The Journal of Toxicology and Health. Photon 105(2014) 477-486
https://sites.google.com/site/photonfoundationorganization/home/the-journal-of-toxicology-and-health
Original Research Article. ISJN: 2294-7439: Impact Index: 4.72

The Journal of Toxicology and Health

Photon

Impact of Paints Exposure and Smoking on oxidative stress and Human fertility

Salem Abdelhady Habib, Elshahat Abomoslem Toson, Rasha Fekry Zahran*

Chemistry Department (Biochemistry Division), Faculty of Science, Damietta University, Egypt

Salem Abdelhady Habib, Elshahat Abomoslem Toson, Rasha Fekry Zahran* receive Photon Young Scientist Award-2014 in Toxicology and Health by Photon Foundation.

Article history:
Received: 13 March, 2014
Accepted: 25 March, 2014
Available online: 26 August, 2014

Abbreviations
E_2: estradiol, EDCs: endocrine disruptors, GSH-Rd: glutathione reductase, GSH: glutathione reduced, GSH-Px: glutathione peroxidase, MDA: malondialdehyde, NO: nitric oxide, NOS: nitric oxide synthase, SOD: superoxide dismutase, TAO: total antioxidant

Keywords
Occupational diseases, hormones, infertility, nitric oxide and free radicals

Corresponding Author:
Zahran R.F.*
Assistant Lecturer
Email: rzahran17@yahoo.com

Habib S.A.
Professor
Email: salem_habib@yahoo.com

Toson E A.
Professor
Email: eatoson@yahoo.com

Abstract
In parallel with industrial advancements, number of the occupational diseases secondary to chemical exposure is increasing. The chemical agents in the work places affect various organ and tissue systems, leading to chronic diseases. Therefore, the aim of this work was to study the effect of the smoking and the exposure to paints on human fertility. In this study, a hundred and forty six male painters diagnosed with occupational diseases related to paints exposure in Damietta were included. In addition, forty of the healthy non-exposed and non-smoker males with the same age range as that of the painters were used as controls. The painters were classified into non-smokers and smokers. The non-smokers were either exposed to paints for less than 15 years (GII) or for more than 15 years (GIII) and the smoker painters were either exposed to less (GIV) or more than 15 years (GV). In sera of all painters, groups the mea levels of testosterone were lowered than that of the control. On the other hand, the levels of estradiol (E2) in sera of all painters, groups were elevated than that of the control, especially in GIII and V. Also, the mean activities of superoxide dismutase (SOD), glutathione reductase (GSH-Rd) and catalase were inhibited in sera of all painters than that of the control. Furthermore, the mean levels of blood reduced glutathione (GSH) in GII-V were lowered than that of the control. The total antioxidant (TAO) was lowered in GII-V than that of the control. On the other hand, the mean levels of nitric oxide (NO) in sera of the same groups were elevated than that of the control group. As was expected, the mean levels of malondialdehyde (MDA) in the red blood cells of GII-V were elevated than that of the control group. In conclusion, the results of this study illustrated that paints, exposure can participate in male infertility possibly via hormonal and free radical mediated mechanisms.

Citation:
Habib S.A., Toson A.E. and Zahran R.F., 2014. Impact of Paints Exposure and Smoking on oxidative stress and Human fertility. The Journal of Toxicology and Health. Photon 105, 477-486.

1. Introduction

In parallel with industrial advancements, the number of the occupational diseases secondary to chemical exposure is increasing. This work environment usually contains a large number of chemicals, which may be inhaled and absorbed by the body, a process which can affect various organ and tissue systems leading to chronic diseases (Yılmaz et al., 2012).

1.1 Paints and sex hormones

In the last few years, there has been a growing interest and concern for the study of a heterogeneous group of environmental chemicals which may act as endocrine disruptors (EDCs) (Harding et al., 2006). Many

EDCs are classified as “xenoestrogen” because their action mimics that of estrogen hormones (Zhou et al., 2009). Multiple lines of evidence from several animal studies indicate that exposure to certain EDCs may drastically alter functional properties of the reproductive, immune, neurologic and endocrine systems (Fusani et al., 2007; Grandjean et al., 2008).

1.1. Paints and oxidative stress

Free radicals and anti-oxidants often play a useful role in cellular signaling. The oxidative balance can be disturbed by several adverse effects including environmental and/or occupational conditions. Oxidative process follow a pro-oxidants mediated mechanism which induce cell death by apoptosis or necrosis via their interacting with cellular unsaturated lipids, proteins, and DNA (Lykkesfeldt, 2007; Basu, 2010).

In this area of study, Ghaffari et al. (2012) observed a significant decrease in sperm motility and a significant increase MDA, nitrite, and nitrate concentrations in the sperm of normozoospermic smokers in comparison with non-smoker men. In humans, spermatozoa generate reactive oxygen species (ROS) which are known to affect hyper activation of spermatozoa, the acrosome reaction, and the attachment of spermatozoa to oocytes thereby contributing to the fertilization of oocytes (Makker et al., 2009; Abd-Elmoaty et al., 2010)

In 2005, Coskun et al., reported that occupational exposure to high concentrations of solvents induce reduction in GSH, SOD, and glutathione peroxidase (GSH-Px). Similarly to organic solvents of paints, lead, another constituent of paints, is involved in the mechanism of oxidative stress (Pande and Flora, 2002).

