Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2020.29.004841

Potential Ameliorative Action of Vitamin E on Spermatogenesis and Sperm Count in Bisphenol A-Treated Rats: Reproductive Health Research

S Naderi Noreini[1], M Malmir*[2], M Soleimani Mehranjani[3], T Faraji[2] and H khodabandehlo[2]

[1]*Sina Specialty and Multispecialty Hospital, Rastak Infertility Center, Iran*

[2]*Department of Midwifery, Tuyserkan Branch, Islamic Azad University, Iran*

[3]*Department of Sciences, Arak University, Iran*

***Corresponding author:** M Malmir, Department of Midwifery, Tuyserkan Branch, Islamic Azad University, Iran

ARTICLE INFO

Received: August 11, 2020

Published: August 21, 2020

Citation: S Naderi N, M Malmir, M Soleimani M, T Faraji and H khodabandehlo. Potential Ameliorative Action of Vitamin E on Spermatogenesis and Sperm Count in Bisphenol A-Treated Rats: Reproductive Health Research. Biomed J Sci & Tech Res 29(4)-2020. BJSTR. MS.ID.004841.

Keywords: Bisphenol A; Vitamin E; Spermatogenesis; Sperm count; Histopathology

ABSTRACT

The aim of this study was to investigate the preventing role of vitamin E (Vit.E) on sperm parameters in Bisphenol A-treatment rats. Bisphenol A (BPA) is an environmental pollutant via Oxidative effects and estrogenic activity. Adult male Wistar rats were randomly divided into 4 groups (n=6): control, BPA (250 mg/kg/day), Vit.E (150 mg/kg/day) and BPA+Vit.E. After three times a week (56 days) oral treatments, left caudal epididymis were taken and cut in Ham's F10 and released spermatozoa were used to sperm parameters analysis. The next, right testis was assessed for apoptosis analysis by the TUNEL method. Also, serum testosterone and malondialdehyde (MDA) levels were measured. Results revealed that count, motility, viability, normal morphology and a tail length of sperms and also testosterone levels significantly declined in the BPA group compared to the control group although vice versa MDA levels and TUNEL-positive cells significantly enhanced. also, no changes in sperm maturation and DNA integrity were observed in different groups. The results of this study indicate that Vit.E has a major impact on the devaluation of the BPA-induced toxic roles on sperm parameters.

Abbreviations: MDF: Modified Davidson's Fluid Fixative; IUR: Uniform Random Sampling; TDI: Tubule Differentiation Index; SPI: Spermatogenic Index; SCI: Sertoli Cell Index; MI: Meiosis Index; TDT: Terminal Enzyme Deoxynucleotidyl Transferase; TBA: Thiobarbituric Acid; SD: Standard Deviation; ANOVA: Analysis of Variance; SI: Spermiogenesis Index; LPO: Lipid Peroxidation

Introduction

Over the past decades, several synthetic compounds, including pesticides and industrial chemicals, have been introduced into the environment, considering that these substances have no negative effects on humans and can improve living standards. However, many of these compounds have adverse effects on wildlife and human health [1]. BPA is one of the compounds that have hormone-like activity and interfere with the action of androgen hormones [2], which has adverse effects on the reproductive system of animals [1] and also it is a carbon-based synthetic compound with C15H16O2 chemical formula [1]. This compound is used in the production of polycarbonate plastics and epoxy resins [3]. Bicarbonate is currently used to produce materials that are in direct contact with food, such as plastic bottles, tableware, microwave ovens, food storage containers, and etc. [4]. Epoxy resins are used for the inner coating of food and beverage cans [3,5]. BPA is also used in products such as sunglasses, building materials, medical devices, dental materials and paper [4].

Exposure to BPA in humans is mainly through diet, and other ways are due to soil contamination, climate, inhalation and skin contact [1]. On the other hand, BPA has a wide range of

adverse effects on the health of both males and females, including congenital defects, fertility disorders, growth disorders and metabolic disorders [6]. Previous epidemiological studies have shown an increase in the level of this pollutant in the environment and the incidence of cancers associated with hormonal disorders, such as breast, prostate, ovarian and endometrial cancers [6,7]. It has also been reported in several articles that exposure to BPA has been associated with a decrease in antioxidant enzyme activity [8,9], sperm count [10], and level of testosterone and vice versa an increase in spermatogenesis cell apoptosis [10]. Considering the account, the oxidative stress characteristic of BPA, which is one of the important factors in its toxicity, we claim that apply a potent antioxidant such as VE can help to prevent oxidative stress and reduces the toxicity of this environmental pollutant.

VE, as an antioxidant molecule, protects cells from oxidative stress by preventing ROS mattress and converts them into harmless products [11]. VE is one of the effective chain breakers and fat-soluble antioxidants in biological membranes, which protects of cell structures and tissues against free radical damage and lipid peroxidation products [12]. There is a large amount of VE in Sertoli cells and spermatocytes (Pactin stage), as well as a small amount in round spermatids [13] and is essential for the maintenance of spermatogenesis in mammals [14]. According to previous studies, obviously that VE can degrade the adverse effects of oxidative stress on the testicles. Therefore, this study aimed to investigate the ameliorative action of VE as a potent antioxidant on spermatogenesis in BPA -treated rats was carried out.

