Urol Res (2011) 39:437–442
DOI 10.1007/s00240-011-0372-z

ORIGINAL PAPER

Pretreatment with low-energy shock waves reduces the renal oxidative stress and inflammation caused by high-energy shock wave lithotripsy

Daniel L. Clark · Bret A. Connors · Rajash K. Handa · Andrew P. Evan

Received: 14 January 2011 / Accepted: 21 February 2011 / Published online: 9 March 2011
© Springer-Verlag 2011

Abstract The purpose of this study was to determine if pretreatment of porcine kidneys with low-energy shock waves (SWs) prior to delivery of a clinical dose of 2,000 SWs reduces or prevents shock wave lithotripsy (SWL)-induced acute oxidative stress and inflammation in the treated kidney. Pigs (7–8 weeks old) received 2,000 SWs at 24 kV (120 SW/min) with or without pretreatment with 100 SWs at 12 kV/2 Hz to the lower pole calyx of one kidney using the HM3. Four hours post-treatment, selected samples of renal tissue were frozen for analysis of cytokine, interleukin-6 (IL-6), and stress response protein, heme oxygenase-1 (HO-1). Urine samples were taken before and after treatment for analysis of tumor necrosis factor-α (TNF-α). Treatment with 2,000 SWs with or without pretreatment caused a statistically significant elevation of HO-1 and IL-6 in the renal medulla localized to the focal zone of the lithotripter. However, the increase in HO-1 and IL-6 was significantly reduced using the pretreatment protocol compared to no pretreatment. Urinary excretion of TNF-α increased significantly ($p < 0.05$) from baseline for pigs receiving 2,000 SWs alone; however, this effect was completely abolished with the pretreatment protocol. We conclude that pretreatment of the kidney with a low dose of low-energy SWs prior to delivery of a clinical dose of SWs reduces, but does not completely prevent, SWL-induced acute renal oxidative stress and inflammation.

D. L. Clark (✉) · B. A. Connors · R. K. Handa · A. P. Evan
Department of Anatomy and Cell Biology, Indiana University School of Medicine, 635 Barnhill Drive, MS 510, Indianapolis, IN 46202, USA
e-mail: danlclar@iupui.edu

Keywords Shock wave lithotripsy · Kidney · Oxidative stress · Heme oxygenase · Inflammation

Introduction

Shock wave lithotripsy (SWL) is the most common method for treating uncomplicated kidney stones of ≤2 cm located in the upper urinary tract [1, 2]. Although clearly effective at breaking stones, SWs also produce acute renal injury involving damage to small blood vessels in the renal medulla and cortex, intraparenchymal bleeding, oxidative stress, inflammation, and impairment of renal hemodynamics [1]. Normal global kidney function usually is restored within hours, but the repair of focal sites of tissue injury results in scar formation and the loss of functional renal tissue [1–6].

SWL is generally considered a low-risk procedure. However, the long-term safety of SWL has been questioned in light of recent studies reporting an association of SWL with an increased incidence of diabetes mellitus [7], the onset of hypertension [8, 9], and the exacerbation of stone disease after multiple SWL sessions [10–12]. Such questions have stimulated basic research studies to better understand the renal response to SWs and to develop protocols to protect the kidney from the injurious effects of SWL.

The notion that oxidative stress contributes to tissue injury after SWL gained support from studies showing that antioxidants decreased urinary markers of tubular damage and reduced tissue injury in the renal cortex after SWL [13, 14]. Most studies have examined oxidative stress in the cortex, but we recently showed that SWs induce a rapid oxidative stress and inflammatory response in medullary tissue located within the focal zone (F2) of the lithotripter

[15]. In these studies, heme oxygenase-1 (HO-1) and interleukin-6 (IL-6) were elevated in the medulla at F2, while urinary excretion of tumor necrosis factor-α (TNF-α) increased by 1 h after treatment. The magnitude of this tissue response was subsequently found to be dependent on SW number [16].

