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The effect of taurine on renal ischemia/reperfusion injury

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Summary. Ischemia-reperfusion (I/R) injury is one of the most common causes of renal dysfunction. Taurine is an endogenous antioxidant and a membrane-stabilizing, intracellular, free beta-amino acid. It has been demonstrated to have protective effects against I/R injuries to tissues other than kidney. The aim of this study was to determine whether taurine has a beneficial role in renal I/R injury. Forty Wistar-Albino rats were allocated into four groups as follows: sham, taurine, I/R, and I/R + taurine. Taurine 7.5 mg/kg was given intra-peritoneally to rats in the groups taurine and I/R + taurine. Renal I/R was achieved by occluding the renal arteries bilaterally for 40 min, followed by 6 h of reperfusion. Immediately thereafter, blood was drawn and tissue samples were harvested to measure 1) serum levels of BUN and creatinine; 2) serum and/or tissue levels of malondialdehyde (MDA), glutathione (GSH), glucose 6-phosphate dehydrogenase (G-6PD), 6-phosphogluconate dehydrogenase (6-PGD) and glutathione reductase (GSH-red); 3) renal morphology; and 4) immunohistochemical staining for P-selectin. Taurine administration reduced I/R-induced increases in serum BUN and creatinine, and serum and tissue MDA levels ($p < 0.05$). Additionally, taurine lessened the reductions in serum and tissue glutathione levels secondary to I/R ($p < 0.05$). Taurine also attenuated histopathologic evidence of renal injury, and reduced I/R-induced P-selectin immunoreactivity ($p < 0.05$). Overall, then, taurine administration appears to reduce the injurious effects of I/R on kidney.

Keywords: Taurine – Ischemia – Reperfusion – Kidney – Malondialdehyde and glutathione

Introduction

Acute renal failure continues to be associated with significant morbidity and mortality, despite increased understanding of its pathogenesis, novel therapeutic approaches, and the development of technical advances in therapeutic delivery (Radhakrishnan and Kiryluk, 2006). Ischemia/reperfusion (I/R) injury, one of the most important causes of acute renal failure, cannot be avoided in some situations, including renal artery surgery, renal transplantation, atheroembolic disease, interventional radiologic manipulations to the renal artery, cardiac arrest, hypotensive states and shock. Injury following I/R depends not only on the duration of ischemia, but also on the reperfusion that follows. During reperfusion, the generation of reactive oxygen species (ROS) leads to increased oxidative damage and organ dysfunction (Cutrin et al., 2000; Noiri et al., 2001; Walker et al., 2001). Anti-oxidative therapy has been discovered to be effective against I/R injury (Aragno et al., 2000; Lloberas et al., 2002).

The beneficial effects of taurine have been demonstrated in I/R injuries in tissues other than kidney (Oz et al., 1999, 2002). Taurine (2-aminoethanesulfonic acid) is the major intracellular free beta-amino acid found in most mammalian tissues (Chesney, 1985). Osmoregulation, prevention of oxidative injury, bile acid conjugation, modulation of the functioning central nervous system and cell proliferation are among its main physiologic roles (Chesney, 1985; Huxtable, 1992). Moreover, taurine protects cellular membranes against toxic compounds – like oxidants, haloalkanes, bile acids and xenobiotics – and reduces the production of malondialdehyde (MDA), which is one of the markers of oxidative stress (Huxtable, 1992; Wright et al.,

1985, 1986). In addition to MDA, glutathione (GSH) is a common marker and non-enzymatic antioxidant to determine oxidative stress, and widely is being used in experimental and clinical studies (Shan et al., 1990). On the other hand, glucose-6-phosphate dehydrogenase (G-6PD) and 6-phosphogluconate dehydrogenase (6-PGD) are known to be fundamental enzymes of the pentose phosphate pathway. These enzymes are the principal source of NADPH, and serve as antioxidant enzymes that modulate the redox milieu. NADPH, in turn, acts as a reducing equivalent to maintain reduced GSH stores, which protect cells against ROS (Ulusu et al., 2005; Ulusu and Tandogan, 2006). Glutathione reductase (GSH-red) also is related to antioxidant metabolism, and I/R injury may cause a decrease in this enzyme's activity (Barnard et al., 1993). Consequently these oxidative stress markers and enzymes were included the present study to evaluate the effect of taurine on renal I/R injury.