Material and Method

Material and Treatments

For this experimental study, 24 adult male Wistar rats were purchased with an average weight of 231±10 grams from the Pasteur Institute of Iran. The animals were kept in an animal house at Arak University under standard conditions (2 ± 21 Celsius and ambient light with 12 hours of darkness and 12 hours of light). All animals were fed equally in the same feeding conditions and free access to water as possible for all of them. Subsequently, one week of adaptation to environmental conditions and after weighing the rats randomly divided into 4 groups. In each group, (6 rats) divided as follows: The first group Control: this group received daily corn oil orally (Gavage). The second group (Bisphenol A: BPA): this group received 250 mg/kg/body weight/day BPA by gavage. The third group (Vitamin E: VE): this group received 150 mg/kg/body weight/day VE by gavage. The fourth group (BPA +VE): this group received BPA + VE daily and with the same previous dose simultaneously by average. The duration of treatment was 56 days, which is the time required to complete course spermatogenesis is considered. All dosage and grouping of this study have been according to previous studies in this field [15,16]. For the treatment of BPA and VE was purchased by Sigma Aldrich Chemie GmbH. For dissolution of BPA, this substance is initially dissolved in absolute alcohol and then diluted in corn oil and then kept at room temperature until use [17]. Consumables in this study, except the mentioned above, from company Merck Germany, was purchased.

Histopathological Assay

The rats were weighed after the end of the treatment period (56 days). The next, after euthanasia and opening the scrotum, the right testis was taken and underwent histopathological examinations. The next, after weighing, testes were transferred to a container containing Modified Davidson's fluid fixative (MDF) and kept at room temperature for one week [18]. It should be noted that all health principles in animal care and extermination were based on ethical protocol. After confirmation, isotropic uniform random sampling (IUR) was performed. This method is a random method. For slicing, there are organs that have a heterogeneous structure, and finally, with this method, uniform cuts of tissue are made [19]. After going through the steps related to tissue processing, the samples were molded applying molten paraffin. In the next step, 5-micrometer sections of paraffin blocks were prepared by a microtome machine. Finally, Heidenhain's Azan method applied for staining samples [20].

Sperm Count Assay

After testis sampling, the left epididymis tail was removed and immediately inserted into a 5 cm plate containing culture medium to examine the sperm count used. Homocytometers were used to sperm counts. 10µl of diluted sperm solution (The culture medium suspension containing sperm from different groups was diluted 1: 9 with a formalin fixative of 2%.) placed on the neobar lam. The sperm with head, middle and tail located in the four corners and center of the square, were counted by light microscope. The number of sperm per each milliliter via n×50000×d formula and 400x magnification was counted. "n" is the number of sperm counted in the five squares of the homocytometer and "d" is the opposite of the dilution of a suspension containing sperm [21]. The count was performed twice for each sample and its mean was announced.

Histomorphometrical Evaluations of Testis

For histomorphometrical evaluation, the diameter of the seminiferous tubules, the diameter of the lumen and the thickness of the germinal epithelium in the groups carried out by motic image software. Coincidentally, a number of fields were selected by microscope (BX41TE) equipped with a model camera Olympus (DP12) Made in Japan, it was photographed by Olysia software with an objective of 10. And randomly diameter 100 seminiferous tubes, its lumen and thickness. The germinal epithelium was measured and recorded using (Motic image 2000) software. Then, the average of these parameters in each rat was calculated.

Spermatogenesis Index Evaluation

For this purpose, 100 seminiferous tubules in each testis to evaluate the following index were examined: Tubule Differentiation Index (TDI): To determine this index in the testicular tissue of each rat, the percentage of semen tubes the device, which had three or more classes of spermatogenesis cells differentiated from type A spermatogonia cells, was calculated [22]. Spermatogenic Index (SPl): This index indicates the percentage of seminiferous tubules with natural spermatogenesis containing sperm [22]. Sertoli Cell Index (SCI): The Sertoli cell index was calculated by comparing the number of germ cells to the number of Sertoli cells, in other words, the sum of the number of spermatogonia and spermatocyte cells and dividing by the number of Sertoli cells per seminiferous tube [23]. Meiosis Index (MI): In order to calculate the meiosis Index, the ratio of the number of round spermatozoa to primary spermatocytes was specified [24].

Estimation of Population of Spermatogenesis, Sertoli and Leydig Cells

Spermatocytes, long and round spermatids, Sertoli and Leydig cells were counted by optical dissector technique and special frame count [25,26]. This used an unbiased counting frame, a 100x magnification, and a regular random method of 20-micron testicular sections in each rat to count cells. Also, a microcator (ND 221 B, Heidenhain, Germany) was used to count the depth of tissue. Finally, the method of Malmir et al. was used to count the number of cells [24].