One method to reduce renal injury after SWL is to reduce the rate at which the SWs are applied. Experiments have shown that reducing the treatment rate from the usual 120 SW/min (2 Hz) to either 30 [17] or 60 [18] SW/min (0.5 and 1 Hz, respectively) gave good stone comminution and decreased both the renal vascular lesion size and the effects on renal hemodynamics [19, 20]. However, employing this method would extend treatment times, so fewer patients could be treated in a day. A second method to protect the kidney from SWs involves an adaptation of a "ramping" protocol: i.e., progressive increases in SW delivery voltage [3, 20]. We have recently shown that pretreatment of the kidney with a small number of SWs, independent of SW voltage, followed by a brief pause (what we have termed the "protection protocol") before delivering a clinical dose of high-energy SWs attenuated the SWL-induced decrease in renal hemodynamics and reduced the size of the resulting lesion [19, 20]. It is not known, however, whether reduced treatment rate or the "protection protocol" will ameliorate or prevent SW-induced renal oxidative stress and inflammation. Therefore, the purpose of this study was to determine if our protection protocol protects the kidney from the tissue injury induced by SWL.

Materials and methods

The experimental protocol used in this study was carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and was approved by the Institutional Animal Care and Use Committee of the Indiana University School of Medicine and Methodist Hospital. Female farm pigs, 7–8 weeks of age (10–15 kg, Hardin Farms, Danville, IN), were assigned to receive either a pretreatment of 100 SWs at 12 kV with a 3 min interval followed by 2,000 SWs at 24 kV or a direct treatment of 2,000 SWs at 24 kV from an HM3 lithotripter; all SWs were delivered at 120 SWs/min. Details of the surgical placement of the vascular and ureteral catheters, and of the use of the lithotripter have been previously described [15]. Prior to SWL, and at intervals of 500 SWs during treatment, the position of the SW focus (on a lower pole) was verified by injection of a small amount of contrast medium (Renografin 60%, Bracco Diagnostics, Princeton, NJ, USA) through the ureteral catheter into the urinary collection system of the treated kidney.

Timed plasma and urine samples were collected throughout the experiment. Aliquots of plasma and urine allocated for cytokine analysis were frozen on dry ice and stored at −80°C. Four hours after treatment, the kidneys were perfused with cold isotonic saline to remove blood and then removed. Transverse tissue sections were cut from the lower and upper poles of both kidneys. Cortex and medulla isolated from each section were snap-frozen in liquid nitrogen and stored at −80°C.

Renal homogenates for analysis of IL-6 were prepared as previously described [15]. Briefly, frozen renal tissue was weighed and then homogenized in two volumes of ice-cold buffer containing 10 mM HEPES, 10 mM KCl, 0.1 mM EGTA, 1 mM dithiothreitol, and 0.25 mM phenyl methylsulfonyl fluoride (PMSF). The homogenate was centrifuged twice at 3,000×*g* for 15 min at 4°C. Protein was assayed using the Coomassie Plus assay (Pierce, Rockford, IL) and aliquots of the final supernatant were stored at −80°C.

Renal microsomes were prepared for analysis of HO-1 by Western blot. Frozen kidney tissue was weighed, then homogenized in three volumes of ice-cold 20 mM potassium phosphate buffer (pH 7.4) containing 135 mM KCl, 0.1 mM EDTA, Complete Protease Inhibitor Cocktail (Roche, Indianapolis, IN), 1 mM sodium orthovanadate, and 0.1 mM PMSF. Following low-speed centrifugation to remove large particles, homogenates were centrifuged at 100,000×*g* for 1 h at 4°C. The microsomal pellet was resuspended in 20 mM potassium phosphate buffer (pH 7.4) containing 1 mM KCl, 10 mM EDTA, and protease inhibitors. After assay of protein, aliquots were stored at −80°C.

Renal microsomal protein (25 μg) prepared in sample buffer was separated on a 10% polyacrylamide gel, followed by electrophoretic transfer to a PVDF membrane (Millipore). After blocking in 10 mM Tris-buffered saline with 0.05% Tween and 5% milk, the membrane was incubated with a rabbit polyclonal anti-HO-1 antibody (1:4,000; Stressgen SPA-895: Assay Designs, Ann Arbor, MI), followed by incubation with a donkey anti-rabbit IgG–HRP conjugated antibody (1:40,000; Jackson Immunoresearch, West Grove, PA). Bands were detected by enhanced chemiluminescence (Pierce, Rockford, IL). Membranes were stripped and probed for *β*-actin using a mouse monoclonal anti-*β*-actin-peroxidase conjugate antibody (1:100,000; Abcam, Piscataway, NJ). Band intensities were quantified by densitometry (Quantity One, BioRad, Hercules, CA).

