Research Article

Evaluation of Taurine Role on Some Biochemical and Histological Alterations in γ - Irradiated Rats

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ABSTRACT

Ionizing radiation is well known to induce oxidative stress on target tissues, mainly through the generation of reactive oxygen species that present an enormous challenge for biological and medical safety. The present study has been designed to investigate the protective role of taurine (TA), a sulfur containing essential amino acid, against oxidative stress induced by gamma (γ) Irradiation. Rats were subjected to single dose of 6 Gray. Five days before or after irradiation, animals received TA daily (100 mg/kg body weight i.p.). In the irradiated animals, the oxidative stress marker malondialdehyde was significantly increased while a marked decrease in the catalase and glutathione peroxidase activities as well as in the reduced glutathione contents in hepatic, cardiac, and renal tissues were demonstrated. In addition, serum lipid profiles, kidney functions and the activities of alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, lactate dehydrogenase, and creatine kinase were disturbed after irradiation. Moreover, γ-Irradiation induced hematological changes as well as histopathological alterations in the hepatic, cardiac and renal tissues. Pretreatment with TA, significantly improved radiation-induced injury as indicated by the reduction of the indices of liver, heart and kidney damage, lipid peroxidation product, the elevation of antioxidants, the attenuation of the hematological disturbances and the tissues histological architecture. Less protection was obtained on TA- post treatment suggesting that administration of TA protected the tissue damage produced by the acute sublethal dose of γ-irradiation in rats by decreasing oxidative stress in a way depending on the order of TA administration.

Keywords: γ-irradiation, oxidative stress, taurine, antioxidants, rats.

INTRODUCTION

Ionizing radiation has a diversity of beneficial uses in medicine including radiotherapy as an important treatment modality for a wide variety of tumors, radiographs for screening, diagnosis and staging of diseases and malignancies, but its acute side effects on the normal tissues limit the effectiveness of therapy[1].Scientific and technological advancements have further increased the radiation burden in humans, because exposure to low levels of radiation has become common during space or air travel, cosmic radiation and using certain electronic gadgets. Other sources of radiation exposure include radon in houses, contamination from weapons testing sites and nuclear accidents[2]. It is well known that ionizing radiations induce oxidative stress on target tissues, mainly through the generation of reactive oxygen species (ROS) resulting in imbalance of the pro-oxidant and antioxidant in the cells, attack diverse cellular macromolecules such as DNA, lipids, and proteins, eventually inducing cell death[3].

The potential application of radioprotective chemicals in the event of planned exposures or radiation accidents has been investigated from the beginning of the nuclear era[4]. It has also been considered that radiation therapy for cancer patients could be improved by the use of radioprotectors to protect normal tissue. They include sulfhydryl compounds, antioxidants, plant extracts, immunomodulators, and other agents[5].

Taurine (TA), 2-aminoethane sulfonic acid, is a sulphur containing β-amino acid. It is an antioxidant that is present at high concentrations in many tissues and play important roles in numerous physiological functions including conjugation with bile acids, modulation of calcium levels and maintenance of osmolarity, antioxidation and stabilization of membranes[6]. The source of TA in the body is biosynthesis and dietary intake from meat and especially sea food[7]. The low toxicological profile of TA combined with its promising therapeutic effects, warrant continued human clinical trials. Several reports of the clinical applications of TA has been reviewed by Parcell[8] who concluded that TA had beneficial effects in the treatment of a number of conditions, such as depression, fibromyalgia, arthritis, interstitial cystitis, athletic injuries, congestive heart failure, diabetes, cancer and acquired immunodeficiency syndrome. In addition, TA has been shown to prevent experimentally toxin-mediated hepatic and renal injuries[9, 10] and cardiovascular diseases[11]. In view of these considerations, the present study was carried out to throw some light on the hazardous effects of γ-radiation on some biochemical and hematological parameters as well as histological changes in liver, heart, and kidney of adult male rats. In addition, the protective effect of TA on

minimizing the induced hazardous effect of radiation was investigated.

MATERIALS AND METHODS

Chemicals

Taurine was purchased from Sigma Chemical Co. (St. Louis, MO). All other chemicals and solvents used in this study were of highest purity and analytical grade and purchased from Sigma-Aldrich chemic (Deisenhofen, Germany). Commercially available reagent kits for aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) assays were obtained from Quimica Clinica Aplicada S.A (Spain). Lactate dehydrogenase (LDH) and creatine kinase (CK) were obtained from Stanbio Laboratory (USA). Reagent Kits for determination of total cholesterol (TC), triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL), urea, creatinine, hemoglobin (Hb), malondialdehyde (MDA), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH) were purchased from Biodiagnostics (Egypt).