Biochemical Assay

TUNEL Assay: For this purpose, TUNNEL Kit (Roch in citu cell death detection kit, Fluorescein,) applied according to the manufacturer's instructions. The basis for the diagnosis in the TUNNEL test is the detection of DNA fracture by the terminal enzyme deoxynucleotidyl transferase (TDT) and the dUTP marker, which marks the free 3.-OH in the end sections of nucleic acids. TUNNEL is capable of detecting two groups of apoptotic cells with damaged DNA (positive TUNNEL) and non-apoptotic cells with healthy DNA (negative TUNNEL).

Serum Testosterone Assay: The serum testosterone evaluation in this study was evaluated by the ELISA method and in accordance with the instructions of the manufacturer kit (Testosterone ELISA kit, Cat No (EIA-1559), DRG International, Inc., USA.

MDA Assay: Buege and Aust's methods were used to measuring malondialdehyde. In this method, MDA with thiobarbituric acid (TBA) reacts and produces a combination with an orange color that is capable of observing rays with a wavelength of about 532-535 nm [27,28].

Statistical Analysis

Results were expressed as mean ± standard deviation (SD) for an animal per group. One-way analysis of variance (ANOVA) followed by Tukey's test was applied to determine the statistical differences among means ($p<0.05$ was considered significant).

Results

Weight in the Body and Testis

The mean bodyweight of the rats, after treatment with BPA, did not differ significantly between any of the groups ($P>0.05$). While the mean testicular weight in the BPA group was significantly reduced compared to the control group ($P<0.01$) and in the VE + BPA group, this decrease was normalized in the control group ($P<0.04$) (Table 1).

Table 1: Comparison of the average Body weight before and after treatment and also Testis weight after treatment in various rat groups treated (for 56 days) with Bisphenol A (250 mg/kg/day) and Vitamin E (150mg/kg/day) and Bisphenol A+ Vitamin E, Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same superscripts do not differ significantly.

Groups	Body Weight Before Treatment (gr)	Body Weight After Treatment (gr)	Testis Weight After Treatment (gr)
Control	231.17±10.57a	292.93±27.11a	1.52±0.08a
Bisphenol A	232.00±11.31a	280.00±14.29a	1.37±0.09b
Bisphenol A + Vit E	229.67±13.69a	283.38±13.42a	1.49±0.07a
Vit E	231.33±8.91a	301.63±15.35a	1.51±0.06a

Findings of Histopathology and TUNNEL Staining

Testicular histological evaluations in different groups showed that BPA causes severe histopathological changes in testicular tissue. Atrophy in the seminiferous tubes, rupture and irregularity of the germinal epithelium, vacuolation and decreased sperm density can be seen in the testicular tissue of BPA-treated treatment scales (Figure 1). In addition, in the evaluation of testicular tissue via TUNNEL staining in the BPA group, positive-TUNNEL cells of spermatogenesis, Sertoli and Leydig were observed, which was considerably lower in other groups.

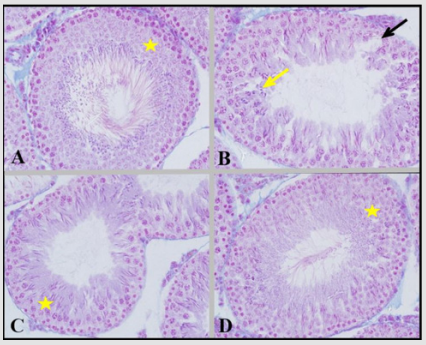

Figure 1: Microscopic images of the testicular tissue of adult rats in different groups, treated with Bisphenol A (250 mg/kg/day) and Vitamin E (150mg/kg/day) and Bisphenol A+ Vitamin E (for 56 days). The thickness of the incisions is 5 microns, the hematoxylin-eosin is staining, and the magnification is 400X.

A. The natural structure of seminiferous tubules in the testicular tissue of the control group with normal germinal epithelial formation (star).

B. Degeneration and vacuolation (arrow black) of the seminiferous tubule, spermatogenesis destruction and immature cell shedding into the lumen space (yellow arrow) in the group treated with Bisphenol A.

C. The almost normal arrangement of germinal epithelium and normal spermatogenesis (star) in the group treated with Bisphenol A + Vitamin E.

D. View of seminiferous tubule similar to the control group with increasing thickness of germinal epithelium (star) in the group treated with vitamin E.

Findings of Histomorphometric in Testicular Tissue

This assessment demonstrated that in the testicular tissue of rats treated with BPA, the mean diameter of the seminiferous tubules (µm) and the thickness of the germinal epithelium (µm) decreased significantly compared to the control group (P <0.001). In addition, the mean thickness of the germinal epithelium in the VE group enhanced significantly compared to the control group (P <0.01). In the BPA + VE group, VE was able to significantly amend tissue changes caused by BPA (P <0.001) (Table 2). The population of spermatocyte, long and round spermatid, and Sertoli cells showed a significant decrease in the BPA group compared to the control group (P <0.05). In addition, the population of Leydig cells in the BPA group showed a significant decline compared to the VE group (P <0.007) (Table 3).

Table 2: Comparison of the average Seminiferous tubule diameter (µm), Lumen diameter (µm) and Germinal epithelium thickness (µm) in various rat groups treated (for 56 days) with Bisphenol A (250 mg/kg/day) and Vitamin E (150mg/kg/day) and Bisphenol A+ Vitamin E, Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same superscripts do not differ significantly.

