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Diverse effects of taurine on vascular response and inflammation in GSH depletion model in rabbits

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Abstract. – OBJECTIVE: A reduction in GSH and an increase in free radicals are observed in inflammatory diseases, indicating oxidative stress. Taurine protects cells from the cytotoxic effects of inflammation. There have been limited studies to date evaluating the effect of taurine in oxidative stress-induced vascular dysfunction and its role in vascular inflammatory diseases. Therefore, we aimed to investigate the effect of taurine on the regulation of vascular tonus and vascular inflammatory markers in rabbit aortae and carotid arteries in oxidative stress-induced by GSH depletion.

MATERIALS AND METHODS: Rabbits were treated subcutaneously with buthionine sulfoximine (BSO), GSH-depleting compound and/or taurine. Cumulative concentration-response curves for acetylcholine (ACh), phenylephrine and 5-hydroxytriptamine (5-HT) were constructed with or without N^{ω}-nitro-L-arginine (LNA) in the carotid artery and aorta rings. Immunohistochemical staining was performed for TNF-α and IL-1β.

RESULTS: BSO increased ACh-induced NO-dependent relaxations, phenylephrine-induced contractions in the carotid artery and 5-HT induced-contractions in both the carotid artery and the aorta. BSO decreased EDHF dependent relaxations only in the aorta. ACh-induced NO-dependent relaxations and augmented contractions were normalized by taurine. BSO increased TNF-α expressions in both carotid arteries and aortas, which were reversed by taurine. The BSO-induced increase in IL-1β was reversed by taurine only in aortae.

CONCLUSIONS: Treatment with BSO resulted in vascular reactivity changes and increased immunostaining of TNF-α in mainly carotid arteries in this model of oxidative stress. The effect of taurine on BSO-induced vascular reactivity changes varied depending on the vessel. The inhibition of the increase in TNF-α expression by taurine in both carotid arteries and aortae supports the proposal that taurine has a beneficial effect in the treatment of inflammatory diseases such as atherosclerosis.

Key Words:
Buthionine sulfoximine, Atherosclerosis, Taurine, Inflammation, Rabbit.

Introduction

Oxidative stress is widely accepted as the main cause of cardiovascular diseases, which is the primary reason for mortality. Oxidative stress occurs when free radical formation and the antioxidant system is unbalanced. Reduced glutathione (GSH) is one of the most important anti-oxidant defence mechanisms in the vascular system. GSH is catalyzed by the enzyme γ-glutamyl-L-cystein synthetase (γ-GCS). Continuous depletion of GSH by Buthionine sulfoximine (BSO), a selective inhibitor of γ-GCS, has been used as an experimental model of GSH deficiency for two decades[1]. A reduction in GSH accompanies an increase in free radicals in inflammatory diseases[2].

Apart from GSH, taurine also takes part in the antioxidant mechanism. In humans the endogenous synthesis of taurine from methionine and cysteine is low and the main source is, therefore, through the diet. Taurine protects cells from the cytotoxic effects of inflammation[3]. Epidemiological studies have suggested that a regular intake of taurine in higher doses reduces the development of cardiovascular diseases[4,5]. Although the regulatory role of taurine in acute inflammation is well-documented[3], its role in vascular inflammatory diseases is not clear. Nevertheless, there have been clinical trials to investigate the therapeutic potential of taurine in hypertension as an antioxidant nutrient[6]. However, studies about the effect of taurine in oxidative stress-induced vascular dysfunction have been limited. Therefore, we investigated the effect of taurine on the regulation of vascular tonus and vascular inflammatory markers in rabbit aortae and carotid arteries in GSH depletion-induced oxidative stress.

Materials and Methods

Materials

Acetylcholine chloride, phenylephrine hydrochloride, 5-hydroxytryptamine creatinine sul-

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phate, potassium chloride, indometacin sodium and the chemicals used to prepare Kreb's solution (NaCl, KCl, $CaCl_2$, KH_2PO_4, $MgSO_4$ and $NaHCO_3$) were purchased from Merck (Darmstadt, Germany), buthionine sulfoximine and N^{ω}-nitro-L-arginine were purchased from Sigma Chemical Co., (St. Louis, MO, USA) and taurine (Tau) from Fluka (Buchs, Switzerland).

Animals

The animal experiments were carried out in accordance with guidelines described by the Ethics Committee of the Faculty of Pharmacy, Ege University. White rabbits of either sex (2.5-3 kg) were divided into four groups. The first group (n = 7, BSO group) received a single subcutaneous (s.c.) injection of BSO (75 mg kg^{-1} body weight day^{-1}). The second group (n = 6, control group) received only the vehicle (0.9% NaCl, 0.8 mL kg^{-1} body weight day^{-1}). The third group (n = 5, Taurine group) received taurine in drinking water (1.0%, w/v). The fourth group (n = 4, BSO+Taurine group) received the same dose of BSO plus Taurine in drinking water. Throughout the 2-week treatment period, each rabbit was kept in a separate cage and allowed free access to rabbit chow and tap water and body weights were recorded. At the end of the treatment period, the rabbits (n = 22) were sacrificed by means of an overdose of sodium pentobarbitone. Carotid artery and aorta were isolated.

Organ Chamber Experiments

After careful removal of loose connective tissue, the rings were suspended in organ chambers filled with physiological salt solution (Krebs buffer) at 37°C, continuously oxygenated with 95%O_2-5%CO_2. In addition, special care was taken not to cause any damage to the endothelium. Indometacin (10^{-5} μM) was added to Krebs solution to inhibit endogenous prostanoid synthesis. Isometric contractile force development was measured by means of a Grass FT3 force transducer and recorded (Panlab®, Cornella, Spain). After a 15-min equilibration, carotid arteries were gradually stretched to a tension of 7 g and aortae were stretched to a tension of 4 g and left to equilibrate for a further 45 min. At the end of the equilibration period the following cumulative concentration–response curves were constructed in either the presence or absence of L-nitro^{w} arginine (LNA 10^{-4} M): acetylcholine (10^{-9} to 10^{-4} M) pre-contracted by 10^{-6} M phenylephrine and phenylephrine (10^{-9} to 10^{-4} M); 5-hydroxytryptamine (5-HT) (10^{-9}M to $3x10^{-5}$M). Each agonist was washed out by changing the bath solution three times in a 30-min before the addition of the next agonist. Krebs solution contained (in mM): NaCl 118, KCl 4.7, $CaCl_2$ 2.5, KH_2PO_4 1.2, $MgSO_4$ 1.2, $NaHCO_3$ 25 and glucose 11.1.