The aim of the present study was to investigate the effects of taurine on kidney function and morphology, serum and renal tissue levels of oxidative stress markers, anti-oxidant and anti-oxidant enzyme levels, and pentose phosphate pathway enzymes in a rat model of renal I/R injury.

Materials and methods

The study was approved by the Animal Ethics Committee and carried out in accordance with the guidelines of the Research Committee of Gazi University.

Animals

Forty male Wistar-Albino rats, weighing 220–250 g, were acquired from the university's vivarium sources and housed in 8 cages at a constant temperature (24 °C), humidity (70%) and light–dark cycle in a controlled environment. They were fed standard rat chow and tap water, *ad libitum*.

Experimental protocols

Rats were randomly divided into four groups as follows: sham (N = 10), taurine (N = 10), I/R (N = 10), and I/R + taurine (N = 10). The mean weight of rats was approximately 230 g in all four groups.

Surgical procedure

Following a 12 h fasting period, rats underwent surgery, using ketamine HCl anesthesia (50 mg/kg) and sterile technique. With each animal, the abdomen was entered through a midline incision and both renal arteries visualized. In the sham group, the abdomen was closed without any further procedure. In the taurine-only group, taurine, 7.5 mg/kg, was injected into the peritoneal cavity just before closure of the abdominal wall. Body temperature was maintained close to 37.5 °C with a heating lamp. In the I/R and I/R + taurine groups, both renal arteries were occluded using microvascular clamps for 40 min, and occlusion of blood flow was confirmed by visual inspection of the kidneys. After de-clamping, we confirmed that renal blood flow had been restored prior to closing the incision. At the beginning of reperfusion, taurine was given to the I/R + taurine group as previously described. The I/R group was not treated. Fluid loss was replaced by administering 5 ml of warm (37 °C) 0.9% NaCl intra-peritoneally prior to abdominal closure in all rats. At the end of 6 h of reperfusion (or the equivalent period of time in the non-I/R rats), 3 ml of blood was drawn from the heart, and, in the process, the animal was sacrificed. The serum was isolated from each animal to study serum blood urea nitrogen (BUN), creatinine and several other biochemical markers. The abdomen was re-entered and bilateral nephrectomies were performed. The kidneys were separated into two halves, one half of which was wrapped with aluminum foil, placed in liquid nitrogen and kept at −80 °C to determine tissue MDA, GSH and enzyme levels. The other half of each kidney was placed in 10% formaldehyde for histopathological and immunochemistry analysis. All specimens were coded in the research laboratory and evaluated by the same individuals, who were blinded to group assignments.

Biochemical studies

BUN and creatinine

Serum BUN and creatinine levels were determined by means of an Abbott-Aeroset autoanalyzer (Chicago, IL, USA) using the original kits.

Malondialdehyde and glutathione

The levels of serum MDA (nmol/ml), tissue MDA (nmol/g of tissue), serum GSH (nmol/ml) and tissue GSH (μmol/g tissue) were determined spectrophotometrically (Aykac et al., 1985; Mihara and Uchiyama, 1978).

Tissue preparation for enzymatic assays

Kidneys were weighed. Then each sample was homogenized with an ultra turax homogenizer with a S18N-10G probe for approximately 3 min, using 3 volumes of 50 mM potassium phosphate buffer pH 7.4. The homogenate was centrifuged at $105\,000 \times g$ for 60 min at 4 °C using a Beckman ultracentrifuge; the resultant supernatants were used for the measurement of enzyme activity.

Chemicals

Glucose-6-phosphate (G-6-P), nicotinamide adenine dinucleotid phosphate ($NADP^+$), reduced nicotinamide adenine dinucleotid phosphate (NADPH), 6-phosphogluconate (6-PG), magnesium chloride ($MgCl_2$), oxidized glutathione (GSSG), sodium phosphate monobasic and dibasic, Tris [Tris (hydroxymethyl) aminomethane] were obtained from Sigma Chemical Co., MO, USA. Coomassie Brilliant Blue G-250 was obtained from SERVA Feinbiochemia GmbH, Heidelberg, Germany. Ethanol (EtOH) was obtained from Merck, Darmstadt, Germany. Orto-phosphoric acid was obtained from Analar BDH Chemical Ltd., England.

