THE EFFECT OF TREATMENT STRATEGY ON STONE COMMINUTION EFFICIENCY IN SHOCK WAVE LITHOTRIPSY

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ABSTRACT

Purpose: The comminution of kidney stones in shock wave lithotripsy (SWL) is a dose dependent process caused primarily by the combination of 2 fundamental mechanisms, namely stress waves and cavitation. The effect of treatment strategy with emphasis on enhancing the effect of stress waves or cavitation on stone comminution in SWL was investigated. Because vascular injury in SWL is also dose dependent, optimization of the treatment strategy may produce improved stone comminution with decreased tissue injury in SWL.

Materials and Methods: Using an in vitro experiment system that mimics stone fragmentation in the renal pelvis spherical BegoStone (Bego USA, Smithfield, Rhode Island) phantoms (diameter 10 mm) were exposed to 1,500 shocks at a pulse repetition rate of 1 Hz in an unmodified HM-3 lithotripter (Dornier Medical Systems, Kennesaw, Georgia). The 3 treatment strategies used were increasing output voltage from 18 to 20 and then to 22 kV every 500 shocks with emphasis on enhancing the effect of cavitation on medium fragments (2 to 4 mm) at the final treatment stage, decreasing output voltage from 22 to 20 and then to 18 kV every 500 shocks with emphasis on enhancing the effect of stress waves on large fragments (greater than 4 mm) at the initial treatment stage and maintaining a constant output voltage at 20 kV, as typically used in SWL procedures. Following shock wave exposure the size distribution of fragments was determined by the sequential sieving method. In addition, pressure waveforms at lithotripter focus produced at different output settings were measured using a fiber optic probe hydrophone.

Results: The rate of stone comminution in SWL varied significantly in a dose dependent manner depending on the treatment strategies used. Specifically the comminution efficiencies produced by the 3 strategies after the initial 500 shocks were 30.7%, 59% and 41.9%, respectively. After 1,000 shocks the corresponding comminution efficiencies became similar (60.2%, 68.1% and 66.4%, respectively) with no statistically significant differences (p = 0.08). After 1,500 shocks the final comminution efficiency produced by the first strategy was 88.7%, which was better than the corresponding values of 81.2% and 83.5%, respectively, for the other 2 strategies. The difference between the final comminution efficiency of the first and second strategies was statistically significant (p = 0.005).

Conclusions: Progressive increase in lithotripter output voltage can produce the best overall stone comminution in vitro.

KEY WORDS: kidney, kidney calculi, lithotripsy

Although shock wave lithotripsy (SWL) has been used routinely for the treatment of symptomatic renal calculi for almost 2 decades, the treatment procedure is still largely empirical. Besides some anecdotal opinions, no well-defined protocols of SWL have been developed to ensure an effective treatment outcome with minimal adverse tissue injury. On the other hand, clinical and animal studies have shown that tissue injury in SWL, such as hematuria, the formation of diffuse hemorrhage and hematomas,1, 2 is dose dependent and increases with the total number of shocks delivered3 and with pulse energy.4 Similarly the comminution of renal calculi in SWL is also a dose dependent process.5 Therefore, it is plausible that optimizing the treatment strategy (ie different ways of using the same total amount of acoustic energy delivered to the patient) in SWL may lead to more effective stone comminution with decreased tissue injury. Such a hypothesis has not been thoroughly evaluated.

