Effect of urine pH on the effectiveness of shock wave lithotripsy: A pilot study

Ahmad Majzoub, Ammar Al-Ani, Tawiz Gul, Hatem Kamkoum, Khalid Al-Jalham
Department of Urology, Hamad Medical Corporation, Doha, Qatar

INTRODUCTION

Urolithiasis is a common medical condition worldwide with prevalence rates reaching up to 20% in some areas of the world. Of particular significance is its tendency to recur; around 50% of stone formers will develop at least one recurrence during their lifetime. This characteristic demands the development of minimally invasive procedures successful in achieving stone clearance. Extracorporeal shock wave lithotripsy (SWL) is the least invasive surgical method with documented levels of success in treating stone disease. Since its

Abstract

Aim: Shock wave lithotripsy (SWL) is a well-established modality in the treatment of urolithiasis. Studying the effect of urine pH on SWL success is appealing as pH can be manipulated before SWL to insure a better outcome.

Materials and Methods: This is a prospective study performed at a tertiary medical center. Patients presenting to the SWL unit with a single renal stone <2 cm in size were included in this study. In addition to standard laboratory and radiologic investigations, urine pH measurement was performed on all patients before their procedure. The number of sessions performed, and the stone-free rate (SFR) were assessed. Patients were divided into two groups according to stone clearance. Group 1 was stone-free, whereas Group 2 had residual stones after three sessions of SWL. Data was also classified according to different pH ranges. Influential factors were compared among the study groups and pH ranges.

Results: A total of 175 patients were included in this study. The SFR was 54.3%. The mean number of sessions performed was 2.2 ± 0.8. Group 1 included 95 patients, whereas Group 2 had eighty patients. Among all studied factors, stone size (P = 0.03) and skin to stone distance (P = 0.04) significantly affected SFR with SWL. Urine pH was not found to have a statistically significant influence on SWL outcome (P = 0.51).

Conclusion: Urine pH was not found in this study population to influence the effectiveness of SWL. Further experimental studies are required to help investigate this notion.

Key Words: Extracorporeal shock wave lithotripsy, urine pH, urolithiasis
first introduction in the early 1980s,[4] SWL underwent major advancements that ultimately revolutionized the treatment of urolithiasis.

Several studies have investigated predictors of success with SWL. In addition to stone size and location, factors such as stone Hounsfield Unit (HU) and urine hardness were also investigated.[5,9] One study acknowledged the use of newer imaging techniques such as dual energy computed tomography (CT) to predict stone composition before SWL.[9] Lim et al. retrospectively studied 223 patients who underwent SWL and suggested that stones with higher radiodensity may be associated with higher failure rate.[6] The influence of urine features on SWL success rate first started with Li et al. who particularly assessed urine specific gravity (SG).[5] He demonstrated that stone breakage is more effective at urine SG of 1.040. In another study, however, this particular association was not detected.[10]

To the best of our knowledge, the effect of urine pH on stone-free rate (SFR) with SWL was never assessed before. In this prospective study, we aim to evaluate this particular factor, in addition to other predictors of SFR with SWL.

**MATERIALS AND METHODS**

This is a prospective study conducted in the lithotripsy unit of a tertiary medical center. The inclusion criteria were patients above 18 years of age presenting with a single renal stone <2 cm in size. While the exclusion criteria were patients taking medications known to alter urine pH such as potassium citrate or ascorbic acid; and the presence of multiple stones, of larger size, in other parts of the urinary system or with indwelling ureteral stents. Patients meeting the inclusion and exclusion criteria were asked to participate in this study. The Local Ethics Committee approved the study, and a waiver of exclusion criteria were asked to participate in this study. The Local Ethics Committee approved the study, and a waiver of signed informed consent was made by the principal investigator.

