African Journal of Pharmacy and Pharmacology Vol. 6(18), pp. 1363-1366, 15 May, 2012
Available online at http://www.academicjournals.org/AJPP
DOI: 10.5897/AJPP12.141
ISSN 1996-0816 ©2012 Academic Journals

Full Length Research Paper

The plerotic effect of Yunnan Baiyao on renal injury after extracorporeal shock wave lithotripsy

Haifeng Yu[1], Dapang Rao[1] and Ping Duan[2]*

[1]Department of Urology, The Second Affiliated Hospital, Wenzhou Medical College, Wenzhou 325000, P. R. China.
[2]Department of Gynecology, The Second Affiliated Hospital, Wenzhou Medical College, Wenzhou 325000, P. R. China.

Accepted 17 April, 2012

The objective of this study was to explore the protective effect of Yunnan Baiyao, a traditional Chinese herbal remedy, on renal function after extracorporeal shock wave lithotripsy (ESWL). 55 patients with renal pelvic stones were randomized to two groups: The control group (n = 25), where the patients were administered with Paishi Chongji (a traditional Chinese herbal granule for removing stones) after ESWL; and the study group (n = 30), where the patients were administered with Paishi Chongji and Yunnan Baiyao after ESWL. Urine microproteins and peripheral venous malondialdehyde (MDA), superoxide dismutase (SOD), endothelin-1 (ET-1) and nitric oxide (NO) were determined before ESWL, and at 24, 72 h and one week after ESWL. Urine, albumin (ALB), immunoglobulin (IgG) and beta-2-microglobulin (β2-MG) levels increased significantly, and urine THP decreased significantly after ESWL. Peripheral ET-1 and MDA at 24 and 72 h after ESWL were significantly lower, while peripheral SOD and NO were significantly higher in the study group than those in the control group (both P < 0.05). In conclusion, Yunnan Baiyao has a definite plerotic effect on renal injury after ESWL and could be spread widely for clinical use.

Key words: Yunnan Baiyao, renal injury, extracorporeal shock wave lithotripsy (ESWL).

INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) is generally accepted as a safe and effective method for the treatment of urinary tract stones. However, clinical studies and experiences in the last 20 years have reported hemoturia, low back discomforts and mild renal injury at the site of ESWL. According to the reports in the literature (May et al., 2004; Rubin et al., 1987), the occurrence of peri-renal or parencymal hematoma after ESWL was 0.1 to 0.6% as shown by B-type ultrasound, and the percentage of renal injury after ESWL was 20 to 25% as shown by computed tomography (CT) or magnetic resonance image (MRI). Pathological examination after ESWL revealed renal hemorrhage, thrombosis of small arteries and veins, tubular expansion and cellular degeneration in many animal studies (Karlsen et al., 1991). Conversion from failing ESWL to open surgery in clinical practices also showed tissue fibrosis around stones. According to the current knowledge, ESWL-induced renal injury is mainly caused by physical and biochemical factors. Physical factors include high pulse pressure produced at the focus because of sudden change in acoustic impedance and stress effect when high-energy waves pass through the tissue-stone interface, causing change of cell structures and rupture of microvessels and lymphatic ducts, resulting in transient ischemia of local renal parenchyma and impairment of renal function. Biochemical factors, including cavitation effect, may induce local high temperature and pressure, causing lysis of water molecules and production of oxygen free radicals. During the course of alternative bombardments, the kidney is in an atypical I/R status. In addition, large numbers of oxygen free radicals are also produced when the prototype xanthine oxidase is being transformed to the oxidized type (Sivagnana et al., 2000). The aforementioned renal injuries could be reflected by changes in urine microproteins and blood biomarkers such as endothelin-1 (ET-1), nitric oxide (NO), superoxide dismutase (SOD) and malondialdehyde (MDA) (Neuhofer and Pittrow, 2006; Aihara et al., 2003).