Effective renal plasma flow was estimated by measuring the renal clearance of para-aminohippuric acid using a colorimetric assay as previously described [21]. TNF-α was quantified in urine using a Quantikine Porcine TNF-α ELISA kit (R&D Systems, Minneapolis, MN). IL-6 was

measured in renal homogenates with a Quantikine Porcine IL-6 ELISA kit (R&D Systems, Minneapolis, MN).

For comparison, we have included data for urinary TNF-α excretion from animals receiving sham treatment or 2,000 SWs from a recently published study on the effect of SWL on renal oxidative stress and inflammation [15]. That study was carried out with the same lithotripter, animals of the same size, and the same protocol as the current experiment. IL-6 assays and Western blots generated to examine the effect of low-dose low-voltage SW pretreatment included samples from the sham and 2,000 SW groups used in the previous studies [15, 16], as well as samples from other animals in these groups which had not been analyzed.

For statistical analysis, mean HO-1 measures from the three groups were compared by ANOVA with post hoc comparisons between pairs of groups following a significant overall ANOVA ($p < 0.05$). Since both IL-6 and TNF-α values were highly skewed, we used non-parametric methods to analyze these data. The Kruskal–Wallis test was used for deriving the overall p values when comparing differences in means of the three groups. Following significant overall p values, post hoc comparisons were conducted using the Wilcoxon test to obtain p values. The criterion for statistical significance was $p < 0.05$.

Results

Animals from all groups had similar weights (14.2 ± 1.9 kg) and basal blood pressure (68.3 ± 1.5 mm Hg). The group of animals treated with the protection protocol showed a modest, but significant, elevation in basal blood pressure compared to sham for the TNF-α measurements (Table 1).

HO-1 in the medulla within F2 was significantly elevated in the groups receiving 2,000 SWs either with ($p < 0.004$) or without ($p < 0.05$) pretreatment than in the sham group (Fig. 1). Direct treatment with 2,000 SWs induced a larger increase of HO-1 than in the pretreatment group ($p < 0.05$).

Similarly, IL-6 levels in the medulla within F2 increased after SW treatment above sham levels (Fig. 2). A smaller increase in IL-6 levels was observed in pretreated kidneys than in those receiving 2,000 SWs without pretreatment ($p < 0.04$).

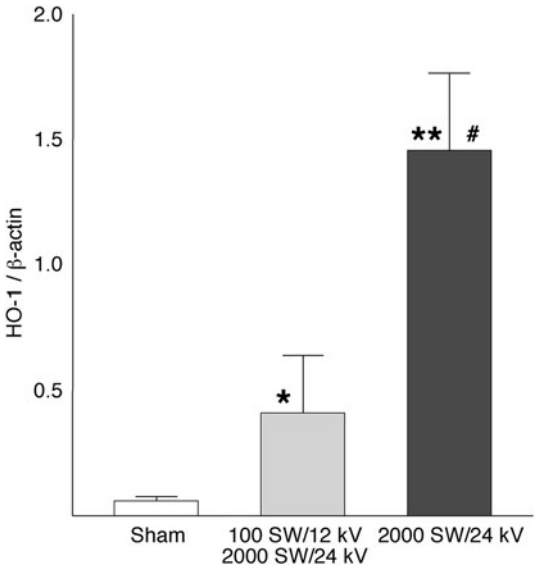

Fig. 1 HO-1 in the medulla (F2 for SWL) for sham and SWL-treated pigs at 4 h after treatment. For each group, $N = 6$. *100 SW/12 kV–2000 SW/24 kV versus sham, $p < 0.05$. **2,000 SW versus sham, $p < 0.004$. #100 SW/12 kV–2000 SW/24 kV versus 2000 SW, $p < 0.05$