Before their participation in the study, all patients were evaluated with laboratory investigations in the form of complete blood count, renal function tests, coagulation profile, and urine culture. Patients were asked to provide a urine sample for analysis of pH and SG before performing each session of the procedure. Radiographic investigations were performed for all patients and include CT scan for accurate evaluation of the anatomy of the renal system and the size and location of the presenting stone. A plain kidney ureter and bladder (KUB) X-ray was also performed for all patients on the day of the procedure.

SWL was performed using the Siemens Lithoskop (Siemens, Erlangen, Germany). Under mild sedation, patients were placed in supine position and stones were localized with the help of fluoroscopic guidance or ultrasound depending on the stone radioluency. A total of 4000 shock waves were administered in each session, starting at low power and reaching a maximum of 4 kV in all participants. Patients were given appointments 1 week apart to assess their stone status using plain KUB X-ray or ultrasound. Patients with residual stones, more than 2 mm in diameter, were subjected to SWL with similar settings. Three sessions in total were given to patients with persistent sizable residual stone fragments after which if no success was achieved, they were referred to their primary urologist for another modality of treatment. A plain KUB X-ray or an ultrasound was performed at the end of treatment to evaluate the success of SWL.

Patients were asked to void through a strainer to collect any sizable fragments for stone analysis, which was performed using the wet chemistry method. Stone composition was displayed as pure or mixed form. Mixed stones are those containing calcium oxalate, protein, and/or carbonate of variable percentages.

Data regarding patients’ demographics, body habitus, urine investigations, stone characteristics, and outcome of SWL were collected. Patients were divided into two groups according to stone clearance. Group 1 was stone-free, whereas Group 2 had residual stones after 3 sessions of SWL. Correlations were made between the patients’ body mass index (BMI), urine pH and SG, stone size, site, HU and skin to stone distance with the number of sessions, and SFR overall. Data were also subclassified according to different pH ranges for analysis. Chi-square and Student’s t-test were used for statistical analysis. Categorical variables and numerical variables were presented as number (%) and mean ± standard deviation (SD), respectively. A P < 0.05 was considered statistically significant. Data analysis was done using SPSS statistical software, version 21 (IBM, Armonk, NY, USA).

**RESULTS**

One hundred and seventy-five patients were recruited in this study. Their mean age ± SD was 40.9 ± 10.3 years. The mean stone size and HU were 10.3 ± 4.7 mm and 776.8 ± 336.3, respectively. In 39 patients, the stone was located in the lower calyx, 81 in the middle calyx, 42 in the upper calyx, and 13 in the pelvis. The overall SFR was 54.3%. Stones were available for analysis in 47 out of 95 patients (49.5%) who had successful stone clearance. Calcium oxalate, mixed stones, and uric acid stones were detected in 27 (15.4%), 13 (7.4%), and 7 (4%) of cases. Other characteristics of the studied population are presented in Table 1. Group 1 included 95 patients, whereas Group 2 included eighty patients. A comparison between both groups is presented in Table 2. Factors found to have a statistically
significant association with SFR were stone size ($P = 0.03$) and skin to stone distance (SSD) ($P = 0.04$). Although BMI was lower in Group 1 than Group 2 patients (26.5 ± 4.1 vs. 29.6 ± 3.6, respectively), the value was not statistically significant ($P = 0.05$). The mean urine pH ± SD was 5.6 ± 0.5 in Group 1 and 5.8 ± 0.5 in Group 2 patients ($P = 0.51$). Stone clearance was highest in the renal pelvis (69.2%), followed by upper calyx (59.5%), middle calyx (56.8%), and lower calyx (38.5%). Table 3 evaluates different ranges of pH. The SFR was not found to be statistically significant among various pH ranges ($P = 0.58$).

### DISCUSSION

SWL is considered the treatment of choice for renal stones <2 cm in size. Despite its documented benefit, the outcome of this management modality depends on different factors assessed in various studies. Aspects such as stone composition, size, density, and location within the renal system as well as the body habitus of patients undergoing SWL were all found to affect SWL success rate. Fewer studies, however, assessed changes in the properties of urine in search for possible influential characteristics. In this study, urine pH was specifically assessed for the first time in medical literature. Our results acknowledged some of the previously reported factors. However, urine pH was not found to carry a statistically significant impact on SFR in this study population.

