Urol Res (2006) 34: 277–282
DOI 10.1007/s00240-006-0057-1

ORIGINAL PAPER

Xiang Li · Dalin He · Linlin Zhang · Xinfa Cheng
Binwu Sheng · Yong Luo

A novel antioxidant agent, astragalosides, prevents shock wave-induced renal oxidative injury in rabbits

Received: 21 October 2005 / Accepted: 27 March 2006 / Published online: 17 June 2006

Abstract Extracorporeal shock-wave lithotripsy (ESWL)-induced renal damage can occur as a result of multiple mechanisms, including small vessel injury and free radical formation. Our previous studies have demonstrated that *Astragalus membranaceus* (AM), a traditional Chinese herb, could significantly alleviate shock wave-induced renal oxidative injury, and its renoprotective effects were superior to those of varapamil, a calcium antagonist, which were considered to be a powerful agent in treating renal damage during ESWL. However, the effective antioxidant ingredient of this herb in the setting of lithotripsy remains unclear. Astragalosides, the major components of AM, was demonstrated to have superior antioxidation properties both in vitro and in vivo. Therefore, in this study we further investigate the potential effects of astragalosides on the shock wave-induced oxidative stress in rabbit kidney. Thirty male rabbits were randomly assigned to two groups, each consisting of 15 rabbits: (1) control group, (2) astragaloside-treated group. Each group of animals underwent 1,500 shock waves to the right kidney. Peripheral blood, urine and kidney tissue samples were collected pre- and post-ESWL. The level of urinary *N*-acetyl-β-glucosaminidase (NAG), serum creatinine, serum or homogenates malondialdehyde (MDA) and superoxide dismutase (SOD), respectively, were detected. Histological alterations were also examined through light microcopy and transmission electron microscopy. In the control group, shock wave significantly increased the level of MDA and decreased SOD activity in both blood and renal homogenates ($P < 0.05$, respectively). The comparison between the control and astragalosides group demonstrated that astragalosides could significantly decrease the level of MDA ($P < 0.05$) and inhibit the decline of SOD activity ($P < 0.05$). After exposure to shock waves, the activity of urinary NAG increased significantly in the control group ($P < 0.05$). However, the concentration of serum creatinine did not change significantly. The comparison between the control and astragalosides group demonstrated that astragalosides significantly reduced the shock wave-induced leakage of NAG into the urine ($P < 0.05$). Histological examination also showed that renal morphological impairments were much milder in astragaloside-treated rabbits than those of the control group. Our results indicated that astragaloside treatment provided significant protection against shock wave-induced renal oxidative injury.

Keywords Shock waves · Renal injury · Astragalosides · Antioxidation · Rabbits

X. Li · D. He (✉) · L. Zhang · X. Cheng · B. Sheng · Y. Luo
Department of Urology, School of Medicine,
Xi'an Jiaotong University, Xi'an, Shaanxi 710061, China
E-mail: Urologistlx@yahoo.com.cn
Tel.: +29-853-23661
Fax: +29-853-24058

Introduction

The advent of extracorporeal shock-wave lithotripsy (ESWL) changed the therapeutic strategy for urolithiasis dramatically. It is currently the first-line treatment for upper urinary tract calculi. However, this treatment is not completely free from side effects. Numerous morphological and functional impairments subject to ESWL have been documented in animals and human patients [1–4]. Although the clinical significance of parenchymal injury secondary to shock-wave treatment is still an open question in healthy patients with two normal kidneys, those with a solitary kidney or baseline renal dysfunction may be at significant risk for permanent renal damage [5]. Initially the adverse effects of ESWL were attributed to renal damage resulting only from the direct action of cavitation bubbles or shear stress, which originated from shock-wave energy [1, 6]. More recently, formation of free radicals has been demonstrated to be a major contributing factor in shock wave-induced tissue damage via lipid peroxidation and the disruption of cellular membranes, which in turn induces calcium

overload and initiates the process of cellular death [7–10].

