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Perinatal taurine exposure affects adult oxidative stress

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Lerdweeraphon W, Wyss JM, Boonmars T, Roysommuti S. Perinatal taurine exposure affects adult oxidative stress. *Am J Physiol Regul Integr Comp Physiol* 305: R95–R97, 2013. First published April 24, 2013; doi:10.1152/ajpregu.00142.2013.— Perinatal exposure to taurine (a β -amino acid) can alter adult physiological functions, including arterial pressure, hormonal and renal functions. Whereas perinatal taurine supplementation appears to have only minor effects on adult physiology, perinatal taurine depletion is associated with multiple adverse health effects, especially in animals postnatally exposed to other insults. New studies indicate that the mechanism for many of the physiological effects of taurine is related to the antioxidant activity of taurine. Thus the perinatal taurine depletion leads to oxidative stress in adult animals. It is likely that perinatal taurine depletion increases oxidative stress throughout life and that the early life taurine depletion leads to perinatal, epigenetic programming that impacts adult physiological function.

arterial pressure; hypertension; oxidative stress; perinatal exposure; taurine

TAURINE (2-aminoethanesulfonic acid) is a free β -amino acid found abundantly in many tissues including brain, myocardium, and kidney and is generally highest during early postnatal life and declines with advancing age (6, 19, 21). Taurine plays diverse physiological functions from conception onward, including regulation of growth and differentiation, osmoregulation, neurohormonal modulation, lipid metabolism, gluco-regulation, and blood pressure control, and the protection of taurine from oxidative stress may underlie many effects. Prenatal taurine deficiency induces low birth weights and in later life, the risk of cardiovascular disease, likely related to oxidative stress (19). Taurine deficiency leads to abnormalities observed in animals that are perinatally (prenatally and early postnatally) protein restricted. In contrast, perinatal taurine supplementation ameliorates neurological deficiencies arising from intrauterine growth restriction (12), and dietary taurine supplementation during pregnancy protects mothers and embryos from diabetes-induced oxidative stress (20). This review focuses on effects of perinatal taurine exposure on adult arterial pressure control, especially as it relates to oxidative stress.

Taurine as an Antioxidant

Oxidative stress results from unbalanced pro-oxidant versus antioxidant factors, which can lead to cellular and tissue damage. The antioxidant activity of taurine has been recognized for a decade. In Sprague-Dawley rats made hypertensive by administration of *N*-nitro-L-arginine methyl ester to reduce nitric oxide

(NO), 2% taurine in drinking water increases serum NO and NO synthase levels and attenuates hypertension (5). The antioxidant and antihypertensive effects of taurine are also observed in lead-induced hypertension (14) and cyclosporine A-induced hyperten-

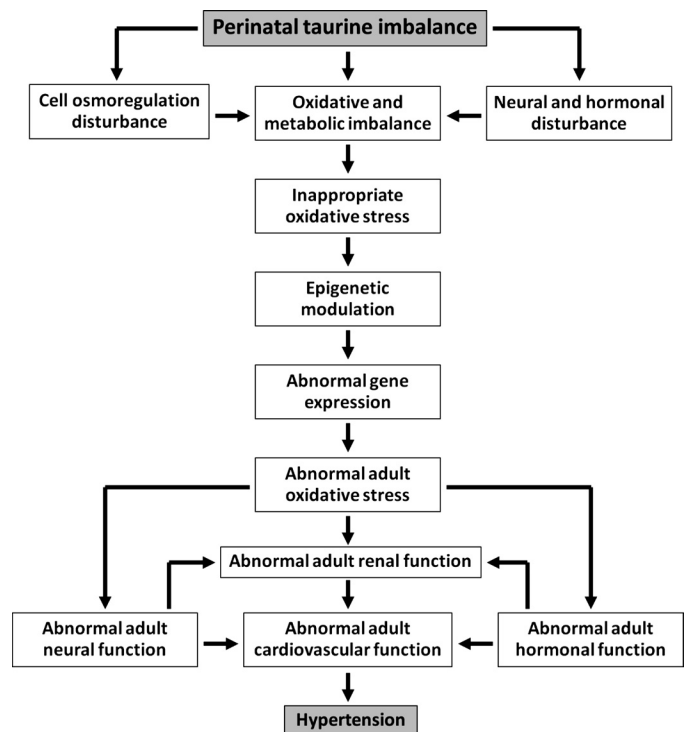


Fig. 1. Potential mechanisms by which perinatal taurine exposure affects adult arterial pressure control via oxidative stress.