Gamma Irradiation

Whole body of the animals was exposed to an acute single dose of 6 Gy delivered at a dose rate of 1.167 rad/sec using cobalt-60 from the biological irradiator gamma cell source belonging to Middle Eastern Regional Radioisotopes Center for Arab Countries, Dokki, Giza, Egypt.

Animals and Experimental Design

Thirty adult male Sprague-Dawley rats weighing about 120-150 g were obtained from Animal House of National Research Center, Cairo, Egypt. All animals were housed in plastic cages and kept under the same laboratory conditions of temperature (25±2°C) and lighting (12:12hr light: dark cycle) for one week prior to starting the experiments. The rats were provided *ad libitum* with tap water and fed with standard laboratory diet. All animals received humane care in compliance with the international guiding principles for animal research. TA was dissolved in saline and injected intraperitoneally to animals at a dose of 100 mg / kg body weight. The dose of TA used was selected based on the previous studies[12].

Animals were randomly divided into 5 groups of 6 animals each:

1- Control group: The animals were received intraperitoneal injection of 0.5 ml saline for 10 consecutive days.

2-γ- irradiated (γ-IR) group: The animals were received intraperitoneal injection of 0.5 ml saline for 5 consecutive days, then were exposed to single dose of 6 Gy whole-body radiation on the 6th day followed by intraperitoneal injection of 0.5 ml saline for another 5 consecutive days.

3-Taurine (TA) treated group: the animals were injected with 0.5 ml freshly prepared TA at dose of 100 mg/kg body weight for 5 consecutive days followed by intraperitoneal injection of saline for another 5 days.

4-γ-IR pre-treated with TA group: the animals were injected with 0.5 ml freshly prepared TA at a dose of 100 mg/kg body weight for 5 consecutive days, then they were exposed to a single dose of 6 Gy whole-body radiation on the 6th day followed by intraperitoneal injection of 0.5 ml saline for another 5 days.

5-γ-IR post-treated with TA group: the animals were injected with 0.5 ml saline for 5 consecutive days and then they were exposed to a single dose of 6Gy whole-body radiation on the 6th day followed by intraperitoneal injection of 0.5 ml TA for another 5 days.

At the end of the experimental period, the animals were fasted for 16-18 hrs. before sacrificing. Animals were decapitated and blood was collected from each animal in two tubes: the first containing 10% EDTA for estimation the hematologic parameters and the second for separation of serum for different biochemical analysis. Portions of liver, heart, and kidney were immediately washed in ice-cold physiological saline and homogenized in 50mM potassium phosphate (pH 7.4) to render 10% homogenate. Small portions of liver, heart and kidney were preserved in 10% neutral buffered formalin, embedded in paraffin wax and sectioned at 5µm. The sections were stained with haematoxyline and eosin for histological examination by methods described by Ross et al.[13]

Biochemical analysis

Blood samples were centrifuged at 3000 rpm for 15 min. to separate serum, which was used for estimation of AST and ALT activities[14], urea[15], creatinine[16,] GGT[17], LDH[18] and CK[19] activities.TC was determined according to Allain et al.[20], TG was estimated according to Fassati and Prencipe[21], HDL was determined according to Burstein et al.[22] and LDL was assayed according to Wieland and Seidel[23]. The tissues homogenate were centrifuged at 4000 rpm for 15 min. at 4 °C. The supernatant was used for MDA [24], CAT[25], GPX[26] and GSH[27]analysis.

Hematological study

Total red blood cells (RBCs) were counted using an improved Neubaurhemocytometer (Clay, Aams, NY). Blood was diluted 1:200 with Hayem's fluid and RBCs were counted in the loaded hemocytometer chamber. Total white blood cells (WBCs) were counted by using improved Neubaurhemocytometer (Clay, Adams, NY). Blood was diluted 1:20 with diluting fluid and four large ($1mm^2$) corner squares of the hemocytometer were counted on light microscope. Hb was determined using the cyanmethemoglobin method[28]. Packed cells volume (PCV) was determined by using microhematocrit capillaries (75mm X 1.1mmI.D.) that were filled with blood, sealed at one side by capillary sealer and

centrifuged at 11.000rpm for 6 minutes in microhematocrit centrifuge, and PCV percentage was measured by microhematocrit reader.

Statistical analysis

The results were expressed as mean ± SE of studied groups using the analysis of variance test (one-way ANOVA) followed by Bonferroni test. Analysis was performed by statistical package for the social science software (SPSS Inc., Chicago, IL). Values of P<0.05 were considered significant.

