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Review Article

TAURINE CYTOPROTECTION: FROM CELL TO SYSTEM

Sanya Roysommuti[1], Junichi Azuma[2], Kyoko Takahashi[2], and Stephen Schaffer[3]

[1]Department of Physiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, [2]Department of Clinical Evaluation of Medicines and Therapeutics, Osaka University, Osaka, Japan, and [3]Department of Pharmacology, College of Medicine, University of South Alabama, Mobile, Alabama, USA

Taurine affects the two major causes of cellular toxicity, namely, Ca^{2+} overload and oxidative stress. Often, the beneficial effects of taurine have been attributed to both an improvement in oxidative stress and Ca^{2+} overload. Nonetheless, it is important to recognize that taurine does not directly scavenge superoxide, hydrogen peroxide and superoxide although it directly scavenges HOCl in the presence of myeloperoxidase. Four mechanisms may contribute to taurine-mediated reductions in oxidative stress. First, there is some evidence that taurine might upregulate the anti-oxidant defenses. Second, N-chlorotaurine suppresses the activity of the neutrophils, thereby reducing their ability to generate free radicals. Third, taurine may prevent Ca^{2+} overload, thereby minimizing free radical generation. Fourth, the major cause of taurine-mediated cytoprotection against certain xenobiotics is the formation of a taurine conjugate that is incapable of generating free radicals. At least three mechanisms contribute to the modulation of Ca^{2+} movement by taurine. First, taurine indirectly alters the activity of the Na^+/Ca^{2+} exchanger. Second, as an osmolyte, taurine affects the activity of a number of key osmotically sensitive ion transporters. These transporters directly affect Na^+ and K^+ transport, which in turn alter Ca^{2+} transport. Third, taurine detoxifies specific xenobiotics that alter Ca^{2+} movement. Taurine displays both short- and long-term cytoprotective activities. Growth retardation, organ damage, and abnormal cardiovascular and renal function have been detected in adult animals that were made taurine deficient in early life. Whether these effects are also found in the human requires further investigation.

Key words: taurine, cell, cytoprotection, kidney, osmoregulation, anti-oxidant, calcium

Taurine, a non-protein sulfur containing amino acid, is the most abundant free amino acid and has been shown to play several essential roles in the human body. It is widely distributed in very high concentrations in brain, heart, kidney, lens, and reproductive organs (Huxtable, 1992). In these tissues, it functions as a neurotransmitter, cell volume regulator, antioxidant, growth-promoting factor, etc. At the cellular level, one of its important functions is cytoprotection. Although the concept that taurine exhibits cytoprotective activity was introduced in 1981, it was only after taurine was found to prevent Ca^{2+}-induced cellular necrosis that its cytoprotective activity was recognized (Kramer et al., 1981). Since that date, numerous reports have documented that high levels of extracellular taurine render cells resistant to an array of damaging stimuli, including ischemia- reperfusion, hyperglycemia,

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Correspondence should be addressed to Dr. S. Schaffer, Department of Pharmacology, College of Medicine, University of South Alabama, Mobile, AL, USA; E-mail: sschaffe@jaguar1.usouthal.edu

reactive oxygen species, heat shock, toxic xenobiotics, cellular excitotoxicity and osmotic derangements. The aim of this review is to discuss the importance of each factor in the cytoprotective actions of taurine. Taurine plays a crucial role from conception until death. Taurine-deficiency in the mother leads to growth retardation of the offspring, and produces long-term effects on several organs (Aerts and Van Assche, 2002). In the adult, taurine delays age-dependent damage of several organs (Dawson, Jr. et al., 1999). The present review discusses its cytoprotective activity and the long-term effect of taurine deficiency and supplementation.

Cell volume regulation

Generally, when cells are subjected to a hyposmotic insult, a rapid efflux of organic and ionic osmolytes ensues, partially normalizing the osmotic balance (Hoffmann and Dunham, 1995). This process, known as the regulatory volume decrease, serves as a safety valve to prevent damage caused by excessive cell swelling. Because the efflux of taurine from the hyposmotically stressed cell is very rapid, taurine loss is an important contributor to the regulatory volume decrease. Intravenous administration of mannitol has been found to reduce cellular edema, minimize swelling-induced disruption of the cell membrane and eliminate the no-reflow phenomenon in the ischemic myocardium. Similarly, a reduction in the intracellular osmotic load through taurine depletion reduces cerebral edema during acute hyponatremia (Trachtman et al., 1990) and protects the heart against ischemia (Allo et al., 1997). Thus, the acute effects of taurine loss can significantly benefit the osmotically stressed cell.

