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# Taurine is protective against oxidative stress during cold ischemia in the rat kidney

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**Aim:** Recent studies in rats have shown that taurine can prevent oxidative changes induced in renal tissue by ischemia and reperfusion. The aim of the present study was to investigate whether taurine can prevent oxidative changes that occur in the renal tissue during a long period of cold ischemia.

**Materials and methods:** Oxidative changes were evaluated histologically and biochemically in kidneys from a total of 40 rats, which were assigned to 1 of 4 groups of 10 rats each: control group (no taurine given, kidneys evaluated immediately after removal), taurine group (as in the control group, except that taurine was given orally at a dose of 150 mg/kg per day for 3 days preceding kidney removal), ischemia group (no taurine given, kidneys evaluated after 72 h of ischemia at 4 °C in University of Wisconsin solution), and taurine plus ischemia group (as in the taurine group, except that kidneys subsequently underwent cold ischemia as in the ischemia group).

**Results:** Compared to the ischemia group, the taurine plus ischemia group showed significantly lower levels of malondialdehyde and significantly higher activities of copper and zinc dependent superoxide dismutase, catalase, and glutathione peroxidase.

**Conclusion:** Orally administered taurine appears to ameliorate the oxidative stress that occurs in kidneys during cold ischemia. Compared to the ischemia group, the taurine plus ischemia group had significantly less tubular necrosis, and glomerular and epithelial injury.

**Key words:** Antioxidants, ischemia, kidney, taurine, transplantation

## Taurinin sıçan böbreğinde soğuk iskemi sırasında oksidatif strese karşı koruyucu etkisi

**Amaç:** Ratlarda yapılan son çalışmalar taurinin böbrek dokusunda iskemi ve reperfüzyon ile indüklenen oksidatif değişiklikleri önleyebileceğini göstermiştir. Bu çalışmanın amacı, taurinin böbrek dokusunda uzun süren soğuk iskemi döneminde oksidatif değişiklik oluşmasına etkisini araştırmaktır.

**Yöntem ve gereç:** Böbreklerde oksidatif değişikliklerin histolojik ve biyokimyasal olarak değerlendirildiği 40 sıçan 4 eşit gruba ayrıldı: Kontrol grubu (taurin verilmedi, böbrek hemen alındıktan sonra değerlendirildi), taurin grubu (böbrek alınmadan önce taurin 150 mg/kg/gün dozunda 3 gün süreyle oral olarak verildi), iskemi grubu (taurin verilmedi, nefrektomi materyalli UW solüsyonu içerisinde + 4 °C'de 72 saat tutulduktan sonra histopatolojik ve biyokimyasal inceleme için örnekleme yapıldı), taurin artı iskemi grubu (iskemi grubunda yapılanlara ilave olarak böbrek alınmadan önce taurin 150 mg/kg/gün dozunda 3 gün süreyle oral olarak verildi).

**Bulgular:** İskemi grubu, taurin artı iskemi grubu ile karşılaştırıldığında malondialdehit anlamlı olarak düşük seviyelerde gözlenirken, süperoksit dismutaz, katalaz ve glutatyon peroksidaz ise anlamlı olarak yüksek seviyelede idi. İskemi grubu,

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taurin artı iskemi grubu ile karşılaştırıldığında anlamlı derecede daha az tubuler nekroz, glomerüler ve epitelyal hasar vardı.

**Sonuç:** Daha önceden oral yoldan uygulanan taurinin böbreklerde soğuk iskemi sırasında ortaya çıkan oksidatif stresi iyileştirdiği görülüyor.

