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Biochemical and histomorphometric comparison of antioxidant (Taurine) and ozone therapy effects on ESWL-induced oxidative damage in rabbit kidney tissue

Tavşan böbrek dokusunda eswl ile indüklenen oksidatif hasar üzerine antioksidan (Taurin) ve ozon terapi etkilerinin biyokimyasal ve histomorfometrik karşılaştırılması

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Abstract

Purpose: This study aimed to investigate the role of free radicals in kidney injury induced by extracorporeal shock wave lithotripsy (ESWL) and to compare the protective effects of taurine and ozone therapy.

Materials and methods: Thirty male New Zealand rabbits were divided into five groups: control, ESWL, ESWL + ozone, ESWL + taurine, and ESWL + ozone + taurine. ESWL was applied in a single session at 14 kV and 2500 shocks. Ozone was administered intraperitoneally and taurine orally for 15 days. Histopathological evaluations and biochemical analyses, including MDA, SOD, CAT, and GSH-Px levels, were performed on renal tissues.

Results: ESWL significantly increased tissue MDA levels and decreased antioxidant enzyme levels. Taurine and ozone treatments reduced oxidative stress by lowering MDA levels and enhancing antioxidant enzyme activity. Histologically, less tissue damage was observed in the treatment groups.

Conclusion: Taurine and ozone therapies effectively reduced ESWL-induced kidney damage both biochemically and histologically. These findings support the potential protective role of these agents in clinical settings.

Keywords: Lithotripsy extracorporeal, kidney injuries, oxidative stress, taurine, ozone therapy.

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Öz

Amaç: Bu çalışmada, litotripsi sonrası oluşan böbrek hasarında serbest radikallerin rolü ve bu hasarın azaltılmasında taurin ve ozon tedavisinin etkileri karşılaştırılmıştır.

Gereç ve yöntem: Otuz erkek Yeni Zelanda tavşanı beş gruba ayrıldı: kontrol, ESWL, ESWL + ozon, ESWL + taurin ve ESWL + ozon + taurin. ESWL uygulaması tek seans 14 kV enerjiyle, 2500 atım olarak gerçekleştirildi. Ozon tedavisi intraperitoneal olarak, taurin ise oral yolla 15 gün süreyle verildi. Histopatolojik değerlendirme yanı sıra doku düzeyinde MDA, SOD, CAT, GSH-Px gibi biyokimyasal parametreler ölçüldü.

Bulgular: ESWL sonrası doku MDA düzeyleri anlamlı şekilde artarken, antioksidan enzim düzeyleri azaldı. Taurin ve ozon tedavileri, MDA düzeylerini düşürüp antioksidan enzim düzeylerini artırarak oksidatif stresi azalttı. Histopatolojik olarak da tedavi gruplarında daha az hasar izlendi.

Sonuç: Taurin ve ozon tedavisi, ESWL'nin neden olduğu böbrek hasarını hem biyokimyasal hem de histopatolojik olarak azaltmada etkili bulunmuştur. Bu sonuçlar, klinik uygulamalarda bu ajanların koruyucu potansiyelini desteklemektedir.

Anahtar kelimeler: Litotripsi ekstrakorporeal, böbrek yaralanmaları, oksidatif stres, taurin, ozon terapisi.

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Introduction

Extracorporeal shock wave lithotripsy (ESWL) represents a significant advancement in the treatment of urinary system stones. The concept of utilizing shock waves to fragment stones was first proposed in the 1950s in the Soviet Union. Concurrently, the German aerospace company Dornier, while studying supersonic aircraft, observed that shock waves generated by raindrops impacting the aircraft wings could erode hard materials. Based on these observations, ESWL technology was developed [1-3].

Although large-scale studies have demonstrated that ESWL is a reliable and effective method, there are also reports indicating its potential for serious adverse effects. These side effects occur not only in the kidneys but also in adjacent organs such as the liver, pancreas, skeletal muscle, and gastrointestinal tract. Adverse effects may manifest acutely or as chronic complications emerging over the long term. It has been suggested that acoustic cavitation induced by shock waves, reactive chemical intermediates (free radicals), microjets, and/or other energetic phenomena contribute to tissue damage. When discussing the biological effects of high-energy shock waves, it is crucial to clearly define both the application parameters and the biological system. Device-related factors such as the total number of shock waves, pulse frequency, and the electrode characteristics of spark gap lithotripters, as well as biological factors including cell type, cell growth phase, and environmental conditions (pH, temperature, oxygen saturation, humidity, osmolality, etc.), play significant roles in determining the effects of shock waves [4, 5].

One of the damaging factors during ESWL is acoustic cavitation, which occurs when the tensile stress exceeds ambient pressure, creating a gas bubble that subsequently collapses when positive pressure is restored [6]. It has been demonstrated that ESWL generates acoustic cavitation in vivo. Alongside compressive and tensile forces, cavitation microjets substantially contribute to stone fragmentation by shock waves [7].

The effects of ESWL on tissue cannot be entirely attributed to mechanical mechanisms. Each shock wave is generated by 18.000-24.000 volts of electrical energy with thermal effects. It has been proposed that this energy may induce biochemical reactions in tissues at the focal point where the stone is targeted [8].