Enzyme activities

Glucose-6-phosphate dehydrogenase

Enzyme activities were determined spectrophotometrically using a LKB Ultraspec Plus (4054 UV/visible) spectrophotometer, monitoring NADPH production at 340 nm and 37 °C (Betke et al., 1967). The assay mixture contained 10 mM $MgCl_2$, 0.2 mM $NADP^+$ and 0.6 mM glucose-6-phosphate in 100 mM Tris/HCl buffer with pH 8.0. Assays were carried out in duplicate and the activities were followed for 60 seconds. The reaction was linear during this time period. One unit (U) of activity was defined as the amount of enzyme required to reduce 1 μmol of $NADP^+$ per min under the assay conditions. Specific activity was defined as the number of units per mg of protein.

6-Phosphogluconate dehydrogenase

6-Phosphogluconate dehydrogenase (6-PGD) activity was measured by substituting 0.6 mM 6-phosphogluconate as substrate in the assay mixture given above for G-6PD measurement (Pearse and Rosemeyer, 1975).

GSH-red

The activity of this enzyme was measured in accordance with the modified Staal method (Acan and Tezcan, 1989). The incubation mixture contained 100 mM sodium phosphate buffer, pH 7.4, 1 mM oxidized glutathione (GSSG), 100 μM reduced nicotinamide adenine dinucleotid phosphate (NADPH), and the tissue supernatants. A decrease in the absorbance of NADPH at 340 nm was monitored spectrophotometrically at 37 °C. A unit of activity (U) was defined as the amount of enzyme that catalyses the oxidation of 1 μmol of NADPH in 1 min under these conditions.

Protein assay

Protein concentrations were determined by the method proposed by Bradford, using BSA as a standard (Bradford, 1976).

Histological study

Tissue samples were fixed in a 4% paraformaldehyde solution and embedded in paraffin, and 5-μm sections were stained with hematoxylin and eosin. A semi-quantitative histologic analysis was conducted in a blinded manner. Ten glomeruli and 10 tubules in each kidney were randomly selected at a 400× magnification, and the damaged glomeruli and tubules were graded on a scale of 0–3+, as follows: 0, normal; 1+, slight; 2+, moderate; and 3+, severe. Additionally, epithelial and interstitial injuries also were noted and graded as mentioned.

Immunohistochemistry

For P-selectin detection, renal tissues were fixed with 10% formalin for 72 h. After fixation, tissues were evaluated by means of light microscopy. Then tissues were washed and dehydrated for 1 h with 50, 60, 70, 80, 90, 96 or 100% ethyl alcohol. Later, tissues were incubated in a 100% ethyl alcohol and immersion oil mixture (1:1 dilution rate) for 1 h, and made transparent in immersion oil with overnight incubation. Following xylol serial dilution in xylol and paraffin (1:1 dilution rate) at 37 °C in an incubator for 1 h, the tissues were embedded in paraffin. A 5 μm slice from the paraffin blockage was incubated at 60 °C overnight, at 37 °C for 2 h, and two times for 15 min with xylol. Tissue specimens were dehydrated in 100, 96 and 80% ethyl alcohol for 10 min each, and two times in distilled water for 5 min. Tissue specimens were boiled with 10% citrate in a microwave. After waiting 20 min at room temperature, the circumference of each tissue specimen was outlined using a pap pen which is designed to provide a water repellant barrier around the specimen. The specimens were washed in water and PBS, and then dripped with hydrogen peroxide. Then the specimens were washed in PBS again and blocked with ultraviolet light. The primary antibody – Fitzgerald CD62P (P-selectin) Human/Mouse/Rat, Fitzgerald Industries International Inc., USA) – was used for staining at room temperature for one hour. After washing in PBS, tissue specimens were left in AEC chromogen for 15 min. The specimens were washed in PBS again, stained with Mayer's hematoxylin, and then viewed under a Leica photo light microscope.

Statistical analyses

All statistical analyses were performed using the statistical package SPSS for windows, version 10.0. All values are expressed as mean ± SEM. Group distributions were analyzed by means of a one-sample Kolmogrov-Smirnov test. All group values exhibited a normal distribution, so that parametric statistical methods were used to analyze the data further. Data then were analyzed using analysis of variance (ANOVA) followed by Bonferroni's post test. Histopathologic data were analyzed by means of the Kolmogorov-Smirnov *Z* test. P values below 0.05 were considered statistically significant.