**Anahtar sözcükler:** Antioksidan, iskemi, böbrek, taurin, transplantasyon

## Introduction

Ischemia is a feature of organ transplantation. In mammalian kidneys, ischemia results in a wide range of physiologic changes, including the generation of reactive species in a process known as oxidative stress (1,2). The reactive species important in this setting appear to include oxygen free radicals, such as superoxide and hydroxyl, and reactive oxygen species, such as hydrogen peroxide (2,3). These molecules can induce complex cascades of pathologic changes involving cellular lipids, proteins, nucleic acids, and other molecules (4,5). Collectively, these events are known as oxidative stress (5). Prevention of oxidative changes with antioxidant substances has been explored in many experimental studies of tissue ischemia; however, most studies have focused on the oxidative damage resulting from a combination of ischemia and reperfusion. Recent studies in rats have shown that taurine can prevent oxidative changes induced in renal tissue by ischemia and reperfusion for a short period of cold ischemia (6-8). The aim of the present study was to investigate whether taurine can prevent oxidative changes that occur in renal tissue during a long period of cold ischemia.

## Materials and methods

After the study design was approved by our institution's ethics committee, 40 adult Wistar albino rats (male, 220-240 g) were randomly assigned to 1 of 4 groups of 10 rats each: control, taurine, ischemia, and taurine plus ischemia. Throughout the experimental part of the study, all rats were fed standard laboratory food and water and were kept in an environment provided with 12 h light/dark cycles, at 25 ± 1 °C with 30% humidity. All experiments were performed in accordance with the 'Principles of Laboratory Animal Care' NIH publication Vol 25, No. 28 revised 1996. Procedures for the groups were as follows.

Control group: The rats were observed for 3 days under laboratory conditions. On day 3, left kidneys were removed and prepared immediately for histological and biochemical evaluation.

Taurine group: Rats in this group received a single oral dose of taurine (Department of Pharmacy, Ruprecht-Karls University, Heidelberg, Germany) 150 mg/kg per day for 3 days (9). The taurine was given via oral gavage.

Ischemia group: Kidneys in this group were placed in University of Wisconsin (UW) solution maintained at 4 °C for 72 h before histological and biochemical evaluation.

Taurine plus ischemia group: After the rats were given taurine (150 mg/kg per day) for 3 days, left kidneys were removed and they were placed in UW solution maintained at 4 °C for 72 h before histological and biochemical evaluation.

Nephrectomy was performed as follows. Anesthesia was provided with a combination of intramuscular ketamine HCl (100 mg/kg) and xylazine HCl (10 mg/kg). The abdominal region was shaved and the rat was fastened, in a supine position, to the operating table. Body temperature was maintained at 37.5 °C with a heating pad placed under the rat. For anticoagulation, 10 IU/kg heparin was given intravenously via the caudal vein. After a wait of 3 min, the abdomen was cleaned with povidone-iodine solution and a midline incision was made. The left kidney was reached in the retroperitoneal space. The renal artery, renal vein, and ureter were identified and clamped, and were then tied with silk suture and transected.

UW solution (3 mL, 4 °C) was injected into the renal artery at a pressure of 100 cm $H_2O$ (Medrad auto-injector, Mark V ProVis, USA), and the solution was permitted to flow from the renal vein. The renal capsule was removed, and the kidney was bisected

longitudinally with a scalpel to provide specimens for the histological and biochemical evaluations. In the ischemia group and the taurine plus ischemia group, the kidneys were kept in UW solution at 4 °C for 72 h before histological and biochemical evaluations.

Specimens for histological evaluation were fixed in 10% formalin and were placed in paraffin blocks, from which 5 μm slices were made. These were stained with hematoxylin-eosin, and were evaluated by a pathologist blinded to the sources of the specimens. The evaluation was made at 200× magnification, in 30 microscopic fields, according to the 0-4 scoring system described by Guan et al. (8). By light microscopy, the following were evaluated: flattening of tubular epithelium, brush border loss, cytoplasmic vacuolization, nuclear condensation, nuclear loss, tubular epithelium debris and casts, and the presence of atrophic tubular epithelium.

For biochemical evaluation of oxidative stress, specimens were cooled in liquid nitrogen to –160 °C and were then wrapped in aluminum foil and stored at –80 °C until immediately before the evaluation procedure. Oxidative stress was evaluated in terms of malondialdehyde (MDA) levels and the activities of copper and zinc dependent superoxide dismutase (CuZn-SOD), catalase (CAT), and glutathione peroxidase (GPx).

