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The Effect of Oxidative Stress and Antioxidants on Men Fertility

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Abstract

***Background*:** Various factors affects men fertility and oxidative stress as an important factor which affects fertility has recently got great concern. Oxidative stress refers to conditions of imbalance between productions of reactive oxygen species (ROS) and antioxidant defense mechanism. Reactive species of oxygen, free radicals and peroxide are produced in the cell when metabolism of oxygen is incomplete in the mitochondrial respiratory chain.

***Materials and Methods*:** In this review we will consider effect of oxidative stress on male fertility and the principal antioxidant defences.

***Results*:** Factors such as hypoxia, cytokines, growth factors, chemotherapy, radio frequency waves and UV radiation can increase ROS production. Oxidative stress as one of the strongest physiological factors can lead to damage of sperm and reduction of seminal plasma quality and thereby cause infertility in men. Enzymatic and non-enzymatic defences inhibit oxidant attack. The enzymatic defense include: superoxide dismutases, glutathione peroxidases, and catalase. The non-enzymatic defences include ascorbate (vitamin C) and a-tocopherol (vitamin E), beta carotene, and albumin, which neutralize free radicals.

***Conclusion*:** Oxidative stress affects male fertility through induction of lipid peroxidation, inactivation of proteins, impair of sperm motility and DNA damage.

Introduction

Infertility is a major clinical problem in the realms of medicine and psychiatry. Infertility is defined as no pregnancy after one year of couples having sex without using contraception [1]. About 5 to 15% of couples are infertile, and the male factor is responsible for 50% of these causes [2, 3]. Many factors in men have been identified as causes of infertility that include: varicocoele, cryptorchidism, infections, obstructive lesions, cystic fibrosis, trauma, and tumors; and a new important cause have been identified, oxidative stress. Oxidative stress is a consequence of an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense mechanism. It also has been implicated in the pathogenesis of many other human diseases and disorder such as atherosclerosis, cancer, diabetes, lung diseases, liver damage, inflammatory bowel disease, central nervous system disorders. Oxidative stress as a potent physiological factor can lead to damage sperm, sperm deformation, and male infertility [4].

A metaanalysis of 61 studies worldwide found a downward trend in sperm count and volume of seminal fluid over the past 50 years [5]. In 1940, the average sperm count was 113 million per ml. By 1990, the count had dropped to 66 million per ml [6]. This decreasing trend in sperm count has led to speculation that recent environmental, dietary and/or lifestyle changes are interfering with a man's ability to produce spermatozoa. It is believed that these factors exert their detrimental effects through oxidative stress. In the past two decades, studies on the causes of male infertility, showed relevance between ROS production and oxidative stress as an important factor for defective sperm activity and sterility [7]. ROS are free radicals and peroxides that are derived from the metabolism of oxygen and are present in all aerobic organisms [8]. An imbalance between the production and removal ROS cause significant damage on cellular and biological organism, which lead to organelles damage, enzymes damage, increase lipid peroxidation, decrease quality of sperm and infertility [9].

In natural conditions of cell metabolism, ROS production in plant and animal cells stimulate signaling pathways of cell's activities, which is due to changes of inside and outside physiological conditions [10]. A spermatozoa like any other aerobic cellular needs oxygen for metabolism. Oxygen is essential to sustain physiological levels of ROS and is necessary for metabolism [11].

Materials and Methods

The term “reactive oxygen species” is applied to both free radicals and their non-radical intermediates (Table 1). Free radicals are defined as species containing one or more unpaired electrons, and it is this incomplete electron shell that confers their high reactivity. Free radicals can be generated from many elements, but in biological systems it is those involving oxygen and nitrogen that are

Table 1. Types of reactive oxygen species (ROS)