Results

BUN and creatinine

Ischemia/reperfusion caused a significant increase in serum BUN and creatinine concentrations ($p < 0.05$) which was

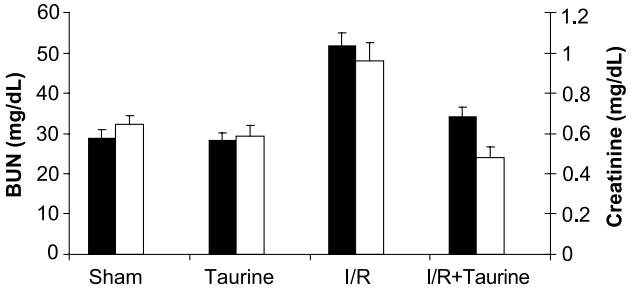


Fig. 1. The rises in serum BUN and creatinine concentrations after I/R were prevented by taurine administration ($p < 0.05$ I/R vs other groups). Values expressed mean ± SEM (■ BUN, □ Creatinine)

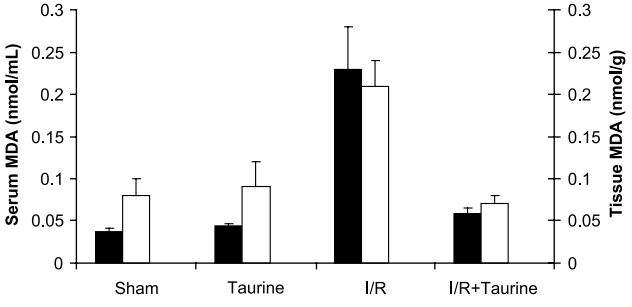


Fig. 2. Serum and tissue MDA levels. Rats subjected to renal I/R had significantly higher serum and tissue MDA levels than the rats in the other groups ($p < 0.05$). Rats in the I/R + taurine group had significantly lower serum and tissue MDA levels than rats in the I/R group ($p < 0.05$). Values expressed mean ± SEM (■ Serum MDA, □ Tissue MDA)

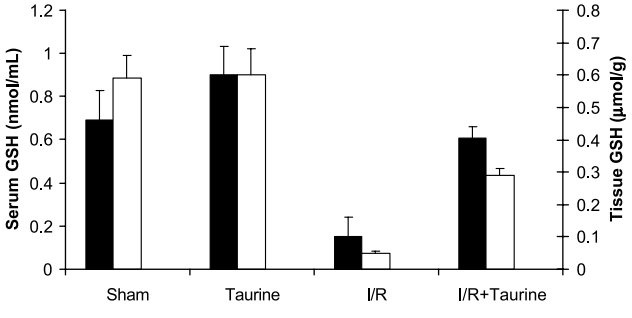


Fig. 3. Serum and tissue GSH levels. Rats subjected to renal I/R had significantly lower serum and tissue GSH levels than the rats in the other groups ($p < 0.05$). Rats in the I/R + taurine group had significantly higher serum and tissue GSH levels than rats in the I/R group ($p < 0.05$). Rats that had been subjected to I/R and received taurine still had significantly lower tissue GSH than sham-operated rats or rats that had received taurine in the absence of I/R injury ($p < 0.05$). Values expressed mean ± SEM (■ Serum GSH, □ Tissue GSH)

Table 1. Activity levels of glucose-6-phosphate dehydrogenase (G-6PD), 6-phosphogluconate dehydrogenase (6-PGD) and glutathione reductase (GSH-red)

Enzymes	Sham	Taurine	I/R	I/R + Taurine
G-6PD (U/mg protein) $\times 10^{-3}$	36.4 ± 2.2	31.1 ± 2.8	$16.5 \pm 2.1^{*}$	$18.6 \pm 1.1^{\dagger}$
6-PGD (U/mg protein) $\times 10^{-3}$	41.3 ± 2.1	36.7 ± 1.3	$30.5 \pm 2.1^{*}$	35.5 ± 1.2
GSH-red (U/mg protein)	0.27 ± 0.01	0.33 ± 0.01	$0.26 \pm 0.02^{\S}$	0.29 ± 0.02

Values expressed mean ± SEM. $^{*}p < 0.05$ I/R vs sham and I/R vs taurine, $^{\dagger}p < 0.05$ I/R + taurine vs sham and I/R + taurine vs taurine, $^{\S}p < 0.05$ taurine vs I/R

prevented by taurine administration ($p < 0.05$). Figure 1 shows serum BUN and creatinine concentrations in all groups.

MDA

Ischemia/reperfusion injury increased serum and tissue MDA levels vs sham ($p < 0.05$). The high serum and tissue MDA levels induced by I/R were reduced by taurine ($p < 0.05$), but taurine alone did not significantly alter MDA levels vs the sham group values (Fig. 2).