Generally, human spermatozoa are vulnerable to oxidative stress, a finding which was supported by Baker and Aitken (2005) who demonstrated that catalase could support the motility of human spermatozoa. Because spermatozoa have discarded most of their cytoplasm during the final stages of spermatogenesis, the availability of cytoplasmic defensive enzymes is limited and, therefore, these cells in particular are susceptible to ROS and lipids peroxidation of spermatozoa plasma membranes (Aitken and De Iuliis, 2007; Shamsi et al., 2010).

The latter process can participates in abnormal sperm concentrations, loss of their motilities, abnormalities of their morphology and finally loss of fertility (Desai et al., 2010; Neagu et al., 2011).

NO is a free radical and a highly reactive central mediator in biological systems which is generated by NO synthase (NOS) (Barnes et al., 2010). Several studies have shown that this enzyme is associated with acrosome and tails of human sperm and it appears to be involved in sperm motility and acrosomal reaction that are the main factors in fertilization process (Herrero et al., 2000).

Aljhni et al. (2012) showed that, ROS and NO are implicated in the steroid hormones binding to albumin thus affecting free hormonal fractions a phenomenon which can explain somewhat the pathophysiological role of free radical in different steroid-hormones related diseases including human infertility.

Several reports support the negative effect of cigarette smoke on sperm motility in a concentration- and time-dependent manner (Hung et al., 2007; Calogero et al., 2009; Hung et al., 2009). However, the literature concerning the effects of cigarette smoking on sperm MDA, nitrite, and nitrate concentration in fertile smoking men is limited. Therefore, the aim of this work was to study the effect of the smoking and the exposure to paints on human fertility.

2. Subjects and Methods

2.1. Subjects

This study was conducted on 146 male painters with an age range of 16 - 58 years. The blood samples were collected from painters from Elshoaraa, Elsinania and Elrawda regions, Damietta Governorate, Egypt. A group of 40 healthy males in the same age range were taken as controls. All individuals know the nature of the research and gave samples with consent.

The 146 painters were classified into non-smokers and exposed to paints less than 15 years (GII) and more than 15 years (GIII) and smokers and exposed to paints less than 15 years (GIV) and more than 15 years (GV).

2.1.2. Preparation of the blood samples

5.0 ml of venous blood were collected in a tube containing ethylene diamine tetra-acetic acid (EDTA) disodium salt from each painter and control subject. 0.5 ml of whole blood was used for GSH determination and GSH-Rd assay, 1.0 ml was refrigerated immediately in ice for malondialdehyde (MDA) determination,

0.5 ml was used for estimating haemoglobin level and counting the blood cells and the remaining 3.0 ml were centrifuged at 3000 rpm for 10 min and the plasma samples were then collected, aliquoted and either directly used or stored at - 80 ºC for the other assays.

2.2. Methods

a- Enzyme-linked immuno-sorbent assay (ELISA):A one-step enzyme linked immunosorbent assay (ELISA) was used for determination of testosterone according to the method of (Marcus 1985; Joshi et al., 1979; Ekins, 1998). Also, E2 was determined by ELISA according to the method of (Tsang et al., 1980; Gore-langton and Armstrong, 1988).

b- Colourimetric assays: NO level was determined by the method of Montgomery et al. (1961) and the total TAO activity was measured according to the method of Koracevie et al. (2001). In addition, GSH-R activity was determined by the method of Goldberg and spooner (1985), SOD activity was determined by the method of Dechatelet et al. (1974) and catalase activity was determined by the method of Aebi (1984). GSH in the blood was determined by the method of Beutler et al. (1963) and MDA level was determined by the method of Stocks and Donnandy (1971).

3. Results

The mean levels of serum testosterone of the non-smoker painters (GII and GIII) were highly significantly decreased (*p<0.001*) when compared with that of the healthy control. Also, serum testosterone levels of the smoker painters groups were highly significantly decreased (*p<0.001*) than that of the control (Table 1). In addition, the smoking status does not affect any of the serum testosterone levels.

On the other hand, the level of serum E2 hormone of non-smoker painters (GII and GIII) was highly significantly elevated (*p<0.001*) than that of the control group. Also, the serum levels of E2 of the smoker painters (GIV and GV), were highly elevated than that of the healthy control (*p<0.001*) (Table 1).

The mean activity of serum SOD of the painters groups (GII, III, IV and V) were highly significantly decreased (*p<0.001*) when compared with that of the healthy control (Tables 2 & 3). In addition, in the smoker painters (GV) serum SOD activity was highly significantly reduced when compared with that of non-smoker painters (GII & III) (*p<0.001*).

On the other hand, the mean levels of MDA and NO of the painters groups (GII, III, IV and V) were highly significantly increased (*p<0.001*) when compared with that of the healthy control group. Also, the results showed that the smoker painters (GV) have a significant increase in MDA level (*p<0.05*) and a very significant increase (*p<0.01*) in NO level than the non-smoker painters (GII) (Tables 2 & 3).

The levels of erythrocytes GSH of the painters groups (GII, III, IV and V) were highly significantly decreased (*p<0.001*) when compared with that of the healthy control. Moreover, the results showed that the smoker painters (GV) have a significant decrease in GSH level (*P<0.05*) than the non-smoker painters (GII) (Tables 2 & 3).

The obtained results revealed that the mean serum activities of catalase and GSH-R of the painters groups (GII, III, IV and V) were highly significantly decreased (*p<0.001*) when compared with that of the healthy control group. Also, the results showed that the smoker painters (GV) have a highly significant decrease in the activities of catalase and GSH-R (*P<0.001*) than the non-smoker painters (GII) (Tables 2-5).