In this study, the effects of taurine, an amino acid with antioxidant properties, and ozone therapy, which can have potential oxidative toxic effects but also protective effects against oxidative stress–induced tissue damage depending on the dose applied, on ESWL-induced oxidative injury in renal tissue were investigated using a rabbit model.

Materials and methods

A total of 30 adult New Zealand White rabbits (15 males, 15 females), with an average age of 5.76±0.12 months (range: 5-8 months) and an average weight of 2518.33±49.80 g (range: 2200-3500 g), were used in this study. Prior to experimentation, all animals were screened for systemic infections, infestations, and anatomical abnormalities. The rabbits were housed in cages accommodating no more than three animals each, maintained in a noise-free environment with ambient temperatures between 20-25°C, and exposed to a 12-hour light/dark cycle. Food and water were provided ad libitum. The animals were randomly assigned to five groups as presented in Table 1, ensuring each group contained three males and three females.

Table 1. Experimental groups

Group I	Control
Group II	ESWL
Group III	ESWL+Antioxidant (Taurine)
Group IV	ESWL+Ozone therapy
Group V	ESWL+Antioxidant (Taurine)+Ozone therapy

ESWL procedure: The rabbits were anesthetized intramuscularly with ketamine hydrochloride (50 mg/kg; Ketalar®, Eczacıbaşı, Türkiye). The right kidney was localized via transabdominal ultrasonography (GE LOGIQ® 400 Ultrasound System, Korea). Rabbits in Groups II, III, IV, and V received ESWL treatment using a third-generation electrohydraulic Stonelith V5 lithotripter (PCK TM, Ankara, Türkiye; ellipse diameter: Ø220 mm, focal length: 130 mm, maximum pressure: 120 MPa). The protocol involved three sessions of ESWL every other day, delivering 2000 shock waves at 18 kV per session.

Taurine administration: A 10% aqueous solution of taurine (Sigma, St. Louis, USA) was prepared by dilution in 0.9% sodium chloride. Animals in Groups III and V received intraperitoneal injections of taurine at a dose of 7.5 ml/kg/day, alternating between the right and left sides for seven consecutive days under sterile conditions. Following the taurine treatment period, these animals underwent three ESWL sessions every other day.

Ozone therapy: Subjects in Groups IV and V received intraperitoneal injections of ozone gas at 2 mg/kg every other day for seven days, alternating administration between the right and left lower abdominal quadrants under sterile conditions. The ozone gas mixture (95% O3 + 5% O2) was generated using an ozone generator (Evozone Basic Plus, Germany). After completing ozone therapy, the animals underwent three ESWL sessions every other day.

Combined taurine and ozone therapy: Group V animals were treated with both intraperitoneal taurine (10% solution) and ozone therapy as described above over a seven-day period, followed by three ESWL sessions every other day.

Surgical procedure and tissue collection

At the end of the experimental period, animals were pre-anesthetized with intramuscular xylazine hydrochloride (1 mg/kg; Rompun®, Bayer, Germany) and sedated with ketamine hydrochloride (10 mg/kg, i.m.). An intravenous catheter was placed in the ear vein for administration of thiopental sodium (20 mg/mL), used for induction of general anesthesia. The animals were positioned supine, and the abdominal area was shaved and disinfected with povidone-iodine (Betadine®, Kansuk, Türkiye) and alcohol. A midline vertical incision (~10 cm) was made to access the intraperitoneal cavity. The intestines were gently retracted laterally, and the right kidney was exposed by carefully dissecting the posterior peritoneum. The renal pedicle was clamped using a Pean clamp, and the right kidney was surgically removed (nephrectomy). After removal, the clamp was released, and the animals were euthanized by exsanguination.

The renal capsules were carefully removed, and each kidney was bisected longitudinally. Tissue samples of approximately 1 cm³ were collected from the upper, middle, and lower regions of each kidney half for histopathological and biochemical analyses. Samples designated for histopathological evaluation were fixed in 40 mL of 10% formalin (pH 7.0 phosphate-buffered) and stored at +4°C. Samples for biochemical analysis were preserved at −80°C in Eppendorf tubes until further examination.

Histomorphometric evaluation

Tissue samples were processed and embedded in paraffin following fixation. Sections of 5–7 µm thickness were obtained using a sliding microtome (Leica, Germany) and stained with hematoxylin-eosin, periodic acid-Schiff (PAS), and modified Masson's trichrome methods. Renal damage criteria were assessed microscopically by two independent investigators using a light microscope connected to a digital camera (Leica DC500, Wetzlar, Germany). Quantitative analysis was performed with Leica Application Suite and QWIN plus image analysis software.

Tubular injury was scored according to the method described by Sharples et al. [9], where tubules appearing normal received a score of 0; those showing swelling, brush border loss, or nuclear condensation in up to one-third of the section were scored 1; involvement of one-third to two-thirds was scored 2; and more than two-thirds involvement was scored 3. Scores from at least 40 sections per kidney were summed, with a maximum possible score of 120 [9].

