaxis and all surgical procedures were performed under ketamine HCl anesthesia (80 mg/kg) by intraperitoneal injection. Rats were positioned supine on the operating table. The abdominal area of each rat was shaved, and the operative field was prepared in a sterile manner using a povidine–iodine solution. The urinary bladder was exposed through a midline suprapubic incision. To evaluate the effects on the bladder wall, the lithotripters were introduced via the cystotomy, and the treatments were delivered in contact with the posterior bladder wall without exerting any pressure. The bladder wall effects were evaluated for the EMS Swiss Lithoclast pneumatic lithotripter and EMS ultrasound lithotripter. For the Lithoclast, a total of 60 shocks were delivered at maximum power with the 3.0 mm rod; for the ultrasonic lithotripter, 36 firing periods of 3 s at maximum power were delivered with the 3.0 mm rod.

At the end of the study (30 days after treatment), the animals were sacrificed for macroscopic and histologic examination of all of the treated sites. These bladder specimens were fixed in 10% formalin solution, embedded in paraffin wax, and the histological sections (4–6 μ) were stained by the immunohistochemical method. A histological evaluation was undertaken by an independent pathologist who had no prior knowledge of the experimental groups from which the specimens were derived. The light microscopy findings were evaluated with haematoxylin and eosin (H&E) stained slides as follows: squamous metaplasia, papillary projection, inflammation, increased stratification, and stone formation. The results were compared in the groups using the Kruskal–Wallis analysis with differences considered statistically significant at $p < 0.05$.

Results

One animal in group I, three animals in group II, and one animal in group III were lost during the follow-up with no apparent cause of the death. No adverse events were noted during the use of the pneumatic or ultrasound lithotripsy. There were no macroscopic differences in the bladder walls between the control and pneumatic lithotripsy groups. However, in five (71.4%) animals of ultrasonic lithotripsy group, bladders were edematous and hemorrhagic. Ultrasound energy induced hemorrhagic and edematous lesions. Furthermore, there was macroscopic stone formation in four of seven rats in the group II, which was thought to be related to mucosal damage during lithotripsy (Fig. 1).

Histologically, the bladder wall was normal in four rats of pneumatic lithotripsy group and there was mild inflammation in two rats (31.5%), squamous metaplasia in three (33.3%), papillary projection in one (11.1%), increased stratification in one (11.1%), and microscopic stone formation in two rats (22.2%). In the ultrasonic lithotripsy group, the bladder wall was normal in only one animal, and there was mild or severe inflammation in four rats (31.5%), squamous metaplasia in six (85.7%), papillary projection in five (71.4%), increased stratification in five (71.4%), and microscopic or macroscopic stone formation in six rats (85.7%) (Fig. 2). Specimens obtained from control group animals had no detectable abnormality except for one which had mild squamous metaplasia.