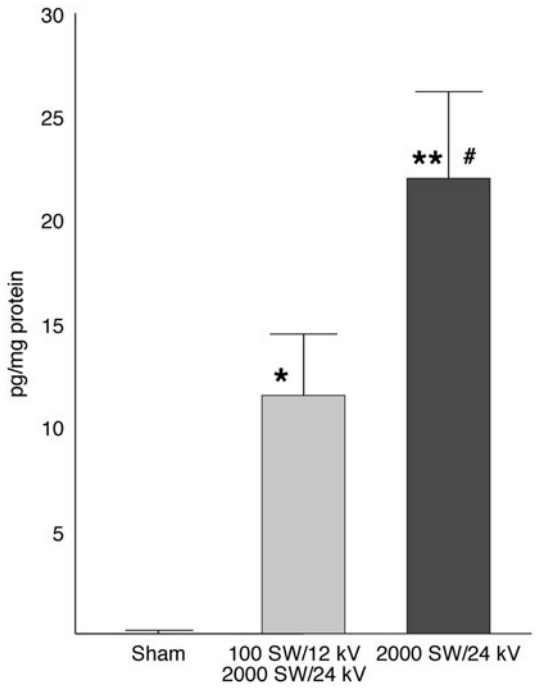

Fig. 2 Tissue IL-6 levels in the medulla (F2 for SWL) of sham- and SWL-treated pigs at 4 h after treatment: *100 SW/12 kV–2000 SW/24 kV versus sham, $p < 0.01$; **2000 SW versus sham, $p < 0.001$; #100 SW/12 kV–2000 SW/24 kV versus 2000 SW, $p < 0.04$

Table 1 Mean (SEM; N) blood pressure by marker analyzed, for treatment groups

Assayed	Sham	100 SW/12 kV	2,000 SW
HO-1	65.2 (2.0; 6)	76.6 (4.5; 6)	72.7 (5.5; 6)
IL-6	64.7 (2.0; 10)	76.6 (4.5; 6)	73.1 (5.2; 6)
TNF-α	65.6 (1.5; 11)	*76.6 (4.5; 6)	67.0 (2.6; 13)

* $p < 0.05$ compared to sham

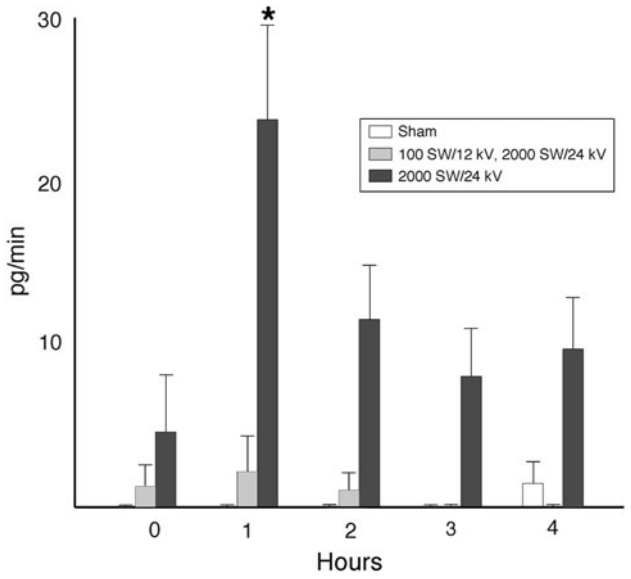

Fig. 3 Urine TNF-α excretion from treated kidneys of sham- and SWL-treated pigs. $*p < 0.001$ versus sham. Values are the mean ± SEM

The urinary excretion of TNF-α from the treated kidney for the group receiving low-energy SW pretreatment prior to the 2,000 SWs did not change from sham values at any sample time (Fig. 3). This is in contrast to kidneys treated with 2,000 SWs, which demonstrated a significant increase in the urinary excretion of TNF-α by 1 h after SWL that declined within 4 h toward baseline values [15].

Discussion

This is the first report to show that pretreatment with a low number of low-energy SWs prevents SWL-induced oxidative stress and inflammation. The elevation of tissue HO-1 and IL-6 typically observed in the medulla within F2 after 2,000 SWs [15] was significantly reduced, but not completely prevented, when 100 low-energy SWs (12 kV) were administered to the kidney followed by a 3 min pause (protection protocol) before administering 2,000 SWs at 24 kV. However, the pretreatment protocol completely abolished the increase in urinary excretion of TNF-α after SWL.

Abnormal cardiovascular or renal function resulting in hypoxia/ischemia can affect systemic and tissue (e.g., renal) stress protein and cytokine levels [22, 23]. Thus, confirmation of normal basal blood pressure for pigs in all groups used in this study was necessary to permit us to conclude that results from the pretreatment protocol are causally related to HO-1 and IL-6 changes observed in renal tissue after SWL. The modest, but significant, difference in blood pressure for the protection protocol group compared to sham for the TNF-α measurements was not in the direction associated with impairment of renal function, nor would it have affected the outcome of these experiments.