Measurement of Tissue GSH and MDA Levels

The levels of reduced GSH and total GSH after dithiothreitol reduction in metaphosphoric acid-denaturated samples were measured by pre-column derivatization with orthopthalaldehyde by HPLC with fluorescence detection. Reversed-phase chromatographic condition included a Macherey/Nagel Nucleosil MN C18 column (250/4.6 mm, 5 μm particle size) (Düren, Germany), an isocratic separation with sodium acetate (50 mM)/acetonitrile (70:30) mixture at a flow rate of 0.7 mL/min, a column temperature at 30°C, and a detector with settings at Ex340/Em420. The level of reduced GSH was directly calculated from oxidized GSH graph and oxidized GSH from "total GSH-reduced GSH/2" equation[7], and was expressed as μmol/g wet tissue. To assess lipid peroxidation, the concentration of malondialdehyde (MDA) was determined on a HPLC system consisting of a fluorescence detector[8].

Immunohistochemical Analysis

The carotid artery and aorta rings were fixed in 10% buffered formalin solution for 24-48 hours and then embedded in paraffin blocks after routine tissue processing. Serial sections (5 μm thickness) were taken onto glass slides. TNF-α and interleukin-1β expressions were determined by immunohistochemical staining with anti-TNF-α (Upstate®, catalogue # 05-331, Darmstadt, Germany) ve anti-interleukin-1β (IL-1β) (Upstate®, catalogue # 01-151, Darmstadt, Germany) antibodies. For immuno scoring, the degree of positive cytoplasmic staining of cells was evaluated by semi-quantitative scoring on a scale of the percentage of positively stained cells in the following range 0: none, 1: 1-10%, 2: 10-50%, and 3: 50-100%.

Statistical Analysis

All data are expressed as mean ± SEM of the groups; n indicates the number of animals. Statistical analyses of data were performed using GraphPad Prism 5 (La Jolla, CA, USA).The sta-

tistical analysis of the significance between groups was carried out using the one-way analysis of variance (ANOVA) or two-way analysis of variance. Bonferroni test was used as a post hoc test when required. Chi-square test was used to evaluate the statistical difference of immunostaining between the groups. Immunoscoring was performed under code by the pathologist (HHO) who had no prior knowledge of the experimental data. The difference was considered significant at p=0.05.

Results

GSH levels in carotid artery and aorta

BSO significantly reduced GSH levels in both the carotid artery (Figure 1a) and the aorta (Figure 1b). Taurine treatment inhibited the effect of BSO on reducing the GSH level in the carotid artery but not in the aorta.

MDA levels in Carotid Artery and Aorta

Treatment with BSO significantly increased MDA levels (Figure 1c and 1d) and these effects were inhibited by taurine in both the carotid artery and the aorta.

Relaxation Responses

Carotid Artery

ACh induced a concentration dependent relaxation in phenylephrine-precontracted carotid arteries. Treatment with BSO caused an increase in ACh-induced relaxations in carotid arteries (Figure 2a), which was reversed by NOS inhibition (Figure 2c).

Although LNA decreased ACh relaxation significantly, it was still present in carotid arteries.

Aorta

ACh induced a concentration dependent relaxation in phenylephrine –precontracted aortae. Neither BSO nor taurine treatment affected ACh-induced relaxation in the aortae, in contrast to the carotid arteries. Although ACh relaxation was significantly decreased by NOS inhibition it was still present in the aortae (Figure 2b, d).

Contractile Responses

Carotid artery

BSO and Taurine caused an increase in contractile response to phenylephrine compared to