Moreover, the mean levels of the serum TAO of the painters groups (GII, III and IV) were significantly decreased (*p<0.05*) and (GV) were very significantly decreased (*p<0.01*) when compared with that of the healthy control. Also, the results showed that the smoker painters (GV) have a significant decrease in the serum TAO levels (*p<0.01*) than the non-smoker painters (GII) (Table 4 & 5).

4. Correlation

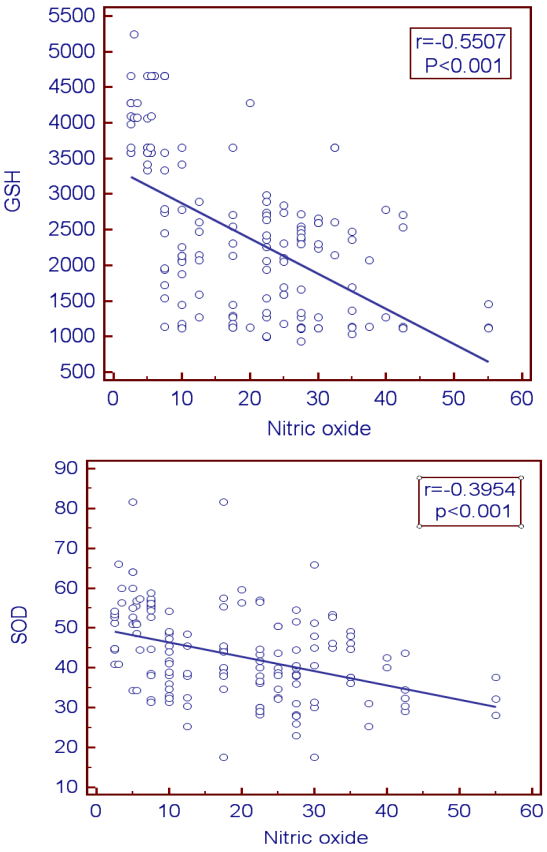
1-Nitric oxide and antioxidants: nitric oxide has a negative correlation with catalase (r=-0.19, *p<0.0004*), GSH-Rd (r=-0.23, p=0.0174), total antioxidants (r=-0.23, *p<0.0073*), GSH (r=-0.55, *P<0.001*) and SOD (r=-0.39, *p<0.001*). On the other hand nitric oxide was positively correlated with MDA (r=0.26, p=0.0013) Figure 1.

2-Nitric oxide and hormones: estradiol has a positive correlation with nitric oxide (r=0.29, *p<0.0028*) Figure 2.

3-Antioxidant and hormones: catalase was positively correlated with testosterone (r=0.23, *p<0.0074*). On the other hand, catalase was

negatively correlated with estradiol (r=-0.19, p=0.0444) Figure 3.

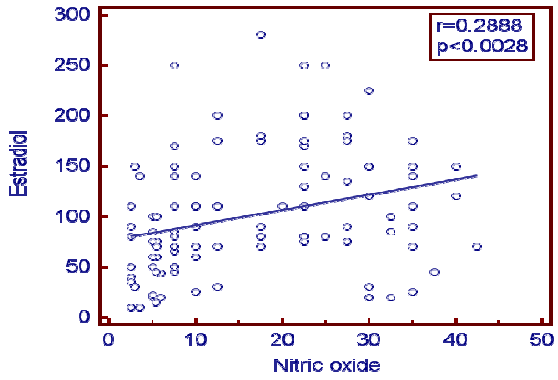
Figure 1: The negative correlation of nitric oxide with GSH and nitric oxide with SOD



5. Discussion

The work environment usually contains a large number of chemicals, which may be inhaled and absorbed by the body. Painters are exposed to an extensive variety of hazardous substances, such as organic solvents, lead-containing pigments, and residual plastic monomers.

Figure 2: The negative correlation of nitric oxide with catalase and the positive correlation of nitric oxide with estradiol



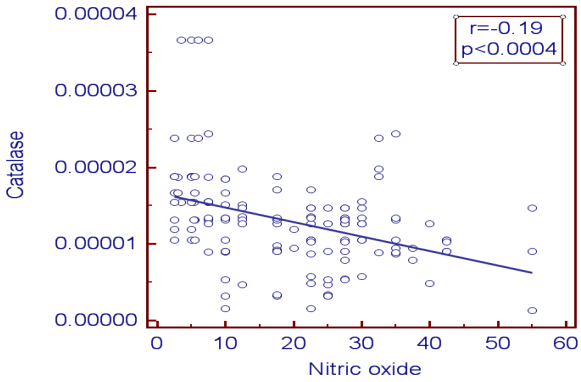
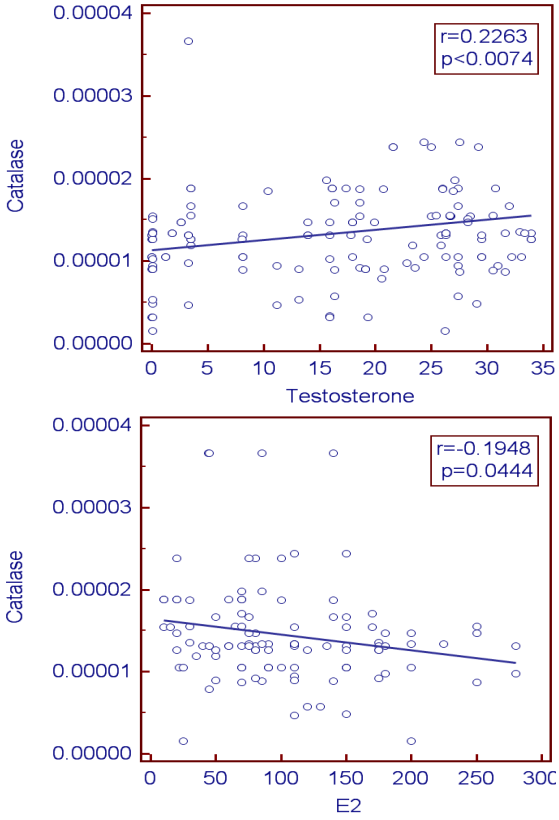