Astragalus membranaceus (AM) is a kind of traditional Chinese herb, which is widely used in treating free-radical-mediated injury in various organs through its anti-oxidant properties [11–13]. In a previous study we demonstrated that AM significantly alleviated shock wave-induced renal parenchymal injury in rabbits, and its renoprotective effects were superior to those of varapamil, a calcium antagonist, which is considered to have powerful renoprotective properties against tissue damage during ESWL [14]. However, the effective ingredient of AM in the setting of lithotripsy remains unclear. Astragalosides, a saponin-like compound, is one of the major active components isolated from AM. It has been shown to have several biological properties: antioxidant [15], antiaging [16], antiviral [17] and inhibiting intracellular calcium overload [18]. Furthermore, astragaloside administration also reduced cardiac ischemia reperfusion injury in a rat model via scavenging free radical species [19]. Therefore, in this study we further investigate the potential protective effect of astragalosides on the shock wave-induced oxidative injury in rabbit kidney.

Materials and methods

Thirty male rabbits weighing between 1,800 and 2,300 g were randomly assigned to two groups: (1) control group and (2) astragaloside-treated group, each consisting of 15 rabbits. The animals of group 2 were administrated astragalosides for 7 days starting 3 days prior to ESWL application at a dosage of 150 mg/kg per 24 h intragastrically. The astragalosides were isolated and purified by the College of Pharmacy, Xi'an Jiaotong University, China. The same volume of isotonic saline solution was administered to the rabbits of the control group.

Before shock-wave exposure all the animals were anesthetized with 2.5% thiopental sodium intraperitoneally at a dosage of 40 mg/kg. After adequate anesthesia all the animals underwent shock-wave lithotripsy at the right kidney under the guidance of ultrasonography. All of the procedures were performed with a HK MZ-V lithotripter (HuiKang, China). This lithotripter has been demonstrated to have approximately equal efficacy and resulting kidney injury compared with Siemens or Dornier machines [20]. The kV values were kept constant (18 kV) and each animal received 1,500 impulses (frequency 70/min). Peripheral blood specimens were collected from the median auricular artery of the animals of each group before, 0 (immediately after), 1, 3, 7 and 14 days after shock-wave treatment. The blood samples were stored at −80°C for the evaluation of plasma superoxide dismutase (SOD), serum malondialdehyde (MDA) and serum creatinine. Urine samples were obtained by putting the animals in the metabolism cages for 8 h on day −1, 0 (immediately after ESWL), 3, 7 and 14. The urine was centrifuged for 10 min at 1,500 rpm and the clear supernatants stored at −80°C prior to analysis.

The kidneys of each animal were removed through bilateral flank incisions under thiopental sodium anesthesia 3, 7 and 14 days after shock-wave treatment. The removed kidneys underwent histological evaluations and were prepared for the determination of homogenate SOD and MDA. All the experiments were conducted in accord with the National Institute of Health Guide for the Care and Use of laboratory Animals and our institutional guidelines of the animal care and use committee.

SOD activity and MDA level were measured by biochemical spectrophotometric analysis according to the manufacturers' instructions (Nanjing Jiancheng Biological Techniques Institute, China) and quantified using a spectrophotometer (Sinco, Korea). SOD activities were detected by a xanthine/xanthine oxidase assay based on a method involving the assay of hydroxylamine 21]. MDA produced by the hydrolysis of lipid hydroperoxides reacts with thiobarbituric acid (TBA) to produce a complex that absorbs at 532 nm. The result of plasma SOD activity was expressed as kU/l, while serum MDA level expressed as mmol/l. The result of homogenate SOD activity was expressed as kU/g protein, while homogenate MDA level was expressed as mmol/g protein. The urinary *N*-acetyl-*β*-glucosaminidase (NAG) activity was measured spectrophotometrically with sodio *m*-cresol sulfonphthaleinyl-*N*-acetyl-*β*-D-glucosaminide as substrate [22]. Serum and urine creatinine was measured by the alkaline picrate method. The excretion ratio of urinary NAG was calculated as NAG activity/urine creatinine concentration (U/g creatinine).

Each rabbit's kidney tissues were evaluated by light microscopy (LM) and transmission electron microscopy (TEM). For LM evaluation, tissue specimens were fixed with 10% formalin solution and then embedded in paraffin blocks. After this procedure, 4-μm sections were obtained with a microtome and stained with hematoxylin and eosin (HE) or periodic acid-Shiff's reagent (PAS). The tissue samples were evaluated for tubular injury and interstitial changes (inflammatory cell infiltration) by an observer masked to the treatment groups.