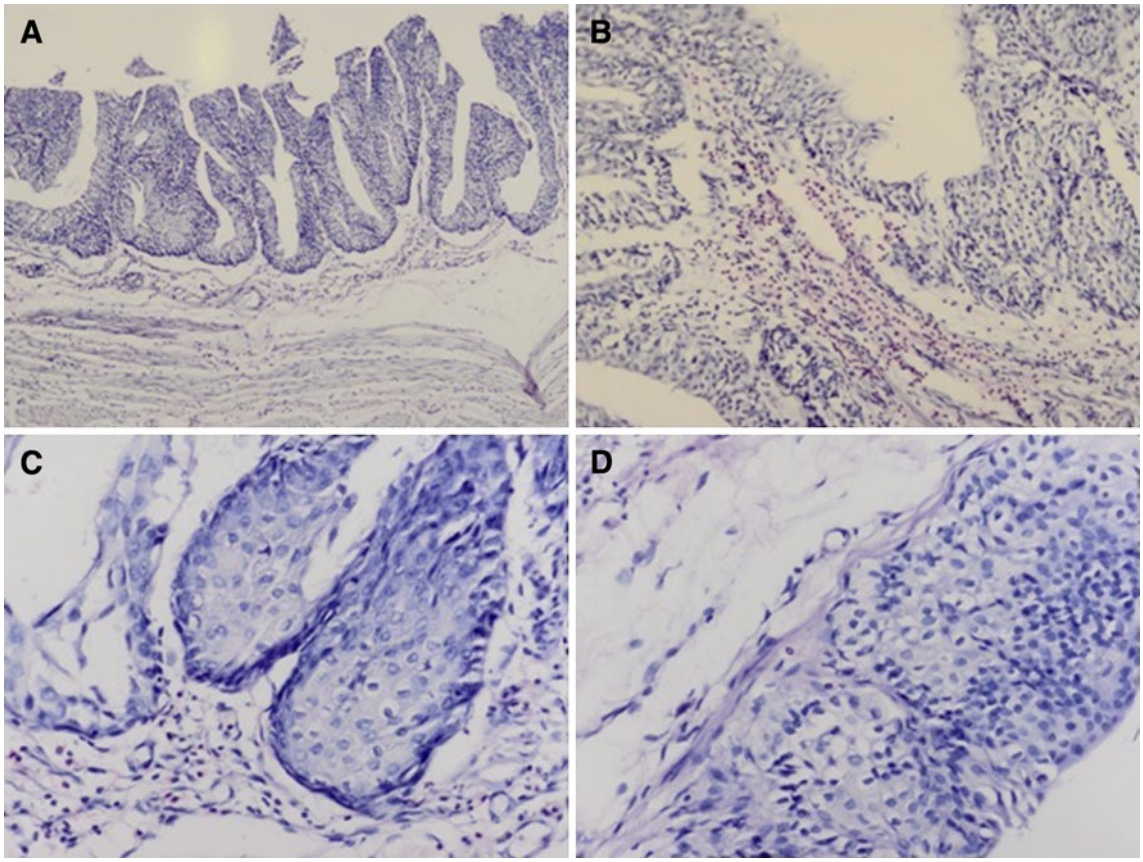

Fig. 2 Tissue effects of lithotripters on rat bladder (H&E; original magnification): **a**. Papillary projection (10 × 10 H&E). **b**. Inflammation (40 × 10 H&E). **c**. Squamous metaplasia (40 × 10 H&E). **d**. Increased stratification (40 × 10 H&E)

Table 1 Tissue effects of lithotripters on rat bladder

	Total	Group I (pneumatic)	Group II (ultrasonic)	*p* value	Group III (control)
No of Rats	25	9	7	0.036*	9
Squamous metaplasia (%)	10 (40%)	3 (33.3%)	6 (85.7%)	0.013*	1 (11.1%)
Papillary projection (%)	6 (24%)	1 (11.1%)	5 (71.4%)	0.152	–
Inflammation (%)	6 (24%)	2 (22.2%)	4 (57.1%)	0.013*	–
Increased stratification (%)	6 (24%)	1 (11.1%)	5 (71.4%)	0.012*	–
Stone formation (%)	8 (32%)	2 (22.2%)	6 (85.7%)		–

* Statistically significant at $p < 0.05$

There was a significant increase in inflammation, squamous metaplasia, papillary projection, increased stratification, and microscopic or macroscopic stone formation in the bladder wall of group II rats (ultrasonic lithotripsy) in comparison with group I (pneumatic lithotripsy) as shown in Table 1.

Discussion

PCNL was established as a minimally invasive treatment option for removal of kidney stones in the 1970s [1]. Today, it is the treatment of choice for large-volume stone disease with the advantages of better stone clearance, cost-effectiveness, and early convalescence as compared with other modalities like SWL or open surgery. An untreated kidney stone can damage the kidney; especially, struvite stones can destroy the kidney and cause life-threatening sepsis [4]. Studies have repeatedly demonstrated the safety and efficacy of this minimally invasive technique, maintaining acceptable stone-free and symptom-free results, while minimizing associated complications [4–7].

