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Treatment protocols to reduce renal injury during shock wave lithotripsy

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Abstract

Purpose of review—Growing concern over the acute and long-term adverse effects associated with shock wave lithotripsy calls for treatment strategies to reduce renal injury and improve the efficiency of stone breakage in shock wave lithotripsy.

Recent findings—Experimental studies in the pig model show that lithotripter settings for power and shock wave rate and the sequence of shock wave delivery can be used to reduce trauma to the kidney. Step-wise power ramping as is often used to acclimate the patient to shock waves causes less tissue trauma when the initial dose is followed by a brief (3–4 min) pause in shock wave delivery. Slowing the firing rate of the lithotripter to 60 shock waves/min or slower is also effective in reducing renal injury and has the added benefit of improving stone breakage outcomes. Neither strategy to reduce renal injury – not power ramping with 'pause-protection' nor delivering shock waves at reduced shock wave rate – have been tested in clinical trials.

Summary—Technique in lithotripsy is critically important, and it is encouraging that simple, practical steps can be taken to improve the safety and efficacy of shock wave lithotripsy.

Keywords

adverse effects; kidney trauma; lithotripsy; shock waves

Introduction

It is well established that unwanted renal and extrarenal side effects can occur as a consequence of shock wave lithotripsy (SWL), and the topic of SWL injury has been the subject of numerous in-depth reviews (Reviewed in [1–5]). Most of what is known about the structural and functional characteristics of renal injury in SWL and the factors that influence the severity of tissue damage come from research with experimental animals [2,5,6,7,8]. This work has shown that injury can be affected by a variety of risk factors, such as age, the size of the kidney, the number of renal units and the presence of renal disease. It has also been shown that renal damage is dependent on the number of shock waves and the shock wave firing rate and power setting of the lithotripter. For example, measurements of lesion size in the acute (4 h posttreatment) juvenile pig SWL injury model have shown that treatment with a conservative dose of shock waves using the Dornier HM3 lithotripter (Dornier MedTech America, Kennesaw, Georgia, USA; 1000 shock waves, 24 kV, 120 shock waves/min) produced a hemorrhagic lesion measuring approximately0.3% of the renal

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parenchyma (functional renal volume, FRV) [6]. Doubling the dose (2000 shock waves) increased the lesion 20-fold (~6% FRV), and raising the dose to 8000 shock waves further doubled the lesion (~14% FRV) [7]. In the same animal model, but with a dose of 2000 shock waves, lesion size was observed to be dependent on the power setting of the lithotripter, increasing from approximately 0.3% FRV at 12 kV to approximately 2.25% FRV at 18 kV and approximately6% FRV at 24 kV [8]. Thus, the severity of acute renal injury in SWL is dose dependent and is affected by the parameters of shock wave delivery.

The long-term consequences of SWL injury are not nearly as well understood, but there is solid evidence to show that acute SWL injury initiates an inflammatory response with progression to scar formation and permanent loss of functional renal mass [9]. Dosedependent parenchymal fibrosis has been observed in dogs [10] and rabbits [11], and there is report of complete atrophy of renal papillae in pigs 3 months following treatment [1]. Clinical reports of long-term effects in SWL have not been extensive, but are concerning just the same. Studies indicate a potential link between SWL and new-onset hypertension with the suggestion that increased age may be a significant risk factor (reviewed in [1,3]). In addition, multiple lithotripsies have been implicated as a risk factor in the exacerbation of stone disease [12]. That is, patients who had received multiple SWL treatment sessions showed a greater tendency over time for transformation from calcium oxalate stone disease to a calcium phosphate or brushite phenotype. There has also been the suggestion that SWL may lead to onset of diabetes mellitus [13]. In this retrospective 19-year follow-up study of patients who underwent SWL for renal stones, lithotripsy increased the risk of developing diabetes mellitus compared with non-SWL controls. In addition, the occurrence of diabetes mellitus in these patients was related to the total number of shock waves they received and the power setting of the lithotripter.

Thus, both the severity of acute renal injury and the potential for long-term adverse effects appear to be dependent on the dose of shock waves applied. This is ample reason to look for ways to reduce the shock wave dose and to identify strategies that will minimize injury that occurs during SWL.