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Disintegration of renal calculi in a lithotripter field is the consequence of dynamic fracture of the stone materials caused by 2 fundamental mechanisms, namely stress wave induced tensile and shear failure (spalling, shear and tear) near the surface and at internal crystalline-matrix interfaces of a kidney stone,6–8 and cavitation erosion at the exterior surface of the stone caused by the violent collapse of cavitation bubbles.9–12 Using an experimental system that mimics stone comminution in the renal pelvis the role of stress waves and cavitation in stone comminution during SWL has been investigated.5 It was shown that stress waves and cavitation have critical roles in the comminution of kidney stones. They act synergistically rather than independently to ensure the effective and successful fragmentation of renal calculi in SWL. Initially stress waves have a much more important role in breaking up kidney stones into distributed pieces than the cavitation erosion mechanism. However, when the size of residual fragments becomes less than half of the compressive wavelength in the stone material, the effectiveness of stress waves, when acting alone, is hindered. In comparison, the collapse of cavitation bubbles produces damage primarily on the surface of the stone (or residual fragments) and consequently weakens the structure of the stone material, making
it much more fragile to the impact of ensuing lithotripter shock waves (LSWs) and associated bombardments of cavitation bubbles. Altogether stress wave induced fracture is dominant in the initial disintegration of kidney stones, while cavitation is necessary to produce fine, passable fragments, which are most critical for the success of clinical SWL. It has been suggested that the optimal use of stress waves and cavitation in SWL may help improve treatment efficiency and decrease adverse tissue injury. In clinical SWL a kidney stone may be fragmented into a group of small pieces in a few hundred shocks, which can be observed by fluoroscopic or ultrasound imaging when the edge of the calculus becomes blurred. At this stage how to proceed with SWL treatment thereafter to ensure successful stone comminution with minimal tissue injury is in dispute. Anecdotally there are 2 common but opposite opinions in clinical practice. The first opinion suggests that the output voltage of the lithotripter should be lowered. This is based on the consideration that the original kidney stone has already been broken into small fragments and, therefore, less acoustic energy is needed to reduce them to less than 2 mm for spontaneous discharge. In addition, by decreasing the output voltage of the lithotripter the propensity of tissue injury is decreased. The second opinion is that the output voltage of the lithotripter should be increased. The rationale is that by increasing to a high energy level the total number of shock waves needed for the complete stone comminution is less, thus, possibly decreasing the propensity for tissue injury. To our knowledge these opinions have not been evaluated systematically in in vitro or in vivo experiments.

In this study we evaluated the effects of 3 treatment strategies on the progressive and overall stone comminution efficiency of SWL using a phantom system that mimics stone disintegration in renal pelvis. All experiments were performed with a Dornier HM-3 lithotripter. For the first strategy the output voltage of the lithotripter was increased in steps from 18 to 20 to 22 kV after every 500 shocks, aiming to enhance SWL induced cavitation effects in the final stage of treatment. For the second strategy an opposite approach was used with lithotripter output voltage decreasing in steps from 22 to 20 to 18 kV after every 500 shocks. In comparison, for the third strategy a constant output voltage of 20 kV was used to mimic the conventional use of the HM-3 lithotripter in clinic. It was found that, although the total acoustic output energies of the 3 strategies were the same or similar, the first strategy could produce better overall comminution efficiency in vitro than the other 2 strategies.

**MATERIALS AND METHODS**

**Lithotripter and pressure waveform measurement.** The experiments in this study were done with an unmodified Dornier HM-3 electrohydraulic shock wave lithotripter, which uses a truncated ellipsoidal reflector with semi-major axis a = 138 mm, semi-minor axis b = 77.5 mm and half focal length c = 114 mm. The lithotripter was operated at an output voltage of 18 kV to 22 kV with a 1 Hz pulse repetition rate. The pressure waveform at the lithotripter focus ($P_z$) was measured using a fiber optic probe hydrophone (FOPH-500, University of Stuttgart, Stuttgart, Germany).

**Stone phantoms.** Spherical stone phantoms (diameter 10 mm) were made of BegoStone material with a powder-to-water ratio of 5:1. The acoustic and mechanical properties of BegoStone have been characterized and found to be similar to those of calcium oxalate monohydrate stones. Before the experiment the weight of each stone phantom in the dry state was measured, which yielded a mean of 1.10 g with an SD of within ± 2% for the samples tested.