Intracorporeal lithotripsy is an integral part of percutaneous stone treatment. With the development of lithotripsy devices in recent decades, several intracorporeal lithotripsy procedures are now available for nephroscopic stone disin-

tegration. Electrohydraulic lithotripsy uses a shockwave generator in connection with a coaxial probe and induces cavitations to break the stone. This method is effective for most stones, but the major disadvantage is its relatively traumatic nature and potential to cause urothelial damage and tissue perforation [8]. The holmium laser uses a series of energy pulses to generate a plasma with subsequent shockwaves [9]. Advantages of laser energy include efficacy in fragmenting all types of urinary calculi, including hard stones, and the fact that the fibers are small enough to be passed through flexible endoscopes. However, in the management of large calculi, application of laser energy can be time consuming [9–11].

Because of the high complication rate noted with electrohydraulic lithotripsy and the inability of laser lithotripsy to concurrently remove stone fragments, currently the most commonly used lithotripters are ultrasonic and pneumatic devices. Ultrasonic lithotripsy uses mechanical energy created by piezo-ceramic elements; vibration is transmitted through rigid probes and the vibration induced at the tip results in a drilling action [12, 13]. Ultrasonic energy devices fragment calculi into small pieces and have the ability to aspirate these small particles through the hollow bore of the transducer, which eliminates manual stone extraction [3]. However, they are not universally successful, especially in the setting of harder cystine or calcium oxalate monohydrate stones. Pneumatic lithotripsy uses pressurized air to accelerate a projectile, which induces a shockwave by striking a probe [14]. Pneumatic lithotripters are effective and economic devices for fragmenting even the hardest of stones, but subsequent extraction of the stone fragments is required.

A large body of literature has developed documenting the clinical efficacy of lithotripsy modalities in performing fragmentation of renal calculi. However, limited data have been published about the potential tissue effects of these endourologic lithotripsy techniques. Teh et al. [9] compared electrohydraulic, pneumatic, and ultrasonic lithotripsy in a stone phantom model, as well as in a porcine model, judging the pneumatic lithotripsy technique as effective and clinically safe. In another investigative study, Denstedt et al. evaluated the acute and long-term tissue effects of the pneumatic devices in an animal model. They showed that pneumatic lithotripsy technique had no acute or long-term harmful effects to the surrounding tissue, especially compared with electrohydraulic and laser lithotripsy [15]. Piergiowanni and coworkers compared the gross tissue effects of the intracorporeal lithotripsy techniques on the pig urothelium [16]. They concluded that the pneumatic lithotripter is as safe as the ultrasonic device and safer than the laser and electrohydraulic lithotripsy devices. However, in this study, they evaluated only macroscopic tissue effects, and they did not make any comment about microscopic examination. In our study, several morphologic changes were noted in the bladder at gross inspection, especially, following ultrasonic lithotripsy, and significant differences were observed within groups on histopathological examination.

In a rat model, we noted that ultrasonic devices could potentially injure tissues. In turn, this was associated with a markedly increased deposition of CaOx stones in the kidney. Previous studies showed that renal tubular epithelial cell injury is a key factor in the stone formation process following shockwave lithotripsy [17–19]. Tissue injury during ultrasound lithotripsy can be due to either thermal or mechanical effect on the urothelium with direct application [15]. Direct application of the ultrasonic probe to the urothelium causes only edema and superficial changes. Nevertheless, overheating of the probe can cause injury. As the probe vibrates, the lost energy is dispersed as heat [20, 21]. Sufficient irrigation is necessary for cooling to prevent tissue damage. In this study, we made continuous irrigation during ultrasound lithotripsy. During pneumatic lithotripsy, only minimal effects appear on elastic tissue, even high energies can be used without significant tissue damage [14].

There are several limitations in our study. The first one is that there are a small number of animals in this study. However, for ethical reasons, we cannot use a large number of rats. A second limitation of this study is that, we analysed our results on bladder urothelium and renal collecting system may not behave in quite the same way. However, it does not seem reasonable to perform a study on kidney urothelial tissue because of rat's small renal collecting system.

Ultrasonic lithotripsy is the standard treatment modality used during PCNL because of its ability to simultaneously fragment stones and clear the resulting fragments with its simultaneous suction. When confronted with harder stones, pneumatic lithotripsy can be more effective while also minimizing tissue injury.

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