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Improvement of stone comminution by slow delivery rate of shock waves in extracorporeal lithotripsy

Kato, Yuji ; Yamaguchi, Satoshi ; Hori, Junichi ; Okuyama, Mitsuhiko ; Kakizaki, Hidehiro

Abstract and Key Words

Aim. We investigated the effect of delivery rate of shockwaves (SWs) on stone comminution and treatment outcomes in patients with renal and ureteral stones.

Methods. Patients with radiopaque stones in upper urinary tract that were treated by extracorporeal shock wave lithotripsy (SWL) were divided into two groups according to two rates (120 or 60 pulses per minute). We compared effective fragmentation after one SWL session and treatment success at 3 months after SWL between the two groups.

Results. Of 134 patients (84 men and 50 women), 68 patients were treated at a fast rate and 66 were treated at a slow rate. Thirty and 38 patients in the fast rate group and 28 and 38 in the slow rate group had renal and ureteral stones, respectively. After one SWL session, effective fragmentation was noted more often in the slow group (65.2%) than the fast group (47.1%) (p=0.035), particularly for smaller stones (stone area less than 100 mm^2) (p=0.005) and renal stones (p=0.005). However, there was no significant difference in treatment success at 3 months after SWL between the two groups. In univariate logistic regression analysis, slow SWs rate and smaller stones were significant factors for effective fragmentation after one SWL session. In multivariate analysis, slow SWs rate and smaller stones were also independent factors.

Conclusions. Slow SWs rate contributed to better stone comminution than fast rate, particularly for small stones and renal stones. We recommend SWL treatment at a slow SWs rate to obtain efficient stone fragmentation.

Short title: Extracorporeal shockwave lithotripsy, shock wave delivery rate, cavitation

Introduction

During the last two decades, development and introduction of extracorporeal shock wave lithotripsy (SWL) has revolutionized treatment strategy to urinary stones. Today SWL is widely applicable to most patients with urinary stone, even those with large stone burden, because of its higher effectiveness, more convenience, less complications and less invasiveness than transurethral or percutaneous approach. At the dawn of SWL therapy, during the treatment by the original Dornier HM3 lithotriptor, shockwaves (SWs) were synchronously triggered by patient's electrocardiogram (ECG) to avoid the cardiovascular events, especially as arrhythmia. Therefore, the delivery rate of SWs could not exceed 60-80 SWs per minute. However, it was revealed that the cardiovascular events during SWL occurred far less than expectations.[1] Therefore, current lithotriptors can be used without synchronization with ECG and the setting of a higher rate, for example over 100 to 120 SWs per minute, is very common today. Consequently, a high frequency rate of SWs contributed to decrease in treatment time. However, precise effects of SWs rate on stone comminution still remain to be clarified.

It is well known that various factors are involved in stone comminution during SWL. Other than stone composition, patients and SWL factors, such as body mass, SWs numbers and SWs power have been considered as important factors for stone comminution. Recently, a variety of in vitro[2,3] and in vivo[4] experimental models have indicated SWs rate as one of the factors affecting stone comminution. However, these experimental models may not exactly reflect a real situation in human stone patients. Although there are a few studies regarding the relation between SWs rate and stone comminution in clinical setting,[5-7] not much has been clarified regarding the effect of different SWs rates on stone fragmentation, leaving the appropriate SWs rate as a controversial issue. Thus, the aim of this study was to investigate whether a fast or slow SWs rate differently affect stone comminution and treatment outcome of SWL in patients with renal and ureteral stones.

Methods

This study included patients with radiopaque solitary stone in upper urinary tract that was treated by SWL in our institute between July 2002 and June 2004. Patients with radiolucent stones were excluded because of difficulty in follow-up with plain x-ray of the kidneys, ureters and bladder (KUB). Patients with cystine stones, staghorn calculus, infectious stone, renal or ureteral anatomical abnormalities, cardiac permanent pace maker or percutaneous nephrostomy placed prior to SWL were excluded. Patients who received other lithotripsy maneuvers (transurethral or percutaneous approach) prior to SWL were also excluded. If the patients had urinary tract infection, it was treated before SWL treatment. SWL was performed in both outpatient and inpatient settings. All participants gave their written informed consent before SWL treatment.

Treatment was performed with Modulith SLX-MX electromagnetic lithotriptor (Storz, St. Louis, Missouri) and stone position was focused by fluoroscopic imaging. No anesthesia was used during the SWL treatment, while some patients were given diclofenac (50mg) suppository, pentazocine (15mg) intramuscular injection or flurbiprofen axetil (50mg) drip infusion 30 minutes before SWL if they requested.

Double pigtail ureteral stent (6Fr.) was inserted prior to SWL if patients had renal colic, obstructed pyelonephritis or stone more than 20 mm in maximum diameter.