The tubular injury was scored semiquantitatively for at least 30 cortical fields of each sample. Tubular injury was defined as tubular dilation or cast formation, atrophy and tubular epithelial cell swelling or necrosis. The following semiquantitative score was used: score 0 = no tubular injury, score 1 = < 10% of tubules were injured, score 2 = 10–25% of the tubules were injured, score 3 = 25–50% of the tubules were injured, score 4 = 50–75% tubules injured and score 5 = > 75% of tubules were injured. The interstitial changes (inflammatory cell infiltration) were graded from 0 to 4 (0 = no changes; 1 = changes affecting less than 25% of the samples; 2 = changes affecting 25–50% of the samples; 3 = changes affecting 50–75% of the samples; 4 = changes affecting more than 75% of the samples) [23, 24].

For TEM evaluation, tissue samples were immediately placed in 2% glutaraldehyde solution and fixed at 4°C for 48 h. Then, the specimens were placed in a 2% solution of osmium tetrahydroxide for 2 h. A graded ethanol series was used for dehydration, and the specimens were embedded in epon. Sections were cut on an ultramicrotome (LKB, Sweden) and stained with both uranyl acetate and lead citrate. Examination was carried out using an H-600 electron microscope (Hitachi, Japan). At least 100 random fields were examined for each tissue sample to determine the percentage of proximal convoluted tubules injury (presenting microvilli loss or brush borders unclear) and podocyte injury (presenting foot process effacement).

All data are presented as mean ± SD. The sample tests were checked for normal distribution (Shapiro-Wilk test). Variance analysis was performed using the O'Brian test. In case of a normal distribution and equal variance the Student's *t*-test was used; otherwise the Wilcoxon test (two-tailed) was used. $P < 0.05$ was considered significant.

Results

In the control series, shock waves significantly elevated the level of serum MDA and reduced the activity of plasma SOD ($P < 0.05$, respectively). In the astragalosides group, there was also a significant increase in the concentration of serum MDA ($P < 0.05$). However, the activity of plasma SOD did not change significantly. The comparison between the control and astragalosides group demonstrated that astragalosides significantly prevented the increase in serum MDA and inhibited the decline of plasma SOD activity ($P < 0.05$, respectively) (Table 1). Compared with the controls, astragalosides also significantly decreased the level of MDA and increased SOD activity in kidney homogenates ($P < 0.05$) (Table 2).

After ESWL, the excretion of urinary NAG was increased significantly in the control group ($P < 0.05$). However, this parameter did not change significantly in the astragaloside-treated group. The comparison between the two groups demonstrated that astragalosides significantly reduced the shock wave-induced leakage of NAG into the urine ($P < 0.05$). Shock waves did not significantly influence the concentration of serum creatinine in either the control or the astragalosides group (Table 3).

In the control, LM revealed the recognized features of tubular and interstitial damage in the shock wave-treated kidneys, with the presence of tubular cast or dilation, tubular epithelial cell swelling or necrosis and tubulo-interstitial inflammatory cell infiltration. In the rabbits treated with astragalosides, the tubular damage was found to be very slight with milder inflammatory cell infiltration (Fig. 1 and Table 4).

TEM revealed a sharp loss in microvilli and unclear brush borders in the epithelial cells of the proximal convoluted tubules in the control. Furthermore the degeneration of podocytes with foot process effacement was also observed. All these subcellular injuries were much milder in the astragalosides group than those of the control group (Fig. 2 and Table 5).

Discussion

Shock-wave lithotripsy is considered safe and effective for fragmenting urinary tract calculi. However, in the last two decades more and more investigators have questioned the adverse effect of this technique. Clinical studies showed that hematuria and postoperative pain or discomfort frequently occurred in patients undergoing shock-wave treatment. The procedure is also demonstrated to cause microtrauma or hemorrhage in normal kidney. The risk of perirenal or intrarenal hematomas is estimated to be 0.1 and 0.6% using ultrasonography and between 20 and 25% using computer tomography or magnetic resonance imaging [25, 26]. Corticomedullary or interstitial hemorrhages, thrombosis of arteries or interlobular veins, tubular dilatation and cellular cast formation have also been documented in several animal models [1–3]. Furthermore, this renal parenchymal injury secondary to shock-wave treatment has also been well characterized by the appearance of urinary marker proteins and enzymes, such as microglobulin and NAG [27, 28].