RESULTS

Effect of TA on lipid peroxidation and antioxidants

As shown in Table 1, γ-irradiation significantly (P<0.01) increased the formation of MDA in the hepatic, cardiac and renal tissues as compared to control group. The administration of TA for 5 days, either before or after γ-irradiation, resulted in a significant (p<0.01) reduction in MDA level when compared with γ-irradiated group (γ-IR group). Insignificant changes in MDA levels were observed in healthy rats treated with TA (TA group).

The results presented in Table 1 also showed that CAT and GPX activities were significantly decreased (p<0.01) in the hepatic, cardiac and renal tissues in the γ-IR group as compared to control group. Pretreatment with TA caused an opposite changes in the activities of CAT and GPX (p<0.01) in all tissues as compared to γ-IR group. The post treatment with TA significantly (p<0.05) attenuated the GPX activity without an obvious effect on CAT activity when compared with γ-IR group. In TA group, insignificant changes were obtained in the activities of the previous enzymes.

From the results summarized in Table 1, it is evident that, in comparison to control values, γ-irradiation was able to reduce GSH level significantly (p<0.01) in the hepatic, cardiac and renal tissues. In the presence of TA, diverging results were obtained. While pretreatment with TA significantly increase (p<0.01) GSH level in all examined tissues, the post-treatment improved the level of GSH (p<0.05) only in hepatic tissues without an obvious effect in cardiac or renal tissue. Treatment with TA in healthy animals induced a markedly increase (p<0.05) in GSH levels in all tissues.

Table 1: Effect of TA on lipid peroxidation and antioxidants in tissues of γ-IR animals.

Group Parameter	Control	γ-IR	TA	γ-IR pre-treated with TA	γ-IR post-treated with TA
MDA (nmol/g tissue)					
Liver	19.51±1.38	97.93±4.76^{**a}	21.96±2.05	23.43±2.01^{*a**b}	51.46 ± .21^{**a**b}
Heart	23.57 ±2.22	89.47 ±6.85^{**a}	22.23 ±1.23	25.51±2.20^{*a**b}	53.51±4.11^{**a**b}
Kidney	24.38±2.27	94.40±4.33^{**a}	26.27±1.76	27.85±2.32^{*a**b}	69.85±3.92^{**a**b}
CAT (U/g tissue)					
Liver	1.78±0.04	0.69±0.07^{**a}	1.71±0.06	1.14±0.05^{*a**b}	0.78±0.04^{**a}
Heart	1.95 ±0.07	0.50 ±0.05^{**a}	1.84 ±0.06	1.37 ±0.08^{*a**b}	0.61 ±0.05^{**a}
Kidney	1.71±0.04	0.62±0.07^{**a}	1.54±0.06	1.07±0.07^{*a**b}	0.71±0.07^{**a}
GPX (U/g tissue)					
Liver	29.04±2.04	17.99±1.21^{**a}	30.50±1.34	27.83±1.98^{**b}	21.72±1.45^{**a*b}
Heart	22.04±1.91	15.21±1.00^{**a}	24.10±1.74	21.50±1.34^{**b}	18.83±1.41^{*a*b}
Kidney	25.13±2.10	14.47±1.02^{**a}	26.23±1.83	23.41±1.29^{**b}	18.31±1.89^{*a*b}
GSH (mg/g tissue)					
Liver	19.13±1.24	12.06±1.05^{**a}	24.15±1.90^{*a}	17.12±1.15^{**b}	16.22±1.00^{*a*b}
Heart	15.22±1.34	10.14±0.98^{**a}	18.34±1.80^{*a}	14.03±1.23^{**b}	13.11±1.20^{*a}
Kidney	12.44±1.00	8.04±0.76^{**a}	15.12±1.04^{*a}	11.22±1.14^{**b}	9.25±0.90^{*a}

Values are expressed as mean ± SE (n=6), ^{a}: groups were compared to the control group,^{b}: groups were compared to IR group,*: significant at P<0.05 and**: significant at p<0.01.

Effect of TA on lipid profile

On its own, daily injection of TA for 5 days produced significant (p<0.05) decreases in serum TC, TG and LDL levels, while it elevated HDL level in comparison with control group (Table 2). As a result of γ-irradiation exposure (γ-IR group), there was a significant increase (p<0.01) in the levels of TC (80%), TG (131%), and LDL (164%) as compared to those of the control group. Treatment with TA before irradiation significantly (p<0.01) decreased the elevation in TC, TG and LDL levels by 36%, 33%, and 58% respectively as regard to γ-IR group. Less protection was found on post-treatment with TA which significantly (p<0.05) decreased the levels of TC, TG, and LDL by 20%, 9% and 38% respectively. On the other hand, radiation exposure resulted in a significant decrease in serum HDL level (p<0.01; 51%). This effect is

significantly inhibited($p<0.01$; 86%) by pre-treatment with TA while post-treatment caused only 11% increment in comparison with γ-IR group.