SWL causes both direct and indirect injury to the kidney. The direct injury comes from the initial effect of SWs on small blood vessels and tubules. Blood vessels are ruptured and tubules are disrupted. The indirect injury consists of hypoxia/ischemia induced by renal vasoconstriction and blood flow disruption by ruptured arterioles. This indirect injury has been implicated in producing an ischemia–reperfusion effect (IR) in the treated kidney [24, 25]. While hypoxia–ischemia and IR may be present, our earlier work suggested that other factors likely make greater contributions to the secondary injury induced by SWs [15]. We have hypothesized that IR coupled with high localized levels of heme and iron, released from red blood cells, create an environment conducive to the development of cellular oxidative stress and inflammation. Exposure of renal tissue to ischemia, heme [26], or iron can induce oxidative stress in several cell types associated with injury caused by SWL [27]. These cell types include renal tubular epithelial cells [28], vascular endothelial cells [29], and macrophages [30]. Future studies will be required to determine which cell types participate in the oxidative stress and inflammatory response we have measured, and how heme and iron contribute to renal injury after SWL.

The induction of oxidative stress in human and pig kidneys post-SWL has been implicated from earlier reports showing increased levels of products of lipid peroxidation in plasma, urine, and renal dialysate [25, 31, 32]. These lipid peroxidation products are normally indicative of free radical activity potentially related to oxidative stress. Pretreatment with the antioxidant, allopurinol, prevented the SWL-induced increase in lipid peroxidation in pigs [13]. Likewise, a calcium antagonist or antioxidants reversed modest changes in urine levels of albumin and β-microglobulin in patients after SWL [14, 33]. We improved upon these observations by reporting that renal injury after SWL can be assessed using markers of oxidative stress (HO-1) and inflammation (HO-1, IL-6, and TNF-α) [15]. The SWL-induced injury was principally localized to the medulla within the focal zone of the lithotripter (F2). We subsequently found that the magnitude of the oxidative stress and inflammatory response after SWL is dependent on SW number [16]. Determination of this injury response has become a sensitive and useful tool for us to assess the impact of SWs on the kidney.

The heme oxygenase family of enzymes is involved in the degradation of heme to biliverdin, carbon monoxide (CO), and iron (Fe). Biliverdin is subsequently converted to bilirubin. Bilirubin and CO have antioxidant and protective properties, while Fe is injurious to cells [23]. One isozyme

of heme oxygenase, HO-1, is induced by various agents, such as heavy metals, free radicals, heme, statins, as well as by conditions resulting in cellular stress (e.g., hypoxia). Induction of HO-1 in most tissues, including the kidney, usually results in protection of tissue from injury. Some reports, however, indicate that under certain circumstances, HO-1 induction may contribute to further cellular damage. Nevertheless, experimental studies using increased HO-1 levels or delivery of its antioxidant metabolic products appear to reduce injury and improve the prognosis in conditions such as acute renal injury, renal inflammation, and kidney transplantation [34]. For SWL, it is necessary to first determine the role of HO-1 in renal injury before an appropriate protocol can be designed to modulate the level of this protein in a way that will reduce the effects of SWs on the kidney.

The parameters chosen for the pretreatment protocol employed in the present study were the minimum number of SWs with the lowest SW voltage accompanied by a rest interval, which have been observed to provide protection to the kidney from a clinical dose of 2,000 SWs. The "protection protocol" developed from a study in which our group found that if kidneys were pretreated with 2,000, 500, or 100 SWs, the resulting injury from a clinical dose of 2,000 SWs was significantly attenuated [19]. Subsequently, when the pretreatment SW voltage was varied (12, 18, or 24 kV) while the pretreatment dose remained constant at 100 SWs, similar levels of protection were observed, indicating that the effect was not explained solely by voltage ramping [20]. Interestingly, the "protection protocol" includes a 3- to 4-min rest interval between the pretreatment and the clinical SW doses. Future studies are needed to clarify the role of this time period in the efficacy of this procedure for protecting the kidney from SWL-induced injury.