According to traditional Chinese medicine (TCM), Yunnan Baiyao (a traditional Chinese herbal remedy) has

*Corresponding author. E-mail: duanping_2011@163.com.

actions of promoting blood circulation, removing stagnation, stopping bleeding, curing inflammation, improving microcirculation and healing traumatic wounds. However, there is little research on the plerotic effect of Yunnan Baiyao on renal injuries. The aim of this study was to explore the plerotic effect of Yunnan Baiyao on renal injury after ESWL by observing changes in urine microproteins, peripheral ET-1, NO, SOD and MDA, in an attempt to provide experimental clues for clinical use of Yunnan Baiyao in the prevention and treatment of renal injury after ESWL.

MATERIALS AND METHODs

General data

Included in this study, 55 clinical patients were treated with ESWL for kidney stones between June 2006 and June 2011, including 29 males and 26 females ranging in age from 21 to 58 years with a mean of 39.7 ± 9.7 years. All the patients had unilateral renal pelvic stones measuring 1.0 - 1.9 cm (mean 1.48 ± 0.23 cm), with normal liver and renal functions without hypertension, diabetes mellitus or severe cardiac, cerebral and pulmonary diseases. Preoperative CT and intravenous pyelography revealed mild renal hydronephrosis in all patients. B-type ultrasound suggested a separation of 1.0 - 2.0cm (mean 1.41 ± 0.24 cm) in the urinary collecting system. No anesthetic was used during ESWL.

Treatment methods

The 55 patients with renal pelvic stones were randomized to two groups: the control group (n = 25), where the patients were administered with Paishi Chongji (a traditional Chinese herbal granule for removing stones) after ESWL, and the study group (n = 30), where the patients were administered with Paishi Chongji and Yunnan Baiyao after ESWL. The dose of Yunnan Baiyao was 2 tablets at a time, t. i. d., which was initiated 30 min before ESWL for 7 consecutive days. The working conditions of the ESWL machine (Huikang type V, Shenzhen) were as follows: working voltage 13 – 15 KV, frequency 80/min and impact times 2500 - 3000. Urine and peripheral venous blood samples were collected before ESWL and at 24h, 72h and 1 week after ESWL. NO, SOD and MDA were determined by immunohistochemistry, and ET-1 was detected by chemical colorimetry.

Statistical treatment

Statistical analysis was performed using SPSS11.0. $P< 0.05$ was considered statistically significant.

RESULTS

Changes in urine microproteins before and after ESWL

The results are indicated in Table 1. There was no significant difference in ALB, IgG, β2-MG and THP before ESWL between the two groups. ALB, IgG and β2 – MG in the control group increased significantly at 24 and 72 h after ESWL as compared with those before ESWL, and urine THP decreased significantly, indicating that shock waves impaired the renal function. The differences before and after ESWL were significant ($P < 0.01$). In the study group, urine ALB, IgG and β2–MG decreased gradually and urine THP increased after administration of Yunnan Baiyao. The differences before and after ESWL were significant ($P < 0.01$). Urine microproteins tended to become normal one week after ESWL, when there was no significant difference in urine microproteins between the two groups ($P > 0.05$).

There was no significant difference in microprotein levels between the two groups before ESWL ($P>0.05$); there were significant differences in microprotein levels between the two groups at 24 and 72 h after ESWL ($P < 0.01$); there were no significant differences in microprotein levels between the two groups at 1 week after ESWL ($P > 0.05$).

Changes in injury-related factor ET-1 and MDA before and after ESWL

The results are shown in Table 2. There was no significant difference in peripheral ET-1and MDA between the two groups before ESWL ($P>0.05$); there was significant difference in peripheral ET-1and MDA between the two groups at 24 and 72 h after ESWL ($P < 0.05$); ET-1 and MDA tended to become normal after ESWL, and there was no significant difference between the two groups ($P > 0.05$).

Changes in protection-related factor SOD and NO before and after ESWL

The results are shown in Table 3. There was no significant difference in peripheral ET-1 and MDA between the two groups before ESWL ($P > 0.05$); there was significant difference in peripheral SOD and NO between the two groups at 24 and 72 h after ESWL ($P < 0.05$); NO at 1 week after ESWL was significantly higher in the study group than that before ESWL and of the control group ($P < 0.05$).