Groups	Seminiferous Tubule Diameter (µm)	Lumen Diameter (µm)	Germinal Epithelium Thickness (µm)
Control	257.72±4.98a	103.27±4.61a	76.37±1.96a
Bisphenol A	224.03±15.18b	89.02±10.33a	66.08±5.49b
Bisphenol A + Vit E	254.52±7.19a	95.36±9.38a	77.529±4.71a
Vit E	269.12±11.73a	102.43±10.1a	84.40±2.86c

Table 3: Comparison of the population cells of Spermatocyte, Long Spermatid, Round Spermatid, Sertoli cells and Leydig in various rat groups treated (for 56 days) with Bisphenol A (250 mg/kg/day) and Vitamin E (150mg/kg/day) and Bisphenol A+ Vitamin E, Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same superscripts do not differ significantly.

Groups	Spermatocyte (×106)	Long Spermatid (×106)	Round Spermatid (×106)	Sertoli Cells (×106)	Leydig Cells (×106)
Control	150.52±9.25a	267.72±4.18a	245.27±14.51a	29.37±2.96a	34.68±4.83ab
Bisphenol A	115.93±11.57b	215.03±23.55b	198.30±19.93b	22.08±3.69b	30.62±3.54b
Bisphenol A + Vit E	141.39±9.99a	254.77±7.19a	111.46±17.08a	28.59±3.01a	32.67±2.26ab
Vit E	161.00±13.58a	269.28±11.83a	261.88±21.16a	31.28±4.86a	38.69±3.87a

Evaluation of Spermatogenesis and Sperm Count

A statistical evaluation comparing the values of spermatogenesis indexes in different groups exhibited that BPA leads to the elimination of germinal cells in the process of spermatogenesis, which this propels to a significant diminution in tubular differentiation index (TDI; P <0.001), spermiogenesis

index (SPI; P <0.001) and meiosis index (MI; P <0.002) compared to the control group. However, treatment with VE increased the significance (P <0.001) in these parameters compared to the group that received only BPA. In addition, in the BPA group, sperm count had a significant decrease compared to the control group, which in the BPA + VE group had a significant increase compared to the BPA group (P <0.03) (Table 4).

Table 4: Comparison of the Sperm count, Tubule Differentiation Index (TDI), Spermatogenic Index (SPI), Sertoli Cell Index (SCI) and Meiosis Index (MI) in various rat groups treated (for 56 days) with Bisphenol A (250 mg/kg/day) and Vitamin E (150mg/kg/day) and Bisphenol A+ Vitamin E, Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same superscripts do not differ significantly.

Groups	Sperm Count	TDI (%)	SPI (%)	SCI (%)	MI (%)
Control	25.83±3.06a	91.9±11.89a	86.45±6.86a	19.36±2.27a	2.61±0.2a
Bisphenol A	18.17±2.23b	80.63±5.88b	60.82±10.59b	18.92±3.42a	1.87±0.27b
Bisphenol A + Vit E	24.50±3.83a	90.59±2.28a	83.40±2.87a	18.59±1.45a	2.8±0.33a
Vit E	26.64±4.88a	92.01±2.7a	90.91±4.27a	18.00±2.49a	2.54±0.34a

Biochemical Findings

Serum Testosterone Levels Evaluation: As shown in Figure 2, BPA resulted in a significant reduction in serum testosterone levels compared with the control group (P <0.02). However, in the BPA + VE group, there was no change in testosterone concentration compared to the BPA group and the control group (P <0.05); (Figure 2).

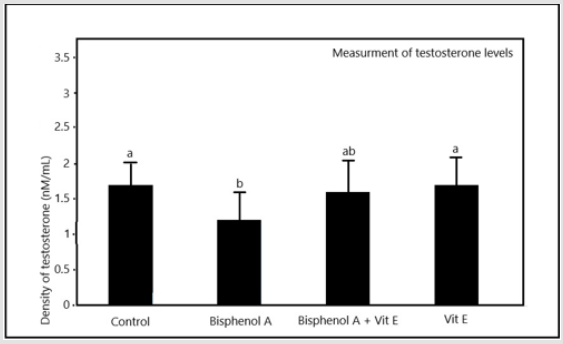

Figure 2: Comparison of serum testosterone (ng/mol), in various rat groups treated (for 56 days) whit Bisphenol A (BPA) (250 mg/kg/day) and Vitamin E (VE) (150mg/kg/day), Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same letters do not differ significantly.

Evaluation of Lipid Peroxidation by MDA: MDA concentration in the BPA group exhibited a significant increase compared to the control group (P <0.03). However, in the BPA + VE group, the MDA level decreased significantly compared to the group BPA (P <0.04); (Figure 3).