Tissue specimens were homogenized in ice-cold 1.15% KCl with a glass homogenizer. Cellular residue was removed by centrifugation of the homogenates at 4400 × *g* for 10 min at 4 °C. The remaining supernatant was analyzed for MDA content and activities of CuZn-SOD, CAT, and GPx as follows.

MDA activity in tissue homogenate was measured by the method of Bulucu et al. (10). MDA levels were measured through the reaction of MDA with thiobarbituric acid. The reaction product was measured spectrophotometrically. A 1,1,3,3-tetramethoxypropane solution was used as a standard. Tissue MDA levels were expressed as nmol/g of tissue.

CuZn-SOD activity in tissue homogenate was measured by the method of Yucel et al. (11). CuZn-SOD activity was measured through the addition of 25 μL of supernatant to a buffer solution containing 50 mmol/L 3-(cyclohexylamino)-1-propanesulfonic acid (CAPS) and 0.094 mmol/L EDTA (pH 10.2), which was mixed with 850 μL of a substrate solution containing 0.05 mmol/L xanthine sodium and 0.025 mmol/L 2-(4-iodophenyl)-3-(4-nitrophenol)-5-phenyl tetrazolium chloride (INT). To this mixture was added 125 μL of xanthine oxidase (80 U/mL) and the increase in absorbance at 505 nm against air was measured for 3 min. As standards, 25-μL samples of phosphate buffer at a range of concentrations were used. CuZn-SOD activity was expressed as U/g of tissue.

CAT activity measurement: CAT activity in tissue homogenate was measured at 25 °C by the method of Aebi (12). Substrate $H_2O_2$ decomposition rate was followed spectrophotometrically at 240 nm for 30 s. Activity was expressed as KU/g.

GSH-Px activity in tissue homogenate was measured by the method of Aydın et al. (13). GPx activity was determined with the use of a reaction mixture at pH 7.6, containing the following: 50 mmol/L Tris buffer, 1 mmol/L disodium EDTA, 2 mmol/L reduced glutathione, 0.2 mmol/L NADPH, 4 mmol/L sodium azide, and 1000 U glutathione reductase. To 950 μL of this reaction mixture, 50 μL of supernatant was added and the mixture was incubated at 37 °C for 5 min. The reaction was started with the addition of 8.8 mmol/L of hydrogen peroxide, and the reduction in NADPH absorbance at 340 nm was followed for 3 min. Enzyme activity was expressed as U/g of tissue.

Statistical analysis was performed with SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). Variables were examined with one-way analysis of variance.

Group comparisons were made via the Kruskal-Wallis test and Mann-Whitney U test. Histological and biochemical results were obtained as mean ± standard deviation. Statistical significance was defined as $P < 0.05$.

## Results

### Histopathological findings

The findings are summarized in Table 1. In the control and taurine groups, renal tissue sections had a normal morphology: tubular necrosis and casts in the tubules were minimal (Figures 1 and 2). In

Table 1. Histological scores in the 4 groups of rats.

| Scores | Control (n = 10) | Taurine (n = 10) | Ischemia (n = 10) | Taurine + Ischemia (n = 10) |
|---|---|---|---|---|
| Glomerular injury score | 0.1 ± 0.1 | 0.4 ± 0.1 | 2.4 ± 0.4* | 1.7 ± 0.2 ** |
| Tubular injury score | 0.1 ± 0.1 | 0.3 ± 0.2 | 2.4 ± 0.6* | 2.1 ± 0.3 ** |
| Epithelial injury score | 0.1 ± 0.1 | 0.3 ± 0.1 | 2.9 ± 0.3* | 2.4 ± 0.3 ** |

* $P < 0.05$ Ischemia group vs. other groups
** $P < 0.05$ Taurine + ischemia group vs. the other groups.