Taurine loss, however, can also have an adverse effect. The volume decrease that accompanies apoptosis appears to be an exaggerated activation of the regulatory volume decrease (Okada and Maeno, 2001). According to Lang et al. (Lang et al., 2000) stimulation of Fas-mediated apoptosis in Jurkat T-lymphocytes is accompanied by taurine release. This is an important step in the apoptotic cascade because preloading cells with taurine significantly inhibits Fas-induced DNA fragmentation and apoptotic cell shrinkage. Although taurine loading does not prevent some of the early apoptotic events, such as initiation of the apoptotic cascade, it can prevent the apoptotic cascade from proceeding beyond the cell shrinkage step. These findings are consistent with earlier studies suggesting that the loss of organic osmolytes might participate in the dismantling of the cell during apoptosis (Lang et al., 1998).

Taurine also contributes to volume regulation following a hyperosmotic insult. In response to an abrupt increase in extracellular osmolality, the cell rapidly accumulates Na^+, K^+ and Cl^-. This process is known as the regulatory volume increase. If the hyperosmotic insult is severe enough, osmotically sensitive cells may experience very severe damage and even die. Ozasa and Gould (1982) found that only 30% of chimpanzee spermatozoa survive a one hour hyperosmotic insult produced by doubling the extracellular osmolality with NaCl. Yet, inclusion of 2 mM taurine in the incubation medium increased the number of living cells to 55%.

Several pathological conditions, including chronic hypernatremia, are associated with a hyperosmotic imbalance. The treatment of chronic hypernatremia requires special care because rapid rehydration can lead to an osmotic imbalance associated with brain damage and the risk of seizures, coma and even death. As one would predict, taurine transport plays a central role in chronic hypernatremia; taurine uptake is enhanced and taurine efflux is retarded (Law, 1995). Trachtman et al. (1988) found that taurine deficient cats are very susceptible to hypernatremic dehydration, experiencing an increased mortality rate, significant brain cell shrinkage and an enhanced rate of seizure activity.

Diabetes mellitus is another clinical condition with a hyperosmotic component. High extracellular glucose causes an osmotic imbalance by increasing both the extracellular osmolality

and the accumulation of glucose end-products, such as sorbitol. The rise in intracellular sorbitol is associated with a corresponding decrease in the levels of other osmolytes, such as taurine (Hansen, 2001; Pop-Busui et al., 2001). This loss of taurine appears to contribute to specific complications of diabetes, as evidenced by the amelioration of hyperglycemia-induced nephropathy (Ha et al., 1999; Trachtman et al., 1995) and neuropathy (Obrosova et al., 2001) and vascular injury (Wu et al., 1999) following chronic administration of taurine. Although these beneficial effects of taurine may be related in part to an improvement in the osmotic balance, hyperglycemia also leads to oxidant stress and the accumulation of advanced glycosylation end-products, effects that are also altered by taurine (see below).

Anti-oxidant and membrane stabilizing activity

It is generally accepted that taurine treatment protects cells against oxidative injury. However, there has been a great deal of debate in the literature regarding the anti-oxidant activity of taurine. Aruoma et al. (1988) clearly showed that taurine does not directly react with superoxide, H_2O_2 or hydroxyl radical. Yet, taurine has been shown to protect hepatocytes against H_2O_2-induced damage (Fukuda et al., 2000). If taurine cannot directly scavenge the classical reactive oxygen species, it is logical to assume that the actions of taurine within the cell are indirect. There are several mechanisms that could explain the anti-oxidant activity of taurine. First, taurine could elevate the levels of the anti-oxidant defenses. Unfortunately, most studies that have examined the effect of taurine on the anti-oxidant defenses were initially designed to evaluate its effectiveness in reversing the actions of a toxic xenobiotic. In one such study, Giri et al. (1994) found that bleomycin increased the activity of superoxide dismutase in hamster lung but the increase was prevented in hamsters fed a diet containing elevated levels of taurine and niacin. Nonetheless, there are a handful of studies that have directly tested the effects of taurine on the anti-oxidant defenses. Vohra and Hui (2001) found that intragastric administration of taurine elevated superoxide dismutase and glutathione peroxidase activity in certain brain regions. They suggested that the increase in glutathione peroxidase activity might account for taurine's effectiveness in preventing carbon tetrachloride toxicity. Similarly, Balkan et al.(2001) found that taurine improved the status of the anti-oxidant defenses in the liver of thioacetamide-treated rats by elevating the levels of vitamin E and increasing the activity of glutathione peroxidase. In another study, Nonaka et al. (2001) found that pretreatment of vascular smooth muscle cells with 10 mM taurine prevented homocysteine-mediated reductions in the expression of superoxide dismutase. Mochizuki et al. (2000), who focused on the organic anti-oxidants, found that taurine altered the metabolism of ascorbic acid while Trachtman et al. (1995) observed a beneficial effect of taurine treatment on serum free iron concentration. While these studies raise the possibility that taurine might increase the levels of the endogenous anti-oxidants, a recent study by Pitari et al. (2000) questions this notion. Pitari et al. (2000) found that taurine treatment reduced superoxide dismutase and catalase activity in muscle of rats maintained under normobaric hyperoxic conditions. Even under normoxic conditions, a reduction in catalase activity was found after taurine treatment. Clearly, further studies are warranted to clarify the effect of taurine treatment on the anti-oxidant defense system.