Pretreatment with shock waves protects against subsequent shock wave lithotripsy injury

The first suggestion that shock waves could be used to trigger a protective response by the kidney came in a preliminary study using the pig model in which it was observed that treatment of the lower pole (2000 shock waves, 24 kV, Dornier HM3) produced a lesion measuring approximately 7% of the renal parenchyma, but immediate retargeting and delivery of the same dose of shock waves to the upper pole resulted in a lesion measuring only 0.1% FRV. Subsequently, four groups of juvenile pigs (6–7 weeks of age) were studied to test the idea that an initial dose of shock waves at a low power setting (12 kV) might prove sufficient to induce protection against injury during continued treatment[14]. An initial dose of either 2000 or 500 shock waves at 12 kV was delivered to the lower pole followed by retargeting and treatment of the upper pole with 2000 shock waves at 24 kV. In both cases, injury to the second pole was significantly reduced compared with that when no pretreatment was performed. Similarly, when a dose of either 500 or 100 shock waves at 12 kV was delivered to the lower pole followed by a dose of 2000 shock waves (24 kV) to the same pole, the injury was significantly less than that when no pretreatment was used. Thus, pretreatment of the kidney with shock waves at a low power setting protected the kidney from injury caused by subsequent shock waves. The effect occurred when both doses of shock waves were delivered to the same pole, and the threshold for this protective effect was 100 shock waves or less. The physiologic mechanism for this response was not assessed in the study, but work has begun in this area [15•].

Clinical implications

These findings suggest that initiating SWL with the delivery of a ‘preemptive’ dose of shock waves – as few as 100 shock waves at low power setting – could protect against injury caused by subsequent shock waves. The treatment protocol at many centers involves some variation on this theme, that is, using a regimen of power ramping or step-wise SWL. Such protocols have been in place for many years and likely came about as a means to help patients adapt to SWL performed under minimal anesthesia [16]. The precise sequence of shock wave delivery (number of shock waves at various power settings) in such a step-wise protocol may vary considerably depending on the preference and experience of the urologist. This includes whether or not there is any pause in shock wave delivery as the power is ramped up, and many groups make this simple adjustment ‘on-the-fly’. From the standpoint of initiating a protective effect, the timing of shock wave administration maybe key. That is, in the pig experiments described above, the initial dose of shock waves was always followed by a 3–4 min pause (dictated by the time it took to retarget the opposite pole of the kidney). In experiments in which both the initial and subsequent shock wave doses were delivered to the same pole, this 3–4 min pause was retained as part of the treatment protocol. As described next, this brief pause in shock wave delivery appears to be the critical factor in the SWL ‘protection protocol’. As such, there maybe no reason to expect that step-wise power ramping without such a pause – a scenario that to our knowledge has yet to be addressed in clinical trials – would be protective.

‘ Pause - protection ’ : allowing the kidney to respond to initial shock wave exposure may be necessary to afford protection from injury

Subsequent studies in the pig model addressed the timing of shock wave delivery when a pretreatment dose was applied [17•]. Experiments were performed to determine if the pause in treatment that was part of the original experimental protocol (see above) played a role in the renal response to shock waves. To test this, pigs were treated with an initial dose of 100 shock waves at 24 kV followed 3 min later by 2000 shock waves also at 24 kV. Injury was significantly reduced compared with no pretreatment (0.51 ± 0.14% versus 3.93 ± 1.29% FRV, $P = 0.0135$) [17•]. This showed that the protection afforded by shock wave pretreatment was not because the pretreatment dose was at a lower power setting but was, instead, a consequence of the delay between the initial dose and the main dose.

It would seem to be a very simple and otherwise noncomplicating step to incorporate a brief pause in treatment following delivery of the first 100 or so shock waves in virtually any SWL treatment protocol. If the results from the renal injury studies in pigs discussed above are any indication of the potential for improved safety in SWL for patients, adding 3–4 min to the treatment protocol could bear substantial benefit.

Step-wise power ramping protocols, in which shock waves are delivered first at a low power setting then the amplitude is gradually increased, appear to give improved stone breakage as well. Artificial stones *in vitro* [18] or implanted in pig kidneys [19] broke better with gradual ramping, and there is a recent report of improved clinical outcome with such a protocol [20]. It is highly unlikely that addition of ‘pause-protection’ to such a protocol would reduce the efficiency of stone breakage. Thus, step-wise power ramping with ‘pause-protection’ could be both protective and a means to enhance stone comminution.