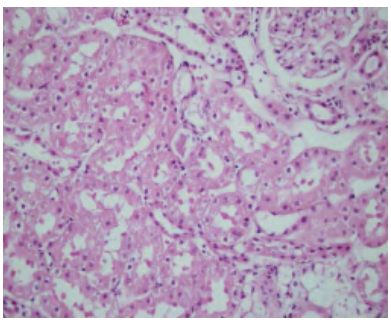

Figure 1. In the control group, tubular necrosis and casts in the tubules were minimal (hematoxylin-eosin, 200×).

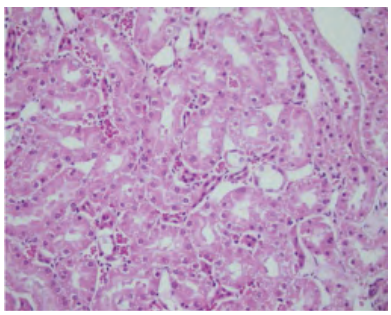

Figure 2. In the taurine group, there was minimal tubular damage, as in the control group (hematoxylin-eosin, 200×).

the ischemia group (Figure 3), tubular necrosis and casts in the tubules were significantly more severe than in the control group ($P < 0.05$). Compared to the ischemia group, the taurine plus ischemia group (Figure 4) had significantly less tubular necrosis and casts in the tubules ($P < 0.05$).

**MDA and antioxidant enzymes**

Biochemical findings are summarized in Table 2. Compared to the control group, the ischemia group had significantly higher levels of MDA ($P < 0.05$) and significantly lower activities of CuZn-SOD, CAT, and GPx. In terms of these parameters, no significant

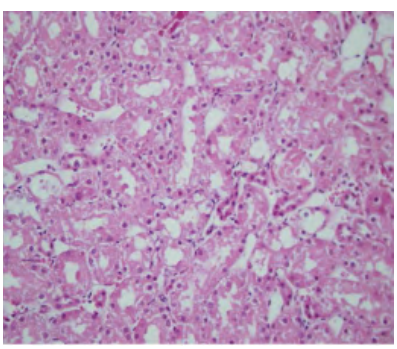

Figure 3. In the ischemia group, tubular necrosis and casts in the tubules were markedly apparent, and were significantly more severe than in the control group ($P < 0.05$) (hematoxylin-eosin, 200×).

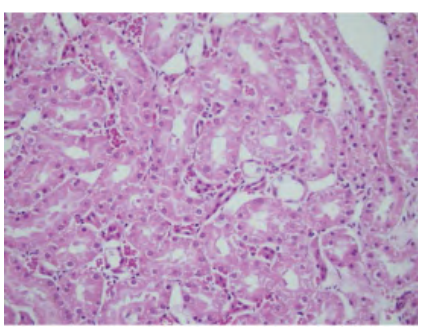

Figure 4. In the taurine plus ischemia group, tubular necrosis and casts in the tubules were significantly less than in the ischemia group ($P < 0.05$) (hematoxylin-eosin, 200×).

Table 2. Oxidative stress parameters in the four groups.

| Groups | MDA | CuZn-SOD | GPx | CAT |
|---|---|---|---|---|
| | nmol/g | U/g | U/g | KU/g |
| Control (n = 10) | 14.26 (± 1.02) | 93.96 (± 8.45) | 18.38 (± 0.92) | 4.25 (± 0.42) |
| Taurine (n = 10) | 14.20 (± 1.26) | 102.22 (± 10.63) | 19.09 (± 2.01) | 5.53 (± 1.21) |
| Ischemia (n = 10) | 21.20 (± 3.65)* | 64.92 (± 4.98)* | 15.47 (± 4.06)* | 2.31 (± 0.23)* |
| Taurine + ischemia (n = 10) | 13.32 (± 0.9)** | 113.52 (± 11.56)** | 20.29 (± 2.98)** | 4.22 (± 1.06)** |

MDA: malondialdehyde; CuZn-SOD: superoxide dismutase; CAT: catalase
GPx: glutathione peroxidase
* P < 0.05 Ischemia group vs. control group
** P < 0.05 Taurine + ischemia group vs. ischemia group

differences were found between the control group and the taurine group. Compared to the ischemia group, the taurine plus ischemia group had significantly lower levels of malondialdehyde and significantly higher activities of CuZn-SOD, CAT, and GPx.