Biochemical analysis

Frozen tissue samples were homogenized, and levels of malondialdehyde (MDA), nitric oxide (NO), total sulfhydryl groups (t-SH), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase were measured. MDA levels were assessed using a modified Yagi method [10], with calibration curves prepared from serial dilutions of 1,1,3-trimethoxypropane. NO levels were measured following the method of Miranda et al. [11], using sodium nitrate standards for calibration. t-SH levels were determined by a modified Sedlak method [12], calibrated with glutathione standards. SOD, GSH-Px, and catalase activities were quantified via manual microplate ELISA assays using Cayman Chemical kits (Cayman Chemical Co., Michigan, USA). Results were expressed in appropriate units relative to protein content.

This study was conducted following approval from the Local Ethics Committee for Animal Experiments of Kırıkkale University (approval date: April 14, 2010; decision number: 10/31).

Statistical analysis

Sample size calculation was performed prior to the study using G*Power software (version X.X, Heinrich-Heine-University, Düsseldorf, Germany). Based on previous experimental studies evaluating oxidative stress parameters in ESWL models, an effect size of 0.50 was assumed, with an alpha error of 0.05 and a statistical power of 80%. Accordingly, a minimum of 6 animals per group was required. Therefore, a total of 30 rabbits were included in the study.

Data were analyzed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA). Normality of data distribution was assessed using the Shapiro–Wilk test, and homogeneity of variances was evaluated with Levene's test. Data are presented as mean ± standard deviation (SD). For comparisons among groups, one-way analysis of variance (ANOVA) was used for normally distributed variables, followed by Bonferroni post hoc test. A *p*-value <0.05 was considered statistically significant.

Results

Biochemical findings

Antioxidant enzyme levels and free oxygen radical concentrations measured in tissue extracts from the groups are presented in Table 2. Analysis of biochemical results revealed that ESWL application and antioxidant treatments caused a statistically significant change in the level of catalase, an antioxidant enzyme (F=4.845, *p*=0.005). A slight increase in catalase levels was observed after ESWL, whereas taurine or ozone therapy alone inhibited this increase, even reducing catalase levels below those of the control group. In Group V, which received both taurine and ozone therapy after ESWL, catalase levels significantly decreased compared to post-ESWL values. The significant difference in catalase levels originated from the values obtained in the combined treatment group (Group V) compared to both the control group (Group I) and ESWL-only group (Group II) (p_Group I vs Group V=0.031, p_Group II vs Group V=0.004, *p*<0.0125) (Figure 1).

Table 2. Antioxidant enzyme and free oxygen radical levels measured in groups (Avg±SD)

	Group-I	Group-II	Group-III	Group-IV	Group-V	*p*
Catalase	8.60±1.20	9.06±0.92	8.18±0.65	7.84±1.06	6.79±0.84	0.005* (F=4.845)
GSH-Px	3.80±0.86	4.77±0.70	3.45±1.18	3.70±0.84	3.49±1.42	0.199 (F=1.625)
SOD	0.24±0.06	0.25±0.07	0.21±0.07	0.18±0.05	0.19±0.07	0.344 (F=1.178)
MDA	34.17±17.52	27.61±25.09	19.11±5.57	28.11±17.37	16.47±5.46	0.335 (F=1.200)
t-SH	0.14±0.03	0.17±0.03	0.13±0.02	0.12±0.04	0.14±0.02	0.095 (F=2.227)
NO	1.89±0.99	2.80±0.58	2.63±1.70	3.04±0.73	2.91±2.00	0.599 (F=0.700)

Data are presented as mean ± SD. Intergroup comparisons were performed using one-way ANOVA. F value is provided for the statistically significant result. *p<0.05