Initially the adverse effects of ESWL were attributed to renal damage resulting only from the direct action of shock-wave energy, which has been known to produce gross areas of hematomas with subsequent cortical fibrosis. The mechanism of tissue injury was believed to be mechanical trauma to renal vasculature and tubules

Table 1 Levels of serum MDA and plasma SOD pre- and post-ESWL

	Serum MDA (nmol/ml)		Plasma SOD (U/ml)	
	Control ($n = 15$)	Astragalosides ($n = 15$)	Control ($n = 15$)	Astragalosides ($n = 15$)
Pre-SWL	3.82 ± 0.73	3.92 ± 0.77	125.32 ± 12.59	127.07 ± 11.60
0-day post-SWL	4.59 ± 0.69	4.26 ± 0.87	108.98 ± 15.76*	120.84 ± 9.29**
1-day post-SWL	6.14 ± 1.59*	4.88 ± 0.67*,**	102.37 ± 17.13*	119.29 ± 10.87**
3-day post-SWL	6.54 ± 1.34*	4.56 ± 0.53**	116.75 ± 8.64	121.65 ± 12.95
1-week post-SWL	4.88 ± 0.63	4.36 ± 0.39	117.29 ± 7.03	123.07 ± 9.46
2-week post-SWL	3.87 ± 0.34	3.89 ± 0.22	124.01 ± 7.63	127.50 ± 8.20

MDA malondialdehyde, *SOD* superoxide dismutase, *ESWL* extracorporeal shock-wave lithotripsy
*$P < 0.05$ indicates pre- versus post-ESWL
**$P < 0.05$ indicates control versus astragalosides group

Table 2 The values of MDA and SOD in kidney homogenates

MDA malondialdehyde, *SOD* superoxide dismutase, *SWL* shock-wave lithotripsy
*$P < 0.05$ indicates control versus astragalosides group

	MDA (nmol/mg protein)		SOD (U/mg protein)	
	Control $n = 5$	Astragalosides $n = 5$	Control $n = 5$	Astragalosides $n = 5$
3-day post-SWL	2.02 ± 0.25	1.17 ± 0.28*	6.09 ± 2.27	8.71 ± 1.83*
1-week post-SWL	1.59 ± 0.32	1.34 ± 0.29	9.63 ± 1.70	10.91 ± 2.04
2-week post-SWL	1.24 ± 0.17	1.18 ± 0.32	10.07 ± 2.01	10.78 ± 0.89

Table 3 The excretion ratio of urinary NAG (U/g creatinine) and serum creatinine (umol/l) pre- and post-ESWL

ESWL extracorporeal shock-wave lithotripsy, NAG *N*-acetyl-β-glucosaminidase
*$P < 0.05$ indicates pre- versus post-ESWL
**$P < 0.05$ indicates control versus astragalosides group

	Urinary NAG (U/g creatinine)		Serum Creatinine (umol/l)	
	Control ($n = 15$)	Astragalosides ($n = 15$)	Control ($n = 15$)	Astragalosides ($n = 15$)
Pre-SWL	2.11 ± 0.83	1.96 ± 0.70	55.47 ± 4.76	53.80 ± 6.46
0-day post-SWL	5.15 ± 0.91*	2.42 ± 0.61**	59.67 ± 7.04	54.40 ± 8.81
1-day post-SWL	2.89 ± 0.61*	2.33 ± 0.44**	53.13 ± 5.88	51.67 ± 5.91
3-day post-SWL	2.20 ± 0.59	1.91 ± 0.26	54.00 ± 0.65	52.53 ± 5.94
1-week post-SWL	2.12 ± 0.44	2.03 ± 0.62	56.10 ± 5.07	54.70 ± 5.36
2-week post-SWL	2.32 ± 0.33	2.04 ± 0.24	55.40 ± 7.16	49.00 ± 2.24