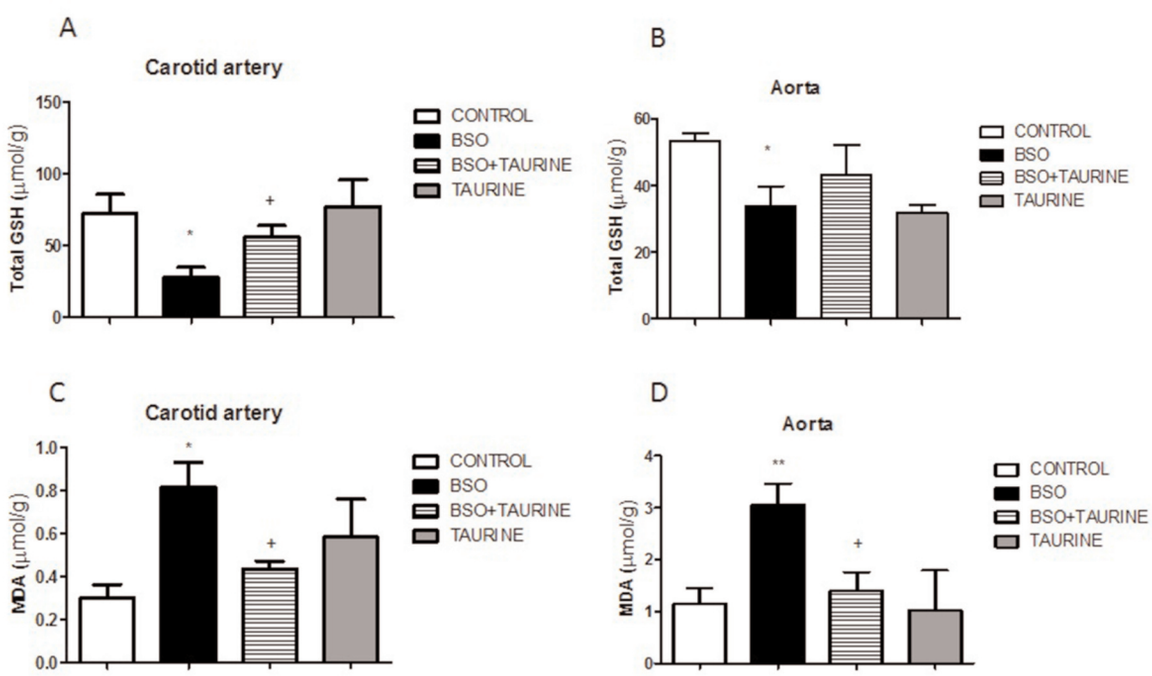

Figure 1. Levels of ***A)*** GSH in carotid artery; ***B)*** GSH in aorta; ***C)*** MDA in carotid arteries; ***D)*** MDA in aorta from Control, BSO, BSO+Taurine and Taurine groups. Data are means ± SEM of values from five rabbits from each group. p<0.05, *Control *vs*. BSO; + BSO *vs*. BSO +Taurine, p<0.01, **Control *vs*. BSO Kruskall Wallis test.

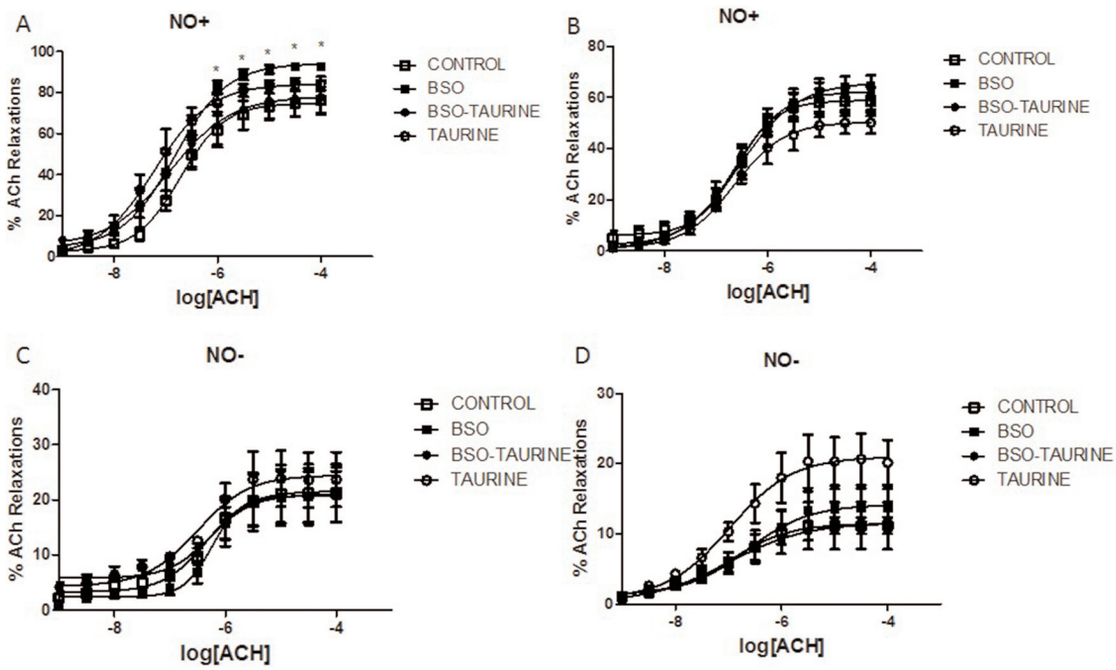

Figure 2. Cumulative acetylcholine (10^{-8}-10^{-4} M) relaxation responses of carotid arteries ***A)*** in the presence and ***C)*** absence of NO, responses of aortae ***B)*** in the presence and ***D)*** absence of NO precontracted with phenylephrine (10^{-6}M) from Control, BSO, BSO+Taurine and Taurine Each point represents the means ± SEM of data from carotid artery or aorta rings obtained from 5-6 animals. $p<0.05$, *Control *vs*. BSO