Effect of TA on serum biochemical markers

As shown in Table 3, γ-irradiation significantly ($P<0.01$) increase the activities of ALT, AST, GGT, LDH and CK by 43%, 17%, 348%, 164% and 229 % respectively as compared to control group. Administration of TA for 5 days before γ-irradiation resulted in a significant ($p<0.01$) reduction in ALT by 21 %; AST by 18%; GGT by 60 %; LDH by 53 % and CK by 62 % when compared to γ-IR group. Less or no improvement was obtained in the enzymes activities in sera of γ-IR group post-treated with TA. No significant change was observed in healthy rats treated with TA. Regarding kidney functions, the levels of urea and creatinine were significantly ($P<0.01$) increased in γ-IR group by 281% and 133 % respectively in comparison with control group. Pre-treatment with TA caused a decrement ($p<0.01$) in urea (48%) and creatinine (21%) levels, while post-treatment caused insignificant alteration when compared to γ-IR group.

Table 2: Effect of TA on lipid profile in serum of γ-IR animals

Group Parameter	Control	γ-IR	TA	γ-IR pre-treated with TA	γ-IR post-treated with TA
TC (mg/dl)	127.31±3.38	229.37±10.11^{**a}	113.96±2.88^{*a}	146.53±8 .39$^{*a\ **b}$	183.21±9.78$^{**a\ *b}$
TG (mg/dl)	93.81±2.86	216.40 ±8.77^{**a}	81.10±2.70^{*a}	145. 30±2.89$^{*a\ **b}$	199.45±8.73^{**a}
HDL (mg/dl)	75.66 ±3.78	37.18 ±1.48^{**a}	89.87 ±3.39^{*a}	69.52 ±2.78 ^{**b}	41.46±1.65$^{**a\ *b}$
LDL (mg/dl)	53.62±1.07	141.32 ±5.43^{**a}	44.60 ±1.95^{*a}	59.80 ±2.40 $^{*a\ **b}$	86.35 ±3.11^{**a**b}

Values are expressed as mean ± SE (n=6), [a]: groups were compared to the control group,[b]: groups were compared to IR group,*: significant at $P<0.05$ and**: significant at $p<0.01$.

Table 3: Effect of TA on biochemical markers in serum of γ-IR animals

Group Parameter	Control	γ-IR	TA	γ-IR pre-treated with TA	γ-IR post-treated with TA
ALT (U/ml)	31.45±2.14	45.13±2.27^{**a}	30.53±2.01	35.85±2.54^{**b}	37.10±2.26$^{**a*\ b}$
AST (U/ml)	70.80±3.54	82.97±4.15^{**a}	68.23±2.73	73.15±3.04^{*b}	76.06±3.10^{**a*b}
GGT (U/L)	20.33±1.16	91.14±4.06^{**a}	21.49±1.19	36.49±2.84$^{**a\ **b}$	81.32±2.54$^{**a\ *b}$
LDH (IU/L)	163.64 ± 13.05	432.16± 34.57^{**a}	185.43 ± 14.66	203.40±16.27^{*a**b}	397.11±18.33^{**a}
CK (IU/L)	118.34± 9.47	389.65± 31.17^{**a}	125.12 ± 10.77	149.36±13.44^{*a**b}	335.95±16.10^{**a}
Creatinine (mg/dl)	0.85±0.07	3.24±0.17^{**a}	0.90±0.06	1.70±0.14^{**a**b}	2.98 ±0.05^{**a}
Urea (mg/dl)	19.68±1.58	45.81±2.00^{**a}	20.66±1.49	36.00±1.61^{**a**b}	43.11 ±1.65^{**a}

Values are expressed as mean ± SE (n=6), [a]: groups were compared to the control group,[b]: groups were compared to IR group,*: significant at $P<0.05$ and**: significant at $p<0.01$.

Effect of TA on hematological parameters

As a result of γ-irradiation exposure, there was a significant decrease ($p<0.01$) in the level of Hb by 28%, RBCs count by46%, WBCs count by 24%, platelets count by 48% and PCV% by 36%, as compared to those of the control group. In γ-IR group pretreated with TA, significantly ($p<0.01$) increased values by 31%, 32%, 21 % 23% and 20%were obtained for Hb, RBCs count, WBCs count, platelets count and PCV% respectively as regarded to γ-IR group. Insignificant variations were obtained in γ-IR post-treated with TA group (Table 4).