through the direct action of cavitation bubbles or shear stress. More recently free radical formation was considered to be an integral element in shock wave-induced renal damage through an indirect mechanism. Using fluorescent dyes, the generation of free radicals induced by ESWL has been demonstrated directly in suspended cells [29]. In in vivo experiments, vascular injuries caused by the direct action of shock waves could induce areas of tissue ischemia and hypoxia, which becomes more susceptible to free radical production as reperfusion occurs. Metabolic alterations caused by ischemia with reperfusion can result in abnormally high levels of free radicals [7, 30]. Thus, free radical formation and subsequent damage to the kidney during the procedure seem to be in the same manner as in the ischemia–reperfusion models. Furthermore, intrarenal hemorrhage from the damaged vessels may compound the problem, because the iron content of red blood cells can also catalyze the formation of free radicals through Fenton reaction [7, 31]. The toxicity of free radicals is attributed to their ability to initiate lipid peroxidation of cellular membranes. Following alteration of cellular membrane integrity, the cellular equilibrium is lost and cell death typically ensues [32]. It is difficult to detect free radical species because of their volatile and transient nature. However, the presence of free radicals can be measured from the elevated lipid peroxidation products or antioxidant consumption under such conditions. MDA is believed to be a reliable marker of free radical-mediated lipid peroxidation. As the breakdown products of cellular lipids, MDA could reflect the degree of tissue oxidative injuries [33]. Enzymes such as SOD, catalase and glutathione peroxidase can functionally protect against the toxic effects of free radicals. SOD can convert oxygen free radical-mediated superoxide to hydrogen peroxide, which in turn converts to water and molecular oxygen by catalase or glutathione peroxidase. Thus, SOD is proved to be a reliable indicator of antioxidation [34].

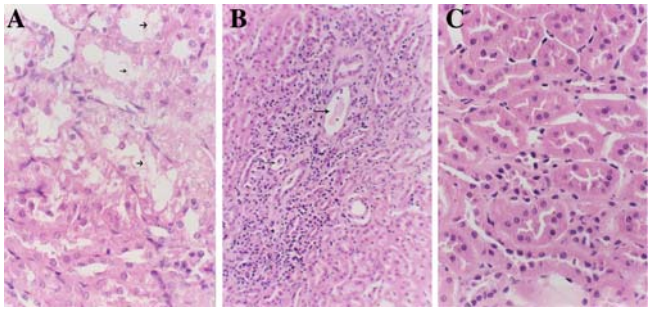

Fig. 1 **a** Proximal convoluted tubular epithelial cell degeneration or necrosis (*arrows*) is observed at 3 days after extracorporeal shock-wave lithotripsy (*ESWL*) application in the control rabbits. **b** Tubular cast formation (*arrows*) with inflammatory cell infiltrations is present at 3 days after ESWL in the control rabbits. **c** There is no obvious damage in tubular epithelial cells in astragaloside-treated rabbits. Magnification: × 400 (**a**, **c**); × 200 (**b**)

Table 4 Renal histology scores in control and astragalosides groups

SWL shock-wave lithotripsy
*$P < 0.05$ indicates control versus astragalosides group

	Tubular damage score		Interstitial damage score	
	Control	Astragalosides	Control	Astragalosides
3-day post-SWL	2.8 ± 0.8	1.6 ± 0.5*	2.6 ± 0.5	1.6 ± 0.5*
1-week post-SWL	2.2 ± 0.4	1.2 ± 0.4*	2.0 ± 0.7	1.2 ± 0.4
2-week post-SWL	1.8 ± 0.4	1.0 ± 0.7	1.2 ± 0.4	0.6 ± 0.5