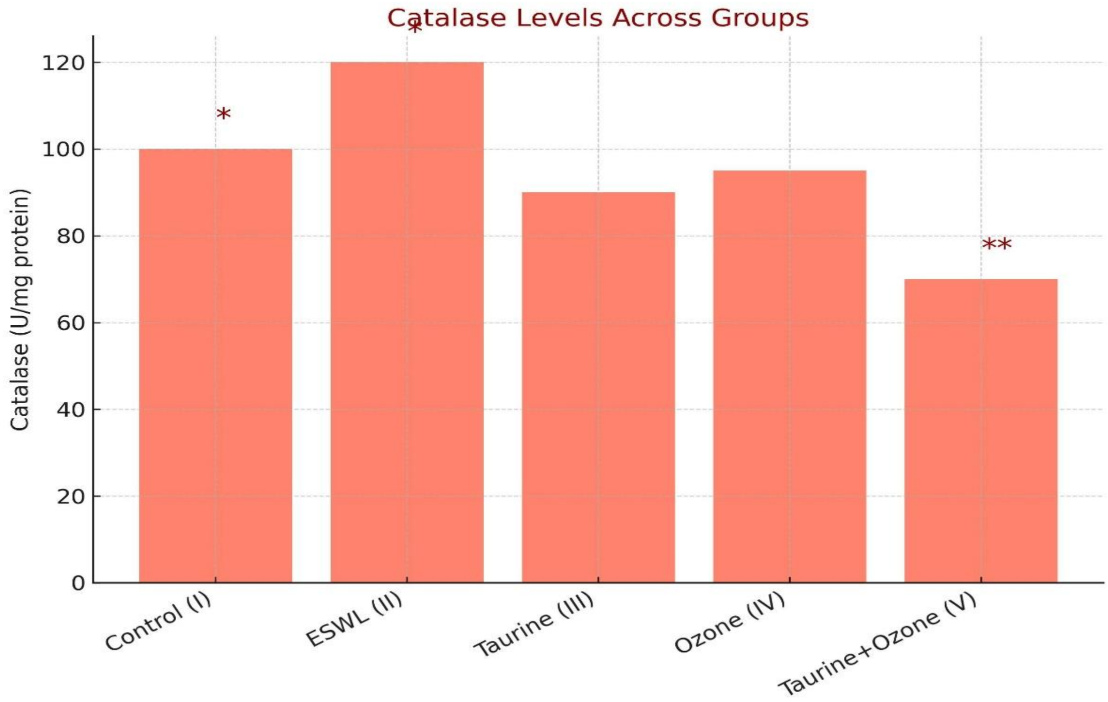


Figure1. Catalase levels across groups

While GSH-Px and SOD levels showed a non-significant increase after ESWL, reductions following taurine and ozone therapy were more pronounced with combined treatment. However, changes in serum GSH-Px and SOD levels were not statistically significant.

Free oxygen radical levels (MDA, t-SH, and NO) showed a non-significant increase after ESWL. Taurine treatment led to a decrease in all three markers. After ozone therapy, MDA and t-SH levels decreased, but NO levels increased. These changes were not statistically significant. Combined treatment resulted in decreases in MDA and t-SH levels reaching control group levels and a slight decrease in NO levels, none of which were statistically significant.

Histomorphometric findings

Qualitative examination showed that the cortico-medullary region was the most affected by ESWL in all experimental groups. Microscopically, renal damage was observed in all groups, including varying degrees of tubular dilatation, epithelial shedding in proximal and/or distal tubules, simplification (flattening) of epithelial cells, and presence of tubular casts. Mild to moderate interstitial inflammation characterized by vascular dilatation, congestion, and mononuclear cell infiltration was present in all groups. Tubular epithelial necrosis, with fragmentation and luminal shedding of cells, was more pronounced in the ESWL-only group (Group II) compared to Groups III, IV, and V. Group V exhibited better tubular and vascular integrity than other groups (Figure 2).

Administration of antioxidant agents or ozone therapy alone did not provide significant protection against epithelial damage in renal tubules induced by ESWL. However, combined treatment reduced this damage and conferred protection against ESWL-induced tubular injury.

Histological scores are presented in Table 3 and Picture 1. Compared to the control group, ESWL caused significant renal damage (p_Group I vs Group II=0.001). Although taurine or ozone therapy alone somewhat improved damage, the difference remained statistically significant compared to the control group (p_Group I vs Group III=0.001; p_Group I vs Group IV=0.001). Combined treatment significantly ameliorated ESWL-induced damage (p_Group II vs Group V=0.010), though the score remained significantly different from the control group (p_Group I vs Group V=0.027).