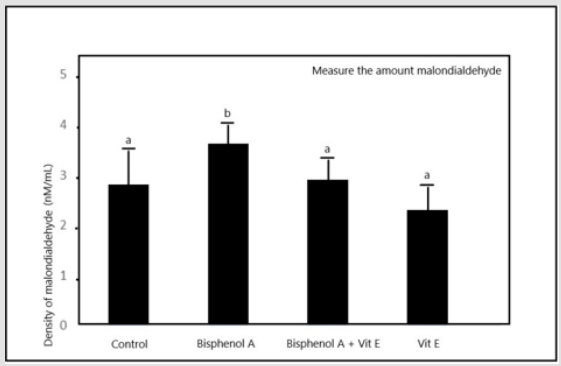

Figure 3: Comparison of serum malondialdehyde (nM/mL) levels, in various rat groups treated (for 56 days) whit Bisphenol A (BPA) (250 mg/kg/day) and Vitamin E (VE) (150mg/kg/day), Date one present as mean ± SD, ANOVA, Tukey's test, the mean with the same letters do not differ significantly.

Discussion

The results of this study indicate a significant reduction in the average of testis weight, seminiferous tubes diameter, germinal epithelium thickness, the population of spermatocytes, long and round spermatids, Sertoli, Tubular Differentiation Index (TDI), Spermiogenesis Index (SI), Meiosis Index (MI), and also sperm count of the epididymis in the BPA group compared to the control group. In the Histopathological studies an enhancement in positive-Tunel cells in spermatogenesis, Sertoli and Leydig cells, also atrophy, germinal epithelium irregularly, and vacuolation was observed in the BPA group compared to the control group. However, by this dose (250mg/kg/day) of BPA in 56 days, this study did not significantly affect the metabolic activity of rats and therefore their weight change, which confirms previous research [17,20,29-31]. Weight loss of testis in rats treated by BPA in this study was accompanied by histopathological changes such as atrophy of the seminiferous tubules, decreased sperm count and impaired spermatogenesis, which confirms previous studies [29,32-34]. By reason of the high mitotic activity of the spermatogenic cycle can be targeted by cytotoxic agents [35].

So, Tan, et al. [30] revealed that BPA could affect spermatogenesis by dysfunction in germinal epithelium. Other researchers in mature male rats treated with different doses of BPA founded out significantly decreases in round spermatids, thickness of germinal epithelium (that accompanied by degeneration and atrophy), seminiferous tubules diameter and daily sperm production [33,34,36,37]. Vice versa increases in shedding out of germinal cells into the lumen [33,37]. All of which indicates the destruction of spermatogenesis in the seminiferous tubules. A diminution in the seminiferous tubule diameter may infer to a decrease in the number of Sertoli and germinal cells affected by apoptosis or disruption on the spermatogenesis process. Decreased thickness of germinal epithelium can be due to the loss of spermatocytes and spermatids and also dispose of premature spermatozoa into the lumen [38,39]. As well as this pollutant can by reducing the expression of proteins in the intercellular connections of germinal and Sertoli cells (in the Ectoplasmic Specialization area) that destroy these connections and the Blood-Testis Barrier and finally leads to the edema and disorder in the germinal epithelium [38,39].

On the other hand, BPA directly and through the effect on the Sertoli cell causes the death of germinal cells in the testicle [40,41]. Also, BPA through the signaling pathway Fas/FasL and trigger the mitochondrial pathway of apoptosis, induces cell death in germinal and Sertoli cells [9,10,41]. Further, this pollutant is talented to motive these cells to death via reducing protein expression N-Cadrin, Oklodin, Zona Oklodens-1 and Conxin-43 or change their position on the membrane [42] and also disrupting the growth and development of germinal cells [17], which together reason infraction of the connection between Sertoli cells and sex cells [39]. From another perspective, based on the vital act of Sertoli cells in spermatogenesis, BPA may have impaired spermatogenesis in this way and TDI, SI, and MI were used as indicators for spermatogenesis assessment, and the results show that BPA disrupted spermatogenesis and the elimination of germ cells and ultimately reduced sperm count in the epididymis [10].

In the biochemical results of this study, a significant decrease in serum testosterone level and a significant increase in Lipid peroxidation in rats treated with BPA compared to the control group were observed, which confirms previous research [9,10]. BPA is an endocrine destroyer and has been reported to reduce serum testosterone and intra-testosterone in mice and rats [36,37,43]. Decreased serum testosterone level by Bisphenol A may result in decreased expression of steroidogenic enzymes and cholesterol-carrying proteins "StAR" which is involved in testosterone synthesis [44,45]. On the other hand, with a note that testosterone is essential for maintaining spermatogenesis and inhibiting apoptosis in germinal cells [30]. Decreasing this hormone in BPA-treated rats can prevent the progression of cell division in cells Germinal, atrophic, genital cell degeneration, and spermatogenesis [12,46]. Therefore, BPA can also interfere with spermatogenesis by reducing testosterone level.

Studies by Cao et al. showed that with increased oxidative stress, the levels of important enzymatic and non-enzymatic antioxidants in Leydig cells decrease and cause reduce the synthesis and secretion of testosterone [47]. In another study decreased testosterone levels were associated with increased levels of MDA in BPA-treated rats [48]. Therefore, one of the reasons for the decrease in serum testosterone levels can be due to oxidative stress caused by BPA. Oxidation of unsaturated fatty acids (PUFA) is called lipid peroxidation (LPO) and as one of the final products of LPO, Malondialdehyde is often the first analyzed parameter to prove the intervention of radical free damage [27,28]. In several studies, treatment with BPA reduced activity Testicular antioxidant enzymes including glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase and increase significant LPO lipid peroxidation was observed [8,9]. In contrast, in the simultaneous treatment group of VE and BPA, VE was able to significantly improve testicular weight loss and tissue changes caused by BPA and reach the control group level. Also, the average thickness of the reproductive epithelium in the group VE increased significantly compared to the control group.