## Discussion

Findings of the present study: (i) tissue GSH-Px, SOD, and CAT levels are significantly higher in the taurine + ischemia group compared to the ischemia group; (ii) tissue MDA levels are significantly lower in the taurine + ischemia group than in the ischemia group, and (iii) tubular, epithelial and glomerular injury are significantly better in the taurine + ischemia group than in the ischemia group.

In the setting of ischemia and reperfusion that occur during kidney transplantation, this approach has led to many reports of clear benefits in animal studies, but clinical applications in humans have been far fewer. In that study ischemia durations are low. In this study, we showed that taurine can prevent oxidative changes, which occur in renal tissue during cold ischemia, even for a period of up to 72 h.

Prevention of oxidative damage to tissues has been the aim of many studies, and the general approach has been to inhibit enzymes that generate reactive species, or to scavenge the reactive species themselves. A possible reason for this is the complexity of events that characterize oxidative damage (5). The rationale for the present study was to limit the possible mechanisms of oxidative changes by focusing on one step in the transplantation process, namely the period of cold ischemia.

Several animal studies have indicated that oxidative changes seen after renal ischemia and reperfusion can be lessened by treatment with taurine (6-8). Michalk et al. (6) induced transient ischemia in rats by clamping the renal artery for 60 min. The authors reported that intravenous administration of taurine at a dose of 40 mg/kg for 10 min before clamping significantly lessened the subsequent rise in serum levels of creatinine and the renal tubular enzymes lactate dehydrogenase and gamma-glutathione-S-transferase. These parameters were measured during reperfusion, at 90 min after the clamp was removed from the renal artery. In a similar study in rats, Guz et al. (7) clamped the renal arteries for 40 min, and then at the beginning of reperfusion they injected taurine into the peritoneal cavity at a dose of 7.5 mg/kg. After 6 h of reperfusion, the rats that had received taurine showed significantly smaller increases in serum creatinine and in serum and tissue levels of MDA, the latter indicating less extensive lipid peroxidation. Renal histologic changes were less extensive in these animals as well, compared to rats that underwent ischemia and reperfusion without receiving taurine. The findings of these 2 studies cannot be directly combined with those of the

present study, due to the lack of cold ischemia in the 2 studies and the lack of reperfusion in the present study. However, the findings of the present study are consistent with those of the previous 2 in suggesting a role for taurine in the prevention or reversal of injury that may occur early in the combined process of renal ischemia and reperfusion.

In a study that included a period of cold ischemia, Guan et al. (8) investigated the effects of taurine given intravenously to rats whose kidneys were then removed, placed in histidine-tryptophan-ketoglutarate solution at 4 °C for 19 h, and transplanted into other rats that had undergone bilateral nephrectomy. After the transplanted kidneys remained 6 h in the recipient rats, serum indicators of renal function and histological specimens of renal tissue were evaluated. The authors reported that taurine significantly decreased blood urea nitrogen, creatinine, aspartate aminotransferase, and lactate dehydrogenase in a dose-dependent manner. Tubular damage was less severe in rats that received taurine, as was the case in our study. Guan et al. (8) also noted that taurine pretreatment was associated with greater expression of superoxide dismutase, and our finding of increased CuZn-SOD activity is consistent with this study. Collectively, these findings suggest an involvement of taurine in multiple cellular events, including those that might be a direct consequence of cold ischemia.

Cold ischemia, even when not followed by reperfusion, has been shown in animal studies to result in oxidative changes in renal tissue (15-18). Human renal tubular cells in cold storage have likewise been found to generate reactive oxygen species (19).