Radicals	Non-Radicals
Hydroxyl (OH°)	Peroxynitrite (ONOO°)
Superoxide (O_2^-)	Hypochloric acid (HOCL)
Nitric Oxide (NO°)	Hydrogen Peroxide (H_2O_2)
Thiyl (RS°)	Singlet Oxygen(O^-)
Peroxyl (RO_2^o)	Ozone (O_3)
Lipid Peroxyl (LOO°)	Lipid peroxide (LOOH)

the most important. Under physiological conditions, the most common oxygen free radical is the superoxide anion, and mitochondria are considered the principal source. The transfer of electrons along the enzymes of the respiratory chain is not totally efficient, and leakage of electrons on to molecular oxygen, in particular from complexes I and III, results in the formation of O_2. The rate of formation is determined by the number of electrons present on the chain, and so is elevated under conditions of hyperoxia and of raised glucose, as in diabetes. Under normal conditions, 2% of oxygen consumed is converted to superoxide anion in the mitochondria. Similarly, superoxide can also be generated through leakage of electrons from the shorter electron transport chain within the ER. The formation of disulphide bonds during protein folding is an oxidative process, and about 25% of superoxide anion within cells is generated within the ER. Other sources of superoxide under physiological conditions include the enzymes nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, cytochrome P450 oxidase, and other oxido-reductases. Under pathological conditions, the enzyme xanthine dehydrogenase becomes an important contributor to produce ROS. This enzyme degrades purines, xanthine and hypoxanthine to uric acid. This enzyme plays a key role in the reperfusion phase of ischaemia–reperfusion injury, when its action is augmented by the build-up of hypoxanthine as a result of ATP breakdown during the hypoxic period [12]. Under hypoxic conditions, the mitochondrial respiratory chain produces nitric oxide that lead to produce nitrogen active species [13].

Effects of lifestyle behavior and environment on oxidative stress and male infertility: In this section, effects of smoking, alcohol consumption and other environmental factors are examined on oxidative stress.

Oxidative stress and smoke: These days, the effects of smoking on male reproductive system are well known. Saleh et al., showed that smoke causes increase ROS levels and decrease total antioxidant capacity of seminal plasma. They showed that persons who are social smoker have high levels of leukocytospermia. They also suggested that oxidative stress caused by increasing ROS production that occur leukocyte activity [14]. Various compounds in smoke (polycyclic aromatic hydrocarbons) and metabolites of smoke act as a chemical stimulus and provoke an inflammatory response that following enhance ROS production of leukocytes [14]. In other study conducted by Gaur et al., were shown that smoking reduces sperm motility and asthenozoospermia [2]. Tobacco contains nearly 4000 harmful substances such as alkaloids, nitrosamines, nicotine and hydroxycotinine. Many of these substances generate ROS and RNS [15]. Smoking by production of ROS cause flagellum and axonemal damage. Sperm motility correlates negatively with the amount of cotinine and hydroxycotinine in the seminal plasma. Their effects through penetrate the blood-testes barrier [16].

Oxidative stress and alcohol consumption: Many processes and factors are involved in causing alcohol-induced oxidative stress. Alcohol metabolism results in the formation of NADH, which enhances activity of the respiratory chain, including heightened O_2 use and ROS formation. One of the by-products of alcohol metabolism, acetaldehyde, interacts with proteins and lipids to form ROS. It is also capable of damaging the mitochondria leading to decreased ATP production. Alcohol also induces hypoxia that is as a cause ROS production [15, 16]. Studies show that excessive alcohol consumption is associated with a decrease in the percentage of normal sperm in asthenozoospermic patients. However, better sperm morphology has been observed in men who drink moderately [17]. Jelodar et al., reported that ethanol causes oxidative stress in testicular and cerebellum tissues of rat, and betaine as an antioxidant neutralize hydroxyl radicals and lipid peroxidation by providing methyl group [18- 20].

Oxidative stress and environment: Many environmental factors such as radiation, some of medications and toxins induce ROS production.

Oxidative stress and the effects of chemical pesticides and insecticides: Induction of oxidative stress caused by the use of chemical pesticides, as a potential mechanism associated with infertility in the past decade has been the focus of researchers [21]. In a study conducted on Danish green house workers, a high count of spermatozoa was found among organic farmers who grew their products without the use of pesticides or chemical fertilizers. These studies categorically suggest the need for a healthy environment [22].