Antioxidant therapy improves sperm repair and increases sperm count against cytotoxic damage and can be effective in reducing BPA toxicity. VE is effective in studies of the protective effect of VE against oxidative damage caused by formaldehyde [49], sodium valproate [50], chromium [51] and sodium aside [12] on the testicles of adult rats, VE was able to significantly prevent testicular weight loss by this toxin were created and the testicular weight returned to the control group range. It also increased the activity of antioxidant enzymes and reduced lipid peroxidation

in the testicles, compensating for the changes caused by these toxins on the testicular tissue, including reducing the diameter and atrophy of the seminiferous tubules and returning them to normal. On the other hand, VE increased sperm count and improved spermatogenesis. In one study, VE was able to in addition to reduction Lipid peroxidation and improved lead-induced histopathological changes also increase serum testosterone levels in rats [15]. The main function of alpha-tocopherol is to inhibit the peroxidation of membrane phospholipids and prevent damage to cell membranes through its antioxidant action [42].

The tocopherol lipophilic property enables it to be located inside the cell membrane [42]. Tocopherols-OH can transfer their hydrogen atom to a single electron from a free radical, thus eliminating it before the free radical interacts with the cell membrane. Therefore, VE can cause stability membranes and prevent lipid peroxidation [42]. VE, as a non-enzymatic defense system in testicular mitochondria [52], is able to inhibit oxidative damage in the testicles [51], which prevents the induction of apoptosis in cells [52,53] and so it plays an important role in keeping sperm alive [51]. Additionally, VE can return glutathione to its normal level on the system Intracellular free radical scavenging is effective and reduces the level of oxidative stress [42,53]. VE may improve spermatogenesis in BPA-treated rats by reducing peroxidation, stabilizing cell membranes, and modulating testosterone levels.

Conclusion

In this study, BPA was able to affect testicular tissue and spermatogenesis and ultimately reduce sperm count. On the other hand, the concomitant use of VE was able to improve the disorder and normalize the spermatogenesis process and ultimately upregulated sperm count. Therefore, the use of VE should be a good strategy to reduce oxidative stress and reduce BPA toxicity in the male reproductive system.