Oxidative damage to the pulmonary system is also responsive to taurine therapy. The lungs are very susceptible to free radical injury due to their exposure to high oxygen tension and toxic gases, such as ozone and the nitrogen oxides. According to the work of Banks et al.(1991) nearly 40% of alveolar macrophages exposed to 0.45 ppm of ozone for 30 min in the absence of taurine were found to lose viability. However, pretreatment of the cells with taurine reduced the extent of ozone-mediated cell death to about 15%, an effect associated with a dramatic reduction in specific measures of oxidative stress, such as lipid peroxidation and reduced glutathione loss. In a related study, Gordon et al. (1986) found that oral taurine administration protected hamster bronchioles

from acute NO_2-induced injury, a condition also associated with severe oxidative stress. Taurine has also been found to protect the lungs against a number of free radical generating xenobiotics. The antineoplastic agent, bleomycin, forms an intracellular bleomycin-Fe^{2+} complex that generates oxygen free radicals and produces a pneumonitis and fibrotic lesions (Bhat et al., 1994; Gurujeyalakshmi et al., 2000). Addition of taurine and niacin to the drinking water reduced the inflammatory response in animals treated with bleomycin (Gurujeyalakshmi et al., 2000). The protective effect was reflected in the degree of lipid peroxidation, nitric oxide production, collagen accumulation and the appearance of acid phosphatase in the bronchoalveolar lavage fluid. Although the authors attributed the cytoprotection to a reduction in oxidative stress, taurine treatment also prevented the increase in total lung calcium content, suggesting that multiple mechanisms might contribute to the beneficial effects of taurine (Bhat et al., 1994; Gurujeyalakshmi et al., 2000). Similar experiments using monocrotaline (Yan and Huxtable, 1996) and amiodarone (Wang et al., 1992) as toxic agents have also revealed the anti-oxidant activity of taurine.

Xenobiotic toxicity is a major problem in the liver, the site of xenobiotic metabolism, as well as taurine biosynthesis. Although the hepatic cytochrome P450 system detoxifies most xenobiotics, some xenobiotics are bioactivated by the cytochrome P450 system. A classical example of the latter is carbon tetrachloride, which is converted by the cytochrome P450 system into a trichloromethyl radical. Like most reactive free radicals, the trichloromethyl radical triggers lipid peroxidation and reacts with a number of proteins to inactivate them. Although the damage from the trichloromethyl radical is restricted to the microsomes, a crucial consequence of the toxicity is the inactivation of microsomal Ca^{2+} accumulation. Consequently, $[Ca^{2+}]_i$ increases and some key Ca^{2+} dependent enzymes are activated (Ungemach, 1987). The hepatocyte eventually dies from disintegration of the cell membrane by the Ca^{2+} dependent enzymes. Waterfield et al. (1993) have found that rat hepatocytes incubated with medium containing various concentrations of taurine are resistant to carbon tetrachloride toxicity, with the higher concentrations of taurine (10-20 mM) exhibiting more protection than intermediate concentrations (5 mM). A similar cytoprotective dose-response curve was observed for hydralazine and naphthoquinone toxicity. Timbrell et al. (1995) proposed that the mechanism underlying the cytoprotection appears to involve the modulation of calcium movement, osmoregulation or membrane stabilization. However, Wu et al. (1997) implicated polyamines in the observed protection against hydrazine and carbon tetrachloride toxicity, although it is unclear how taurine can affect polyamine biosynthesis. Other toxicity studies appear to agree with the Timbrell hypothesis, as taurine was found to minimize oxidative damage and hepatotoxicity in rats exposed to cadmium (Hwang and Wang, 2001), thioacetamide (Balkan et al., 2001) and oxidized fish oil (Hwang et al., 2000).