The mechanisms of renal injury that are active during cold ischemia are diverse and include ATP depletion, acidosis, mitochondrial swelling, calcium influx into the cytosol, iron release, and free radical generation (20). In a study of rabbit kidneys kept at 0 °C for 24 or 48 h, Green et al. found that lipid peroxidation was more extensive when kidneys were kept in isotonic saline rather than in hypertonic citrate solution (15). Gower et al. (16), also working with rabbit kidneys kept at 0 °C for 24 h in isotonic saline, found that lipid peroxidation in the renal cortex was predominantly non-specific and iron-catalyzed, while in the medulla about half of the detected lipid peroxidation was formed enzymatically from arachidonic acid by cyclooxygenase. In a subsequent study, Gower et al. reported that the iron chelator desferrioxamine, when given intravenously to the rabbits before the kidneys were removed, resulted in less lipid peroxidation in the renal cortex during cold storage. In the same study, intravenous administration of the cyclooxygenase inhibitor indomethacin had no effect on lipid peroxidation in the cortex, but lessened it in the medulla (17). Cotterill et al. (18) investigated the effect of adding calcium to the solution in which rabbit kidneys were stored at 0 °C for 24 h, and found a significant increase in lipid peroxidation when calcium was present. In a study of human renal tubular cells kept in UW solution at 4 °C for 24, 48, or 72 h, Salahudeen et al. (19) reported that cold-induced lactate dehydrogenase release, ATP depletion, DNA damage, and membrane degradation were suppressed by the antioxidants 2-methyl aminochroman or deferoxamine.

Taurine, or 2-aminoethanesulfonic acid, due to its capacity to ameliorate oxidative injury, has frequently been described as an antioxidant. However, in vitro taurine has little direct antioxidant activity (21,22). According to a study designed by Mozaffari et al. (23), in rats taurine 1% against renal ischemia-reperfusion injury does not provide a functional improvement. In fact, the lack of taurine against renal ischemia-reperfusion injury may be more useful. This apparent inconsistency raises the question of how taurine might influence the events involved in oxidative damage in vivo. Mitochondrial enzymes have been implicated in the generation of reactive species (2). Hansen et al. (24) have hypothesized that taurine exerts its antioxidative effect by buffering the pH in the mitochondrial matrix and thereby preventing the leakage of the reactive compounds. This hypothesis appears to be consistent with the mitochondrial swelling and leakage reported by Salahudeen et al. in their study of cultured human tubular cells that were kept in cold storage (25).

In this study, we showed that taurine can prevent oxidative changes that occur in renal tissue during cold ischemia even for up to 72 h. Because patients can be delayed in arriving to the hospital, and because in cadaveric transplantation the period of cold ischemia

can sometimes be extensive, taurine might truly be effective in protecting donor kidneys from damage related to long periods of cold ischemia. However, to reach this conclusion definitively, more animal and human studies are needed. Whether such changes occur in intact kidneys undergoing cold storage or if taurine can prevent or lessen these changes are questions for further research.