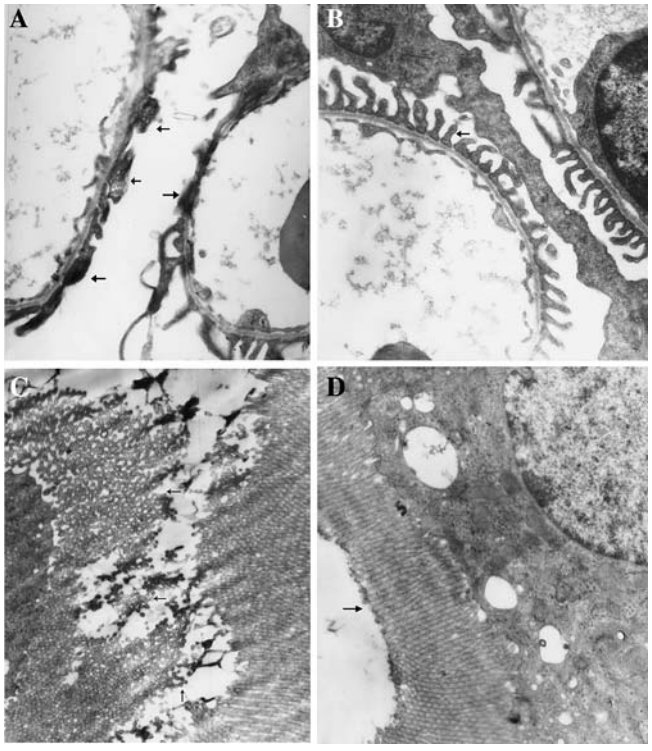

Fig. 2 **a** Degeneration of podocytes with foot process effacement (*arrows*) is seen in the control rabbits at 3 days after extracorporeal shock-wave lithotripsy (*ESWL*) application. **b** The structure of the foot process (*arrow*) is clear in astragaloside-treated rabbits. **c** Sharp loss in microvilli and unclear brush borders in proximal convoluted tubular epithelial cells are present in control rabbits at 3 days after ESWL application. **d** The structure of brush borders in tubular epithelial cells is clear in astragaloside-treated rabbits at 3 days after ESWL. Magnification: × 15,000 (**a**, **b**); × 8,000 (**c**, **d**)

In this study, the two markers combined with the activity of urinary NAG and serum creatinine were used to evaluate shock wave-induced oxidative stress in rabbit kidney. The results demonstrated that shock waves could increase the level of MDA and exhaust SOD activity both in blood and renal homogenates. It also showed a significant increase of urinary NAG activity. NAG is a lysosomal enzyme present in high concentrations in the renal proximal tubular cells. It also exists in serum but its molecular weight does not permit glomerular filtration; thus, increased urinary NAG activity is one of the most sensitive markers of renal tubular damage [35]. The concentration of serum creatinine, however, did not change significantly after shock-wave treatment, probably because the animal model used in this study had only one side of kidney treated with ESWL. Thus, the contralateral untreated kidney may be compensating for the loss of renal function. Furthermore, the histological examination revealed the characterized glomerular or tubular damage with interstitial inflammatory cells infiltration. All these findings in our results are consistent with numerous previous reports. Up till now, several agents, such as vitamins [9], melatonin [10], mannitol [28], caffeic acid phenethyl ester [35], varapamil [36] and selenium [37] have been shown to have protective effects against shock wave-induced renal oxidative stress.

AM, the traditional Chinese herb, has been widely used as a folk medicine for a long time in East Asia. In several animal experiments, it has been demonstrated to alleviate cerebral and intestinal ischaemia following reperfusion injury through its anti-oxidant properties [12, 13]. In our previous study, it has also been shown to have protective effects against shock wave-induced tissue damage through scavenging free radicals [14]. However, the effective ingredient of AM in alleviating oxidative stress in tissues remains unclear. Astragalosides are an active and natural component isolated from AM. It has been shown to have antioxidation properties both in vitro and in vivo [15, 17, 19]. Our current data demonstrated that astragalosides could significantly reduce the shock wave-induced leakage of NAG into the urine. Furthermore, it also effectively decreased MDA level and increased SOD activity in peripheral blood or renal homogenates. Histological examination also demonstrated the renal morphological impairments to be much milder in astragaloside-treated rabbits than those of the controls. Since MDA and SOD are validated measures of free radical-mediated tissue damage, and urinary NAG is a sensitive marker of tubular damage, our results indicated that astragalosides has renoprotective effects in the setting of lithotripsy for antioxidation properties.

In conclusion, in the light of our findings and the results reported in the literature, we think that production of free radicals and the subsequent damage is one of the contributing factors in shock wave-induced renal parenchymal injury. In this study, we demonstrated the potential protective effects of astragalosides on the shock wave-induced oxidative stress in rabbit kidneys. Further investigations are needed to determine the dose–response relationship between the damaging effects of ESWL application and its treatment with astragalosides in various renal changes.

Table 5 Percentage of proximal convoluted tubules and podocyte injury in control and astragalosides groups

	Proximal convoluted tubules injury (%)		Podocyte injury (%)	
	Control	Astragalosides	Control	Astragalosides
3-day post-SWL	50.8 ± 7.3	20.6 ± 4.9*	29.6 ± 4.8	14.4 ± 4.7*
1-week post-SWL	34.8 ± 3.9	13.8 ± 3.8*	10.2 ± 2.8	7.8 ± 2.4
2-week post-SWL	19.4 ± 5.3	9.2 ± 3.9*	7.0 ± 2.1	5.6 ± 2.0

SWL shock-wave lithotripsy
*$P < 0.05$ indicates control versus astragalosides group