**Stone comminution experiment and treatment strategy.** The fragmentation test was performed using a phantom system that mimics stone comminution in the renal pelvis (fig. 1). The stone sample was placed in a plastic holder with a disposable finger cot (QRP, Tucson, Arizona) (diameter 20 mm) attached to the bottom. The holder was connected to the hydraulic gantry of the HM-3 system, so that the stone phantom could be aligned with $F_2$ under biplanar fluoroscopic imaging guidance. To simulate tissue attenuation on the incident LSW the stone holder was immersed in an acrylic chamber ($254 \times 254 \times 152$ to $216$ mm, length × width × height) filled with castor oil and with a slab of 25.4 mm tissue mimicking phantom placed at the bottom (with a polyester membrane window). In addition, a piece of tissue mimicking material was also placed inside the holder above the stone phantom. The acoustic properties of the tissue mimicking phantom have been previously characterized and were found to simulate reasonably well LSW attenuation in vivo.

Before the experiment each stone phantom was immersed in degassed water for at least 20 minutes until no visible bubbles could be seen coming from it. According to our experience prolonged immersion of stone samples does not change the comminution results significantly. During the experiment the position of the fragments was assessed every 50 shocks using the biplanar fluoroscopic imaging system of the HM-3 lithotripter. If necessary, re-positioning was done to align the largest fragment with $F_2$. After 1,000 shocks most of the original stone mass was reduced to small fragments with a few large residual pieces, which were difficult to discern on fluoroscopic imaging. Therefore, for the last 500 shocks the lithotripter focus was scanned throughout the distribution of the fragments after every 50 shocks to ensure sufficient shock wave exposure to all residual pieces. After shock wave treatment all fragments were carefully removed from each sieve and weighed. Stone comminution efficiency was determined by the percentage of fragments less than 2 mm, which could be discharged spontaneously in urine following clinical SWL. Six samples were used under each test configuration. Student’s t test was performed to determine statistical difference among the test groups.

Three treatment strategies with a total exposure of 1,500 shocks using different combinations of output settings were tested. Stone phantoms were divided into 3 groups with each...
group subdivided into 4 treatment units to document and quantify the pattern of stone comminution after 300, 500, 1,000 and 1,500 shocks, respectively. The first group was treated with a progressive increase in steps of lithotripter output voltage from 18 to 20 and then to 22 kV after every 500 shocks. In the second group the opposite strategy was used with lithotripter output voltage started at 22 kV and decreased progressively to 20 and then to 18 kV after every 500 shocks. In the third group a constant output voltage of 20 kV was used to mimic the conventional use of the HM-3 lithotripter in clinic.

RESULTS

Pressure waveforms. Figure 2 shows representative pressure waveforms at F2 generated by the HM-3 lithotripter at 18, 20 and 22 kV. The table lists corresponding shock wave physical parameters. Although the temporal profile, and positive (t+\(P^+\)) and negative (t-\(P^-\)) pulse durations of the pressure waveforms were similar, peak positive (\(P^+\)) and negative (\(P^-\)) pressure, and the corresponding derived pulse intensity integrals at F2 (\(P_{II}^+\) and \(P_{II}^-\)) increased with lithotripter output voltage.

Stone comminution. All 3 strategies produced a progressive comminution of BegoStone phantoms (fig. 3). However, as shown quantitatively in figure 4, the rate of stone comminution varied significantly in a dose dependent manner. Using the second strategy, which started treatment at 22 kV, much higher treatment efficiency was produced after the initial 500 shocks than the first strategy, which started at 18 kV, and the third strategy, which operated at a constant 20 kV. Quantitatively the comminution efficiencies produced by the 3 strategies after the initial 300 and 500 shocks were 14.5%, 46% and 22.4%, and 30.7%, 59% and 41.9%, respectively. In this initial treatment phase a higher output voltage (22 kV) produced mainly medium (2 to 4 mm) and small (1 to 2 mm) fragments, while a lower output voltage (18 kV) yielded more large fragments (greater than 4 mm) (fig. 5). As treatment progressed to 1,000 shocks, comminution efficiencies produced by the 3 strategies became similar (60.21%, 68.1% and 66.4%, respectively) with no statistically significant differences (p = 0.08). Size distributions of the fragments in this intermediate range of treatment were found to be comparable with slightly more medium fragments produced by the first strategy (fig. 5). Figure 4 shows that the rate of stone comminution achieved by the second and third strategies began to slow down while, in contrast, the rate of stone