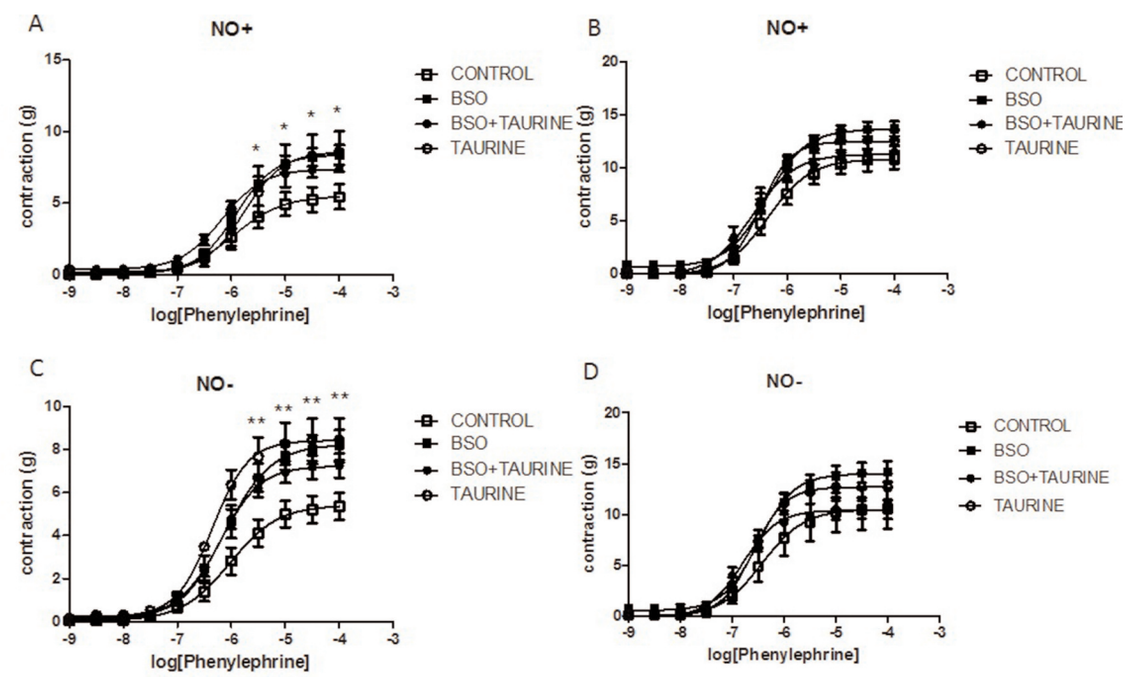

Figure 3. Cumulative phenylephrine (10^{-8}-10^{-4} M) contraction responses of carotid arteries ***A)*** in the presence and ***C)*** absence of NO, responses of aortae ***B)*** in the presence and ***D)*** absence of NO from Control, BSO, BSO+Taurine and Taurine groups. Each point represents the means ± SEM of data from carotid artery rings obtained from 5-6 animals. $^{*}p<0.05$ Control *vs*. BSO, Control *vs*. BSO+Tau, Control *vs*. Tau $^{**}p<0.01$.

the control group in the presence or absence of LNA (Figure 3a, c).

Taurine normalized the BSO-induced enhancement of contraction to phenylephrine in the absence of NO, but not in the presence of NO (Figure 3c).

5-HT induced contractions in carotid arteries from all groups. BSO augmented contraction to 5-HT and taurine normalized it in both the presence and absence of NO (E_{max}: 2.74±0.64 g, 5.67±0.88 g, 3.33±1.04 g and 4.89±1.59 g in Control, BSO, BSO+Taurine and Taurine groups respectively, One Way ANOVA, following Tukey's test, $p<0.05$, n=5-6). However, taurine caused an increase itself (Figure 4 a, c) in the absence of NO.

Taurine significantly increased pD_2 value of 5-HT when NO was inhibited by LNA 5.98± 0.17, 6.12± 0.25, 6.35± 0.16, 6.74± 0.08, in Control, BSO, BSO+Tau and Tau groups respectively, One Way ANOVA, following Tukey's test, $p<0.05$, n=5-6.

Aorta

Neither BSO nor taurine treatment affected phenylephrine E_{max} or pD_2 values in any group (Figure 3 b, d).

BSO caused an increase in 5-HT-induced contraction in aortas and this augmentation was normalized by taurine (Figure 4b, d). pD_2 values of 5-HT-induced contractions remained unchanged in all groups from the aortae (Data not shown).

Immunohistochemistry

Immunoscoring revealed that TNF-α and IL-1β expressions were significantly increased in both aortae and carotid arteries from the BSO-treated group. The increase in TNF-α expression was reversed by taurine in both aortae and carotid arteries (Figures 5 and 6, respectively). The enhancement in IL-1β expression was reversed by taurine in aortae and remained unaltered in carotid arteries (Figures 7 and 8, respectively).

Discussion

The findings of our study are:

1. The BSO-induced increase in MDA levels was normalized by taurine in both the aorta and the

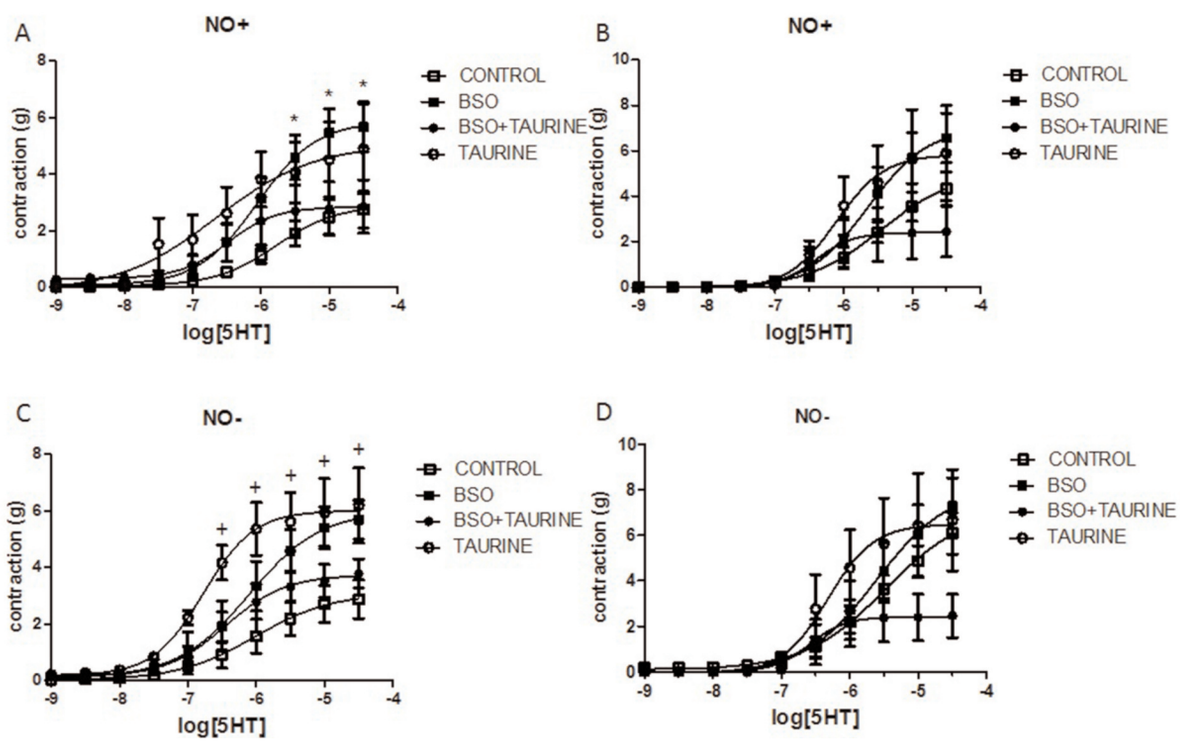

Figure 4. Cumulative 5-HT (10^{-8}-$3x10^{-5}$ M) contraction responses of carotid arteries ***A)*** in the presence and ***C)*** absence of NO, responses of aortae ***B)*** in the presence and ***D)*** absence of NO from Control, BSO, BSO+Taurine and Taurine groups. Each point represents the means ± SEM of data from carotid artery rings obtained from 5-6 animals. *$p<0.05$ Control *vs.* BSO, $^{+}p<0.05$ Control *vs.* BSO, Control *vs.* Taurine