## References


1. Weinberg JM. The cell biology of ischemic renal injury. Kidney Int 1991; 39: 476-500.
2. Kosieradzki M, Rowiński W. Ischemia/reperfusion injury in kidney transplantation: mechanisms and prevention. Transplant Proc 2008; 40: 3279-88.
3. Paller MS. Free radical-mediated postischemic injury in renal transplantation. Ren Fail 1992; 14: 257-60.
4. Halliwell B, Whiteman M. Measuring reactive species and oxidative damage in vivo and in cell culture: how should you do it and what do the results mean? Br J Pharmacol 2004; 142: 231-55.
5. Halliwell B. Biochemistry of oxidative stress. Biochem Soc Trans 2007; 35: 1147-50.
6. Michalk DV, Hoffmann B, Minor T. Taurine reduces renal ischemia/reperfusion injury in the rat. Adv Exp Med Biol 2003; 526: 49-56.
7. Guz G, Oz E, Lortlar N, Ulusu NN, Nurlu N, Demirogullari B et al. The effect of taurine on renal ischemia/reperfusion injury. Amino Acids 2007; 32: 405-11.
8. Guan X, Dei-Anane G, Liang R, Gross ML, Nickkholgh A, Kern M et al. Donor preconditioning with taurine protects kidney grafts from injury after experimental transplantation. J Surg Res 2008; 146: 127-34.
9. J Das, J Ghosh, P Manna, PC Sil. Taurine protects acetaminophen-induced oxidative damage in mice kidney through APAP urinary excretion and CYP2E1 inactivation. Toxicology 2010; 269: 24-34.
10. Bulucu F, Vural A, Aydın A, Sayal A. Oxidative stress status in adults with nephrotic syndrome. Clin Nephrol 2000; 53: 169-173.
11. Yucel O, Uçar E, Tozkoparan E, Gunal A, Akay C, Sahin MA et al. Proanthocyanidin to prevent formation of the reexpansion pulmonary edema. J Cardiothor Surg 2009; 28: 40-8.
12. Aebi H. Catalase in vitro. In: Packer L (ed). Methods Enzymol. Orlando: Academic Press 1984; 105-26.
13. Aydın A, Orhan H, Sayal A, Özata M, Şahin G, Isımer A. Oxidative stress and nitric oxide related parameters in type II diabetes mellitus: effects of glycemic control. Clin Biochem 2001; 34: 65-70.
14. Norio K, Wikström M, Salmela K, Kyllönen L, Lindgren L. Ascorbic acid against reperfusion injury in human renal transplantation. Transpl Int 2003; 16: 480-5.
15. Green CJ, Healing G, Lunec J, Fuller BJ, Simpkin S. Evidence of free-radical induced damage in rabbit kidneys after simple hypothermic preservation and autotransplantation. Transplantation 1986; 41: 161-5.
16. Gower J, Fuller B, Green C. Lipid peroxidation in the cortex and medulla of rabbit kidneys subjected to cold ischaemia and the value of protective agents. Free Radic Res Commun 1987; 3: 107-15.
17. Gower JD, Healing G, Fuller BJ, Simpkin S, Green CJ. Protection against oxidative damage in cold-stored rabbit kidneys by desferrioxamine and indomethacin. Cryobiology 1989; 26: 309-17.
18. Cotterill LA, Gower JD, Fuller BJ, Green CJ. Oxidative damage to kidney membranes during cold ischemia. Evidence of a role for calcium. Transplantation 1989; 48: 745-51.
19. Salahudeen AK, Huang H, Patel P, Jenkins JK. Mechanism and prevention of cold storage-induced human renal tubular cell injury. Transplantation 2000; 70: 1424-31.
20. Salahudeen AK. Cold ischemic injury of transplanted kidneys: new insights from experimental studies. Am J Physiol Renal Physiol 2004; 287: 181-7.
21. Aruoma OI, Halliwell B, Hoey BM, Butler J. The antioxidant action of taurine, hypotaurine and their metabolic precursors. Biochem J 1988; 256: 251-5.
22. Gaté L, Paul J, Ba GN, Tew KD, Tapiero H. Oxidative stress induced in pathologies: the role of antioxidants. Biomed Pharmacother 1999; 53: 169-80.
23. Mozaffari M, Abdelsayed R, Patel C, Wimborne H, Liu JY, Schaffer SW. Differential effects of taurine treatment and taurine deficiency on the outcome of renal ischemia reperfusion injury. J Biomed Sci 2010; 17(Suppl 1): 32.
24. Hansen SH, Andersen ML, Birkedal H, Cornett C, Wibrand F. The important role of taurine in oxidative metabolism. Adv Exp Med Biol 2006; 583: 129-35.
25. Salahudeen AK, Huang H, Joshi M, Moore NA, Jenkins JK. Involvement of the mitochondrial pathway in cold storage and rewarming-associated apoptosis of human renal proximal tubular cells. Am J Transplant 2003; 3: 273-80.