<table>
<thead>
<tr>
<th>Output Voltage (kV)</th>
<th>18</th>
<th>20</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P^+) (MPa)</td>
<td>44.90 ± 1.32</td>
<td>47.01 ± 2.55</td>
<td>50.01 ± 3.19</td>
</tr>
<tr>
<td>(P^-) (MPa)</td>
<td>-6.54 ± 0.32</td>
<td>-7.73 ± 0.38</td>
<td>-9.40 ± 0.30</td>
</tr>
<tr>
<td>t+ ((\mu)sec)</td>
<td>2.13 ± 0.12</td>
<td>2.19 ± 0.06</td>
<td>2.29 ± 0.11</td>
</tr>
<tr>
<td>t- ((\mu)sec)</td>
<td>6.17 ± 0.44</td>
<td>6.01 ± 0.28</td>
<td>6.14 ± 0.54</td>
</tr>
<tr>
<td>(P_{II}^+) (J/m²)</td>
<td>198.31 ± 12.60</td>
<td>240.40 ± 16.05</td>
<td>257.60 ± 10.54</td>
</tr>
<tr>
<td>(P_{II}^-) (J/m²)</td>
<td>31.62 ± 3.20</td>
<td>49.87 ± 6.75</td>
<td>72.32 ± 4.10</td>
</tr>
</tbody>
</table>

Pulse duration was measured by the zero crossing duration of the wave component of the shock wave.

FIG. 2. Representative pressure waveforms measured by fiber optic probe hydrophone (FOPH-500) at focal point of HM-3 lithotripter at output voltage of 18 (A), 20 (B) and 22 (C) kV.

FIG. 3. Photographs of fragments of BegoStone phantoms treated with Dornier HM-3 lithotripter with voltage increasing from 18 to 20 and then to 22 kV every 500 shocks (A) with constant 20 kV during treatment (B) and with voltage decreasing from 22 to 20 and then to 18 kV every 500 shocks (C). SN, shock number.
comminution achieved by the first strategy did not change significantly. Finally, toward the end of treatment (1,500 shocks) the comminution efficiency produced by the first strategy (88.7%) became better than that of the other 2 strategies (81.2% and 83.5%, respectively). In particular the difference between the final comminution efficiency of the first 2 strategies was statistically significant (p = 0.005). Since total output energies of the first and second treatment strategies were the same, this finding suggests that the treatment strategy is important for determining overall stone comminution in SWL.

**DISCUSSION**

In clinical SWL about 2,000 shocks are usually required for the successful comminution of renal calculi. How to administrate these shock waves in a manner that can achieve effective and complete stone comminution with minimal tissue injury is an important issue of clinical significance. To date despite anecdotal opinions the effects of treatment strategy on SWL outcome and safety have not been thoroughly evaluated. In this study we performed a series of in vitro experiments to compare the progressive stone fragmentation pattern produced by 3 lithotripsy strategies under clinically relevant SWL conditions. Specifically, lithotripter output was gradually stepping up, gradually stepping down or maintained constant during the treatment. The total acoustic dose

![Figure 4](image4.png)

**FIG. 4.** Dose dependent comminution efficiency of BegoStone phantoms after shock wave treatment with Dornier HM-3 lithotripter using 3 treatment strategies, namely increasing from 18 to 20 and then to 22 kV, decreasing from 22 to 20 and then to 18 kV, and maintaining a constant voltage of 20 kV. Student's t test was performed to determine statistically differences (p <0.05) between results of first and second strategies.

![Figure 5](image5.png)

**FIG. 5.** Dose dependent size distribution of BegoStone fragments produced by Dornier HM-3 lithotripter using 3 lithotripsy treatment strategies after 300 (A), 500 (B), 1,000 (C) and 1,500 (D) shocks.

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of the first 2 strategies were identical and similar to that of the third strategy, which mimics the conventional use of a Dornier HM-3 lithotripter. Overall it was found that a progressive increase in lithotripter output energy could produce the best stone comminution toward the end of SWL treatment despite a low initial fragmentation rate.