Slowing shock wave rate reduces renal injury in the pig model

With constraints on facilities at busy stone centers, it is likely that most patients are treated at a firing rate of 120 shock waves/min. Recent studies with pigs indicate, however, that

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choice of shock wave rate in the clinical range (30–120 shock waves/min) can affect lesion size and slowing the firing rate to 30–60 SW/min delivers a significant reduction in renal injury [21••]. The first suggestion that lowering the firing rate of the lithotripter below 120 shock waves/min could reduce injury came as an unexpected finding during studies to characterize the performance of the low-pressure wide-focalzone electromagnetic XX-ES lithotripter [22]. In those tests, pigs were treated at the same settings used to treat patients with this machine (27 shock waves/min, ~17 MPa at 9.3 kV, 1500 shock waves) [23], and for comparison pigs were treated using the Dornier HM3 to deliver the same number of shock waves at roughly similar settings (30 shock waves/min, ~32 MPa at 18 kV). The lesion in the XX-ES animals was too small to effectively quantify, but as this lithotripter did not maintain consistent output at 120 shock waves/min, a direct comparison of the effect of shock wave rate on renal injury could not be made. However, lesion size in the HM3 group was also very low (<0.1% FRV) compared with previous studies using 120 shock waves/min in which the lesion measured approximately 5% FRV [5,6]. A follow-up study with the HM3 subsequently demonstrated a significant reduction in lesion size when pigs were treated (2000 shock waves, 24 kV) at 30 shock waves/min compared with 120 shock waves/min (0.08 ± 0.02% versus 4.6 ± 1.7% FRV, $P < 0.005$) [21••]. Thus, reducing the shock wave rate had a significant protective effect.

Clinical implications

Several prospective clinical trials [24–26] supported by an independent metaanalysis[27•] have now reported a significant improvement in stone breakage outcomes when patients are treated at 60 shock waves/min compared with 120 shock waves/min. This strongly suggests a stone breakage advantage in reducing the firing rate of the lithotripter. The potential for reduced injury at slow shock wave rate is added reason to use slower rate. Many urologists would likely find it difficult to treat their patients at the extremely slow rate of 30 shock waves/min shown to be protective. Therefore, it is encouraging that recent studies in the pig model show that injury is also reduced at 60 shock waves/min compared with 120 shock waves/min (0.42 versus 3.93% FRV, $P = 0.034$). Thus, there are solid laboratory data to show that injury is reduced when slower shock wave rate is used, and this finding is complemented by clinical studies reporting improved outcomes at reduced shock wave rate. On the basis of these data, it seems reasonable to suggest that slowing the firing rate of the lithotripter improves both the safety and the efficacy of SWL.

Improved acoustic coupling can improve the efficiency of treatment

Acoustic coupling with modern dry-head lithotripters is not as efficient as when a water bath is used. Defects (air pockets) at the coupling interface arise when coupling is first established and worsen if the patient moves or is repositioned. In-vitro studies using a test tank, with an acoustic window as a surrogate patient, have demonstrated that the quality of coupling is highly variable and that coupling defects can interfere with the transmission of shock waves to the target, thereby requiring more shock waves to break stones [28]. Laboratory tests have shown that simple measures – such as minimizing handling of the gel, using an excess volume of gel and employing the inflation feature of the treatment head to smooth out the gel can significantly improve coupling [29••].

Clinical Implications

The problem of coupling is three-fold: inefficient coupling diminishes the effectiveness of treatment, the high variability of coupling likely contributes to variability in clinical outcomes and ineffective coupling leads to exposure of the patient to more shock waves than are needed, thereby increasing the potential for adverse effects – and is made more difficult by the fact that there is currently no method to monitor the coupling interface during SWL.

Conclusion

The safety and effectiveness of SWL can be improved by attention to technique. Animal studies clearly demonstrate that the sequence of shock wave administration can have a dramatic effect on the severity of renal injury. Step-wise power ramping can be a useful strategy to reduce injury but appears only to be effective when the initial dose of shock waves is followed by a brief pause in treatment ('pause-protection'). Slowing the firing rate of the lithotripter to 60 shock waves/min or slower is equally effective in reducing renal injury and offers the advantage of a significant improvement in stone breakage outcomes documented by multiple prospective clinical trials. The poor quality and variability of acoustic coupling is an additional challenge that needs to be addressed. This aspect of SWL is largely taken for granted but is a factor that is critical to successful outcomes.

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• of special interest

•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 634).

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