While the liver regulates taurine content through biosynthesis, the kidney regulates whole body taurine through excretion. Like the liver, the kidney benefits from the cytoprotective activity of taurine. Trachtman et al. (1992) found that chronic puromycin aminonucleoside administration induces a proteinuric renal disease that resembles focal segmental glomerulosclerosis. The drug-induced nephropathy is characterized by the infiltration of mononuclear cells and neutrophils into the renal parenchyma. The inflammatory response is important because neutrophils produce HOCl, a highly reactive oxygen species that can be scavenged by taurine. Therefore, it is not surprising that taurine treatment reduces the degree of segmental glomerulosclerosis and improves creatinine clearance (Trachtman et al., 1992). However, taurine protection is selective, having little effect on the excretion of protein and albumin. Based on these findings, Trachtman et al. (1992) proposed that the cytoprotective activity of taurine must be related in part to the scavenging of HOCl. However, the effects of taurine may also include the suppression of neutrophil activity by N-chlorotaurine (see below). In this regard, Trachtman et al. (1992) found that a number of other reactive oxygen species and free radicals are produced during the inflammatory response. Based on

electron spin resonance measurements, taurine treatment reduces the levels of these other free radical species in the kidney. Whether the anti-oxidant effect of taurine is related to a reduction in free radical generation by the neutrophil or a secondary effect of taurine on free radical generation remains to be determined.

The heart contains low levels of the antioxidant defenses; therefore, it is also susceptible to oxidative damage. Two agents that produce oxidative stress and respond favorably to taurine thereapy are doxorubicin and isoproterenol. Toxic concentrations of isoproterenol have been shown to elevate malondialdehyde content, reduce the levels of glutathione and decrease the activity of glutathione peroxidase, taurine treatment partially prevents these changes (Hamaguchi et al., 1988). Similarly, taurine treatment prevents the elevation in malondialdehyde content in the doxorubicin treated mouse, but does not prevent the decline in glutathione peroxidase activity (Ohta et al., 1988). While these data support a role for taurine as an anti-oxidant, taurine also attenuates the excessive accumulation of Ca^{2+} in hearts exposed to the two toxins (Hamaguchi et al., 1988; Ohta et al., 1988).

Although taurine is incapable of scavenging the classical reactive oxygen species, but readily reacts with HOCl to form N-chlorotaurine (Wright et al., 1985). This reaction is catalyzed by myeloperoxidase, an enzyme found in the neutrophil. Neutrophils are also rich in both taurine and HOCl, making the leukocyte a major source of N-chlorotaurine. Although N-chlorotaurine exhibits bactericidal and fungicidal activity, it is less cytotoxic than hypochlorous acid (Cantin, 1994; Nagl et al., 2001). In fact, the formation of N-chlorotaurine may protect the neutrophil itself against oxidative stress from excessive HOCl production (Weiss et al., 1982). Another important property of N-chlorotaurine is the ability to regulate the severity of the inflammatory response (Giri et al., 1994; Kato et al., 2002; Son et al., 1996). Several groups have shown that N-chlorotaurine downregulates the generation of inflammatory mediators, such as superoxide, nitric oxide, tumor necrosis factor, interleukin-6 and prostaglandin E_2 (Marcinkiewicz et al., 1998; Quinn et al., 1996; Schuller-Levis et al., 1994). It also inhibits the expression of chemokines involved in the recruitment of neutrophils into the lung during pulmonary inflammation (Liu and Quinn, 2002). Moreover, there is some evidence that taurine may reduce neutrophil activation and adherence to endothelial cells. These findings are supported by Raschke et al. (1995), who found that taurine protects the heart against neutrophil-induced reperfusion injury, an effect involving oxidative stress. Therefore, one of the important functions of N-chlorotaurine and taurine is to restrict the cytotoxicity of the neutrophil, setting limitations on the amount of damage done during inflammation. This is likely the most important anti-oxidant action of taurine.