Glutathione levels

After ischemia and 6 h of reperfusion, the serum and tissue GSH decreased significantly ($p < 0.05$). The rats that in I/R + taurine group had significantly higher serum and tissue GSH levels than the rats that experienced I/R alone ($p < 0.05$; Fig. 3); however, only tissue levels of GSH were significantly lower in the I/R + taurine group than in the sham group ($p < 0.05$). Serum and tissue levels of GSH for sham-operated rats were no different than for rats that received taurine without I/R.

Enzyme activity

Glucose-6-phosphate dehydrogenase and 6-PGD activity both decreased significantly after I/R compared vs the sham-operated group ($p < 0.05$). Taurine administration increased these enzyme activities, especially 6-PGD, following I/R; however, the increase did not reach statistical significance. Additionally G-6PD and 6-PGD activities were similar in the sham and taurine-administrated groups. On the other hand, GSH-red activity was not changed secondary to I/R. This enzyme's activity was no different in the sham, taurine and I/R + taurine groups. Enzyme activity levels are shown in Table 1.

Table 2. Histopathological results obtained from the light microscopic analysis of kidney sections

	Sham ($n = 10$)	Taurine ($n = 10$)	I/R ($n = 10$)	I/R + taurine ($n = 10$)
Glomerular injury score	0.1 ± 0.1	0.3 ± 0.2	$2.3 \pm 0.3^{*}$	$1.8 \pm 0.2^{\dagger}$
Tubular injury score	0.1 ± 0.1	0.2 ± 0.1	$2.4 \pm 0.4^{*}$	$1.9 \pm 0.3^{\dagger}$
Epithelia injury score	0.1 ± 0.1	0.2 ± 0.1	$2.8 \pm 0.3^{*}$	$2.2 \pm 0.2^{\dagger}$
Interstitial injury score	0.1 ± 0.1	0.2 ± 0.1	$3 \pm 0^{*}$	$2.2 \pm 0.1^{\dagger}$

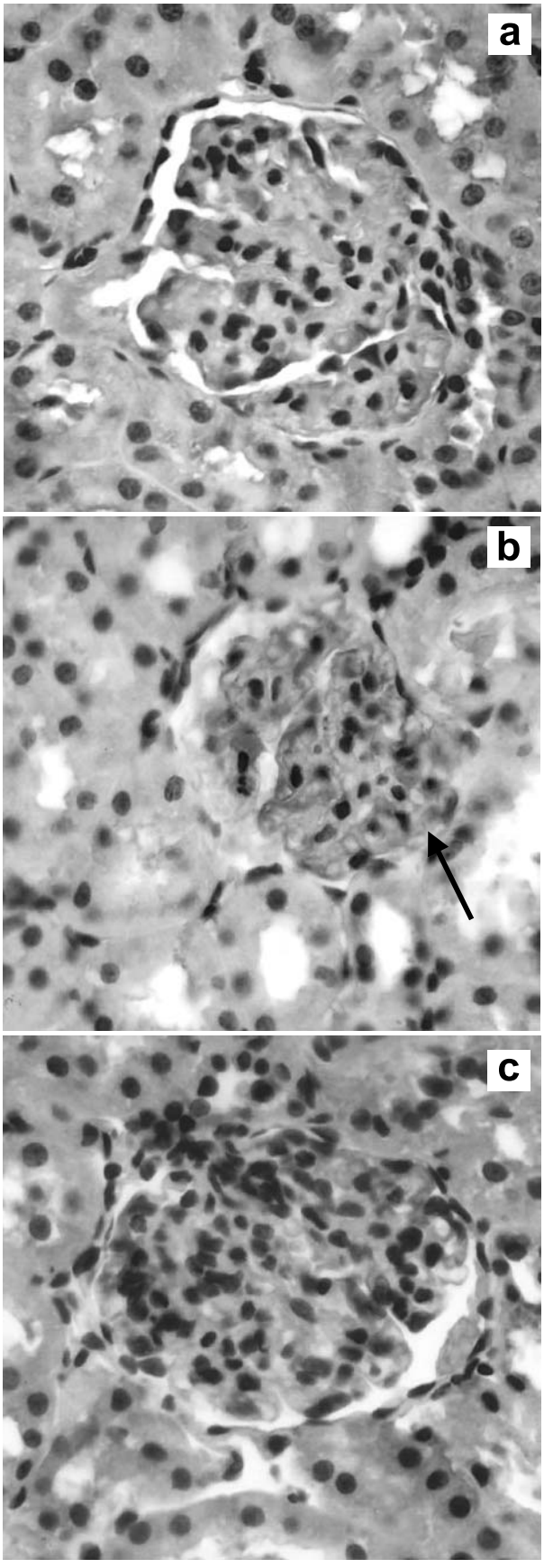
Values expressed mean ± SEM. $^{*}p < 0.05$ I/R vs the other groups, $^{\dagger}p < 0.05$ I/R + taurine vs sham and I/R + taurine vs taurine