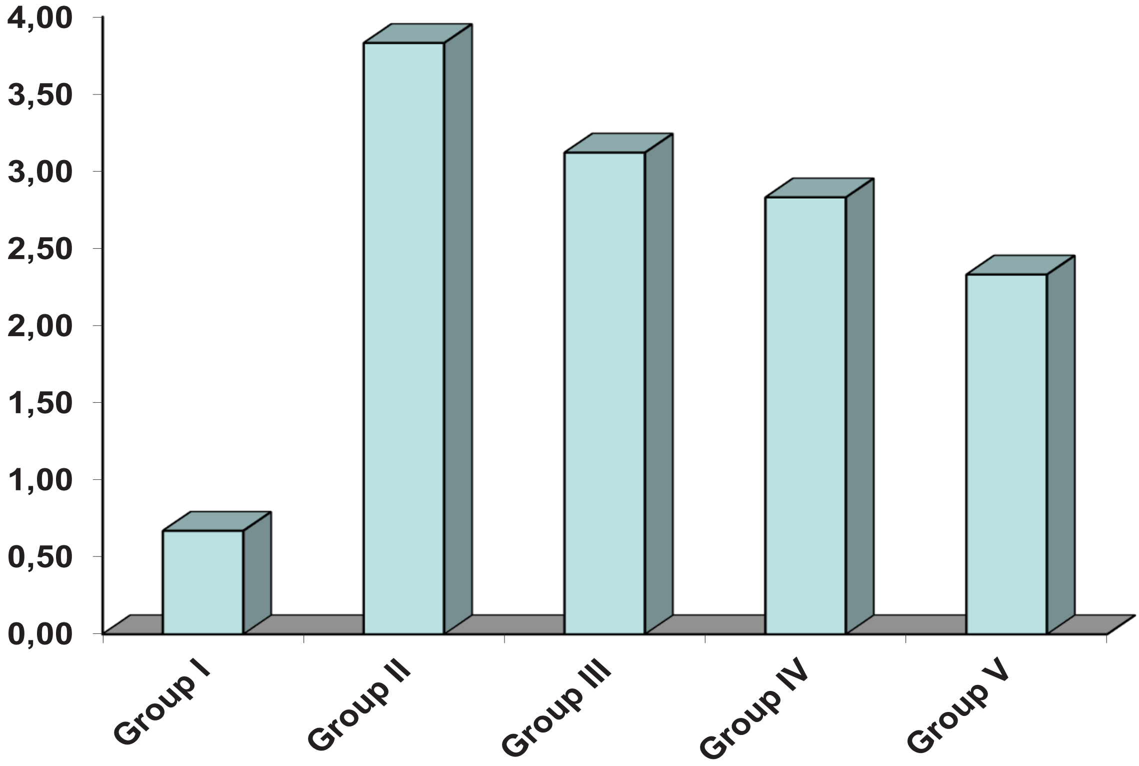


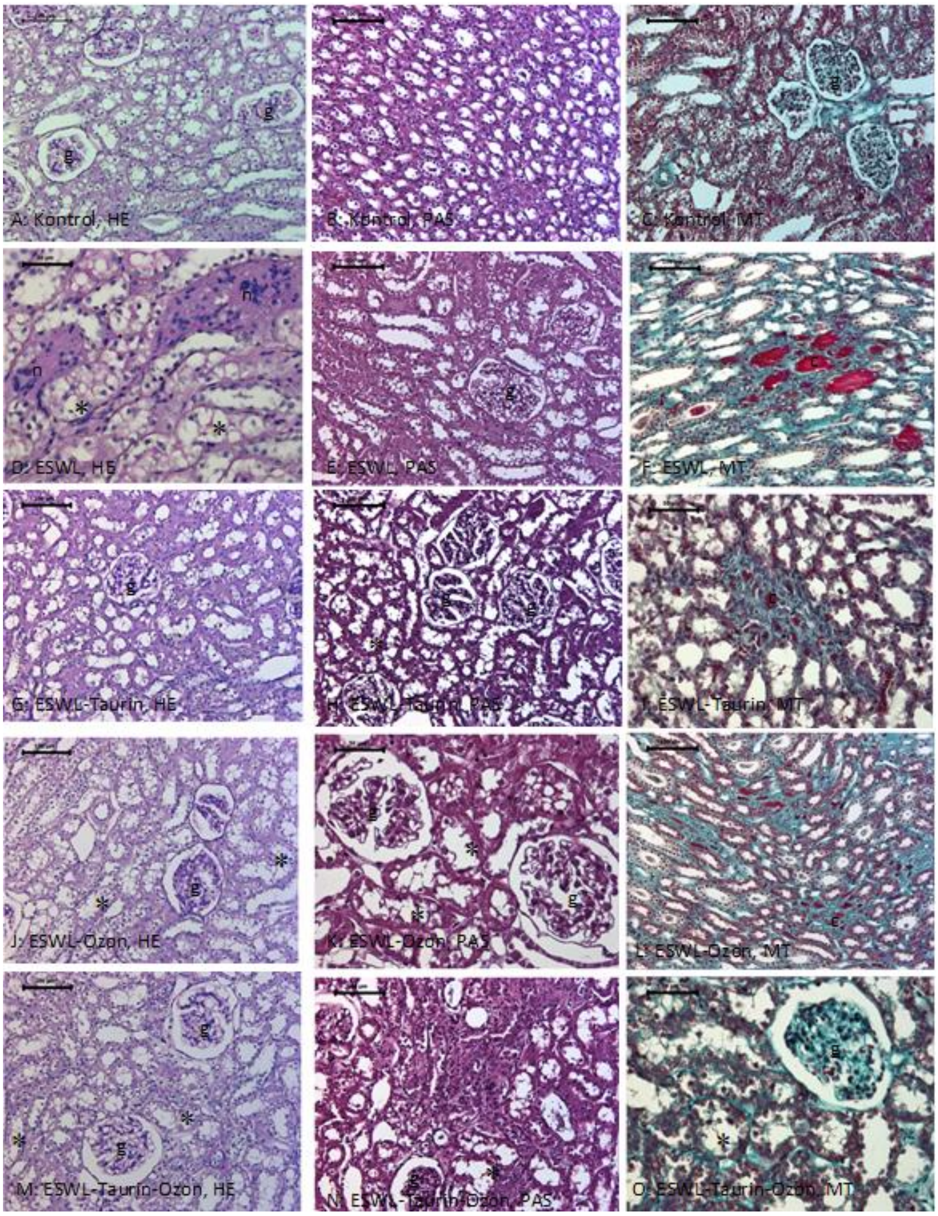
Figure 2. Distribution of kidney tissue damage in groups according to the Sharples scoring system

* One-way analysis of variance, F=14.093, *p*=0.001

Table 3. Evaluation of the damage observed in the kidney tissue according to the Sharples scoring system

Groups	Avarage Damage Score (Ort±SD)	Min-Max
Group I	0.67±0.52*	0-1
Group II	3.83±0.41	3-4
Group III	3.12±0.75	3-4
Group IV	2.83±0.75	2-4
Group V	2.33±1.21	1-4