During the SWL treatment, the maximum number of SWs in each session was limited to 4000. SWL was also terminated when complete fragmentation was achieved in fluoroscopic imaging prior to reaching 4000 SWs. SWs power (from power level 1 to 9) was adjusted as high as possible within the patient’s tolerability. SWs were fired without synchronization with ECG and patients were divided into two groups according to the SWs delivery rate. Between July 2002 and May 2003, patients were treated by a fast rate (120 SWs per minute). Between June 2003 and June 2004, patients were treated by a slow rate (60 SWs per minute). These two rates are the fastest and slowest rates available on this device. Retreatment of SWL was performed after an interval of a week for renal stones and of 3 days for ureteral stones. After one SWL session, KUB was taken within a treatment interval. We defined effective fragmentation as no residual fragments or presence of clinically insignificant residual fragments (less than 4 mm) in KUB film. If residual fragments were 4 mm or over or stone was not broken, retreatment was applied. At 3 months after termination of SWL, we evaluated treatment success that was defined as stone free or clinically insignificant residual fragments (less than 4 mm) in KUB. Patients with failed SWL treatment underwent ancillary procedures, such as transurethral lithotripsy with holmium laser or percutaneous lithotripsy if indicated. Stone fragments were collected to determine the compositions by infrared spectrophotometry if available.

We analyzed patient characteristics (height, body weight, body mass index), stone area (mm^2), stone position, stone compositions, number of SWL sessions, total SWs numbers, SWs power level and treatment time of one session. We compared the stone fragmentation after one SWL session and treatment success at 3 months after SWL between the fast and slow rate groups. Complications of SWL such as subcapsular hematoma were also compared between the two groups.

Statistical Analysis

Continuous variables are presented as mean and plus or minus standard deviation. All statistical analysis was performing using commercially available software (Stat View 5.0 for Windows, SAS Institute Inc., Cary NC). Statistical analysis was conducted using Mann-Whitney U-test for continuous parameters or chi square test for categorized parameters, and p value < 0.05 was accepted as significant. Parameters proven significant in univariate analysis were entered into multivariate logistic regression analysis.

Results

This study included 134 patients, which were comprised of 84 men and 50 women with a mean age 57.6 ± 12.9 years (range 19 to 85), as shown in Table 1. Thirty and 38 patients in the fast rate group and 28 and 38 in the slow rate group had renal and ureteral stones, respectively. Most patients underwent SWL in situ, while 10 in the fast rate group and 14 in the slow rate group had a ureteral stent insertion prior to SWL. Twelve patients in the fast rate group and 15 in the slow rate group needed analgesia before treatment. The two groups were comparable in regard to male to female ratio, patients' age, body weight, height and body mass index. Stone position and insertion of ureteral stent were not significantly different between the two groups. A mean of stone area (mm^2) calculated by major and minor axis (mm) was 108.6 in the fast rate group and 111.5 in the slow rate group. Stone composition was predominantly calcium oxalate in both groups. Number of SWL sessions, total SWs numbers or SWs power level were not significantly different between the two groups. Treatment time of one SWL session was significantly longer in the slow rate group (38.7±9.5 versus 67.5±13.7 min, $p<0.0001$) (Table 1).

After one SWL session, the overall rate of effective fragmentation was 47.1% (32 of 68) in the fast rate group versus 65.2% (43 of 66) in the slow rate group and this difference was significant ($p=0.035$) (Table 2). When stone area was less than 100 mm^2, the rate of effective fragmentation was better in the slow rate group than in the fast rate group (50.0% versus 76.7%, $p=0.005$). No significant difference was noted if stone area was 100 mm^2 or greater. The rate of effective fragmentation for renal stones was better in the slow rate group than in the fast rate group (39.3% versus 75.0%, $p=0.005$). However, significant difference was not noted for ureteral stones (54.3% versus 57.9%, Table 2). Treatment success rate at 3 months after SWL was 76.9% (103 of 134) in all patients and there was no significant difference between the two groups (76.4% versus 77.2%, Table 2). Stone area or stone position did not have any significant influence on the treatment success rate at 3 months (Table 2). Because of failed SWL treatment, 9 patients (25.7%) in the fast rate group and 13 (34.2%) in the slow rate group underwent transurethral lithotripsy with a holmium laser (Table 2). One patient in the fast rate group suffered from retroperitoneal hematoma after the second SWL, with a total of 8000 SWs administered for left renal stone. No other complications occurred in either group during the study period.

In univariate logistic regression analysis, slow SWs rate and stone area less than 100 mm^2 were only significant factors related to effective fragmentation after one SWL session (Table 3). In multivariate analysis, SWs rate and stone area were independent factors each other for effective fragmentation after one SWL session. No factors significantly affected treatment success at 3 months after SWL.