Taurine may also affect oxidative damage by limiting the availability of lipids for lipid peroxidation. Biological membranes are naturally arranged as bilayers. However, some of the phospholipids found in the membrane are capable of disrupting the bilayer structure. Phosphatidylethanolamine belongs to a group of disrupting phospholipids known as hexagonal formers. Interestingly, phosphatidylethanolamine can be converted into a bilayer former, phosphatidylcholine. Hamaguchi et al. (1991) found that taurine inhibits the enzyme phospholipid N-methyltransferase, which catalyzes the conversion of phosphatidylethanolamine to phosphatidylcholine. Besides blocking the conversion of a hexagonal former into a bilayer former, taurine also affects the distribution of phospholipids within the membrane. Phosphatidylethanolamine is preferentially located on the inner bilayer (the cytosolic side) of the cell membrane, while phosphatidylcholine is preferentially found on the outer bilayer facing the extracellular space. By inhibiting the N-methyltransferase reaction, taurine prevents the movement of phospholipids from the inner bilayer to the outer bilayer. Taurine is also capable of forming an ionic interaction with the headgroups of certain phospholipids (Schaffer et al., 1995). Because of these myriad of actions, it would not be surprising if taurine indirectly affects lipid peroxidation.

Cellular calcium metabolism

Prevention of calcium overload was the first recognized cytoprotective action of taurine (Kramer et al., 1981). In their 1981 study, Kramer et al. (1981) found that hearts exposed to a period of Ca^{2+} free perfusion followed by reperfusion with buffer containing Ca^{2+} underwent severe necrosis. The damage resulting from the Ca^{2+} paradox resulted from excessive accumulation of Ca^{2+} during the reperfusion period. Inclusion of taurine in the perfusion medium minimized the degree of cellular necrosis. In a subsequent study, Nakashima et al. (1990) attributed to protection against the oxygen and calcium paradoxes of the hepatocyte to taurine-mediated reductions in Ca^{2+} influx. More recently, El Idrissi and Trenkner (1999) and Chen et al. (2001) reported that neuronal cells incubated with medium containing taurine exhibit a reduction in glutamate-induced excitotoxicity, an effect attributed to inhibition of Ca^{2+} influx via the Na^+/Ca^{2+} exchanger. Interestingly, the Na^+/Ca^{2+} exchanger has also been implicated in the effects of taurine depletion on doxorubicin cardiotoxicity. Harada et al. (1990) found that both taurine deficiency and doxorubicin suppress the activity of the Na^+/Ca^{2+} exchanger, a transporter that functions in the cardiomyocyte to extrude Ca^{2+}. Since doxorubicin also facilitates the release of Ca^{2+} from intracellular stores, it dramatically increases $[Ca^{2+}]_i$. Taurine treatment improves Ca^{2+} homeostasis by facilitating the efflux of Ca^{2+} via the Na^+/Ca^{2+} exchanger. These effects of taurine can be traced in part to its membrane stabilizing activity (Schaffer et al., 1995). High rates of phospholipid N-methylation are associated with a decrease in Na^+/Ca^{2+} exchanger activity. Therefore, taurine-mediated reductions in phospholipid N-methyltransferase activity enhance flux through the Na^+/Ca^{2+} exchanger and lower tissue Ca^{2+} content (Hamaguchi et al., 1991). Taurine also promotes Ca^{2+} efflux via the Na^+/Ca^{2+} exchanger by increasing $[Ca^{2+}]_i$ in the vicinity of the exchanger (Schaffer et al., 1995). The delivery of more Ca^{2+} to the Na^+/Ca^{2+} exchanger partially overcomes limitations arising from its high Km for Ca^{2+}.

Chronic osmotic stress and taurine treatment affect the cell, not only by acutely improving the osmotic balance, but also by affecting the activity of several key ion transporters. Among the transporters, whose flux is altered by osmotic stress and taurine treatment are the Na^+/Ca^{2+} exchanger, the ATP-sensitive K^+ channel, the L-type Ca^{2+} channel and the fast Na^+ channel (Schaffer et al., 2000). Although not directly measured, there is every reason to believe that taurine also affects the activity of the osmotically sensitive Na^+/H^+ exchanger. All of these taurine-sensitive transporters are key players in ischemia-reperfusion injury (Karmazyn and Moffat, 1993) and presumably in other forms of Ca^{2+}-dependent cytotoxicity.