Histological study

As shown in Table 2, compared with the total severity score measured from kidneys obtained from sham-operated animals, renal I/R produced a significant increase in total morphology scores ($p < 0.05$). With administration of taurine following ischemia, the total severity scores were significantly reduced ($p < 0.05$). Administration of taurine without I/R did not have a significant effect on total severity score vs the sham operated rats.

Immunohistochemistry

The I/R procedure resulted in significantly higher P-selectin immunoreactivity levels on glomeruli, but administration of taurine at the beginning of reperfusion significantly reduced P-selectin immunoreactivity ($p < 0.05$). The kidneys from rats that had been subjected to the sham operation did not show significant differences in P-selectin immunoreactivity on glomeruli vs the kidneys from the non-I/R rats administered taurine ($p < 0.05$). Figure 4 shows P-selectin immunoreactivity staining for the four groups.



Discussion

The main findings of the present study were that the administration of taurine attenuated increased serum BUN and creatinine levels in rats subjected to 40 min of renal ischemia and 6 h of reperfusion. In addition, renal I/R induced oxidative stress determined by serum and tissue MDA and GSH levels, which generally were restored to normal levels by taurine administration. Moreover, taurine administration resulted in less morphologic injury to the kidney, and prevented high P-selectin immunoreactivity due to renal I/R.

Several investigators have used I/R-induced acute renal failure in rats as an experimental model, and 30–60 min ischemia time followed by reperfusion is widely accepted as appropriate to evaluate serum and tissue changes (Aragno et al., 2000; Seth et al., 2000; Williams et al., 1997). In the present I/R study, serum BUN and creatinine concentrations significantly increased secondary to I/R. Also, significant morphologic damage and high-level P-selectin immunoreactivity occurred in the I/R group, which suggests that our experimental model should be adequate to examine the effects of a therapeutic intervention. Taurine, a conditionally-semi-essential beta-amino acid, is one of the most abundant amino acids in mammalian cells. We selected taurine as a potential tissue-sparing agent for this model, because of its proven protective effect against ischaemia-reperfusion in other tissues. The dosage we used was similar to what it had been used in a previous study investigating the protective effect of taurine in a rat model of acute tubular necrosis (Erdem et al., 2000). It has been reported that the greatest significant protective effect of taurine is observed when it exclusively is present during the reperfusion phase after membrane damage has occurred. Taurine does not prevent the degree of damage, but it reduces the consequences of that damage (Huxtable, 1992). Therefore, taurine was administered just at the beginning of reperfusion in the present study.

Treatment of rats with taurine reduced the functional and morphologic injury that is characteristic of I/R. It significantly prevented the usual rise in serum BUN and creatinine and attenuated the morphologic injury, although the morphologic protection only was partial. Additionally, taurine treatment following ischemia decreased high

Fig. 4. Immunochemistry staining for P-selectin. **a** Non-specific immunoreactivity for P-selectin in the taurine group, **b** strong immunoreactivity for P-selectin on capillary walls of the glomerulus (arrow) in the I/R group, **c** weak immunoreactivity for P-selectin in the I/R + taurine group (×40). P-selectin immunoreactivity in the sham group was not different from that in the taurine group (not shown)

P-selectin immunoreactivity secondary to I/R. These effects probably were due to the antioxidant activity of taurine against the oxidative stress induced by I/R, as evidenced by it preventing serum and tissue MDA increases and serum and tissue GSH decreases.