References

1. Vandenberg LN, Hunt PA, Myers JP, Vom Saal FS (2013) Human exposures to bisphenol A: mismatches between data and assumptions. Rev Environ Health 28(1): 37-58.
2. Colborn T, Clement C (1992) Wingspread consensus statement in Chemically Induced Alterations in Sexual and Functional Development: He Wildlife/Human Connection. Princeton scientific Publishing, Princeton, p. 1-8.
3. Soleimani Mehrnjani SM, Naderi Noreini S (2016) The protective effect of vitamin E on spermatogenesis indicators in rats treated with Bisphenol A. Cell & Tissue Journal 7(1): 81-89.
4. Geens T, Aerts D, Berthot C, Bourguignon JP, Goeyens L, et al. (2012) A review of dietary and non-dietary exposure to bisphenol-A. Food Chem Toxicol 50(10): 3725-3740.
5. Yang O, Kim HK, Weon J Il, Seo YR (2015) Endocrine-disrupting Chemicals: Review of Toxicological Mechanisms Using Molecular Pathway Analysis. J Cancer Prev 20(1): 12-24.
6. Rochester JR (2013) Bisphenol A and human health: a review of the literature. Reprod Toxicol 42: 132-155.
7. Keri RA, Ho SM, Hunt PA, Knudsen KE, Soto AM, et al. (2007) An evaluation of evidence for the carcinogenic activity of bisphenol A. Reprod Toxicol 24(2): 240-252.
8. EI Beshbishy HA, Aly HA, El Shafey M (1999) Lipoic acid mitigates Bisphenol Ainduced testicular mitochondrial toxicity in rats". Toxicology and Industrial Health 29(10): 875-887.
9. El Henafy HM, Ibrahim MA, Abd El Aziz SA, Gouda EM (2019) Oxidative Stress and DNA methylation in male rat pups provoked by the transplacental and translactational exposure to bisphenol A. Environmental Science and Pollution Research 27(4): 4513-4519.
10. Kaur S, Sadwal S (2020) Studies on the phytomodulatory potential of fenugreek (Trigonella foenum-graecum) on bisphenol-A induced testicular damage in mice. Andrologia 52(2): e13492.
11. Ghojaie M, Barzegar A, Asadzadeh R (2014) Evaluating the function of IRFI005 on removing intra and extracellular free radicals. Scientific Journal of Ilam University of Medical Sciences 22(2): 158-166.
12. El Shenawy NS, AL Harbi MS, Hamza RZ (2015) Effect of vitamin E and selenium separately and in combination on biochemical, immunological and histological changes induced by sodium azide in male mice. Exp Toxicol Pathol 67(1): 65-76.
13. Yoganathan T, Eskild W, Hansson V (1989) Investigation of detoxification capacity of rat testicular germ cells and Sertoli cells. Free Radic Biol Med 7(4): 355-359.
14. Aziz N, Saleh RA, Sharma RK, Lewis Jones I, Esfandiari N, et al. (2004) Novel association between sperm reactive oxygen species production, sperm morphological defects, and the sperm deformity index. Fertil Steril 81(2): 349-354.
15. Ayinde OC, Ogunnowo S, Ogedegbe RA (2012) Influence of Vitamin C and Vitamin E on testicular zinc content and testicular toxicity in lead exposed albino rats. BMC Pharmacology and Toxicology 13: 17.
16. Hassan AA, Ismail AA, Khudir AN (2013) Effects of Pre-and Postnatal Exposure to Bisphenol- A on the Reproductive Efficacy in Male Albino Rats. Journal of Kerbala University 11(3): 158-172.
17. Wu HJ, Liu C, Duan WX, Xu SC, He MD, et al. (2013) Melatonin ameliorates bisphenol A-induced DNA damage in the germ cells of adult male rats. Mutat Res 752(1-2): 57-67.
18. Latendresse JR, Warbrittion AR, Jonassen H, Creasy DM (2002) Fixation of testes and eyes using a modified Davidson's fluid: comparison with Bouin's fluid and conventiona Davidson's fluid. Toxicol Pathol 30(4): 524-533.
19. Mandarim de Lacerda CA (2003) Stereological tools in biomedical research. An Acad Bras Cienc 75(4): 469-486.
20. Soleimani Mehranjani Malek, Taefi Rezvan (2012) The protective role of vitamin E on the testicular tissue in rats exposed to sodium arsenite during the prenatal stage till sex maturity: A stereological analysis. Iran J Reprod Med 10(6): 571-580.
21. Zambrano E, Rodriguez Gonzalez GL, Guzman C, Garcia Becerra R, Boeck L, et al. (2005) A maternal low proteindiet during pregnancy and lactation in the rat impairs male reproductive development. J Physiol 563(Pt 1): 275-284.
22. Rezvanfar MA, Sadrkhanlou RA, Ahmadi A, Shojaei Sadee H, Rezvanfar M, et al. (2008) Protection of cyclophosphamide-induced toxicity in reproductive tract histology, sperm characteristics, and DNA damage by an herbal source; evidence for role of free-radical toxic stress. Hum Exp Toxicol 27(12): 901-910.
23. Malmir M, Soleimani Mehranjani M, Noreini SN, Faraji T (2018) Protective antioxidant effects of N-acetylcysteine against impairment of spermatogenesis caused by paranonylphenol. Andrologia 50(10): e13114.
24. Malmir M, Faraji T, Noreini NS, Mehranjani SM (2018) Protective Antioxidant Effects of N-acetylcysteine on Testicular Tissue and

Serum Testosterone in Paranonylphenol-Treated Mice (A Stereological Analysis). Reprod Syst Sex Disord 7(2): 1-6.

25. Howard C, Reed M (1999) Unbiased Stereology: Three-Dimentional Measurment in Microscopy. Journal of Microscopy 193(1): 89-90.

26. Peng B, Zhang RD, Dai XS, Deng XZ, Wan Y, et al. (2002) Quantitative (stereological) study of the effects of vasectomy on spermatogenesis in rhesus monkeys (Macaca mulatta). Reproduction 124(6): 847-856.

27. Buege JA, Aust SD (1978) Microsomal lipid peroxidation. Methods in Enzimology 52: 302-310.

28. Esterbauer H, Cheeseman KH (1990) Determination of aldehydic lipid peroxdation products; Malondialdehyde and 4-hydroxynonenal. Methods in Enzimology 186: 407-421.

29. Tamilselvan P, Bharathiraja K, Vijayaprakash S, Balasubramanian MP (2013) Protective role of lycopene on sperm characteristics, testicular damage and oxidative stress in rats. International Journal of Pharma and Bio Sciences 4(4): 131-143.

30. Tan B, Kassim NM, Mohd MA (2003) Assessment of pubertal development in juvenile male rats after sub-acute exposure to bisphenol A and nonylphenol. Toxicology Letters 143(3): 261-270.

31. Kovačevič K, Budefeld T, Majdič G (2006) Reduced seminiferous tubule diameter in Mice neonatally exposed to perfume. Slov Vet Res 43(4): 177-183.

32. Li YJ, Song TB, Cai YY, Zhou JS, Song X, et al. (2009) Bisphenol A Exposure Induces Apoptosis and Upregulation of Fas/FasL and Caspase-3 Expression in the Testes of Mice. Toxicological Sciences 108(2): 427-436.

33. Takahashi O, Oishi S (2001) Testicular toxicity of dietary 2,2-bis(4-hydroxyphenyl) propane (bisphenol A) in F344 rats. Arch Toxicol 75(1): 42-51.