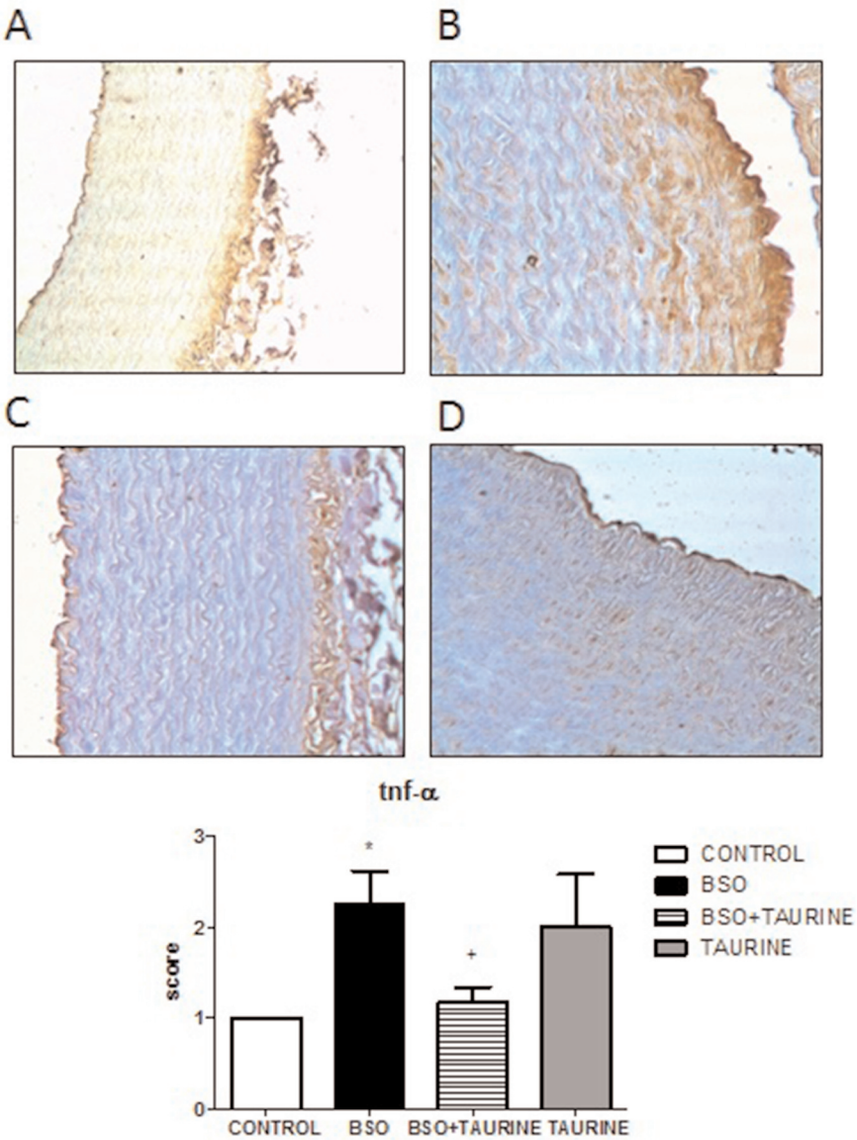

Figure 5. Representative photomicroscopic images of immunohistochemically stained rabbit aortae for TNF-α. ***A)*** control animals, ***B)*** animals treated with BSO, ***C)*** animals treated with BSO and taurine, ***D)*** animals treated with taurine. Immunoblots showing TNF-α expression and densitometric quantification. Original magnification x 10. *, +, $p<0.05$, control *vs*. BSO, BSO *vs*. BSO and taurine, respectively, n=5-6, Chi-square test.

carotid artery. However, taurine did not normalize the decrease in GSH level in aorta, while restoring it in carotid arteries.

2. BSO increased ACh-induced NO-dependent relaxations in the carotid artery only, and it was normalized by taurine. However, BSO decreased possibly endothelium-derived hyperpolarizing factor (EDHF) dependent relaxations in the aorta.

3. BSO increased contraction to 5-HT in both aortae and carotid arteries. However, phenylephrine-induced contractions were increased only in carotid arteries. Taurine normalized all augmented contractions.

4. BSO increased the immunoreactivities of inflammatory markers such as TNF-α ve IL-1β in both carotid arteries and aortae.

The model of continuous depletion of GSH used in this study depends on the inhibition of the enzyme γ-GCS by BSO in mice[9-11], rats[12-14] and rabbits[15]. This experimental model of GSH defi-

ciency has also been used as a model of oxidative stress[16] and as an experimental model of hypertension[14,17]. During the last decade, we have been using this model of oxidative stress to investigate the effects of BSO and taurine on several pathological parameters such as DNA damage and telomere regulation[18,19]. Consistent with the results of our previous studies[18-21] and others[10], subcutaneously administered BSO significantly decreased GSH levels and increased MDA levels in carotid arteries and aortae of animals, while taurine reversed this decrease in GSH levels and increased MDA levels in these arteries.