Histological investigation

In the histological study, the liver sections of control (Fig. 1a) and TA treated (Fig. 1c) rats display normal hepatic architecture. The central vein is appeared and the cellular architecture is formed of cords composed of hepatocytes, one to two cell layers thick, separated by blood sinusoid. In γ-IR group, liver section showed discontinued the endothelial lining of the central vein and severely dilated blood sinusoids. Most hepatocytes in centrilobular area show focal necrosis. Many hepatocytes are swollen and vacuolated (Fig.1b). Liver of γ-IR group pretreated with TA

showed sinusoidal dilatation, preserved the endothelial lining of central vein and ill-defined nuclei of the hepatocytes (Fig.1d). Liver of γ-IR group post-treated with TA showed the central vein filled with acidophilic materials. The hepatocytes were replaced with homogenous ill-defined acidophilic material and dilated blood sinusoids (Fig.1e).

Table 4: Effect of TA on hematological changes in blood of γ-IR animals

Group Parameter	Control	γ-IR	TA	γ-IR pre-treated with TA	γ-IR post-treated with TA
Hb (g/dl)	13.8±0.96	9.89±0.56^{**a}	14.2±0.89	12.91±.0.47^{**b}	11.52 ± 0.81^{*a}
RBCs (×10^{6}cells/ µl)	5.27±0.28	2.87±0.14^{**a}	5.89±0.23	3.79±0.17^{**a**b}	3.01 ± 0.15^{**a}
PCV (%)	44.12±1.76	28.44±1.43^{**a**b}	45.34±2.27	35.17±1.29^{**a**b}	29.64±1.48^{**a}
WBCs (×10^{3}cells/µl)	11.80±0.38	8.97±0.21^{**a}	11.95±0.41	10.89±0.30^{*a**b}	9.52±0.28^{**a}
Platelets (x103/mm3)	294.10^{a}±17.64	154.35±9.24^{**a}	317.21 ±19.02	190.32±11.74^{**a**b}	176.65± 12.32^{**a}

Values are expressed as mean ± SE (n=6), ^{a}: groups were compared to the control group,^{b}: groups were compared to IR group,*: significant at P<0.05 and**: significant at p<0.01.

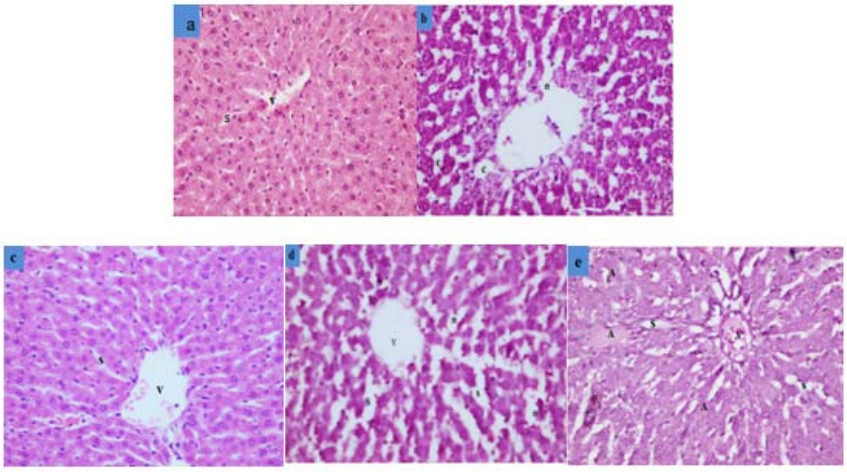

Figure 1: Photomicrographs of sections in the hepatic tissue of rats (H&E X200). **a) control:** the cellular architecture of the liver is formed of cords composed of hepatocytes , one to two cell layers thick, separated by blood sinusoid (S) and the central vein (V) is appeared, **b) γ-IR group** : discontinued endothelial lining of the central vein (V), severely dilated blood sinusoids (S), most hepatocytes in centrilobular area show focal necrosis and many hepatocytes are swollen and vacuolated (c), **c) TA treated group**: no deviation from the control, **d) γ-IR group pretreated with TA:** better-preserved appearance of tissue, sinusoidal dilatation (S), preserved the endothelial lining of central vein (V), ill-defined nuclei of hepatocytes, **e**) **In γ-IR group post-treated with TA**: the central vein (V) filled with acidophilic materials, some hepatocytes are replaced with homogenous ill-defined acidophilic material (A) and blood sinusoids (S) are dilated.