*One-way analysis of variance; F=14.03, *p*=0.001



Picture 1. Histomorphometric Evaluation: Renal damage primarily affects the corticomedullary region, the proximal and distal tubules there

Tubular necrosis (n) is observed in D. In all experimental groups, widespread tubule damage characterized by simplification of the tubule epithelium, apical bleb formation in the cells, and separation from the basement membrane is observed. Cast-like material accumulation (c) and vascular congestion are noted in the tubular lumens in F, I, and L. Glomeruli (g) appear relatively healthy in the tumor groups. Although the ESWL-Ozone and ESWL-Ozone-Taurine groups appear relatively healthier than the ESWL group, local tubular damage persists in these groups. (K, O). HE: Hematoxylin-Eosin, PAS: Periodic Acid Schiff, MT: Masson Trichrome

Discussion

The exact mechanism of cellular damage caused by ESWL in kidney tissue is not fully understood. One likely cause is tissue damage from reactive oxygen species (ROS) generated during the procedure. Each shock wave, created by 18-24 kV electrical energy and focused on the stone, can produce heat leading to biochemical reactions that contribute to ROS formation. These free radicals can damage important molecules inside cells due to their high reactivity [4, 5]. In our study, markers of oxidative damage such as MDA, total sulfhydryl groups (t-SH), and nitric oxide (NO) increased in kidney tissues after ESWL compared to controls, indicating oxidative stress caused by ESWL.

Normally, the body has a complex antioxidant defense system to fight oxidative stress caused by free radicals from internal or external sources. Reactive oxygen species generated during normal cell function are neutralized by antioxidants, maintaining balance and protecting the body. When the production of free radicals exceeds antioxidant capacity, this balance breaks down, leading to oxidative stress [13].

Free oxygen radicals can cause many harmful effects, including cell toxicity, mutations, and changes in gene expression. For example, MDA is produced during lipid peroxidation and serves as a marker for free radical damage [14]. Lipid peroxidation products can also damage DNA directly [15, 16].

Kidney tissue contains antioxidants to protect against damage from excessive oxygen radicals. For example, superoxide dismutase (SOD) converts harmful superoxide radicals into less harmful substances [17, 18]. SOD levels increase with oxidative stress and then return to normal over time.

Glutathione (GSH) is a key non-enzymatic antioxidant that helps defend against oxidative stress. Under normal conditions, GSH reacts with oxidants to form oxidized glutathione (GSSG), a process catalyzed by glutathione peroxidase (GSH-Px). When oxidative stress is prolonged, GSH is depleted, leading to reduced enzyme activity and increased cell damage [19-21].

Previous studies on ESWL's effects on oxidative stress have shown mixed results. Aksoy et al. [22] found that SOD and catalase decreased one hour after ESWL but returned to baseline by day five, while MDA increased and stayed high. They suggested that oxidative stress activates antioxidant defenses but temporarily lowers antioxidant enzyme levels.

Li et al. [23], studying rabbits, also found decreased SOD and increased MDA after ESWL, linking this to renal damage and antioxidant response. They showed that antioxidants could reduce this damage.

In our study, both ROS and antioxidants increased after repeated ESWL sessions over seven days, likely reflecting a compensatory response to ongoing oxidative stress.

ESWL-induced kidney damage has been widely reported and includes damage to glomeruli, tubules, blood vessels, and surrounding tissues, leading to fibrosis and hemorrhage [4, 7, 24, 25]. In our study, the corticomedullary area was most affected, showing tubular dilation, degeneration, cell loss, and inflammation.

Previous research showed that giving antioxidants before or after ESWL can reduce damage. Al Awadi et al. [26] reported that oral antioxidants protected kidney tissue by reducing free radical damage caused by shock waves. Serel et al. [27] found that melatonin, an endogenous antioxidant, reduced oxidative stress after ESWL. Biri et al. [28] showed that vitamins E and C helped prevent endothelial and glomerular damage after ESWL.

Taurine is known for its antioxidant properties and ability to reduce lipid peroxidation [29, 30]. Hagar et al. [31] demonstrated taurine reduced oxidative stress and kidney damage caused by cyclosporine in rats.

Studies on taurine's effect on ROS are mixed. Taurine reacts with hypochlorous acid to form chlorotaurine, which neutralizes harmful substances and regulates nitric oxide and inflammatory factors [32, 33]. Some studies show taurine deficiency increases oxidative damage, while others do not [34-36]. Overall, taurine is thought to protect against oxidative stress.

In our study, taurine reduced oxidative markers after ESWL, even below control levels. Antioxidant enzyme levels also decreased, possibly due to feedback inhibition by external antioxidants.

Ozone therapy is used increasingly in medicine but remains controversial due to potential side effects and limited clinical evidence [37-40]. Some studies showed ozone reduces oxidative stress and protects kidneys in diabetic and ischemic models [41, 42].

As expected, ozone therapy reduced ROS and antioxidant levels in our study, with stronger effects when combined with taurine. NO levels increased with ozone but decreased somewhat with combination therapy, likely due to taurine's scavenging effect.

Histologically, kidney damage was worst with ESWL alone and less with ozone or ozone+taurine, with the combination showing the best preservation of kidney structures. This suggests antioxidants or ozone alone do not fully protect against ESWL damage, but combined therapy can reduce injury, possibly by protecting blood vessels.