References

1. Evan AP, Wills LR, McAteer JA, Bailey MR, Connors BA, Shao Y, Lingeman JE, Williams JC Jr, Finberg NS, Crum LA (2002) Kidney damage and renal functional changes are minimized by waveform control that suppresses cavitation in shock wave lithotripsy. J Urol 168:1556–1562
2. Jaeger P, Redha F, Marquardt K, Uhlschmid G, Hauri D (1995) Morphological and functional changes in canine kidneys following extracorporeal shock wave treatment. Urol Int 54:48–58
3. Karlsen SJ, Smevik B, Hovig T (1991) Acute morphological changes in canine kidneys after exposure to extracorporeal shock waves: a light and electron microscopic study. Urol Res 19:105–115
4. Villanyi KK, Szekely JG, Farkas LM, Javor E, Pusztai C (2001) Short-term changes in renal function after extracorporeal shock wave lithotripsy in children. J Urol 166:222–224
5. Lipski B, Miller J, Rigaud G, Stack G, Marsh C (1997) Acute renal failure from a subcapsular hematoma in a solitary kidney: an usual complication of extracorporeal shock wave lithotripsy. J Urol 157:224–225
6. Williams JC Jr, Stonehill MA, Colmenares K, Evan AP, Andreoli SP, Cleveland RO, Bailey MR, Crum LA, McAteer JA (1999) Effect of macroscopic air bubbles on cell lysis by shock wave lithotripsy in vitro. Ultrasound Med Biol 25:473–479
7. Delvecchio F, Auge BK, Munver R, Brown SA, Brizuela R, Zhong P, Preminger GM (2003) shock wave lithotripsy causes ipsilateral renal injury remote from the focal point: the role of regional vasoconstriction. J Urol 169:1526–1529
8. Munver R, Delvecchio F, 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
9. Biri H, Ozturk HS, Buykkocak S, Kacmaz M, Cimen MY, Unal D, Birey M, Bozkirli I, Durak I (1998) Antioxidant defense potential of rabbit renal tissue after ESWL: protective effects of antioxidant vitamins. Nephron 79:181–185
10. Serel TA, Ozguner F, Soyupek S (2004) Prevention of shock wave induced renal oxidative stress by melatonin: an experimental study. Urol Res 32:69–71
11. Tada S, Yase Y, Shirataki Y (2000) Inhibitory effects of astragali radix, crude drug in Oriental medicines on lipid peroxidation and protein oxidative modification of mouse brain homogenates by copper. Phytother Res 14:294–296
12. Hei ZQ, Huang HQ, Zhang JJ, Cheng BX, Li XY (2005) Protective effects of astragalus membranaceus on intestinal mucosa reperfusion injury after hemorrhagic shock in rats. World J Gastroenterol 11:4986–4991
13. Jia RZ, Jiang L, Qiao LX (2005) Study on effect of radix astragali on injury of cerebral cortex in neonatal rats after hypoxia/ischemia brain damage. Zhongguo Zhong Xi Yi Jie He Za Zhi 25:54–57
14. Sheng BW, Chen XF, Zhao J, He DL, Nan XY (2005) Astragalus membranaceus reduces free radical-mediated renal tubules injury in rabbits receiving High energy shock waves. Chin Med J 118:43–49
15. Wang D, Shen W, Tian Y, Sun Z, Jiang C, Yuan S (1996) Protective effect of active components extracted from radix Astragali on human erythrocyte membrane damage caused by reactive oxygen species. Zhongguo Zhong Yao Za Zhi 21:746–748
16. Lei H, Wang B, Li WP, Yang Y, Zhou AW, Chen MZ (2003) Anti-aging effect of Astragalosides and its mechanism of action. Acta Pharmacol Sin 24:230–234
17. Lu S, Zhang J, Yang D (1999) Effects of Astragaloside in treating myocardial injury and myocardial Sarco/Endoplasmic Ca2 + _ATPase of viral myocarditis mice. Zhongguo Zhong Yi Xi Jie He Za Zhi 19:672–674
18. Meng D, Chen XJ, Bian YY, Li P, Yang D, Zhang JN (2005) Effect of Astragaloside on intracellular calcium overload in cultured cardiac myocytes of neonatal rats. Am J Chin Med 33:11–20