Histological study of the cardiac tissue represented in (Fig 2a-e). Photomicrographs of cardiac muscle cells of the control (Fig 2a) and TA treated group (Fig 2c) are composed of irregular branched cells with nuclei in the center of the muscle fibers. Degeneration of muscle fiber with necrosis of nucleus and fibrinoid necrosis of myofibril were clearly seen in γ-IR group (Fig 2b). Although animals of of γ-IR group pretreated with TA showed better-preserved appearance of cardiac muscle fibers, some cardiac muscle fiber are degenerated and some nuclei are pyknotic (Fig 2d). In γ-IR group post-treated with TA, some cardiac muscle fibers showed swelling of the cytoplasm, the nuclei are pyknotic and extravasated blood elements are seen between the muscle fibers (Fig 2e).

Histological study of the kidneys of the control rats revealed normal glomerulus surrounded by the Bowman's capsule, proximal and distal convoluted tubules without any inflammatory changes (Fig 3a). In γ-IR group, glomerular capillary tuft necrosis, degenerated the cellular lining of proximal and distal tubules were seen (Fig 3b).Treatment with TA alone has no histopathological effects on renal tissues of rats (Fig 3c). Ameliorated architecture of glomeruli, proximal tubule and distal convoluted tubules was seen in γ-IR group pretreated with TA (Fig 3d), whereas in γ-IR group post-treated with TA, the glomerulus with focal necrosis surrounded by wrinkled Bowman's capsule was observed (Fig 3e).

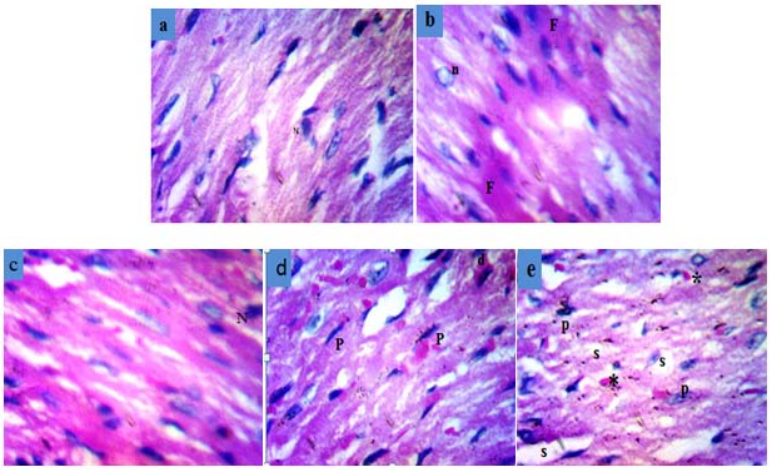

Figure 2: Photomicrographs of sections in the cardiac muscle of rats (H&E X400).**a) control**: irregular branched cells with nuclei (N) in the center of the muscle fiber, **b) γ-IR group**: Degeneration of muscle fiber with necrosis (n) of nucleus and fibrinoid necrosis of myofibril (F), **c) TA treated group:** no deviation from the control, **d) γ-IR group pretreated with TA**: better-preserved appearance of cardiac muscle fibers, some cardiac muscle fiber are degenerated (d) and some nuclei are pyknotic (p), **e) γ-IR group post-treated with TA:** some cardiac muscle fibers showed swelling of the cytoplasm(s), the nucleus are pyknotic (p) and extra vasated blood elements(*) are seen between the muscle fibers.

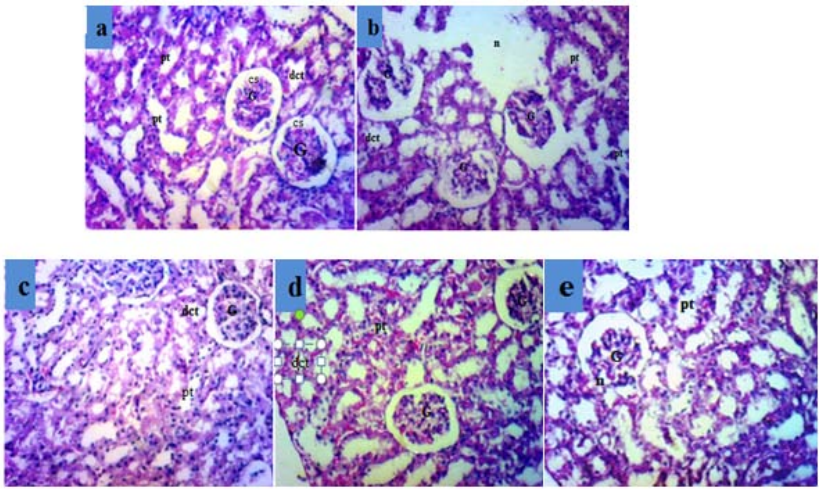

Figure 3: Photomicrographs of sections in the renal cortex of rats (H&EX100). **a) control:** normal architecture of glomerulus (G) of capillaries surrounded by the capsular space (cs), proximal tubule (pt), distal convoluted tubules (dct), **b) γ-IR group**: glomerular (G) capillary necrosis (n), degeneration of the cellular liningof proximal tubule(pt) and distal convoluted tubules (dct), **c) TA treated group:** no deviation from the control, **d) γ-IR group pretreated with TA**: ameliorated architecture of glomeruli (G), proximal tubule (pt) and distal convoluted tubules (dct), **e) γ-IR group post-treated with TA**: the glomerulus with focal necrosis surrounded by wrinkled the Bowman's capsule.