In summary, the present studies have demonstrated the effectiveness of the "protection protocol" and the sensitivity of the oxidative stress and inflammatory response in assessing SWL-induced renal injury. One potential clinical benefit of this low-voltage SW pretreatment derives from it being a non-pharmacological method to reduce the deleterious consequences of SWL on the kidney. We recognize, however, that since the "protection protocol" did not completely prevent SWL-induced tissue injury, any long-term effect resulting from even such modest trauma to the renal parenchyma remains as yet unidentified. Once the role of HO-1 in renal injury after SWL is defined, pharmacologic manipulation of HO-1 prior to SWL, alone or in combination with other strategies for renal protection, may improve the safety of this procedure and minimize the risk of chronic effects implicated with this procedure.

Acknowledgments The authors express appreciation to Dr. Lynn R. Willis for review of the manuscript, to Dr. Alex Robling for support on technical aspects of this study, and to Cynthia Johnson for laboratory support. This project was funded in part by PHS Grants P01-DK43881 and R01-DK67133.

References

1. Evan AP, Willis LR, Lingeman JE, McAteer JA (1998) Renal trauma and the risk of long-term complications in shock wave lithotripsy. Nephron 78:1–8
2. McAteer JA, Evan AP (2008) The acute and long-term adverse effects of shock wave lithotripsy. Semin Nephrol 28:200–213
3. McAteer JA, Bailey MR, Williams JC Jr, Cleveland RO, Evan AP (2005) Strategies for improved shock wave lithotripsy. Minerva Urol Nefrol 57:271–287
4. Newman R, Hackett R, Senior D, Brock K, Feldman J, Sosnowski J, Finlayson B (1987) Pathologic effects of ESWL on canine renal tissue. Urology 29:194–200
5. Morris JS, Husmann DA, Wilson WT, Denstedt J, Fulgham PF, Clayman RV, Preminger GM (1991) A comparison of renal damage induced by varying modes of shock wave generation. J Urol 145:864–867
6. Koga H, Matsuoka K, Noda S, Yamashita T (1996) Cumulative renal damage in dogs by repeated treatment with extracorporeal shock waves. Int J Urol 3:134–140
7. Krambeck AE, Gettman MT, Rohlinger AL, Lohse CM, Patterson DE, Segura JW (2006) Diabetes mellitus and hypertension associated with shock wave lithotripsy of renal and proximal ureteral stones at 19 years of followup. J Urol 175:1742–1747
8. Janetschek G, Frauscher F, Knapp R, Hofle G, Peschel R, Bartsch G (1997) New onset hypertension after extracorporeal shock wave lithotripsy: age related incidence and prediction by intrarenal resistive index. J Urology 158:346–351
9. Barbosa P, Makhlouf A, Thorner D, Ugarte R, Monga M (2010) Shockwave lithotripsy is associated with a higher prevalence of hypertension. J Urology 183(4, Suppl):e562
10. Parks JH, Worcester EM, Coe FL, Evan AP, Lingeman JE (2004) Clinical implications of abundant calcium phosphate in routinely analyzed kidney stones. Kid Int 66:777–785
11. Parks JH, Coe FL, Evan AP, Worcester EM (2009) Urine pH in renal calcium stone formers who do and do not increase stone phosphate content with time. Nephrol Dial Transplant 24:130–136
12. Evan AP, Lingeman JE, Coe FL, Shao Y, Parks JH, Bledsoe SB, Phillips CL, Bonsib S, Worcester EM, Sommer AJ, Kim SC, Tinmouth WW, Grynpas M (2005) Crystal-associated nephropathy in patients with brushite nephrolithiasis. Kid Int 67:576–591
13. Munver R, Delvecchio FC, Kuo RL, Brown SA, Zhong P, Preminger GM (2002) In vivo assessment of free radical activity during shock wave lithotripsy using a microdialysis system: the renoprotective action of allopurinol. J Urol 167:327–334
14. Li B, Zhou W, Li P (1995) Protective effects of nifedipine and allopurinol on high energy shock wave induced acute changes of renal function. J Urol 153:596–598
15. Clark DL, Connors BA, Evan AP, Willis LR, Handa RK, Gao S (2009) Localization of renal oxidative stress and inflammatory response after lithotripsy. BJU Int 103:1562–1568
16. Clark DL, Connors BA, Evan AP, Handa RK, Gao S (2010) Effect of shock wave number on renal oxidative stress and inflammation. BJU Int 107:318–322. doi:10.1111/j.1464-410X.2010.09311.x
17. Evan AP, McAteer JA, Connors BA, Blomgren PM, Lingeman JE (2007) Renal injury during shock wave lithotripsy is significantly reduced by slowing the rate of shock wave delivery. BJU Int 100:624–627