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sion (4). Taurine may act directly to reduce oxidative stress by converting superoxides into taurine chloramine (10) and indirectly through a variety of mechanisms, especially the renin-angiotensin system (5). In addition, the antioxidant effects of taurine may include prevention of endoplasmic reticulum (ER) stress, a cellular response to accumulated unfolded protein or dysfunction of ER, particularly in islets (2), nerve cells (11), myocardium, and blood vessels (9).

In 2012, the likely cellular mechanism of taurine was discovered in isolated cardiomyocytes in which taurine content was decreased 45% by addition of β -alanine into the medium for 48 h (8). The decreased taurine led to increased mitochondrial oxidative stress, as evidenced by enhanced superoxide generation, the inactivation of the oxidant-sensitive enzyme aconitase, and the oxidation of glutathione. Furthermore, Cheong et al. (3) has tested the in vitro antioxidant properties of taurine versus different reactive species at various concentrations by using a spin-trap electron method comparing signal intensity with electron spin resonance. They reported that taurine scavenged 1,1-diphenyl-2-picrylhydrazyl radical, hydroxyl radical, superoxide radical, and alkyl radical.

Perinatal Taurine Effects on Adult Oxidative Stress

Fetuses and newborns are exposed to more oxidative stress than adults due to increased pro-oxidants and immature development of antioxidant system (1). This normal oxidative stress may underlie perinatal programming effects in adult life and may interact with many stimuli, including foods, hormones, chemicals, and other environmental conditions. Low birth weight and preterm babies display higher oxidative stress than normal newborns, and low birth weight stress is correlated with adult hypertension (15). Postnatal treatment with antioxidants can significantly decrease adult cardiovascular disorders (13).

In spontaneously hypertensive rats (SHR), short-term, early life treatment with L-arginine or taurine can greatly reduce hypertension at later life (16). Lifetime inhibition of the renin-angiotensin system can also greatly reduce hypertension in the adult SHR (23). Increased renin-angiotensin system activity increases oxidative stress, especially in blood vessels and cardiomyocytes (9). This effect is blunted or prevented by taurine-conjugated ursodeoxycholic acid and 4-phenylbutyric acid. Furthermore, taurine transporter knockout mice display low taurine content in plasma and tissues, and these animals develop cardiac myopathy (7), probably due to increased pro-oxidants and decreased antioxidants (8). These data suggest that taurine depletion-induced perinatal oxidative stress may adversely alter adult oxidative status. Thus antioxidants including taurine can reduce hypertension in animal models and hypertensive humans (19).

Adult Sprague-Dawley rats that were given normal rat chow with 3% β -alanine (taurine deficient, TD), 3% taurine (taurine supplemented, TS), or water alone (control) from conception through weaning (via maternal feeding) displayed significant differences in arterial pressure control and oxidative stress (19). At 7–8 wk of age, plasma malondialdehyde levels (a bio-marker of oxidative stress from lipid peroxidation) were significantly higher in TD and intermediate in TS compared to control rats. The TD rats, but not the TS rats, displayed blunted baroreflex sensitivity for heart rate and renal nerve activity, decreased autonomic function, and abnormal renal function. Surprisingly, a high-glucose diet after weaning exacerbated baroreflex and renal dysfunction in these rats and led to

sympathetic overactivity in the TD but not TS rats (17, 18, 22). It is likely that perinatal taurine depletion increases perinatal oxidative stress, leading to increased adult oxidative stress (Fig. 1). It remains unclear whether this increased oxidative stress plays a key role in arterial pressure dysregulation in adult rats that are perinatally deprived of taurine.

Perspectives and Significance

Taurine is very important for fetal and perinatal programming of adult cardiovascular health and disease, and the current evidence indicates that the antioxidant properties of taurine contribute importantly to these effects during perinatal life, programming oxidative stress of the adult animals, and thereby influencing adult health and cardiovascular disease. Interestingly, both increase and decrease of perinatal taurine can alter adult arterial pressure control and the oxidative stress. These findings could provide important insights into the effects of perinatal excess and deficiency of taurine in humans.

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