Figure 3: The positive correlation of testosterone with catalase and the negative correlation of estradiol with catalase



In the present study, there was an extremely significant decrease (*p<0.001*) in the mean level of male sex hormone (testosterone) of the non-smoker painters (GII & III) (40.8%, 51.2%) and smoker painters (GIV & V) (44.6% & 51.5%) when compared to that of the control group, respectively. On the other hand, the results showed that the mean level of female sex hormone (estradiol, E2) has an extremely significant increase (*p<0.001*) in serum of non-smoker painters (group II & III) (97.1% & 138.2%) and in serum of smoker painters (group IV & V) (117.8% and 147.6%), Table (1). Normally, LH stimulates the testis to produce testosterone which stimulates testicular spermatogenesis (Champ et al., 2005).

Table 1: The mean serum levels of testosterone and E2 of non-smoker and smoker painters who exposed to paints either for less than 15 years or for more than 15 years compared to those of the healthy control

Parameters / Groups	Non-Smokers painters		Smokers painters	
	Testosterone (nmol/l)	Estradiol (E_2) (pg/ml)	Testosterone (nmol/l)	Estradiol (E_2) (pg/ml)
Control *Mean ±S.E* *N*	26.0 ± 1.1 24	51.0 ± 6.8 21	26.0 ± 1.1 24	51.0 ± 6.8 21
Less than 15 year *Mean ±S.E* *n* *Percent*	15.4 ± 1.94*** 36 [40.8%]^{a}	100.5 ± 11.9*** 18 [97.1%]^{b}	14.4 ± 2.4*** 27 [44.6%]^{a}	111.1 ± 13.9*** 18 [117.8%]^{b}
More than 15 year *Mean ±S.E* *n* *Percent*	12.7 ± 1.85*** 30 [51.2%]^{a}	121.5 ± 13.6*** 26 [138.2%]^{b}	12.6 ± 2.17*** 27 [51.5%]^{a}	126.3 ± 12.3*** 26 [147.6%]^{b}

- Values were expressed as mean ±Standard error (S.E) in each case. ***= extremely significant when compared with the corresponding values of control. [ ]^{a} = Percent of reduction and [ ]^{b} = Percent of elevation than those of the control. [ ]^{a} &[ ]^{b}=(Mean of the control – Mean of the tested group)/Mean of the control.

Table 2: The mean serum activity of SOD and the mean levels of MDA, GSH and NO of the non-smoker painters who either exposed to paints for less than 15 years or for more than 15 years compared to those of the healthy control

Parameters / Groups	SOD (% of inhibition)	MDA (Moles/100ml packed cells)	GSH x 10^{-2} (m moles/ ml cells)	Nitric oxide (µmol/l)
Control *Mean ±S.D* *n*	54.0 ± 9.7 40	0.5 ± 0.1 40	39.86 ± 4.8 40	4.2 ± 0.25 28
Non-Smokers painters Less than 15 year *Mean ±S.D* *n* *Percent*	40.6 ± 10.6*** 39 [24.8%]^{a}	0.7 ± 0.2*** 39 [40.0%]^{b}	20.0 ± 6.5*** 39 [49.8%]^{a}	18.0 ± 1.6*** 35 [328.6%]^{b}
Non-Smokers painters More than 15 year *Mean ±S.D* *n* *Percent*	37.8 ± 8.9*** 47 [30%]^{a}	0.76 ± 0.3*** 47 [52.0%]^{b}	18.9 ± 6.1*** 47 [52.6%]^{a}	24.5 ± 2.2*** 26 [483.3%]^{b}

- Values were expressed as mean ±Standard deviation (S.D) in each case. ***= extremely significant when compared with the corresponding values of control. [ ]^{a} = Percent of reduction and [ ]^{b} = Percent of elevation than those of the control. [ ]^{a} &[ ]^{b}=(Mean of the control – Mean of the tested group)/Mean of the control.

Table 3: The mean serum activity of superoxide dismutase (SOD) and the mean levels of malondialdehyde (MDA), reduced glutathione (GSH) and nitric oxide of smoker painters who either exposed to paints for less than 15 years or for more than 15 years compared to those of the healthy control

Parameters / Groups	SOD (% of inhibition)	MDA (Moles/100ml packed cells)	GSH x 10^{-2} (m moles/ ml cells)	Nitric oxide (µmol/l)
Control *Mean ±S.D* *n*	54.0 ± 9.7 40	0.005 ± 0.001 40	39.86 ± 4.8 40	4.2 ± 0.25 28
Smokers painters Less than 15 year *Mean ±S.D* *n* *Percent*	40.5 ± 5.6*** 21 [25%]^{a}	0.008 ± 0.003** 21 [60.0%]^{b}	17.8 ± 5.9*** 21 [55.3%]^{a}	23.0 ± 1.5*** 21 [447.6%]^{b}
Smokers painters More than 15 year *Mean ± S.D* *n* *Percent*	27.5 ±7.9*** 39 [49%]^{a}	0.0086 ± 0.003*** 39 [72.0%]^{b}	16.1± 5.2*** 39 [59.6%]^{a}	25.7 ± 1.9*** 42 [511.9%]^{b}

- Values were expressed as mean ±Standard deviation (S.D) in each case. **=very significant and ***= extremely significant when compared with the corresponding values of control. [ ]^{a} = Percent of reduction and [ ]^{b} = Percent

of elevation than those of the control. [ ]a &[ ]b=(Mean of the control – Mean of the tested group)/Mean of the control.