18. Connors BA, Evan AP, Blomgren PM, Handa RK, Willis LR, Gao S, McAteer JA, Lingeman JE (2009) Extracorporeal shock wave lithotripsy at 60 shock waves/min reduces renal injury in a porcine model. BJU Int 104:1004–1008
19. Willis LR, Evan AP, Connors BA, Handa RK, Blomgren PM, Lingeman JE (2006) Prevention of lithotripsy-induced renal injury by pretreating kidneys with low-energy shock waves. J Am Soc Nephrol 17:663–673
20. Connors BA, Evan AP, Blomgren PM, Handa RK, Willis LR, Gao S (2009) Effect of initial shock wave voltage on shock wave lithotripsy-induced lesion size during step-wise voltage ramping. BJU Int 103:104–107
21. Willis LR, Evan AP, Connors BA, Shao Y, Blomgren PM, Pratt JH, Fineberg NS, Lingeman JE (2005) Shockwave lithotripsy: dose-related effects on renal structure, hemodynamics, and tubular function. J Endourol 19:90–101
22. Bonventre JV (2004) Pathophysiology of ischemic acute renal failure. Inflammation, lung–kidney cross-talk, and biomarkers. Contrib Nephrol 144:19–30
23. Hill-Kapturczak N, Chang SH, Agarwal A (2002) Heme oxygenase and the kidney. DNA Cell Biol 21:307–321
24. Sarica K, Kosar A, Yaman O, Beduk Y, Durak I, Gogus O, Kavukcu M (1996) Evaluation of ischemia after ESWL: detection of free oxygen radical scavenger enzymes in renal parenchyma subjected to high-energy shock waves. Urol Int 57:221–223
25. Cohen TD, Durrani AF, Brown SA, Ferraro R, Preminger GM (1998) Lipid peroxidation induced by shockwave lithotripsy. J Endourol 12:229–232
26. Nath KA, Balla G, Vercellotti GM, Balla J, Jacob HS, Levitt MD, Rosenberg ME (1992) Induction of heme oxygenase is a rapid, protective response in rhabdomyolysis in the rat. J Clin Invest 90:267–270
27. Tracz MJ, Alam J, Nath KA (2007) Physiology and pathophysiology of heme: implications for kidney disease. J Am Soc Nephrol 18:414–420
28. Alam J, Killeen E, Gong P, Naquin R, Hu B, Stewart D, Ingelfinger JR, Nath KA (2003) Heme activates the heme oxygenase-1 gene in renal epithelial cells by stabilizing Nrf2. Am J Physiol Renal Physiol 284:F743–F752
29. Bernardini C, Zannoni A, Turba ME, Fantinati P, Tamanini C, Bacci ML, Forni M (2005) Heat shock protein 70, heat shock protein 32, and vascular endothelial growth factor production and their effects on lipopolysaccharide-induced apoptosis in porcine aortic endothelial cells. Cell Stress Chaperones 10:340–348
30. Lang D, Reuter S, Buzescu T, August C, Heidenreich S (2005) Heme-induced heme oxygenase-1 (HO-1) in human monocytes inhibits apoptosis despite caspase-3 up-regulation. Int Immunol 17:155–165
31. Aksoy Y, Malkoc I, Atmaca AF, Aksoy H, Altinkaynak K, Akcay F (2006) The effects of extracorporeal shock wave lithotripsy on antioxidant enzymes in erythrocytes. Cell Biochem Funct 24:467–469
32. Brown SA, Munver R, Delvecchio FC, Kuo RL, Zhong P, Preminger GM (2000) Microdialysis assessment of shock wave lithotripsy-induced renal injury. Urology 56:364–368
33. Al-Awadi KA, Kehinde EO, Loutfi I, Mojiminiyi OA, Al-Hunayan A, Abdul-Halim H, Al-Sarraf A, Memon A, Abraham MP (2008) Treatment of renal calculi by lithotripsy: minimizing short-term shock wave induced renal damage by using antioxidants. Urol Res 36:51–60
34. Nath KA (2006) Heme oxygenase-1: a provenance for cytoprotective pathways in the kidney and other tissues. Kid Int 70:432–443