Discussion

Previous studies have already reported that better comminution effect was obtained at a slow SWs rate than at a fast rate. In vitro study of Greenstein and Matzkin,[2] four different rates of SWs (30, 60, 120 and 150 SWs/min) were administered to 118 ceramic stones using Econolith 2000 electrohydraulic lithotriptor. They demonstrated that a slower rate (30 and 60 SWs/min) had better fragmentation than a faster rate (120 and 150 SWs/min). Likewise, Weir et al showed that plaster stones were fragmented earlier at a slower rate (60 and 80 SWs/min) than at a faster rate (117 SWs/min) using Dornier MFL5000 at fixed energy setting of 20kV.[3] Peterson et al established an in vivo porcine model in which gypsum cylinder was inserted via upper pole percutaneous tract to the lower pole calyx.[4] They demonstrated better stone comminution at a rate of 30 SWs/min than at 120 SWs/min. There have already been two prospective clinical studies regarding the effect of SWs rate. Madbouly et al[6] assessed prospectively the effect of SWs rate in 156 stone patients using Siemens Lithostar multiline. They showed that total number of SWs was significantly lower in the slow rate group (60 SWs/min) than in the fast rate group (120 SWs/min), and that success rate, defined as complete stone free or clinically insignificant residual fragments, was higher in the slow rate group. In other study by Pace et al,[7] 220 patients with renal stones were treated prospectively using LithoTron lithotriptor at a rate of 60 or 120 SWs/min. They concluded that treatment at a slow rate had better outcomes on stone fragmentation and stone free rate than at a fast rate. They emphasized that patients with larger stone burden (100 mm^2 or greater), not smaller stones, had a greater benefit with slow rate treatment.

We showed that effective stone fragmentation after one SWL session was obtained more frequently after treatment at 60 SWs/min than at 120 SWs/min. Particularly, for patients with stone area less than 100 mm^2 or patients with renal stones, treatment at a slow rate accomplished more effective stone fragmentation. In logistic regression analysis, SWs rate and stone area were significant factors affecting stone fragmentation after one SWL session by a univariate model, and SWs rate was demonstrated to be an independent factor by multivariate analysis. Regarding stone burden, our results are not in line with those reported by Pace et al[7] and we cannot explain the reason for different results. We speculate that the different results between their and our studies might have come from the differences in recruited patients (renal versus renal and ureteral stones), treatment protocols (only one SWL session versus one or more SWL sessions) and timing of treatment outcome evaluation (2 weeks and 3 months after SWL versus after one SWL session and 3 months after the final SWL session).

On the other hand, regarding treatment success at 3 months after SWL, we could not find a significant difference between the fast and slow rate groups. Furthermore, percentage of patients who needed ancillary procedures due to SWL failure did not differ significantly between the two groups. Treatment outcome of SWL is usually evaluated as condition of complete stone free or clinically insignificant residual fragments. It is well known that stone free rate is influenced by several factors, including patients' activity of daily life, quantity of fluid intake or anatomical dimension of renal pelvic and calyces.[8] Because we performed one or more SWL treatments until stone fragments became small enough for spontaneous passage, it seems likely that significant difference did not appear in treatment success rate at 3 months in the present study.

The exact mechanism of superiority in slow rate treatment is not well understood. Several mechanisms are advocated, for example, decreased acoustic impedance mismatch, improved cavitation bubble production on the stone surface or improved bubble dynamics due to water gas content surrounding the stone.[9] The most plausible mechanism of SWs rate effect is related to cavitation phenomenon. The cavitation phenomenon is one of the mechanisms for stone fragmentation. Briefly, SWs administration causes creation of gas bubble in both the liquid and tissues. This air bubble rapidly collapses and formed wave strikes the stone surface, and subsequently stone is broken.[10] These bubbles may act as an air "cloud" barrier to efficient shock wave energy transmission if persistent air bubbles may not have time to dissipate until next SWs arrival in fast rate treatment.[11] However, this hypothesis is not yet proved exactly, thus further studies regarding impact of cavitation phenomenon on stone comminution are warranted.

Stones may not remain in the focal zone during all treatment time and respiratory movement may influence stone comminution. Cleveland et al performed an in vitro study to investigate the effect of stone motion using Storz Modulith SLX-MX lithotriptor and showed that motion of 10 mm led to significant aggravation in stone comminution.[12] Moreover, the stone comminution was slightly but consistently improved when SWs were administrated at 60 SWs/min rather than at 120 SWs/min regardless of several settings of stone movement. SLX-MX lithotriptor has a tight focal area in 6×6 mm diameter and 28 mm depth and high peak pressure in 105 mPa. Because of this tight focal area, respiratory movement may influence stone comminution in treatment at a fast rate rather than at a slow rate.