Table 4: The mean serum activity of catalase and glutathione reductase and the mean levels of total antioxidants capacity of non-smoker painters who either exposed to paints for less than 15 years or for more than 15 years compared to those of the healthy control

Parameters / Groups	Catalase x 10^7 sec^{-1} (KU/mg protein)	Glutathione reductase (U/L)	Total antioxidants (mmol/l)
Control			
Mean ±S.D	18.5 ±7.1	41.8 ± 13.0	3.0 ± 0.8
N	40	33	26
Non-Smokers painters Less than 15 year			
Mean ±S.D	11.5 ± 5.7***	29.0 ± 9.8***	2.3 ± 0.4*
n	39	40	35
Percent	[37.8%]a	[30.6%]a	[23.3%]a
Non-Smokers painters More than 15 year			
Mean ±S.D	12.8 ±1.3***	26.2 ± 8.5***	2.2 ± 0.6*
n	47	36	23
Percent	[30.8%]a	[37.3%]a	[26.7%]a

- Values were expressed as mean ±Standard deviation (S.D) in each case.
*= Significant and ***= extremely significant when compared with the corresponding values of control.
[ ]a = Percent of reduction and [ ]b = Percent of elevation than those of the control.
[ ]a &[ ]b=(Mean of the control – Mean of the tested group)/Mean of the control.

Table 5: The mean serum activity of catalase and glutathione reductase and the mean levels of total antioxidants capacity of smoker painters who either exposed to paints for less than 15 years or for more than 15 years compared to those of the healthy control

Parameters / Groups	Catalase x 10^7 sec^{-1} (KU/mg protein)	Glutathione reductase (U/L)	Total antioxidants (mmol/l)
Control			
Mean ±S.D	18.5 ±7.1	41.8 ± 13.0	3.0 ± 0.8
N	40	33	26
Smokers painters Less than 15 year			
Mean ±S.D	7.0 ± 2.8***	24.1 ± 9.7**	2.1 ± 0.6*
n	20	18	20
Percent	[62.1%]a	[42.3%]a	[30%]a
Smokers painters More than 15 year			
Mean ±S.D	6.4 ± 2.9***	15.3 ± 3.0***	2.0 ± 0.6**
n	36	24	32
Percent	[65.4%]a	[63.4%]a	[33.3%]a

- Values were expressed as mean ±Standard deviation (S.D) in each case.
*= Significant, **=very significant and *** = extremely significant when compared with the corresponding values of control.
[ ]a = Percent of reduction.
[ ]a =(Mean of the control – Mean of the tested group)/Mean of the control.

Therefore, the reduction in serum testosterone levels of the painters who exposed to both paints and cigarettes smoke may cause defects in the process of spermatogenesis and thence infertility. This reduction in testosterone level may be due to damage of tissues due to oxidative stress including gonads and pituitary glands tissues (Denicola et al., 1998; Pacher et al., 2007).

This explained in Aljhni et al., 2012 study, who have showed that free radicals (reactive oxygen species and nitric oxide) changed the steroid hormone binding on albumin and therefore their free-fraction levels. This change affected the hydrogen bond or van der Waals interaction which were modified after the oxidation of some residues as the free thiol or hydroxyl of the albumin binding sites (cys, tyr, etc.). The change of hormone free fractions levels induced by free radicals can explain somewhat the pathophysiological role of free radical in different steroid-hormones related diseases.

In addition, E2 has been shown to directly affect steroidogenesis in the rat testis via accumulation of estrogen-regulated proteins (Tong et al., 2004). Therefore, one can expect that, the elevation of serum E2 levels in sera of the painters included in this study may stimulates Leydig cell hyperplasia which has

been associated with cryptorchidism, testicular cancer, and impaired spermatogenesis as was previously reported by Abney (1999) who found association between E2 level and Leydig cell hyperplasia in rodents.

Also, (Turner et al., 2000; D'Souza et al., 2005) demonstrated that the circulating LH and FSH concentrations were effectively reduced by E2. Our results were confirmed by the results of Gao et al. (2013) who found that the sex hormone balance in the male reproductive system was disrupted by TiO2 NPs exposure and thereby suppressed spermatogenesis through pathological changes in the testis.

Also, (Svensson, 1992b; Yilmaz et al., 2001) found that several organic solvents and environmental contaminants have been suggested to affect neurochemical mechanisms in the brain, which control gonadotropin release from the anterior pituitary. Chronic occupational toluene exposure in male subjects resulted in reduced luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels (Svensson, 1992a). Yilmaz et al., (2001) found that paint thinner exposure for 15 days decreased serum LH and testosterone concentrations in parallel.

The oxidative balance can be disturbed by several adverse environmental and/or occupational conditions, causing an uncompensated increase of pro-oxidants (Basu, 2010).

The results in the present study indicate that oxidants and antioxidants status were altered with periods of paints exposure and cigarettes smoke. Serum SOD activity was extremely decreased ($p<0.001$) while, MDA (lipid peroxidation marker) level was extremely increased ($p<0.001$) in groups (II-V) when compared to that of the healthy control group (Table 2 & 3).