DISCUSSION

Under normal physiological conditions, only a small amount of protein in the blood passes through glomerular filtration, and therefore only a very small amount of protein was detectable in urine. Glomerular damage would cause urine ALB, IgG and β2-MG to increase and THP to decrease. Urine ALB and IgG levels are often correlated with the extent of injury to the glomerular membrane. β2-MG and THP are markers used to monitor the degree of damage to the proximal and distal tubules respectively. Compared with the control group, urine ALB, IgG and β2-MG decreased fast and THP increased fast in the study group in which the animals were administered with Yunnan Baiyao after ESWL. The

Table 1. Changes in urine microproteins before and after ESWL in the two groups (mg/d, $\overline{X}$ ± S).

Group	Pre-operation	24 h post-operation	72 h post-operation	1 week post-operation
ALB in study group	12.59 ± 1.96	36.36 ± 6.87	13.34 ± 1.75	12.62 ± 2.33
ALB in control group	12.81 ± 1.95	46.38 ± 10.59	30.86 ± 6.08	12.30 ± 2.38
IgG in study group	3.41 ± 0.17	12.06 ± 2.70	3.35 ± 0.19	3.34 ± 0.24
gG in control group	3.18 ± 0.43	22.94 ± 5.51	12.41 ± 2.62	3.10 ± 0.21
β2MG in study group	0.31 ± 0.10	0.39 ± 0.15	0.32±0.11	0.20 ± 0.10
β2MG in control group	0.26 ± 0.14	0.55 ± 0.15	0.37±0.09	0.29 ± 0.10
TPH in study group	23.36 ± 7.43	17.01 ± 1.65	21.80±4.99	21.92 ± 6.63
TPH in control group	21.21 ± 6.94	12.31 ± 2.33	16.51±3.15	24.38 ± 3.64

Table 2. Changes in serum MDA (nmol/ml) and ET (pg/ml) before and after ESWL in the two groups.

Group	Pre-operation	24 h post-operation	72 h post-operation	1 week post-operation
ET-1 in study group	43.66 ± 7.55	63.17 ± 18.59	44.68 ± 8.34	45.67 ± 8.08
ET-1 in control group	45.10 ± 6.55	73.59 ± 16.15	61.56 ± 20.61	46.52 ± 9.47
MDA in study group	4.43 ± 0.40	6.76 ± 0.80	4.53 ± 0.39	4.35 ± 0.39
MDA in control group	4.54 ± 0.41	9.06 ± 1.02	7.33 ± 0.93	4.52 ± 0.38

Table 3. Changes in plasma SOD (nU/ml) and NO (μmol/ml) before and after ESWL ($\overline{X}$ ± S).

Group	Pre-operation	24 h post-operation	72 h post-operation	1 week post-operation
SOD in study group	257.17 ± 65.69	163.50 ± 29.21	267.20 ± 68.08	284.23 ± 54.26
SOD in control group	281.32 ± 70.00	125.41 ± 20.96	186.09 ± 32.14	279.09 ± 66.13
NO in study group	70.47 ± 16.62	66.29 ± 18.71	69.30 ± 14.12	76.61 ± 17.23
NO in control group	72.39 ± 18.41	55.81 ± 19.83	62.33 ± 19.15	70.33 ± 15.47

differences between the two groups were significant, indicating that the drug had a plerotic effect on injury to the glomerular filtration barrier and tubules. These abnormal changes restored to the normal status in about one week after ESWL in the control group, suggesting that the interval between two ESWL episodes should be more than one week. ET-1, an active polypeptide containing 21 amino acids, is the most potent vasoconstrictor that has been known, and is considered one of the co-existing pathogenic factors contributing to all vascular endothelial injuries (Ogiste et al., 2003). Various kidney intrinsic cells such as glomerular epithelial cells, mesangial cells and tubular epithelial cells can synthesize and secrete ET-1, and at the same time the kidney contains abundant ET-1 receptors. The kidney is by far more sensitive to them than other organs. It was found in our study that ET-1 elevated significantly after ESWL impact in the control group and remained elevated for about one week, indicating that there is a close relationship between ESWL and ET-1. Shock waves many cause damage to vascular endothelial cells and kidney tissue when they are releasing energy. By increasing the expression of ppET-1mRNA, large amounts of mature ET-1 are released, which decreases the renal blood flow and cause ischemia of the kidney tissue, which in turns promotes ET-1 release, thus forming a vicious cycle. In the study group where Yunnan Baiyao was administered, ET-1 decreased gradually, and this difference was statistically significant as compared with the control group ($P<0.05$). NO is a pleiotropic biogas molecule, acting as both a vasoactive substance to participate in regulating vasodilation and synaptic transmission, and an important chemical inflammatory mediator to regulate the bactericidal activity of macrophages and immune responses. Studies (Park et al., 2002) have shown that NO plays different roles in different tissue environments, either preventing injury or inducing injury. In the control group, plasma NO decreased after ESWL and then increased, and restored to the level before ESWL in about one week ($P > 0.05$), while in the study group NO at day 7 after ESWL was still significantly higher than that before ESWL ($P < 0.05$). This change may be due to the two different mechanisms of NO synthesis and different roles of NO. NO synthesis may be regulated by two