Oxidative stress and cell phone: Mobile phones are using radiofrequency waves ranging between 850-1900 MHz. Energy produced by cell phone (Radiofrequency electromagnetic waves: RF-EMW) in comparison with ionizing radiation (such as X-ray which frequency range 10^{10}-10^{18} MHz) is very low and does not cause ionization of biomolecules. Although RF-EMW exposure is applied various effects on biological systems, conflicting results of studies is on the effects of mobile phone on male fertility. These discrepancies are probably due to the heterogeneity of the data and research methods [23]. Epidemiologic studies shows that cell phone reduce the sperm parameters [24, 25]. Some studies show that cell phone causes a decrease in sperm motility in the men who own cell phones more than four hours a day for 90 days, compared with men who did not use cell phones [25]. RF-EMW exposures to chronic causes damage the mitochondrial genome and epididymal spermatozoa genome [26]. Dasdag et al., showed that rats exposed to cell phone radiation show reduced diameter of seminiferous tubules [24]. Jelodar and Talebzadeh

showed that electromagnetic waves decrease motility and viability of epididymal sperm [27]. Exposure to radio frequency waves of 900 MHz was reported to decreased antioxidant enzymes activity and increased lipid peroxidation in the testis [28] and eye [29] and vitamin C could improves antioxidant enzyme activity and decreased lipid peroxidation in these tissues [28, 29].

However, various studies in the animals indicate that animals are not suitable models for evaluation effect of oxidative stress in the reproductive system of a man, because testicular size and duration of test animals compared with humans in a real situation is different [18, 30].

Origin of ROS in male reproductive system: Human semen consists of different types of cells such as mature and immature spermatozoa, round cells from different stages of the spermatogenesis process, leukocytes and epithelial cells. Of these, leukocytes and immature spermatozoa are the two main sources of ROS [7, 18, 31]. Gomez et al., showed that droplet cytoplasmic due to a defect in spermatogenesis is as an important source of lipid peroxidation by ROS in spermatozoa [32]. During spermatogenesis, lack the release of spermatozoa from the germinal epithelium and plenty of droplet cytoplasmic cause immature and dysfunctional in spermatozoa [33]. There are two major systems of ROS production in sperm:

1. The NADPH oxidase system at the level of the sperm plasma membrane.
2. The other is NADH-dependent oxido-reductase (diphorase) system at the mitochondrial level.

There is a strong positive correlation between immature spermatozoa and ROS production, which in turn is negatively correlated with sperm quality [34]. Leukocytes particularly neutrophils and macrophages, have been associated with excessive ROS production, and they ultimately cause sperm dysfunction. Leukocytes act either directly by ROS synthesis or indirectly by other neighboring white cells via soluble factors as cytokines [31]. DNA structural damage can be found in spermatozoa from leukocytospermic patients [35]. World Health Organization (WHO) defines leukocytospermia (increased leukocyte infiltration in semen) as the presence of leukocytes in concentrations of $>1\times10^6$ per milliliter of semen [36]. On one side, sperm parameters such as, decreased hyperactivation, and defective sperm function have been attributed to leucocytospermia [37]. Studies conducted in non leukocytospermic samples show that ROS levels were lower in fertile men than in subfertile patient's samples ($p\leq0.01$) [38]. In other study Pasqualotto et al., showed that occurrence of oxidative stress with increasing of leukocytes has a positive correlation [39]. Seminal plasma are contains several nuclear leukocytes (60-50%) and macrophages (30-20%). The prostate gland and the seminal vesicles are the main sources of these leukocytes in human [37]. Leukocytes may be activated in response to various stimuli such as infection and inflammation.