A possible cytoprotective mechanism of taurine is mediated by reductions in $[Ca^{2+}]_i$. Foremost among the agents that interfere with the accumulation of Ca^{2+} during ischemia-reperfusion are the Na^+/H^+ exchange inhibitors (Karmazyn and Moffat, 1993). During ischemia the hydrolysis of ATP and the generation of certain metabolic intermediates lead to a reduction in pH_i. The Na^+/H^+ exchanger senses the decline in pH_i and promotes an exchange between extracellular Na^+ and intracellular H^+. Some of the Na^+ that enters the cell undergoes further exchange with extracellular Ca^{2+}. When influx of Ca^{2+} via the Na^+/Ca^{2+} exchanger is excessive, severe cellular damage ensues. Osmotic stress and taurine treatment appear to affect the activities of both the Na^+/H^+ and Na^+/Ca^{2+} exchangers. According to Earm et al. (1993), cells exposed to medium containing taurine show enhanced Na^+/Ca^{2+} exchanger activity. Therefore, the effects of taurine on the Na^+/H^+ and Na^+/Ca^{2+} exchangers are unlikely to be cytoprotective. Indeed, there is every reason to believe that the combination of taurine treatment and a Na^+/H^+ exchange inhibitor will be more cytoprotective than either the Na^+/H^+ exchanger inhibitor alone or taurine alone.

Long-term effect of taurine depletion or supplementation in the early life

It is well known that taurine plays an important role in cell growth and development. During pregnancy, taurine is mainly supplied to the fetus by the mother via the placenta, and in the newborn via maternal milk (Huxtable, 1992). The taurine content of the body is highest in the early life period, and then declines with increasing age (Aerts and Van Assche, 2002; Huxtable, 1992). Most of data implicating a role for taurine's cytoprotective activity were performed in short-term experiments, especially using in vitro models. The systemic and long-term effect of taurine supplementation or depletion in early life has remained unclear. Previous experiments have indicated that depletion of taurine decreases renal function in the adult animal (Dawson, Jr. et al., 1999). In contrast, supplementation improves renal function in rats with nephrotic syndrome (Mozaffari and Schaffer, 2002; Trachtman and Sturman, 1994) or advancing age (Cruz et al., 2000). We tested the hypothesis that either depletion or supplementation of taurine in early life alters cardiovascular and renal function of the animal when it reaches adulthood. Accordingly, female Sprague Dawley (SD) rats were fed from conception until delivery (fetal period) or from delivery until weaning (lactation period) with normal rat chow and tap water containing either 3% β-alanine (taurine depletion), 3% taurine (taurine supplementation) or water alone (Control). After weaning, the male offspring were fed normal rat chow and tap water ad libitum. At 7-8 weeks of age, arterial pressure, heart rate, and renal function were studied in the conscious animal placed under a restrained condition (Roysommuti et al, 2002). Body weight, kidney weight, and the kidney weight to body weight ratio were not significantly different among the groups, whereas the heart weight of the taurine depleted fetus group (TDF) was slightly higher than the other groups. When compared to the Control, TDF or TDL groups, the mean arterial pressure was significantly elevated in the rats supplemented with taurine during either the fetal (TSF group) or lactation periods (TSL group) (baseline: Control 111 ± 2 mm Hg, TDF 113 ± 2 mm Hg, TDL 116 ± 1 mm Hg, TSF 120 ± 3 mm Hg, TSL 120± 2 mm Hg; $P < 0.05$). However, the heart rates of all treated groups were not significantly different from those of the Control. The basal plasma sodium concentration was not significantly different among the groups, whereas basal plasma potassium content of the TSF group was significantly ($P < 0.05$) lower than that seen in the other groups (Control 4.0 ± 0.1 mEq/L, TDF 3.4 ± 0.2 mEq/L, TDL 4.2 ± 0.3 mEq/L, TSF 3.3 ± 0.2 mEq/L, TSL 3.6 ± 0.1 mEq/L). Despite a higher mean arterial pressure, adult rats that had been supplemented with taurine during the fetal and lactation periods, displayed diuretic and natriuretic responses to an acute saline load similarly to those of the other groups (percent water excreted in 90 minutes per gram kidney weight: Control 44.7 ± 6.7 %, TDF 38.8 ± 5.8 %, TDL 36.4 ± 6.1 %, TSF 41.2 ± 4.7 %, TSL 43.5 ± 3.7 % ; percent sodium excreted in 90 minutes per gram kidney weight: Control 44.7 ± 6.0 %, TDF 37.8 ± 4.4 %, TDL 44.1 ± 7.0 %, TSF 38.9 ± 4.4 %, TSL 42.2 ± 3.0 %). The present data indicate that taurine supplementation in early life elevates arterial pressure when the animal reaches adult hood, raising the possibility that taurine supplementation might alter the pressure-diuresis/natriuresis in the adult conscious rat. Other than the long-term effect of taurine on phenotypic expression in the early life, alterations in taurine content and action in the mature period need to be elucidated.

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