In the present study GSH contents and catalase and GSH-R activities were extremely decreased ($p<0.001$) in painters groups (group II, III, IV & V) when compared to that of the healthy control group (Table 2 - 5).

Nitric oxide (NO), a short-lived freely diffusible radical gas that acts as an important biological signal, regulates an impressive spectrum of physiological functions in vertebrates. In the present study, there was an extremely significant increase ($p<0.001$) in the mean levels of NO in serum of smoker and non-smoker painters groups (GII, III, IV & V) by (328.6%, 483.3%, 447.6% & 511.0%), respectively (Table 2 & 3).

These changes in the oxidative balance have shown in (Georgieva et al., 2002; Ilgazli et al., 2004; Coskun et al., 2005) studies which illustrated that occupational exposure to high concentrations of solvents induces lipid peroxidation and decreases in the endogenous antioxidants in the body, such as reduced glutathione (GSH), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px).

The change of antioxidant enzymes (e.g. SOD, CAT, GSH-Px, GSH-Rd) by various pollutants like metals, PAHs, and other organic compounds, have been documented in detail by Moro et al., (2010); Moro et al., (2012) who suggested that these contaminants can induce ROS (e.g., O− 2, H2O2, HO−, and 1O2, etc.) inciting oxidative stress and even lipid peroxidation.

The total antioxidant capacity in the obtained results was significantly reduced ($p<0.05$) in painters groups compared to control. The percent of reduction was 30% and 33.3% in serum of smoker painters GIV & GV, respectively and 23.3% & 26.7% in serum of non-smoker painters GII & GIII, respectively (Table 4 & 5).

In agreement with a toluene-induced increase in ROS production, reports in the literature have indicated that exposure to paint thinners containing toluene increased serum malondialdehyde (a measure of OS) levels in humans, (Halifeoglu et al., 2000) as well as increasing lipid peroxidation in different rat brain regions (Baydas et al., 2003; Baydas et al., 2005).

In the obtained results, estradiol has a positive correlation with nitric oxide ($r=0.29$, $p<0.0028$) and a negative correlation with catalase ($r=-0.19$, $p=0.0444$). Also, testosterone has a positive correlation with catalase ($r=0.23$, $p<0.0074$).

These results confirmed that, there is a relation between nitric oxide and antioxidant enzymes in male infertility. In 2012, Ji et al. found that the PON1 R192Q (rs662) and SOD2 V16A (rs4880) variant genotypes were associated with sperm integrity and risk of male infertility. The results of this study might be helpful in improving the understanding of the genetic susceptibility of sperm DNA

integrity and in providing diagnostic implications for assisted reproduction success rates.

Also, Scichilone et al. 2013 found that the exhaled nitric oxide is associated with cyclic changes in sexual hormones.

In 2012, Aly et al. demonstrated that exposure of NP This induces testicular toxicity and impairs sperm functions, at least partly, by induction of oxidative stress in epididymal sperm of rat. Moreover, the reduction in sperm transit time may affect sperm quality and fertility potential.

In conclusion, these results demonstrate that exposure to paints has an effect on antioxidant balance by a reduction in the activities of antioxidant enzymes and increase in free radicals and nitric oxide, which was associated with cyclic changes in sexual hormones and then risk of infertility.

Research Highlights

1- Exposure to paints and cigarette smoking induces oxidative stress.
2- Exposure to paints and cigarette smoking disturbs the sex hormones.
3- Paints, exposure can participate in male infertility possibly via hormonal and free radical mediated mechanisms.

References

Abd-Elmoaty M.A., Saleh R., Sharma R., Agarwal A., 2010. Increased levels of oxidants and reduced antioxidants in semen of infertile men with varicocele. Fertility and Sterility, 94(4), 1531–1534.

Abney T.O., 1999. The potential roles of estrogens in regulating Leydig cell development and function: a review Steroids 64, 610–617.

Aebi H., Catalase. In: L. Packer (Ed), methods in enzymology. Academic pres, Orlando; 105, 121–126.

Aitken R.J., De Iuliis G.N., 2007. Origins and consequences of DNA damage in male germ cells. Reproductive Biomedicine Online, 14(6), 727–733.

Aljhni R., Ibrahim F., Guillaume Y.C., Andre C., 2012. Reactive oxygen species and nitric oxide effect on the steroid hormone binding with serum albumin. Journal of Pharmaceutical and Biomedical Analysis, 62, 129–134.

Aly H.A.A., Domènech Ò., Banjar Z.M., 2012. Effect of nonylphenol on male reproduction: Analysis of rat epididymal biochemical markers and antioxidant defense enzymes. Toxicology and Applied Pharmacology, 261(2), 134–141.

Baker M.A., Aitken R.J., 2005. Reactive oxygen species in spermatozoa: methods for monitoring and significance for the origins of genetic disease and infertility. Reproductive Biology and Endocrinology, 3, 67.

Barnes P.J., Dweik R.A., Gelb A.F., Gibson P.G., George S.C., Grasemann H. et al. 2010. Exhaled nitric oxide in pulmonary diseases: a comprehensive review. Chest, 138, 682–692.

Basu S., 2010. Fatty acid oxidation and isoprostanes: oxidative strain and oxidative stress. Prostaglandins eukotrienes and essential fatty acids, 82(4–6), 219–225.