34. Takahashi O, Oishi S (2003) Testicular toxicity of dietarily or parenterally administered bisphenol A in rats and mice. Food and Chemical Toxicology 41(7): 1035-1044.

35. Endo F, Manabe F, Takeshima H, Akaza H (2003) Protecting spermatogonia from apoptosis induced by doxorubicine using the luteinizing hormone-releasing hormone analog leuprorelin. Int J Urol 10(2): 72-77.

36. Mohamed DA, Arafa MH (2013) Testicular toxic changes induced by bisphenol A in adult albino rats: a histological, biochemical, and immunohistochemical study. The Egyptian Journal of Histology 36(1): 233-245.

37. Gurmeet KSS, Rosnah I, Normadiah MK, Das S, Mustafa AM (2014) Detrimental effects of bisphenpl a on development and functions of the male reproductive system in experimental. EXCLI Journal 13: 151-160.

38. Toyama Y, Yuassa S (2004) Effects of bneonatal administration of 17 beta estradiol , beta estradiol 3 benzoate or BPAon mouse and rat spermatogenesis. Reprod Toxicol 19(2): 181-188.

39. Anahara R, Yoshida M, Toyama Y, Maekawa M, Kai M, et al. (2006) Estrogen agonists, 71 betaestradiol, Bisphenol A, and diethylstilbestrol decrease cortactin expression in the mouse testis. Arch Histol Cytol 69(2): 101-107.

40. Wang Q, Zhao XF, Ji YL, Wang H, Liu P, et al. (2010) Mitochondrial signaling pathway is also involved in bisphenol A induced germ cell apoptosis in testes. Toxicology Letters 199(2): 129-135.

41. Qi S, Fu W, Wang C, Liu C, Quan C, et al. (2014) BPA-induced apoptosis of rat Sertoli cells through Fas/FasL and JNKs/p38 MAPK pathways. Reproductive Toxicology 50: 108-116.

42. Krishnamoorthy G, Venkataraman P, Arunkumar A, Vignesh RC, Aruldhas AM, et al. (2007) Ameliorative effect of vitamins) alphatocopherol and ascorbic acid) onPCB (Aroclor 1254) induced oxidative stressin rat epididymal sperm. Reprod Toxicol 23(2): 239-245.

43. Wisniewski P, Romano RM, Kizys MML, Oliveira KC, Kasamatsu T, et al. (2015) Adult exposure to bisphenol A (BPA) in Wistar rats reduces sperm quality with disruption of the hypothalamic-pituitary-testicular axis. Toxicology 392: 1-9.

44. Nakamura D, Xanagika Y, Duan Z, Ito Y, Okamura A, et al. (2010) Bisphenol A may cause testosterone reduction by adversely affecting both testis and pituitary systems similar to estradiol. Toxicology Letters 194(1-2): 16-25.

45. Xi W, Lee CKF, Yeung WSB, Giesy JP, Wong MA, et al. (2011) Effect of perinatal and postnatal Bisphenol A exposure to the regulatory circuits at the hypothalamus- pituitary-gonadal axis of CD-1 mice. Reproductive Toxicology 31(4): 409-417.

46. Singh J, Handelsman DJ (1996) The Effects of Recombinant FSH on Testosterone-Induced Spermatogenesis in Gonadotrophin-Deficient (hpg) Mice. Journal of Andrology 17(4): 382-393.

47. Cao L, Leers Sucheta S, Azhar S (2004) Aging alters thefunctional expression of enzymatic and non-enzymatic anti-oxidant defense systems in testicularrat Leydig cells. J Steroid Biochem Mol Biol 88(1): 61-67.

48. Eshak, Mariam G, Hala F Osman (2014) Biological effects of chitosan against bisphenol-A induced endocrine toxicity and androgen receptor gene expression changes in male rats. Int J pharmaceutical Clin Res 6(4): 300-311.

49. Zhou DX, Qiu SD, Zhang J, Tian H, Wang HX (2006) The protective effect of vitamin E against oxidative damage caused by formaldehyde in the testes of adult rats. Asian J Androl 8(5): 584-588.

50. Shalaby MA, El Zorba HY (2010) Protective Effect of celery oil, vitamin E and their combination against testicular toxicity in male rats. Global veterinaria 5(2): 122-128.

51. Chandra AK, Chatterjee A, Ghosh R, Sarkar M (2010) Vitamin E-supplementation protect chromium (VI)-induced spermatogenic and steroidogenic disorders in testicular tissues of rats. Food and Chemical Toxicology 48(3): 972-979.

52. Ahmed AE, Alshehri A, Al Kahtani MA, Elbehairi SEI, Alshehri MA, et al. (2020) Vitamin E and selenium administration synergistically mitigates ivermectin and doramectin-induced testicular dysfunction in male Wistar albino rats. Biomedicine & Pharmacotherapy 124: 109841.

53. Mumtaz S, Ali S, Khan R, Shakir HA, Tahir HM, et al. (2020) Therapeutic role of garlic and vitamins C and E against toxicity induced by lead on various organs. Environmental Science and Pollution Research 27(9): 8953-8964.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2020.29.004841

M Malmir. Biomed J Sci & Tech Res