The role of ROS in I/R injury has been examined by measuring the products of target molecule oxidation (lipid peroxidation and protein oxidation) – like MDA – and determining the consumption of tissue antioxidants – like GSH. Numerous studies have indicated a positive correlation between increased antioxidant enzymes and/or decreased antioxidant defenses (Azuma et al., 1987; Erdem et al., 2000; Heffner and Fracica, 1996; Oz et al., 1999, 2002). Taurine may play a significant role in preventing I/R injury by acting as an antioxidant. In the literature, taurine has been found to be protective in adriamycin-induced cardiotoxicity, in post-ischemic myocardial injury, in gentamycin-induced acute tubular necrosis, and in I/R-induced lung injury, at least in terms of oxidative stress indicators like MDA and GSH (Azuma et al., 1987; Erdem et al., 2000; Oz et al., 1999, 2002). Malondialdehyde is relatively stable as an end product of lipid peroxidation. In the present study, both serum and tissue MDA levels decreased significantly in the taurine-administered group at the beginning of reperfusion vs the I/R rats that did not receive taurine. Additionally, renal I/R caused a decrease in GSH levels, which is consistent with previous studies (Slusser et al., 1990). Glutathione, a substrate for GSH peroxidase and an important intracellular antioxidant, scavenges reactive oxygen species. Under conditions of oxidative stress, cells may become oxidized, so that they have adequate antioxidant defense to prevent irreversible damage, such as lipid peroxidation (Meister, 1991). In our ischemic rats, both tissue and serum GSH levels decreased secondary to I/R injury, but taurine prevented these decreases.

Glucose-6-phosphate dehydrogenase and 6-PGD are fundamental enzymes in the pentose phosphate pathway, and their activities are important for the maintenance of intracellular NADPH concentration. These enzymes participate in multiple metabolic pathways, such as reductive biosynthesis, which includes lipogenesis, protection from oxidative stress, and cellular growth. Additionally, G-6PD and 6-PGD are necessary to respond rapidly in case increased demands for NADPH. That is why these enzymes are used as an early marker of oxidative stress. In the present study, G-6PD and 6-PGD activities decreased after I/R, similar to what has been reported in the literature (Khundmiri et al., 2004). The activities of G-6PD and 6-PGD also tended towards increase with taurine administration; however, the increase with taurine did not reach statistical significance. On the other hand, GSH-red activity did not change following I/R, similar to previous studies (Barnard et al., 1993; Seth et al., 2000). Likely, more prolonged ischemia or a longer period of reperfusion would have been helpful in evaluating this enzyme's activity and the impact of taurine on this enzyme in I/R injury.

The pattern of morphologic damage seen in our animals, in many respects, resembles that described in other studies on I/R injury (Aragno et al., 2000; Park et al., 2004). Additionally, male rats are known to be more susceptible to I/R injury than female (Park et al., 2004). That is why male rats were chosen for our experiment. Morphologic damage was significantly prominent after I/R, and taurine administration significantly, but only partially, attenuated this morphologic damage. Selectins, that are similar to other adhesion molecules, like the integrins and the immunoglobulin superfamily, mediate leukocyte-endothelium interactions. P-selectin resides in endothelial cells. It mobilizes rapidly to the cell surface following cell activation. It has been shown that, in mice I/R renal injury, P-selectin expression begins at 20 min of reperfusion following 30 min ischemia; expression then peaks at 5 h and falls at 10 h (Zizzi et al., 1997). In the present study, P-selectin expression in I/R group kidneys was significantly higher than in either the sham or taurine group kidneys. Furthermore, taurine inhibited P-selectin expression secondary to I/R. These results again suggest that taurine protects kidney from I/R injury.

The exact mechanism by which taurine prevents I/R injury are not yet fully understood. There are various known and proposed roles for taurine. Taurine may play an important role in preventing I/R injury by acting as an antioxidant. Taurine, an amino acid also found in large quantities in neutrophils, is a powerful endogenous antioxidant. Taurine was effective in preventing neutrophil-mediated microvascular injury (Barry et al., 1997). The other proposed functions include removal of hypochlorous acid in tissues where oxidants are generated such as neutrophils and retina, modulation of calcium levels, maintenance of osmolarity and stabilization of membranes (Timbrell et al., 1995).

The present study demonstrated that the administration of taurine, the major intracellular free β-amino acid, prevents renal dysfunction, oxidative damage and increasing P-selectin immunoreactivity, and decreases morphologic kidney injury due to renal I/R in rats. Consequently, taurine might be a good option for patients who carry renal I/R risk. The presence of taurine in most mammalian tissues seems to be an advantage in terms of availability and toxicity, and should

encourage continued investigations, examining its effect when used at different doses and time points, by different administration routes, and in different models.

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