Baydas G., Ozveren F., Tuzcu M., Yasar A., 2005. Effects of thinner exposure on the expression pattern of neural cell adhesion molecules, levels of lipid peroxidation in the brain and cognitive function in rats. European Journal of Pharmacology, 512, 181–187.

Baydas G., Reiter R.J., Nedzvetskii V.S., Yasar A., Tuzcu M., Ozveren F., Canatan H., 2003. Melatonin protects the central nervous system of rats against toluene-containing thinner intoxication by reducing reactive gliosis. Toxicology Letters, 3, 169–174.

Beutler E., Duron O., Kelly B., 1963.

Improved method for the determination of blood glutathione. Journal of Laboratory and Clinical Medicine, 61, 882–890.

Calogero A., Polosa R., Perdichizzi A., Guarino F., La Vignera S., Scarfia A., et al. 2009. Cigarette smoke extract immobilizes human spermatozoa and induces sperm apoptosis. Reproductive Biomedicine Online, 19(4), 564–71.

Champe P.C., Harvey, D.E. Ferrier, 2005.

Lippincott Illustrated Reviews, (3rd edn). Lippincott Williams & Wilkins. 351 West Camden Street Baltimore, MD 21201, 238.

Coskun O., Oter S., Korkmaz A., Armutcu F., Kanter M., 2005.

The oxidative and morphological effects of high concentration chronic toluene exposure on rat sciatic nerves. Neurochemical Research, 30, 33–38.

Dechatelet L.R., Mc. Call C.E., Mc. Phial L.C., Johnston R.B., 1974. Superoxide dismutase activity in leukocytes. Journal of Clinical Investigation, 53, 1197–1201.

Denicola A., Souza J.M., Radi R., 1998. Effect of thinner inhalation on lipid peroxidation and some antioxidant enzymes of people working with paint

thinner. Cell Biochemistry and Function, 18, 263–267.

Desai N., Sabanegh Jr. E., Kim T., Agarwal A., 2010. Free radical theory of aging: implications in male infertility. Urology, 75(1), 14–19.

D'Souza R., Gill-Sharma M.K., Pathak S., Kedia N., Kumar R., Balasinor N., 2005. Effect of high intratesticular estrogen on the seminiferous epithelium in adult male rats. Molecular and Cell Endocrinology, 241, 41–48.

Ekins R., 1998. The science of free testosterone measurement. Proc. UK NEQAS meeting. 3, 35–39.

Fusani L., Seta D. D., Dessì-Fulgheri F., Farabollini F., 2007. Altered reproductive success in rat pairs after environmental-like exposure to xenoestrogen. Proceeding of the Royal Society, 274, 1631–1636.

Gao G., Ze Y., Zhao X., Sang X., Zheng L., Ze X., Gui S., Sheng L., Sun Q., Hong J., Yu X., Wang L., Hong F., Zhang X., 2013. Titanium dioxide nanoparticle-induced testicular damage, spermatogenesis suppression, and gene expression alterations in male mice. Journal of Hazardous Materials, 258–259, 133–143.

Georgieva T., Michailova A., Panev T., Popov T. 2002. Possibilities to control the health risk of petrochemical workers. International Archives of Occupational and Environmental Health, 75, 21–26.

Ghaffari M.A., Rostami M., 2012. Lipid peroxidation and nitric oxide levels in male smokers' spermatozoa and their relation with sperm motility. Journal of Reproduction and Infertilty, 13(2), 81–87.

Goldberg D.M., Spooner R.J., 1985. Glutathione reductase. H.U. Bergmeyer (Ed.), Methods in enzymatic analysis (3rd ed.), 3, 258–265.

Gore-Langton R.E., Armstrong D.T., 1988.

Follicular steroidogenesis and its control. In: Knobil, E., and Neill, J. et al., ed. The physiology of reproduction. Raven press, New York, 331–385.

Grandjean P., Bellinger D., Bergman A., Cordier S., Davey-Smith G., Eskenazi B., Gee D., Gray K., Hanson M., van den Hazel P., Heindel J.J., Heinzow B., Hertz-Picciotto I., Hu H., Huang T.T., Jensen T.K., Landrigan P.J., McMillen I.C., Murata K., Ritz B., Schoeters G., Skakkebaek N.E., Skerfving S., Weihe P., 2008. The faroes statement: human health effects of developmental exposure to chemicals in our environment. Basic & Clinical Pharmacology & Toxicology, 102, 73–75.

Halifeoglu I., Canatan H., Ustundag B., Illhan N., Inanc F., 2000. Effect of thinner inhalation on lipid peroxidation and some antioxidant enzymes of people working with paint thinner. Cell Biochemistry and Function, 18, 263–267.

Harding A.K., Daston G.P., Boyd G.R., Lucier G.W., Safe S.H., Stewart J., Tillitt D.E., Van Der Kraak G., 2006. Endocrine disrupting chemicals research program of the U.S. Environmental Protection Agency: summary of a peer-review report. Health Perspectivies, 114, 1276–1282.

Herrero B.M., Chatterjee S., Lefievre L., de Lamirande E., Gagnon C., 2000. Nitric oxide interacts with the cAMP pathway to modulate capacitation of human spermatozoa. Free Radical Biology & Medicine, 29(6), 522–36.

Hung P.H., Baumber J., Meyers S.A., Voort C.A.V., 2007. Effects of environmental tobacco smoke in vitro on rhesus monkey sperm function. Reproductive Toxicology, 23(4), 499–506.