The 2 fundamental mechanisms known to contribute to stone comminution in SWL are stress waves and cavitation. The results of previous studies show that stress waves have an important and often dominant role in initial stone fragmentation when the size of the stone or its residual fragments is larger than half of the compressive wavelength in the stone material.\(^{5,8}\) In comparison, cavitation induced by the tensile component of the LSW is responsible for surface erosion produced by the violent collapse of cavitation bubbles with resultant strong secondary shock wave emission or high speed microjet impingement.\(^{3–12}\) Although damage produced by individual cavitation bubbles does not penetrate deep into the bulk of the stone material, the collective impact of numerous bubbles may weaken the structure of residual fragments making them much more fragile to the ensuing shock wave pulses. Therefore, stress waves and cavitation are believed to work synergistically to produce effective and successful stone comminution in SWL.\(^5\)

The progressive stone comminution pattern produced by different treatment strategies is also intriguing. Figure 4 shows that, although the initial rate of stone fragmentation produced by the first strategy was low compared to that of the other 2 strategies, a gradual increase in output voltage helped maintain a relatively constant rate of fragmentation throughout the entire course of SWL treatment. In contrast, although the rate of stone fragmentation produced by the second strategy was high initially, it decreased significantly after the first 500 shocks when the output voltage of the lithotripter was decreased. For the third strategy of a constant output voltage comminution efficiency was also found to decrease between 500 and 1,000 shocks. Together these results suggest that a gradual increase in lithotripter output voltage is the best strategy to achieve the highest overall stone comminution efficiency in SWL.

Several factors may attribute to this observation. 1) The fracture strength of most renal calculi is not high. Therefore, relatively low pressure (about 30 MPa) is sufficient to initiate stone fragmentation, which is supported by a recent clinical study using a wide focus and low pressure electromagnetic shock wave generator.\(^{17}\) 2) When a stone is disintegrated, fine powders of the stone materials may accumulate around some residual large pieces, which scatter and attenuate the ensuing LSWs, thus, decreasing subsequent stone comminution efficiency.\(^5\) Similar problems in SWL treatment for ureteral stones have also been reported.\(^{18,19}\) Under these circumstances an increase in lithotripter output voltage, as in the first strategy, could compensate for the increased attenuation from accumulated small fragments and, thus, maintain a high stone comminution rate toward the end of SWL treatment. 3) A gradual increase in lithotripter output voltage also enhances cavitation activity and a strong synergistic interaction between stress waves and cavitation in the latter part of SWL treatment should yield better overall stone comminution.

In comparison, if SWL treatment is started at a higher output voltage, as in the second strategy, the initial fragmentation rate is high but treatment is incomplete. As a result of the high initial fragmentation rate, small fragments accumulate more rapidly and increase the attenuation on ensuing LSWs. In addition, when the size of residual fragments becomes smaller than half of the compressive wavelength in the stone material (about 4.4 mm for BegoStone phantoms), the effectiveness of stress waves is hindered. These factors, compounded by the fact that lithotripter output voltage was gradually decreased in the latter part of treatment, led to dramatically decreased fragmentation efficiency toward the end of treatment with a low overall stone comminution rate.

Finally, when evaluating strategies for improving SWL treatment, not only stone comminution, but also the adverse effects of SWL should be considered. Preliminary evidence in animal studies suggests that staged SWL treatment combining low energy shock waves followed by high energy shock waves could decrease the potential for vascular injury.\(^{20}\)

Therefore, of the 3 lithotripsy strategies evaluated in this study the first strategy is likely to produce the least amount of tissue injury, although further confirmation in animal studies \textit{in vivo} is needed. From the patient point of view the first strategy would also be most tolerable in terms of treatment, noise and pain produced by the incident LSWs.

CONCLUSIONS

Stone comminution in SWL is dose dependent and the rate of fragmentation varies significantly during the course of treatment depending on the strategies used. Based on \textit{in vitro} phantom studies it was observed that a progressive increase in lithotripter output voltage could produce the best overall comminution efficiency, while the potential of causing tissue injury and discomfort to the patient was minimal compared to other treatment strategies. The implication of this finding is significant for the clinical practice of SWL and it warrants further confirmation by \textit{in vivo} animal and clinical studies.

REFERENCES


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