In conclusion, ozone therapy reduces oxidative damage caused by ESWL, especially when combined with antioxidants. Further research is needed to clarify its long-term safety and optimal use.

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Conflict of interest: No conflict of interest was declared by the authors.

References

1. Hill AJ, Basourakos SP, Lewicki P, et al. Incidence of Kidney Stones in the United States: The Continuous National Health and Nutrition Examination Survey. *J Urol*. 2022;207(4):851-856. doi:10.1097/JU.0000000000002331
2. Walsh PC, Retik AB, Vaughan ED, Wein AJ. Urinary stone disease and endourology. In: Campbell's Urology. 8th ed. Philadelphia, PA: Saunders; 2006.
3. Chow GK, Streem SB. Extracorporeal lithotripsy: update on technology. *Urol Clin North Am*. 2000;27(2):315322. doi:10.1016 /s0094-0143(05)70260-3
4. Kaude JV, Williams CM, Millner MR, Scott KN, Finlayson B. Renal morphology and function immediately after extracorporeal shockwave lithotripsy. *AJR Am J Roentgenol*. 1985;145(2):305313. doi:10.2214/ajr.145.2.305
5. Rubin JI, Arger PH, Pollack HM, Banner MP, Coleman BG, Mintz MC, VanArsdalen KN. Kidney changes after extracorporeal shockwave lithotripsy: CT evaluation. *Radiology*. 1987;162(1):2124.
6. Delius M, Jordan M, Eizenhoefer H, et al. Biological effects of shock waves: kidney haemorrhage by shock waves in dogs—administration rate dependence. *Ultrasound Med Biol*. 1988;14(7):689694. doi:10.1016/0301-5629(90)90024-7
7. Gillenwater JY. Extracorporeal shock wave lithotripsy for the treatment of urinary calculi. In: Gillenwater JY, Grayhack JT, Howards SS, Duckett JW, eds. Adult and Pediatric Urology. 2nd ed. St Louis, MO: Mosby Year Book; 1991:695710.
8. Stoller ML. Extracorporeal shockwave lithotripsy. In: Tanago EA, McAninch JW, eds. Smith's General Urology. 14th ed. Stamford, CT: Appleton & Lange; 1995:305313.
9. Sharples EJ, Patel N, Brown P, et al. Erythropoietin protects the kidney against the injury and dysfunction caused by ischemiareperfusion. *J Am Soc Nephrol*. 2004;15(7):21152124. doi:10.1097/01.ASN.0000135059.67385.5D
10. Yagi K. Lipid peroxides in hepatic, gastrointestinal and pancreatic diseases. *Adv Exp Med Biol*. 1994;366:165169.
11. Miranda KM, Espey MG, Wink DA. A rapid simple spectrophotometric method for simultaneous detection of nitrate and nitrite. *Nitric Oxide*. 2001;5(1):6271. doi:10.12691/ajfn-11-3-5
12. Sedlak J, Lindslay RH. Estimation of total proteinbound and nonprotein sulfhydryl groups in tissue with Ellman's reagent. *Anal Biochem*. 1968;25(1):192205. doi:10.1016/0003-2697(68)90092-4
13. McCord JM. Human disease, free radicals and the oxidant/antioxidant balance. *Clin Biochem*. 1993;26(6):351357. doi:10.1016/0009-9120(93)90111-i
14. Ray G, Batra S, Shukla NK, et al. Lipid peroxidation, free radical production and antioxidant status in breast cancer. *Breast Cancer Res Treat*. 2000;59(3):163170. doi:10.1023/a:1006357330486
15. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. 2nd ed. Oxford, UK: Clarendon Press; 1989. doi:10.1007/0-387-26741-7-3
16. Rikans LE, Hornbrook KR. Lipid peroxidation, antioxidant and aging. *Biochim Biophys Acta*. 1997;362(2):116127. doi:10.1016/s0925-4439(97)00067-7
17. Nath KA, Croatt AJ, Hostetter TH. Oxygen consumption and oxidant stress in surviving nephrons. *Am J Physiol*. 1990;258(6Pt2):F13541362. doi:10.1152/ajprenal.1990.258.5.F1354
18. Waz WR, Feld LG. Reactive oxygen molecules in the kidney. *Adv Exp Med Biol*. 1994;366:171183. doi:10.1007/978-1-4615-1833-4_13
19. Dröge W, Schulze Osthoff K, Mihm S, et al. Functions of glutathione and glutathione disulfide in immunology and immunopathology. *FASEB J*. 1994;8(10):1131138.