Stone-related characteristics are perhaps most influential on SWL success. It is well known that stone fragility is closely related to its composition. Among all stone types, the hardest composition belongs to calcium oxalate monohydrate, which predictably had a lower success rate with SWL and greater need for adjuvant procedures to achieve a stone-free state. Evaluation of stone density through CT was found to be a reliable method for predicting its composition, indicating a potential benefit for HU evaluation before SWL. In this study, HU was not found to have a statistically significant effect on SFR with SWL ($P = 0.63$).

SWL has long been considered to be less effective in patients with large body habitus. Obese patients have a longer

### Table 1: Characteristics of the study population

| Variable                      | Result                                      |
|-------------------------------|---------------------------------------------|
| Age, years (mean±SD)          | 40.9±10.3                                   |
| BMI, kg/m² (mean±SD)          | 27.9±9.6                                    |
| ST size, mm (mean±SD)         | 10.3±4.7                                    |
| ST HU (mean±SD)               | 776.8±336.3                                 |
| SSD, cm (mean±SD)             | 8.4±1.7                                     |
| Urine SG (mean±SD)            | 1.026±0.026                                 |
| Urine pH (mean±SD)            | 5.8±0.5                                     |
| ST site, n (%)                |                                             |
| Lower calyx                   | 39 (22.3)                                   |
| Middle calyx                  | 81 (46.3)                                   |
| Upper calyx                   | 42 (24)                                     |
| Pelvis                        | 13 (7.4)                                    |
| Composition, n (%)            |                                             |
| Calcium oxalate               | 27 (15.4)                                   |
| Mixed                         | 13 (7.4)                                    |
| Uric acid                     | 7 (4)                                       |
| ST free, n (%)                |                                             |
| Yes                           | 95 (54.3)                                   |
| No                            | 80 (45.7)                                   |
| Number of sessions, n (%)     |                                             |
| 1                             | 43 (24.6)                                   |
| 2                             | 38 (21.7)                                   |
| 3                             | 94 (53.7)                                   |

BMI: Body mass index, SG: Specific gravity, HU: Hounsfield Unit, ST: Stone, SSD: Skin to stone distance, SD Standard deviation

### Table 2: Comparison between Groups 1 and 2

| Variable                      | Group 1 (n=95) | Group 2 (n=80) | P    |
|-------------------------------|---------------|---------------|------|
| Age, years (mean±SD)          | 39.9±9.8      | 42.1±10.3     | 0.16 |
| BMI, kg/m² (mean±SD)          | 26.5±4.1      | 29.6±13.6     | 0.05 |
| Urine pH (mean±SD)            | 5.6±0.5       | 5.8±0.5       | 0.51 |
| Urine SG (mean±SD)            | 1.028±0.03    | 1.025±0.01    | 0.38 |
| ST HU (mean±SD)               | 761.5±311.7   | 795.5±365.7   | 0.63 |
| ST size, mm (mean±SD)         | 9.3±4.2       | 11.4±4.9      | 0.03 |
| ST site, n (%)                |               |               |      |
| Pelvis                        | 9 (9.5)       | 4 (5)         | 0.12 |
| LC                            | 15 (15.8)     | 24 (30)       | 0.02 |
| MC                            | 46 (48.4)     | 35 (43.8)     | 0.83 |
| UC                            | 25 (26.3)     | 17 (21.2)     | 0.56 |
| SSD, cm (mean±SD)             | 8.4±1.6       | 10.2±2.4      | 0.04 |

BMI: Body mass index, SG: Specific gravity, HU: Hounsfield Unit, ST: Stone, SSD: Skin to stone distance, SD Standard deviation