19. Zhou JY, Fan Y, Kong JL, Wu DZ, Hu ZB (2000) Effects of components isolated from Astragalus membranaceus Bunge on cardiac function injured by myocardial ischemia reperfusion in rats. Zhongguo Zhong Yao Za Zhi 25:300–302
20. Sun XZ, Zhang ZW (2004) Domestic shock wave lithotripters and their characteristics. Chin Med Equip J 8:28–29
21. Koo DD, Welsh KI, West NE, Channon KM, Penington AJ, Roake JA, Morris PJ, Fuggle SV (2001) Endothelial cell protection against ischemia reperfusion injury by lecithinized superoxide dismutase. Kidney Int 60:786–796
22. Noto A, Ogawa Y, Mori S, Yoshioka M, Kitakaze T, Hori T, Nakamura M, Miyake T (1983) Simple, rapid spectrophotometry of urinary N-acetyl-beta-D-glucosaminidase, with use of a new chromogenic substrate. Clin Chem 29:1713–1716
23. Benigni A, Corna D, Maffi R, Benedetti G, Zoja C, Remuzzi G (1998) Renoprotective effect of contemporary blocking of angiotensin II and endothelin-1 in rats with membranous nephropathy. Kidney Int 54:353–359
24. Tamada S, Nakatani T, Asai T, Tashiro K, Komiya T, Sumi T, Okamura M, Kim S, Iwao H, Kishimoto T, Yamanaka S, Miura K (2003) Inhibition of nuclear factor-κB activation by pyrrolidine dithiocarbamate prevents chronic FK506 nephropathy. Kidney Int 63:306–314
25. Knap PM, Kulb PB, Lingeman JE, Newman DM, Mertz JH, Mosbaugh PG, Steele RE (1988) Extra corporeal shock wave lithotripsy induced perirenal hematomas. J Urol 139:700–703
26. Rubin JI, Arger PH, Pollack HM, Banner MP, Coleman BG, Mintz MC, Van Arsdalen KN (1987) Kidney changes after shock wave lithotripsy: CT evaluation. Radiology 162:21–24
27. Strohmaier WL, Billes IC, Abelius A, Lahme S, Bichler KH (2002) Selenium reduces high energy shock wave induced renal injury in rats. Urol Res 30:31–34
28. Ogiste JS, Nejat RJ, Rashid HH, Greene T, Gupta M (2003) The role of mannitol in alleviating renal injury during extracorporeal shock wave lithotripsy. J Urol 169:875–877
29. Suhr D, Brummer F, Hulcer DF (1991) Cavitation-generated free radicals during shock wave exposure: investigations with cell-free solutions and suspended cells. Ultrasound Med Biol 17: 761–768
30. Cohen TD, Durrani AF, Brown SA, Ferraro R, Preminger GM (1998) Lipid peroxidation induced by shockwave lithotripsy. J Endourol 12:229–232
31. Sarica K, Kosar A, Yaman O, Beduk Y, Durak I, Gogus O, Kavukcu M (1996) Evaluation of ischemia after ESWL: detection of oxygen free radical scavenger enzymes in renal parenchyma subjected to high energy shock waves. Urol Int 57:221–223
32. Defraigne JO, Detry O, Pincemail J, Franssen C, Meurisse M, Lamy M, Limet R (1994) Direct evidence of free radical production after ischemia and reperfusion and protective effect of desferrioxamine: ESR and vitamin E studies. Eur J Vasc Surg 8:537–543
33. Boaz M, Matas Z, Biro A, Katzir Z, Green M, Fainaru M, Smetana S (1999) Serum malondialdehyde and prevalent cardiovascular disease in hemodialysis. Kidney Int 56: 1078–1083
34. Vaziri ND, Lin CY, Farmand F, Sindhu RK (2003) Superoxide dismutase, catalase, glutathione peroxidase and NADPH oxidase in lead-induced hypertension. Kidney Int 63:186–194
35. Ozguner F, Armagan A, Koyu A, Caliskan S, Koylu H (2005) A novel antioxidant agent caffeic acid phenethyl ester prevents shock wave-induced renal tubular oxidative stress. Urol Res 33:239–243
36. Yaman O, Sarica K, Ozer G, Soygur T, Kutsal O, Yaman LS, Gous O (1996) Protective effect of varapamil on renal tissue during shock wave application in rabbit kidney. J Endourol 10:329–333
37. Walter LS, Inge CB, Annette A, Sven L, Karl-Horst B (2002) Selenium reduces high energy shock wave-induced renal injury in rats. Urol Res 30:31–34