different mechanisms, thus producing dual actions during the course of renal recovery after ESWL (Ogiste et al., 2003). ESWL induces the kidney to produce large amounts of oxygen free radicals, and at the same time SOD synthesis is decreased due to ischemia and hypoxia, causing damage to renal tissue cytomembranes and producing large amounts of MDA. In the study group, MDA decreased significantly 24 and 72 h after ESWL, thus attenuating injury to the kidney.

Yunnan Baiyao mainly contains Sanqi (Radix Notoginseng), Binpian (Dryobalanops aromatica Gaertn. f.), Gengxiang and Pimacao (Tali falsehellebore herb). Sanqi is a perennial plant of the family Araliaceae containing Sanqi Panax Notoginseng, flavones and other alkaloids. Modern pharmacological studies have demonstrated that Sanqi can lower the permeability of capillaries, improve mucosal vascular fragility and intrinsic mucosal vascular inflammation, and repair wounds. Sanqi Panax Notoginseng that it contains can contract blood vessels, shorten prothrombin time and promote platelet aggregation. Therefore, it has the action of repairing vascular endothelial cells and kidney tissue injured by ESWL, lower the glomerular permeability of microproteins and promote tubular reabsorption. Yunnan Baiyao exerts its plerotic effect on renal injury and protective effect on renal function by repairing ruptured renal microvessels and lymphatic ducts and injured glomerular infiltration and renal tubular cell function, thus reducing the production of ET-I, promoting clearance of oxygen free radicals and lipid metabolites, and attenuating I/R injury after ESWL.

Many researchers have attempted various methods to prevent and treat ESWL-related renal injury, but they can hardly be used in clinical practice because of unsatisfactory outcomes. The results of the present study have proven that Yunnan Baiyao has a definite therapeutic effect on ESWL-related renal injury, and therefore may be applied widely in more clinical practices.

REFERENCES

May M, Gunia S, Helke C (2004), An unusual comp lication of extracorporeal shock wave lithotrip sy: rup ture of the kidney with consecutive nephrectomy, J. Aktuelle Urol., 35: 316-319.

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.

Karlsen SJ, Smevik B , Stenstrm J (1991). Physiological changes following exposure to entracoporeal shock waves. J. Urol., 68: 337.

Sivagnana M, Masui N, Paymond LH (2000). Free radical scav2 engers catalase and superoxide dismutase p rovide protection from oxalate2associated injury t o LL C2p k1 and Mdck Cells [J]. J. Urol., 164 (1): 224–229.

Neuhofer W, Pittrow D (2006). Role of endothelin and endothelin receptor antagonists in renal disease. Eur. J. Clin. Invest., 36 (3): 78-88.

Aihara K, Byer KJ, Khan SR (2003). Calcium phosphate-induced renal epithelial injury and stone formation: involvement of reactive oxygen species. Kidney. Int., 64(4): 1283-1291

Ogiste JS, Nejat RJ, Rashid HH (2003). The role of mannitol in alleviating renal injury during extracorporeal shock wave lithotripsy [J], J. Urol., 169(3): 875-877.

Park JK, Cui Y, Kim MK (2002). Effects of extracorporeal shock wave lithotripsy on plasma levels of nitric oxide and cyclic nucleotides in human subjects[J].J Urol,, 168(1): 38- 42.