Hung P.H., Froenicke L., Lin C.Y., Lyons L.A., Miller M.G., Pinkerton K.E., et al. 2009. Effects of environmental tobacco smoke in vivo on rhesus monkey semen quality, sperm function, and sperm metabolism. Reproductive Toxicology, 27(2), 140–8.

Ilgazli A., Sengul C., Maral H., Ozden M., Ercin C. 2004. The effects of thinner inhalathion on superoxide dismutases activities, malondialdehyde and glutathione levels in rat lungs. Clinica Chimica Acta, 343, 141–144.

Ji G., Yan L., Liu W., Qu J., Gu A., 2013. OGG1 Ser326Cys polymorphism interacts with cigarette smoking to increase oxidative DNA damage in human sperm and the risk of male infertility. Toxicology Letters, 218(2), 144–149.

Joshi U.M., et al., 1979. A sensitive specific enzyme immunoassay for serum testosterone. Steroids, 34, 35.

Koracevic D., Koracevic G., Djordjevic V., Andrejevic S., Cosic V., 2001. Method for the measurement of antioxidant activity in human fluids. Journal of Clinical Pathology, 54, 356–361.

Lykkesfeldt J., 2007. Malondialdehyde as biomarker of oxidative damage to lipids caused by smoking. Clinica Chimica Acta, 380, 50–58.

Makker K., Agarwal A., Sharma R., 2009.

Oxidative stress & male infertility. Indian Journal of Medical Research, 129(4), 357–367.

Marcus G.J., et al., 1985. A simple linked immunoassay for testosterone. Steroids, 46, 975.

Montgomery H.A.C., Dymock J.F., 1961. The determination of nitrate in water. Analyst, 86, 414–416.

Moro A.M., Brucker N., Charão M., Bulcão R., Freitas F., Baierle M., Nascimento S., Valentini J., Cassini C., Salvador M., Linden R., Thiesen F., Buffon A., Moresco R., Garcia S.C., 2012. Evaluation of genotoxicity and oxidative damage in

painters exposed to low levels of toluene. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 746(1), 42–48.

Moro A.M., Charão M., Brucker N., Bulcão R., Freitas F., Guerreiro G., Baierle M., Nascimento S., Waechter F., Hirakata V., Linden R., Thiesen F.V., Garcia S.C., 2010. Effects of low-level exposure to xenobiotics present in paints on oxidative stress in workers. Science of the Total Environment, 408(20), 4461–4467.

Neagu V.R., García B.M., Rodríguez A.M. , et al. 2011. Determination of glutathione peroxidase and superoxide dismutase activities in canine seminal plasma and its relation with sperm quality and lipid peroxidation post thaw. Theriogenology, 75(1), 10–16.

Pacher P., Beckman J.S., Liaudet L., 2007.

Nitric oxide and peroxynitrite in health and disease. physiological Reviews, 87, 315–424.

Pande M., Flora S.J., 2002. Lead induced oxidative damage and its response to combined administration of alpha-lipoic acid and succimers in rats. Toxicology, 177(2-3), 187–96.

Scichilone N., Battaglia S., Braido F., Collura A., Menoni S., Arrigo R., Benfante A., Bellia V., 2013. Exhaled nitric oxide is associated with cyclic changes in sexual hormones Pulmonary. Pharmacology & Therapeutics, 26(6), 644–8.

Shamsi M.B., Venkatesh S., Kumar R., et al. 2010. Antioxidant levels in blood and seminal plasma and their impact on sperm parameters in infertile men. Indian Journal of Biochemistry and Biophysics, 47(1), 38–43.

Stocks J., Donnandy T., 1971. The autoxidation of human red cell lipids induced by hydrogen peroxide. British Journal of Haematology, 20, 95–111.

Svensson B.G., Nise G., Erfurth E.M., Nilsson A., Skerfving S., 1992a. Hormone status in occupational toluene exposure. American Journal of Industrial Medicine, 22, 99–107.

Svensson B.G., Nise G., Erfurth E.M., Olsson H., 1992b. Neuroendocrine effects in printing workers exposed to toluene. British Journal of Industrial Medicine, 49, 402–408.

Tong M.H., Christenson L.K., Song W.C., 2004. Aberrant cholesterol transport and impaired steroidogenesis in Leydig cells lacking estrogen sulfotransferase. Endocrinology, 145, 2487–2497.

Tsang B.K., Armstrong D.T., Whitfield J.F., 1980. Steroid biosynthesis by isolated human ovarian follicular cells in vitro. Journal of clinical Endocrinology and Metabolism, 51, 1407–1411.

Turner K.J., Morley M., Atanassova N., Swanston I.D., Sharpe R.M., 2000. Effect of chronic administration of an aromatase inhibitor to adult male rats on pituitary and testicular function and fertility. Journal of Endocrinology, 164, 225–238.

Yilmaz B., Kutlu S., Canpolat S., Sandal S., Ayar A., Mogulkoc R., Kelestimur H., 2001. Effects of paint thinner exposure on serum LH, FSH and testosterone levels and hypothalamic catecholamine contents in the male rat. Biological and Pharmaceutical Bulletin, 24, 163–166.

Yılmaz H., Keten A., Karacaoğlu E., Tutkun E., Akçan R., 2012. Analysis of the hematological and biochemical parameters related to lead intoxication. Journal of Forensic and Legal Medicine, 19(8), 452–454.

Zhou J., Cai Z.H., Zhu X.S., 2009. Endocrine disruptors: an overview and discussion on issues surrounding their impact on marine animals. Journal of Experimental Marine Biology & Ecology, 2, 7–12.