Under oxidative stress conditions, it is well known that vascular responses are considerably different and that this differentiation is mainly a result of the vessel type and animal species. It should prove possible to directly demonstrate these differences in response to oxidative stress by means of functional *in vitro* experiments. The different contractile and relaxation responses to vasoactive agents among the various vessels from different animals have been attributed to the receptor types/subtypes of the plasma membrane of the smooth vessel and their density, the presence of functional endothelium and/or the

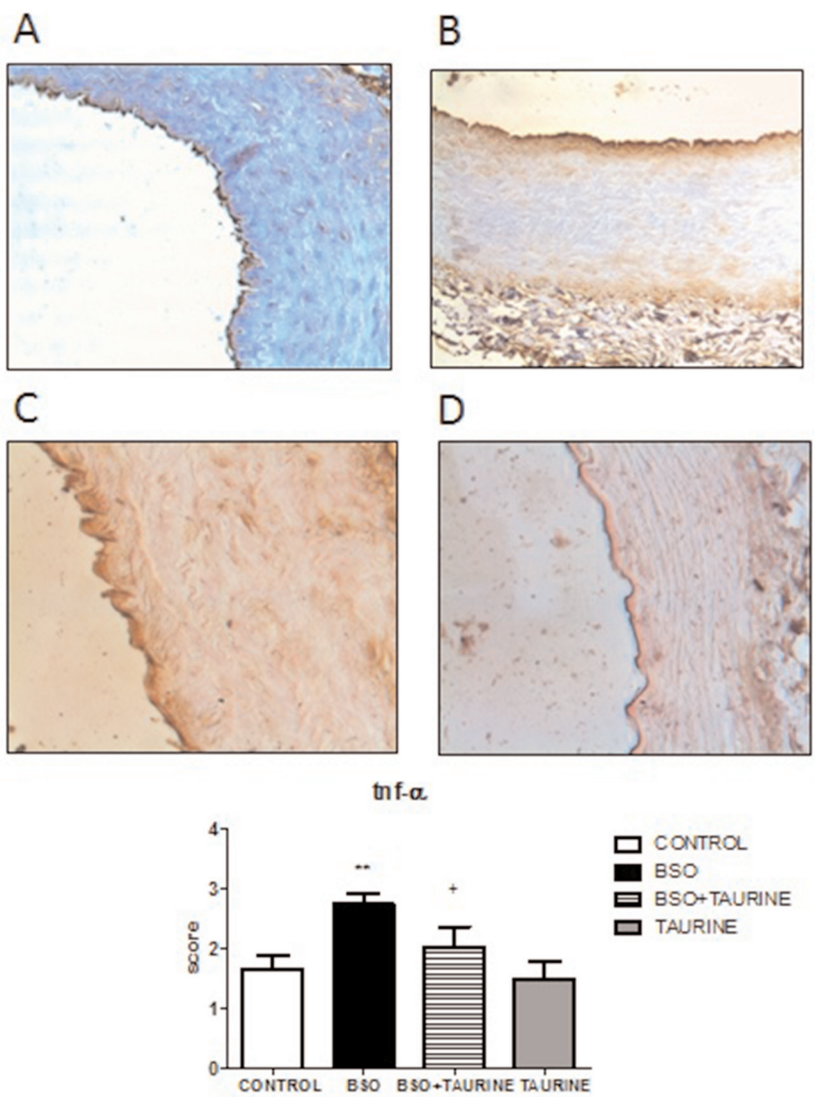

Figure 6. Representative photomicroscopic images of immunohistochemically stained rabbit carotid arteries for TNF-α. ***A)*** control animals, B) animals treated with BSO, ***C)*** animals treated with BSO and taurine, ***D)*** animals treated with taurine. Immunoblots showing TNF-α expression and densitometric quantification. Original magnification x 10. **, $p<0.01$, control *vs.* BSO, +, $p<0.05$, BSO *vs.* BSO and taurine, n=5-6, Chi-square test.

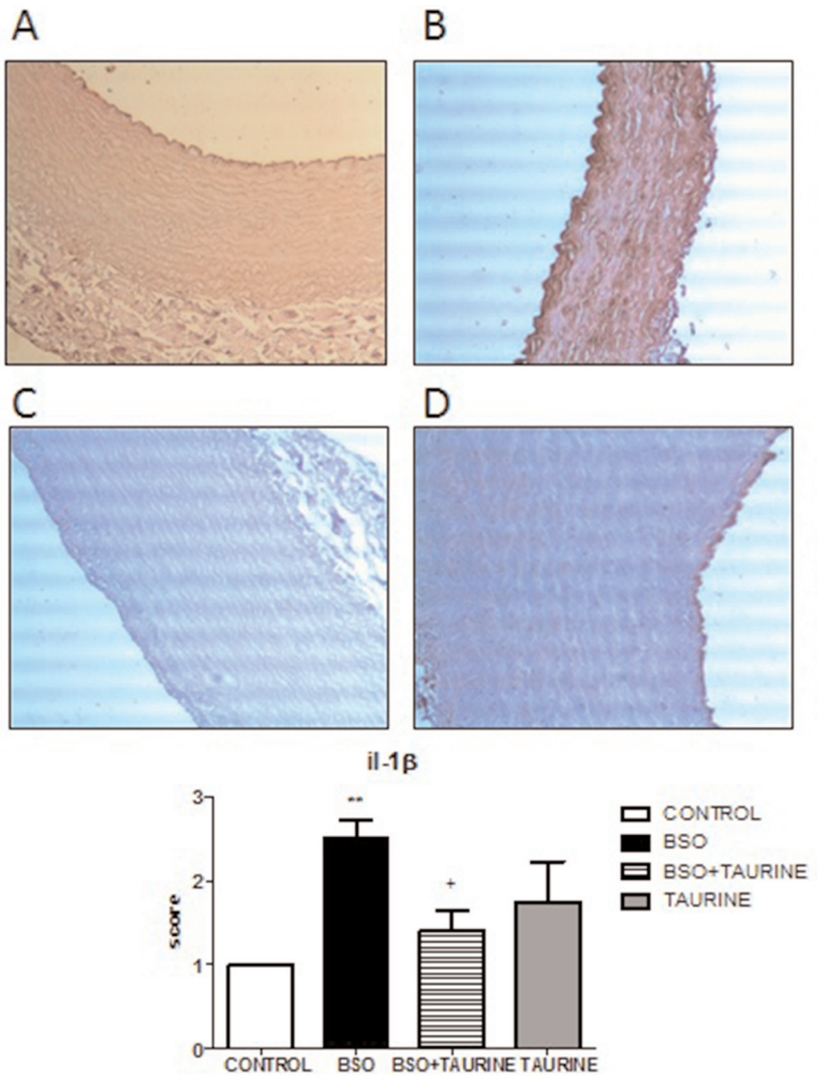

Figure 7. Representative photomicroscopic images of immunohistochemically stained rabbit aortae for IL-1β. ***A)*** control animals, ***B)*** animals treated with BSO, ***C)*** animals treated with BSO and taurine, ***D)*** animals treated with taurine. Immunoblots showing IL-1β expression and densitometric quantification. Original magnification x 10. **, $p<0.01$, control *vs*. BSO, +, $p<0.05$, BSO *vs*. BSO and taurine, n=5-6, Chi-square test.

nature of the nitric oxide release and to the difference in contractile machinery and/or the amount of smooth muscle[22].