Physiological role of ROS in sperm activity: Pioneering work in the field of reactive oxygen species was conducted by Aitken and his group. According to his research, ROS was exclusively considered toxic to human spermatozoa. Based on these studies, small amounts of ROS are necessary for spermatozoa to acquire fertilizing capabilities [40]. Low levels of ROS are essential for fertilization, acrosome reaction, hyperactivation, motility, and capacitation [41]. Capacitation is a maturation process of spermatozoa that take place in the female genital tract. During this process, the levels of intracellular calcium, ROS, and tyrosine kinase all increase, leading to an increase in cyclic adenosine monophosphate (cAMP). This increase in cAMP facilitates hyperactivation of spermatozoa, a condition in which they are highly motile [42]. However, only capacitated spermatozoa exhibit hyperactivated motility and undergo a physiological acrosome reaction. Studies have shown that co-incubation of spermatozoa with low concentrations of hydrogen peroxide stimulate sperm capacitation, hyperactivation, acrosome reaction, and oocyte fusion [18, 42]. Nitric oxide (NO), a free radical with a relatively long half-life (8s), promotes capacitation. Low concentrations of NO cause a significant increase in capacitation and zona pellucida binding [43]. NO regulates cyclic adenosine monophosphate (cAMP) concentration and induces capacitation of spermatozoa through the action of adenyl cyclase. Finally, NO also plays a role in sperm hyperactivation [44]. Other ROS such as nitric oxide and the superoxide anion also are shown to promote capacitation and the acrosome reaction [45].

Pathological role of ROS in sperm activity: In this section pathological effects of ROS are examined on lipid peroxidation, mobility, damage to DNA, protein damage and apoptosis in spermatozoa. All cellular compounds (carbohydrates, proteins, lipids and nucleic acids) are potential targets of ROS. The extent of ROS-induced damage depends not only on the nature and amount of ROS, but depends the duration of ROS exposure and extracellular factors such as temperature, oxygen tension; the composition of the surrounding environment (e.g., ions, proteins) and ROS scavengers [45].

ROS and lipid peroxidation: Lipids are considered to be the most susceptible macromolecules and are present in sperm plasma membrane in the form of polyunsaturated fatty acids (PUFA), fatty acids that contain more than two carbon-carbon double bonds. Most membrane PUFA contain unconjugated double bonds that are separated by methylene groups. The presence of a double bond adjacent to a methylene group makes the methylene carbon-hydrogen bond weaker, and as a result, the hydrogen is more susceptible to abstraction. When this abstraction has occurred, the radical produced is stabilized by the rearrangement of double bonds. The PUFA rearranges to form a conjugated diene radical that subsequently can be oxidized [42]. The PUFA are necessary for the plasma membrane fluidity and normal physiological function of sperm. Also ion pumps located in the membrane help to maintain concentrations of nutrients and ions (calcium and sodium) in the cell. The normal function of the pump is related to membrane

fluidity. Changes in membrane fluidity impair activity of this pump thereby cause accumulation of ions inside the cell and leads to disruption of the normal functioning of the cell [9]. ROS attack PUPA in the cell membrane leading to a chain of chemical reactions called lipid peroxidation [46]. The reaction occurs in three distinct steps-initiation, propagation and termination. During initiation, the free radicals react with fatty acid chain and releases lipid free radical. This lipid radical further reacts with molecular oxygen to form lipid peroxyl radicals. Peroxyl radicals again react with fatty acid to produce lipid free radical and this reaction is propagated. During termination, the two radicals react with each other, and the process comes to an end [42]. This process of fatty acid breakdown produces hydrocarbon gases (ethane or pentane) and aldehydes. Malondialdehyde (MDA) is one of the byproducts of lipid peroxidation. This byproduct has been used in various biochemical assays to monitor the degree of peroxidative damage sustained by spermatozoa [42].

ROS and sperm motility: Sperm obtains mobility and maturity as passed through epididymis. Maturation process is re-arranged sperm membrane molecules. Uptake and secretory epididymal functions provides a suitable environment for sperm maturation [47]. Epididymal activity is controlled by androgens. Therefore, anything that can damage leydig cells, leads to androgen deficiency in the blood and it decrease in interstitial fluid that can be prevented testicular sperm maturation and infertility [7]. Increased ROS levels have been correlated with decreased sperm motility [42]. However, the exact mechanism through which ROS causes decreased motility is not understood. Thus, many hypotheses have been proposed to explain the link between ROS and decreased motility. One hypothesis shows that H_2O_2 can diffuse across the membranes into the cells and inhibit the activity of some vital enzymes such as glucose-6-phosphate dehydrogenase (G6PD). Another hypothesis involves a series of interrelated events resulting in a decrease in axonemal protein phosphorylation and sperm immobilization, both of which are associated with a reduction in membrane fluidity that is necessary for sperm-oocyte fusion [48]. Alvarez et al, showed that low NADPH and glutathione levels decrease GPx activity. This enzyme removes metabolite of lipid peroxidation and maintains intracellular Ca-homeostasis. Change of concentration Ca affect on sperm motility [35].