### Table 3: Correlation between different pH ranges

| pH Range | Group 1 (n=13) | Group 2 (n=77) | Group 3 (n=61) | Group 4 (n=24) | P     |
|----------|----------------|---------------|---------------|---------------|-------|
| <5.5     | 43.3±10.9      | 41.4±9.2      | 39.1±10.8     | 42.8±11.8     | 0.29  |
| 5.5-6.0  | 29.3±5.7       | 27.6±6.5      | 28.2±4.3      | 27.3±4.2      | 0.93  |
| 6.0-6.5  | 1.025±0.008    | 1.026±0.012   | 1.024±0.012   | 1.037±0.066   | 0.24  |
| >6.5     | 972.2±373.8    | 776.4±337.8   | 726.1±32.9    | 784.1±344.9   | 0.13  |
| SSD, cm (mean±SD)              | 6.8±1.8       | 8.1±1.8      | 8.6±1.7      | 8.2±1.5      | 0.56  |
| Number of sessions (mean±SD)   | 2.3±0.9       | 2.4±0.8      | 2.4±0.8      | 2.2±0.9      | 0.82  |
| SCR, n (%)                      | 6 (46.2)      | 41 (53.2)    | 32 (52.4)    | 16 (66.7)    | 0.58  |
| Composition, n (%)             |               |               |               |               | 0.23  |
| Calcium oxalate                | 0 (0)         | 14 (18.2)     | 10 (16.4)     | 3 (12.5)     |      |
| Mixed                           | 0 (0)         | 6 (7.8)       | 4 (6.5)       | 3 (12.5)     |      |
| Uric acid                       | 1 (7.6)       | 4 (5.2)       | 2 (3.2)       | 0 (0)        |      |

BMI: Body mass index, SG: Specific gravity, HU: Hounsfield Unit, ST: Stone, SSD: Skin to stone distance, SD Standard deviation, SCR: Stone clearance rate
SSD, which tends to reduce the efficacy of the shock waves administered. The usefulness of SSD as a clinical predictor for SWL success has been stressed by Park et al., who demonstrated the presence of an inverse relationship. Awareness of such a relationship has led few researchers to modify the positioning of obese patients during the procedure. Karatzas et al. tried placing patients in a modified lateral position in attempt to reduce the SSD against the SWL water cushion. Patients' SSD significantly affected SWL success in our study population (P = 0.04). Although BMI was lower in patients with a successful SWL outcome, the value was not statistically significant (P = 0.05).

The correlation between urine-related properties and success of lithotripsy has not been fully explored. Few studies evaluated urine SG aiming to investigate the effect of fasting before SWL on its outcome. An optimal SG of 1.040 was found to be associated with superior SWL results indicating a beneficial effect of fasting before the procedure. On the other hand, Hosseini et al. failed to find any significant impact of urine SG on SWL success rate. In this study, urine SG also was not found to have any statistically significant influence on SFR after SWL.

The influence of urine pH on the success of stone fragmentation in SWL has never been studied previously. Urinary pH is an important factor playing a major role in urinary stone formation. An alkaline pH favors the crystallization of calcium- and phosphate-containing stones, whereas an acidic pH promotes uric acid or cystine stones. It is thus plausible that if urine pH is a key factor in determining the composition of stones; then, it should also have an influence on their fragility. A comprehensive example comes from Pierratos et al. depicting the association of a higher urine pH with the more fragile dihydrate stones compared to a lower pH with the more resilient monohydrate stones.

Alteration of urinary pH has become a standard in the management and prevention of certain stone types. Urine alkalization is currently considered the treatment of choice in uric acid and cystine stones. While urine acidification is praised in struvite and phosphate-containing stones. Extrapolating this management modality into lithotripsy is tempting by requires it being based on scientific facts.