In the present study, it was found that the contractile responses of rabbit carotid artery and aorta to phenylephrine and 5-HT (such as E_{max} values) were different under oxidative stress conditions induced by GSH depletion by BSO. Similarly, the present study demonstrated that acetylcholine-induced endothelium-dependent relaxations differ between the vessels.

BSO increased ACh-induced NO-dependent relaxations in the carotid artery only, and it was normalized by taurine. However, BSO decreased EDHF dependent relaxations in the aorta. The increased ACh-induced relaxation in carotid arteries by BSO was reversed by LNA, suggesting the role of eNOS or iNOS. There is conflicting data in the literature regarding the effect of BSO on ACh-induced relaxation in aortae, either hyperreactivity[13] or decreased response[23] in rat aortae. We observed an unaltered response to ACh in rabbit aortae. In rat carotid arteries Dennis et al[24] found that endothelium-derived relaxing factor (EDRF) relaxation is unaltered in the carotid arteries of the rat. However, we have found that it

is increased. This may depend on using different species or methodological differences, since in our study the cyclooxygenase (COX) pathway was inhibited, whereas in the other study the COX pathway was active. On the other hand, we found that taurine restored BSO-induced hyperreactivity to ACh.

In our study, LNA did not completely block acetylcholine-induced relaxations in either the carotid artery or the aorta, suggesting an involvement of another factor apart from NO and prostacyclin, possibly EDHF.

In this study, BSO increased phenylephrine-induced maximum contraction responses in carotid arteries without changing the pD_2 values in the absence or presence of LNA. The increase in contractile responses (phenylephrine and 5-HT) in carotid arteries were independent of NO. In the above-mentioned study by Ford et al[23], a ten-day administration of BSO (20 or 30 mM in drinking water) to rats had no significant effect on systolic blood pressure in conscious animals. However, as was consistent with our study, contractile responses to phenylephrine (PE) were greater in the BSO group compared to the control group and BSO shifted the PE dose–response curve to the left. Phenylephrine exerts its contracting effects through α_1 receptors. It has been

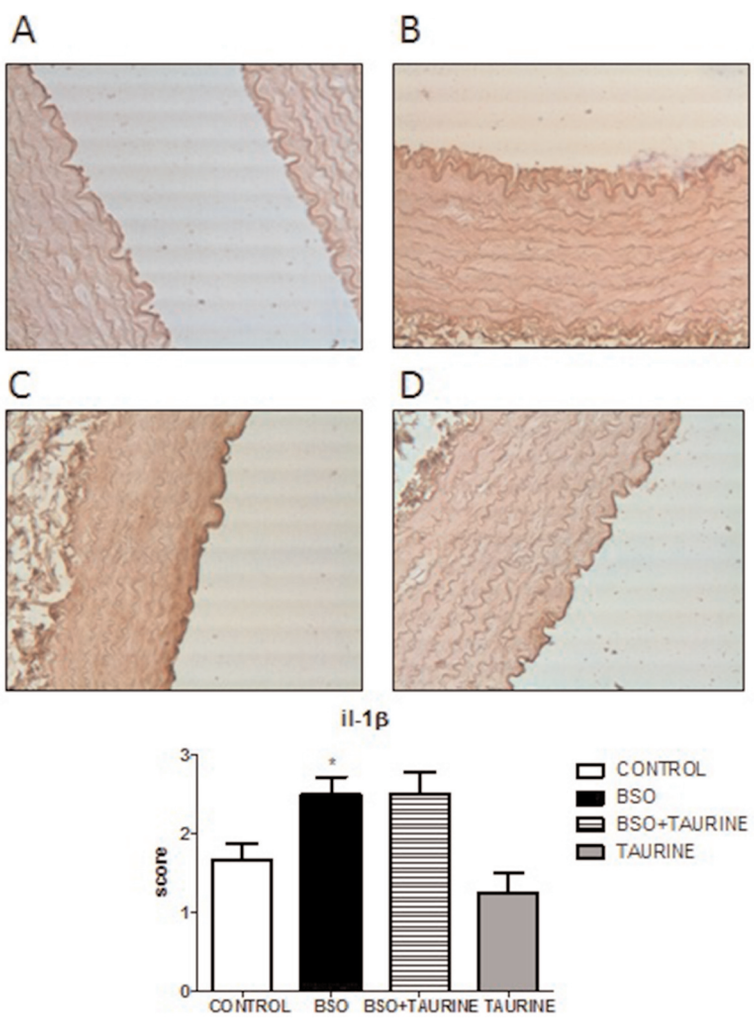

Figure 8. Representative photomicroscopic images of immunohistochemically stained rabbit carotid arteries for IL-1β. ***A)*** control animals, ***B)*** animals treated with BSO, ***C)*** animals treated with BSO and taurine, ***D)*** animals treated with taurine. Immunoblots showing IL-1β expression and densitometric quantification. Original magnification x 10. *, $p<0.05$, control *vs.* BSO, n=5-6, Chi-square test.

shown that glutathione depletion causes an increase in intracellular Ca^{++} through melastatin-related transient receptor potential 2 (TRPM2) and transient receptor potential vanilloid type 1 (TRPV1) channels[25]. Morelli et al[26] revealed that there is a cross-talk between α_{1D}-adrenoceptors and TRPV1 which triggers prostate cancer cell proliferation. On the other hand, in the present study, the increased TNF-α expressions observed in both arteries (see infra) might be a plausible explanation since TNF-α has been shown to increase cytosolic Ca^{++} [27]. Thus, the increasing effect of BSO on phenylephrine contraction suggests a possible increase in intracellular Ca^{++}. However, we did not detect BSO-induced blunted contractile responses in aortae, possibly because of dissimilar responses of α_1-adrenoceptor-mediated responses in this vessel.