Another superiority in treatment at a slow rate is related to less tissue damage, which was revealed by in vitro and vivo studies.[13-15] In a dog model using Dornier HM II lithotriptor, renal parenchymal hemorrhage occurred more often at a fast rate (100 SWs/sec) than at a slow (1 SWs/sec).[14] Similarly, an in vitro study demonstrated that cellular injury, estimated by hemoglobin release from suspended red blood cell to medium, was diminished by administration of slow rate (0.2 Hz) SWs rather than of fast rate (1 Hz).[15] However, these experimental situations were not physiologic and not necessarily mimicking clinical SWL setting. In the aforementioned studies,[6,7] treatment at a slow rate significantly reduced total SWs numbers compared to fast rate although there was no significant difference in our study. Because renal tissue damage is related to quantity of SWs energy and administered SWs numbers, slow rate SWL may minimize renal tissue damage by reducing total SWs numbers and number of SWL sessions. Consequently, slow rate treatment will contribute to better treatment quality with acceptable increase in treatment time of one SWL session.

The limitations of the present study include a small population of patients, non-randomized methods, disagreement of study duration between two groups, and the lack of assessment of tissue damage. It is ethically difficult to evaluate directly renal tissue damage by examining renal tissue samples. To clarify the superiority in slow rate treatment regarding tissue damage, indirect evaluations, such as measurement of urine LDH or NAG (*N*-acetyl-β-D-glucosaminidase) as indicators of renal tissue damage, may be required in the future.

In conclusion, we showed that SWL treatment at a slow SWs rate contributed to better stone comminution than at a fast rate in clinical setting, particularly for renal stones and small stones (stone area less than 100 mm^2). To obtain efficient fragmentation and potentially minimize renal tissue damage, we recommend treatment at a slow SWs rate.

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Table 1: Parameters of patients, urinary stones, and SWL treatment in the fast and slow SWs rate groups.

Characteristics	Fast rate group (120/min)	Slow rate group (60/min)	p value
No. patients	68	66	
Male	45	39	
Female	23	27	
Age (y)	58.3 ± 11.9	56.8 ± 13.9	NS
Body weight (kg)	61.4 ± 9.0	62.1 ± 11.0	NS
Height (cm)	161.4 ± 8.2	161.3 ± 8.9	NS
BMI (kg/m^2)	23.5 ± 2.8	23.8 ± 3.2	NS
Stone area (mm^2)	108.6 ± 117.3	111.5 ± 121.8	NS
Major axis (mm)	11.6 ± 5.9	11.5 ± 6.2	NS
Minor axis (mm)	7.7 ± 4.3	7.8 ± 4.3	NS
No. stone location			
Renal	30	28	
Ureteral	38	38	
No. ureteral stent before SWL	10	14	
No. stone composition			
CaOx	17	19	
CaP	3	1	
CaOx + CaP	20	31	
unknown	28	15	
Number of SWL sessions	1.8 ± 1.1	1.7 ± 0.87	NS
Total SWs numbers	6838.8 ± 4573.2	6348.3 ± 3701.9	NS
SWs power level	4.1 ± 1.1	4.0 ± 1.1	NS
Treatment time of 1 session (min)	38.7 ± 9.5	67.5 ± 13.7	<0.0001

NS: no significant difference, CaOx: calcium oxalate, CaP: calcium phosphate

Table 2: Effective fragmentation after one SWL session and treatment success at 3 months in the fast and slow SWs rate groups.

	Number of Patients (%)		
	Fast rate (120/min)	Slow rate (60/min)	p value
Effective fragmentation after 1 session			
Overall effective rate	32 (47.1)	43 (65.2)	0.035
Stone area less than 100 mm^2	21 (50.0)	33 (76.7)	0.005
Stone area 100 mm^2 or greater	11 (45.8)	10 (43.5)	NS
Renal stone	13 (39.3)	21 (75.0)	0.005
Ureteral stone	19 (54.3)	22 (57.9)	NS
Treatment success at 3 months			
Overall success rate	52 (76.4)	51 (77.2)	NS
Stone area less than 100 mm^2	33 (75.0)	36 (83.7)	NS
Stone area 100 mm^2 or greater	19 (79.2)	15 (65.2)	NS
Renal stone	27 (81.8)	26 (92.9)	NS
Ureteral stone	25 (71.4)	25 (65.8)	NS
Subsequent TUL	9 (25.7)	13 (34.2)	NS

NS: no significant difference

Table 3: Logistic regression analysis of effective fragmentation after one SWL session

Variable	Odds ratio (95%CI)	p value
Univariate analysis		
Slow SWs rate (60/min)	2.1 (1.1-4.2)	0.036
Stone area less than 100 mm^2	2.0 (1.0-4.2)	0.049
Multivariate analysis		
Slow SWs rate (60/min)	2.1 (1.1-4.4)	0.034
Stone area less than 100 mm^2	2.1 (1.0-4.3)	0.049