Investigating the influence of urine pH on SWL is maybe based on sound speculation that pH must have an influence on SWL activity. Wave propagation and intensity may differ according to the properties of the conducting medium. In addition, continuous stone fragmentation could also be affected by a medium of urine pH suitable for the individual stone composition. Such an understanding has been recently explored by Mendez-Probst et al. who demonstrated significant variations in fragmentation in different media. Although this clinical study failed to find an association between urinary pH and SWL success rate, it does not unfavor conducting experimental studies on the mechanics of stone fragmentation in media of different acidity.

Failure of having pH ranges toward the alkaline state could have affected the study results and can be considered as a limitation to this study. Such pH levels could have been achieved through the administration of urine alkalinizers. However, we aimed to reflect the natural situation of patients in this observational study. Another limitation is that stone analysis was available in only 49.5% of cleared stones with only 4% of them being urine acid. This may have prevented a better understanding of the effect of urine pH on different stone compositions during SWL.

CONCLUSION

SWL is a minimally invasive procedure with documented benefit in treating renal stones <2 cm in diameter. The study of factors influencing the success rate of this procedure serves to select most suitable cases coupled with the highest outcome. Urine pH was not found in this study population to significantly affect SWL results. However, it remains an attractive factor that needs to be explored in the future experimental studies.

Financial support and sponsorship
Medical Research Center, Hamad Medical Corporation.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Tiselius HG. Epidemiology and medical management of stone disease. BJU Int 2003;91:758-67.
2. Yasui T, Okada A, Hamamoto S, Hirose M, Ando R, Kubota Y, et al. The association between the incidence of urolithiasis and nutrition based on Japanese National Health and Nutrition Surveys. Urolithiasis 2013;41:217-24.
3. Hesse A, Brändle E, Wilbert D, Köhrmann KU, Alken P. Study on the prevalence and incidence of urolithiasis in Germany comparing the years 1979 vs 2000. Eur Urol 2003;44:709-13.
4. Schmidt E, Chaussy C. Extracorporeal shock-wave lithotripsy (ESWL) of kidney and ureteric stones. Int Urol Nephrol 1984;16:273-83.
5. Li CC, Finley DS, Urbe C, Eichel L, Lee DI, McDougall EM, et al. Effect of urine specific gravity on effectiveness of shockwave lithotripsy. J Endourol 2005;19:167-9.
6. Lim KH, Jung JH, Kwon JH, Lee YS, Bae J, Cho MC, et al. Can stone density on plain radiography predict the outcome of extracorporeal shockwave lithotripsy for ureteral stones? Korean J Urol 2015;56:56-62.
7. Tehranchi A, Rezaei Y, Mohammadi-Fallah M, Mokhtari M, Alizadeh M, Abedi F, et al. Effects of hydrochlorothiazide on kidney stone therapy with extracorporeal shock wave lithotripsy. Urol Ann 2014;6:208-11.
8. Gück A, Uyetürk U. Usefulness of hounsfield unit and density in the
assessment and treatment of urinary stones. World J Nephrol 2014;3:282-6.

9. Bres-Niewada E, Dybowski B, Radziszewsk B. Predicting stone composition before treatment – Can it really drive clinical decisions? Cent European J Urol 2014;67:392-6.

10. Hosseini SR, Mohseni MG, Mohammadi A, Tajik P. Impact of fasting on shockwave lithotripsy in renal stones: A randomized controlled trial. J Endourol 2007;21:1403-5.

11. Türk C, Knoll T, Petrlik A, Sarica K, Skolarikos A, Straub M, et al. Guidelines on Urolithiasis. European Association of Urology Guidelines; 2014. Available from: http://uroweb.org/wp-content/uploads/22-Urolithiasis_LR.pdf. [Last accessed on 2016 Feb 06].

12. Takahara K, Ibuki N, Inamoto T, Nomii H, Ubai T, Azuma H. Predictors of success for stone fragmentation and stone-free rate after extracorporeal shockwave lithotripsy in the treatment of upper urinary tract stones. Urol J 2012;9:549-52.