20. Hayes JD, McLellan LI. Glutathione and glutathionedependent enzymes represent a coordinately regulated defence against oxidative stress. *Free Radic Res*. 1999;31(4):273300. doi:10.1080/10715769900300851
21. Haddad JJ, Olver RE, Land SC. Antioxidant/prooxidant equilibrium regulates HIF1 alpha and NFkappa B redox sensitivity: evidence for inhibition by glutathione oxidation in alveolar epithelial cells. *J Biol Chem*. 2000;275(28):211302140. doi:10.1074/jbc.M000737200
22. Aksoy Y, Malkoc I, Atmaca AF, et al. The effects of extracorporeal shock wave lithotripsy on antioxidant enzymes in erythrocytes. *Cell Biochem Funct*. 2006;24(4):467469. doi:10.1002/cbf.1239
23. Li X, He D, Zhang L, Cheng X, Sheng B, Luo Y. A novel antioxidant agent, astragalosides, prevent shock waveinduced renal oxidative injury in rabbits. *Urol Res*. 2006;34(4):277282. doi:10.1007/s00240-006-0057-1
24. Orestano F, Caronia N, Gallo G. Functional aspects of the kidney after shock wave lithotripsy. In: Lingeman JE, Newman DM, eds. Shockwave Lithotripsy 2: Urinary and Biliary Lithotripsy. New York, NY: Plenum Press; 1989:1517.
25. Back W, Kohrmann KU, Bensemann J, Rassweiler J, Alken P. Histomorphologic and ultrastructural findings of shockwaveinduced lesions in the isolated perfused kidney of the pig. *J Endourol*. 1994;8(4):257261. doi:10.1089/end.1994.8.257
26. Al Awadi KA, Kehinde EO, Loutfi I, et al. Treatment of renal calculi by lithotripsy: minimizing shortterm shock wave induced renal damage by using antioxidants. *Urol Res*. 2008;36(1):5160. doi:10.1007/s00240-007-0126-o
27. Serel TA, Ozguner F, Soyupek S. Prevention of shock waveinduced renal oxidative stress by melatonin: an experimental study. *Urol Res*. 2004;32(1):6971. doi:10.1007/s00240-003-0397-z
28. Biri H, Oztürk HS, Büyükkoçak S, et al. Antioxidant defense potential of rabbit renal tissues after ESWL: protective effects of antioxidant vitamins. *Nephron*. 1998;79(2):181185. doi:10.1159/000045022
29. Huxtable R. Physiological actions of taurine. *Physiol Rev*. 1992;72(1):101163. doi:10.1152/physrev.1992.72.1.101
30. Chesney RW. Taurine: its biological role and clinical implications. *Adv Pediatr.* 1985;32:1-142.
31. Hagar HH, El Etter E, Arafa M. Taurine attenuates hypertension and renal dysfunction induced by cyclosporine A in rats. *Clin Exp Pharmacol Physiol*. 2006;33(2):189196. doi:10.1111/j.1440-1681.2006.04345.x
32. Park E, Schuller Levis G, Quinn MR. Taurine chloramine inhibits production of nitric oxide and TNFalpha in activated RAW 264.7 cells by mechanisms that involve transcriptional and translational events. *J Immunol.* 1995;154(9):47784784.
33. Cunningham C, Tipton KF, Dixon HB. Conversion of taurine into Nchlorotaurine (taurine chloramine) and sulphoacetaldehyde in response to oxidative stress. *Biochem J*. 1998;330(Pt 3):939945. doi:10.1042/bj3300939
34. ElAbhar HS, ElGaward HM. Modulation of cortical nitric oxide synthase, glutamate, and redox state by nifedipine and taurine in PTZkindled mice. *Epilepsia*. 2003;44(3):276-281. doi:10.1046/j.1528-1157.2003.22302.x
35. Guz G, Oz E, Lortlar N, et al. The effect of taurine on renal ischemia/reperfusion injury. *Amino Acids*. 2007;32(3):405411. doi:10.1007/s00726-006-0383-1
36. Gürer H, Özgünes H, Saygin E, Ercal N. Antioxidant effect of taurine against leadinduced oxidative stress. *Arch Environ Contam Toxicol*. 2001;41(3):397402. doi:10.1007/s002440010265
37. Bocci V. Ozone as Janus: this controversial gas can be either toxic or medically useful. *Mediators Inflamm*. 2004;13(1):3-11. doi:10.1080/0962935062000197083
38. Souza YM, Fontes B, Martins JO, et al. Evaluation of the effects of ozone therapy in the treatment of intraabdominal infection in rats. *Clinics (Sao Paulo)*. 2010;65(2):195202. doi:10.1590/s1807-593220100000200012
39. Pryor WA. Mechanisms of radical formation from reactions of ozone with target molecules in the lung. *Free Radic Biol Med*. 1994;17(3):451465. doi:10.16/0891-5849(94)90172-4
40. Bhalla DK, Gupta SK, Reinhart PG. Alteration of epithelial integrity, alkaline phosphatase activity, and fibronectin expression in lungs of rats exposed to ozone. *J Toxicol Environ Health A*. 1999;57(5):329343. doi:10.1080/009841099157647
41. Morsy M, Hassan WN, Zalat SI. Improvement of renal oxidative stress markers after ozone administration in diabetic nephropathy in rats. *Diabetol Metab Syndr*. 2010;2:29. doi:10.1186/1758-5996-2-29
42. Barber E, Menéndez S, León OS, et al. Prevention of renal injury after induction of ozone tolerance in rats submitted to warm ischaemia. *Mediators Inflamm*. 1999;8(1):3741. doi:10.1080/09629359990702