DISCUSSION

Radiations are commonly used in a number of medical and industrial situations. Exposure to ionized radiation leads to serious systemic damage to various cellular and subcellular structures. It is well known that ionizing radiation induced oxidative stress through generation of ROS resulting in an imbalance in pro-oxidant/antioxidant status in the cells.[3] The present study shows that γ-irradiation from cobalt-60 source produced significant oxidative damage 5 days following radiation exposure. This damage is indicated by the significant enhancement of MDA level (a marker of lipid peroxidation) in hepatic, cardiac and renal tissues accompanied by depletion in the enzymatic antioxidants CAT and GPX activities and the non-enzymatic antioxidant GSH level. Our data were in consistent with previous studies reported by Mansour and Hafez[29] and Pradeep et al.[30] who recorded a significant depletion in the antioxidant system in parallel with enhancement of lipid peroxidation after whole blood gamma irradiation. In the current study, the elevated level of MDA in γ-irradiated rats might be due to the interaction of free radicals with polyunsaturated fatty acids in the phospholipids portion of cellular membranes[31].The decrease in the activities of CAT and GPX could be as a result of their utilization by the enhanced production of ROS, which interacts with the enzyme molecules causing their denaturation and partial

inactivation[32]. The significant reduction in GSH level following radiation exposure in the present study is in accordance with Mathur and Sharma[33]who concluded that the reduction in GSH content was attributed to the enhanced utilization of the antioxidant system as an attempt to detoxify the free radicals generated by radiation.

In the present study, considerable beneficial effects of TA were noted when it administered at a dose of 100 mg/kg on biochemical variables suggestive of oxidative stress. In both TA pre- and post-treated γ-irradiated groups, there was attenuation in the MDA level and GPX activity in hepatic, cardiac and renal tissues. Regarding to CAT activity and GSH level, in the presence of TA, diverging results obtained depending on the timing of TA administration and the damaged tissue. While a pretreatment with this amino acid virtually abolished the effect of γ-irradiation on GSH level and nearly brought it towards the normal values in hepatic, cardiac, and renal tissues, the post-treatment with TA improved the level of GSH only in hepatic tissue without an obvious effect in cardiac or renal tissue. The improvement in CAT activity occurred only in TA pretreated group. Treatment with TA in healthy animals induced a markedly increase in GSH levels in all tissues.

Taurine might offset lipid peroxidation either by scavenging ROS directly or by binding to ferrous ion or copper ion through its sulphonic acid group as suggested by Franconi et al.[34] The free sulfhydryl group in TA seems to play a significant role as a ROS scavenger. TA is neither metabolized nor incorporated into cellular proteins in mammals suggesting ready availability of sulfhydryl moiety in cytosol[35]. Furthermore, TA might protect the cells through intercalating into the membrane and stabilizing it[36]. On the other hand, Hansen et al.[37] hypothesized that TA exerts its antioxidative effect by buffering the pH in the mitochondrial matrix which implicated in the generation of ROS and thereby preventing the leakage of the reactive compounds. Moreover, TA and GSH biosynthesis have the common precursor cysteine[38], so treatment with TA might increase the GSH levels as a result of directing more amount of cysteine into GSH biosynthesis.

The TC, TG, HDL as well as LDL are the indicators of cardiac dysfunction. In the current study, the recorded events pointed to a significant rise in the serum level of TC, TG and LDL associated with a decline in the HDL values 5 days post radiation exposure, possibly as a result of liver injury. These changes are in agreement with previous studies in rats[39]. This indicates that ionized radiation-induced oxidative stress might alter hepatic lipid metabolism and serum lipoproteins. The whole body γ-irradiation of rats produced high level of serum cholesterol fractions through its release from tissues, destruction of cell membranes and increase rate of cholesterol biosynthesis in the liver and other tissues[40]as an early reaction necessary for restoration of biomembranes[41]. In addition, radiation could modify LDL and HDL metabolism indirectly through the action of various inflammatory products and might decreased the lipoprotein lipase activity (clearing factor) in adipose tissues leading to reduction in the uptake of lipids[41].