13. Al-Ansari A, As-Sadiq K, Al-Said S, Younis N, Jaleel OA, Shokeir AA. Prognostic factors of success of extracorporeal shock wave lithotripsy (ESWL) in the treatment of renal stones. Int Urol Nephrol 2003;35:413-8.

14. Abdel-Khalik M, Sheir K, Elsobky E, Showkey S, Kenawy M. Prognostic factors for extracorporeal shock-wave lithotripsy of ureretic stones – A multivariate analysis study. Scand J Urol Nephrol 2003;37:413-8.

15. Ansari MS, Gupta NP, Seth A, Hemal AK, Dogra PN, Singh TP. Stone fragility: Its therapeutic implications in shock wave lithotripsy of upper urinary tract stones. Int Urol Nephrol 2003;35:387-92.

16. Ringdén I, Tiselius HG. Composition and clinically determined hardness of urinary tract stones. Scand J Urol Nephrol 2007;41:316-23.

17. Pareek G, Armenakas NA, Fracchia JA. Hounsfield units on computerized tomography predict stone-free rates after extracorporeal shock wave lithotripsy. J Urol 2003;169:1679-81.

18. Hwang I, Jung SI, Kim KH, Hwang EC, Yu HS, Kim SO, et al. Factors influencing the failure of extracorporeal shock wave lithotripsy with Pieszolith 3000 in the management of solitary ureteral stone. Urolithiasis 2014;42:263-7.

19. Park BH, Choi H, Kim JB, Chang YS. Analyzing the effect of distance from skin to stone by computed tomography scan on the extracorporeal shock wave lithotripsy stone-free rate of renal stones. Korean J Urol 2012;53:40-3.

20. Karatzas A, Gravas S, Tzortzis V, Aravanitos E, Zachos I, Kalogeras N, et al. Feasibility and efficacy of extracorporeal shock-wave lithotripsy using a new modified lateral position for the treatment of renal stones in obese patients. Urol Res 2012;40:355-9.

21. Wagner CA, Mohhebbi N. Urinary pH and stone formation. J Nephrol 2010;23 Suppl 16:S165-9.

22. Pierratos AE, Khalaff H, Cheng PT, Psirrannis K, Jewett MA. Clinical and biochemical differences in patients with pure calcium oxalate monohydrate and calcium oxalate dihydrate kidney stones. J Urol 1994;151:571-4.

23. Cicciollo E, Merlo F, Maccarruso L. Urinary alkalization for the treatment of uric acid nephrolithiasis. Arch Ital Urol Androl 2010;82:145-6.

24. Pizzarelli F, Peacock M. Effect of chronic administration of ammonium sulfate on phosphatic stone recurrence. Nephron 1987;46:247-52.

25. Méndez-Probst CE, Fernández A, Erdeljan P, Vanjecek M, Cadieux PA, Razvi H. Third prize: The impact of fluid environment manipulation on shockwave lithotripsy artificial calculi fragmentation rates. J Endourol 2011;25:397-401.

New features on the journal’s website

Optimized content for mobile and hand-held devices
HTML pages have been optimized of mobile and other hand-held devices (such as iPad, Kindle, iPod) for faster browsing speed. Click on [Mobile Full text] from Table of Contents page.
This is simple HTML version for faster download on mobiles (if viewed on desktop, it will be automatically redirected to full HTML version)

E-Pub for hand-held devices
EPUB is an open e-book standard recommended by The International Digital Publishing Forum which is designed for reflovable content i.e. the text display can be optimized for a particular display device. Click on [EPub] from Table of Contents page.
There are various e-Pub readers such as for Windows: Digital Editions, OS X: Calibre/Bookworm, iPhone/iPod Touch/iPad: Stanza, and Linux: Calibre/Bookworm.

E-Book for desktop
One can also see the entire issue as printed here in a ‘flip book’ version on desktops. Links are available from Current Issue as well as Archives pages. Click on [View as eBook]