As observed with phenylephrine, BSO increased 5-HT-induced maximum contraction responses in the carotid arteries only, without changing the pD_2 values in the absence or presence of LNA, suggesting a nitric oxide-independent effect. It has been concluded that 5-HT induces contractions via $5\text{-}HT_{2A}$, $5\text{-}HT_{1B}$ or $5\text{-}HT_{1D}$ receptors in rabbit arteries and responses by receptors are shown to be mediated by the activation of L-type voltage-dependent calcium channels[28,29]. In the present work, chronic BSO treatment augmented 5-HT-induced contractions in this model of oxidative stress. The investigation of 5-HT receptor subtypes was outside the scope of this study. However, BSO-induced augmented E_{max} values of 5-HT, as seen in phenylephrine, could be related to the increased intracellular Ca^{++} and TNF-α expression[28]. Our result which showed that BSO-induced augmented 5-HT contractions in rabbit carotid arteries were independent of NO, once again reveals the importance of 5-HT in different pathologies associated with oxidative stress such as atherosclerosis.

Effects of Taurine

Taurine exerts a diversity of biological effects, enabling it to influence the functions of multiple organ systems. More commonly reported effects include cardiovascular regulation, antioxidation, modulation of ion transport, membrane stabilization, osmoregulation, modulation of neurotransmission, bile acid conjugation, hypolipidemia, antiplatelet activity and fetal development[30,31].

We have previously carried out studies revealing the beneficial effects (effect against DNA damage, effects on atherosclerosis, etc.) of taurine using oxidative stress model induced by GSH depletion[18-21]. On the other hand, in view of the vasculature, there have been both *in vivo* and *in vitro* studies which investigate the effects of taurine on vascular reactivity to elucidate the molecular mechanism(s) involved[30,32].

In the present report, we aimed to investigate the functional role of taurine in the regulation of vascular tonus in GSH depletion-induced oxidative stress in rabbits. Given the effects of taurine supplementation on endothelium-mediated relations, Abebe et al[33] referred that taurine treatment attenuates vascular contractility non-specifically in rats, and this effect is partly mediated via the endothelium. Conversely, both noradrenaline- and potassium-chloride-induced maximum contractile responses of endothelium-denuded aortae are enhanced in taurine-depleted rats[34]. Taurine exerts either a vasodilation or vasoconstriction depending on cellular Ca^{++} concentrations[35]. A study using porcine coronary arteries showed[36] that taurine antagonizes and relaxes the contractions of arteries, associated with the activation of potassium channel including K_{IR}, K_{ATP}, K_{Ca}. Taurine supplementation has been shown to normalize impaired endothelium-dependent vasodilation in mice fed with a high-cholesterol diet and in streptozotocin-induced diabetic mice[37].

Our results revealed that chronic taurine treatment restored the reduced pD_2 values of acetylcholine-induced relaxations without affecting E_{max} values in the absence of NO in BSO-induced model of oxidative stress. However, further studies of the mechanism(s) of this effect of taurine in oxidative stress conditions in this model are warranted.

On the other hand, we have found that taurine, when administered with BSO, normalized BSO-induced increased E_{max} values of phenylephrine in the absence of NO in carotid arteries. Taurine itself increased the 5-HT E_{max} values in the presence of LNA in carotid arteries, suggesting that taurine may interact with 5-HT.

In addition, taurine itself caused an increase in contraction to phenylephrine. Taurine is a sulfur containing aminoacid. A recent clinical trial and our preliminary data showed that taurine is able to increase H_2S level in vessels[6,38]. Hydrogen sulfide is a gasotransmitter engaged in the regulation of vascular tonus. In mice aortae, H_2S causes first contraction and then relaxation. The increased contraction induced by taurine in aortae may be due to inducing a low level of H_2S. Confirming

this, our preliminary study showed increased contraction and relaxation in response to L-cysteine, a substrate of H_2S synthesizing enzymes. H_2S is produced in smooth muscle and thereby shows endothelium-independent effects[38]. This finding suggests that taurine may affect vascular tone in both endothelium-dependent and independent manner. H_2S acts through TRPV1 channels which have been shown to decrease by BSO treatment[39]. Thus, it may be possible that the beneficial effect of taurine in BSO-induced oxidative stress may involve the H_2S pathway.

Inflammation Markers

It has been known that oxidative stress participates in initiating acute inflammatory responses and ultimately leads to vasculature dysfunction[40].

According to the classical view of inflammation, cytokines (such as IL-1β, IL-6 and TNF-α) are produced by cells of the innate immune system (monocytes, neutrophils, NKT cells), toxic reagents, trauma, oxidative stress, antibodies, or immune complexes[27].

In the present work, the finding that BSO resulted in an increase in both TNF-α and IL-1β immunostaining in the carotid artery and the aorta in this model of oxidative stress in rabbits agrees with Speciale et al[41]. It is commonly accepted that taurine plays an important role in the immune system as an antioxidant to protect cells from oxidative stress[31]. Thus, in our study, the inhibitory effect of taurine on increased immunostaining of TNF-α in both carotid arteries and aortae supports the hypothesis that cellular adaptive response induced by glutathione depletion may be triggered by TNF-α. However, we are aware that taurine did not affect IL-1β immunostaining in aortae.

Conclusions

We have shown that treatment with BSO resulted in vascular reactivity changes in mainly the carotid arteries in this model of oxidative stress. Besides, the effect of taurine on these BSO-induced reactivity changes varies in terms of the contractile and relaxation responses of the vessels examined in this study. Finally, the fact that taurine inhibited the increased immunostaining of TNF-α in both carotid arteries and aortae supports the proposal that taurine has a beneficial effect in inflammatory diseases such as atherosclerosis.

Acknowledgements

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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