In the present study, TA administration prior irradiation could increase serum HDL and decrease TC, TG and LDL. Such hypolipidemic effects of TA with an increase in HDL level were demonstrated previously in cardiac impairment induced by cadmium in rats[12]. The protective effects of TA against lipid metabolism disturbance were greater when given as pre-treatment than as a post-treatment to γ-irradiation. The effects of TA were mostly related to increased degradation and excretion of cholesterol as bile in the feces. Specific hypolipidemic mechanisms were postulated include increased activity of cholesterol 7α-hydroxylase activity, the rate-limiting enzyme in the catabolism of cholesterol into bile acids and increased LDL receptor binding and turnover of LDL among others[42].

Moreover, TC, TG, LDL and free radicals are also risk factors that tend to damage arteries leading to heart disease. Increases in the levels of circulating cardiac damage markers, such as CK and LDH, represent a powerful and sensitive predictor of increased cardiac complications[43]. In the present study, γ-irradiation caused a marked increase in the activities of serum LDH and CK in addition to the histopathological alterations in cardiac tissue. These findings are in harmony with those obtained earlier by Park et al.[32] and could be explained on the bases that ionizing radiation instigates the alterations in the dynamics permeability of membranes allowing leakage of biologically active materials out of the injured cells[44]. In the present study, only pretreatment of γ-irradiated animals with TA alleviated the alterations in the activities of LDH and CK and could improve to some extent the altered heart histopathology. The cardioprotective potential of TA was probably due to a counter action of free radicals by its antioxidant nature or to strengthening of myocardial membrane by its membrane stabilizing property[45].

Several enzymes in blood are considered as indicators of hepatic dysfunction and damage and the leakage of hepatic enzymes such as AST, ALT and GGT into blood are routinely used as a reliable biochemical index for hepatocellular damage. In the current study, it could be noticed that γ-irradiation caused a significant increase in the activities of AST, ALT and GGT and the breakdown of hepatocytes and necrotic degeneration of liver cells. These results are in accordance with other studies[32] and could be attributed to the drastic dysfunction of the hepatic cells as a consequence of radiation interaction with membranes and also related to extensive breakdown of hepatocytes and necrotic degeneration of liver cells. Pre- and post-treatment with TA attenuated the increase in the activities of the enzymes. The hepatoprotective property of TA might be due to its ability to decrease

oxidative stress, enhance mitochondrial function and amend cytoplasmic and mitochondrial Ca^{2+} homeostasis in biological systems[10].

In the current study, elevated urea and creatinine levels associated with kidney histological disorders were observed in rats exposed to γ-irradiation. These results came similar to previous investigations by Barakat et al.[46] These increments in serum urea and creatinine could be attributed to the destruction and malfunction of kidney cells due to the action of ROS released post radiation exposure. Roushdy et al.[47] demonstrated that, radiation causes an increase in glutamate dehydrogenase enzyme levels, which may increase carbamoyl phosphate synthetase activity leading to an increase in urea concentration. In the present study, urea and creatinine measurements, showed marked improvements only in γ–irradiated group pretreated with TA. Several studies have suggested that TA progressively accumulates in the renal medulla and plays a physiologic role in protecting the tubule cells from apoptosis[48]. The protective property of TA may also reside in its ability to become chlorinated in the presence of hypochlorous acid, thereby preventing the direct attack of this oxidant on cell membranes of organs, including the kidney[49]. In addition, TA exhibits nephron protection by regulating blood flow in the renal vasculature and Na^+ transport in the proximal tubules, maintaining osmoregulation and scavenging ROS in the glomerulus[50].

Furthermore, data of the present study have indicated that whole body γ-irradiation resulted in disorders in the hematological constituents as manifested by a significant decrease in Hb content as well as in RBCs, WBCs, and platelets counts and hematocrit percentage. These observations are similar to those recorded by Azab et al.[51] RBCs are considered as a major target for the free radicals owing to the presence of both high membrane concentration of polyunsaturated fatty acids and the oxygen transport associated with redox active hemoglobin molecules, which are potent promoters of activated oxygen species[52]. In the current study, pretreatment with TA ameliorated the alterations in hematological indices. The protective effect of TA might be attributed to its cytoprotective, osmoregulatory and membrane stabilization properties.

CONCLUSION

The present study demonstrates that administration of TA protected the tissue damage produced by the acute sublethal dose of γ-irradiation in rats by decreasing oxidative stress in a way depending on the order of TA administration. Pre-treatment with TA gave more protection than post-treatment and this implies that the antioxidant action of TA depend upon a rise in its intracellular levels prior γ-irradiation.

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