ROS and damage to DNA: Two factors protect spermatozoa DNA from oxidative stress, one the characteristic tight packaging of sperm DNA and other the antioxidants defense in seminal plasma [49]. Singlet oxygen and agents that generate oxygen free radicals, such as ionizing radiation, induce numerous lesions in DNA that lead to deletions, mutations and other lethal genetic effects. Pyrimidine bases are most susceptible to oxidative stress as are purines and deoxyribose sugar. Oxidation of the sugar by the hydroxyl radical is the main cause for DNA strand breaks. Oxidative damage can cause base degradation, DNA fragmentation and crosslinking [49]. 8-hydroxy-2-deoxyguanosine (8-OH-2-deoxyguianosine), a common byproduct of DNA oxidation, has been considered a key biomarker of this oxidative DNA damage. When the extent of DNA damage is small, spermatozoa can undergo self-repair, and moreover, the oocyte also is capable of repairing damaged DNA of spermatozoa [50, 51].

ROS and protein damage: Singlet oxygen can to react to five amino acid tryptophan, histidine, tyrosine, methionine and cysteine form peroxides formation. Rate of react singlet oxygen and protein related to number and type of amino acids that have double bond or thiol groups. Tryptophan, histidine, and tyrosine are containing double bonds and they directly react with singlet oxygen. Methionine and cysteine are containing a sulfur atom with four electrons non-pair that react to singlet oxygen. The reaction rate of singlet oxygen and proteins depended to pH, temperature, dielectric of the cellular environment and the 5-amino acid tryptophan, histidine, tyrosine, methionine and cysteine. Many amino acids undergo specific irreversible modifications when a protein is oxidized. The oxidative degradation of protein is enhanced in the presence of metal cofactors that are capable of redox cycling, such as Fe [15].

ROS and apoptosis: Apoptosis is programmed cell death that occurs in a genetically determined fashion. It is initiated by ROS-induced oxidative damage. Too much oxidative stress agents can terminate apoptosis by inactivating the caspase enzyme cascade [41]. High levels of ROS disrupt the integrity of the mitochondrial membrane, which in turn releases cytochrome c. It activates the caspase enzyme cascade and triggers apoptosis. Studies in infertile men have shown that high levels of ROS are correlated positively with apoptosis, which in turn is negatively correlated with conventional semen parameters [52]. Apoptosis in sperm also may be initiated by ROS-independent pathways involving the cell surface protein Fas. Fas is a type I membrane protein that belongs to the tumour necrosis factor-nerve growth factor receptor family and mediates apoptosis. When Fas ligand or agonistic anti-Fas antibody binds to Fas, apoptosis occurs [53].

Antioxidants: The body against damage commence of free radicals has the mechanism as antioxidant defense system, which is divided the two broad groups of enzymatic and non-enzymatic. Antioxidant enzymes system is an important defense mechanism intracellular. Seminal plasma contains three important enzymatic antioxidants-SOD, glutathione peroxidase and catalase. Non-enzymatic antioxidants system is including: vitamin E, A, C and proteins such as albumin, seroloplasmin, haptogobulin, glutathione, ubiquinol, melatonin, L-carnitine and pyruvate. Seminal plasma antioxidants are essential to protect spermatozoa to damage ROS, because spermatozoa contain a low volume of cytoplasm, which makes weak defense against ROS. Human spermatozoa contain mainly enzymatic antioxidants. Of them, SOD plays a prominent role in protecting spermatozoa against lipid peroxidation.

Superoxide dismutase (SOD): Spermatozoa possess primarily enzymatic antioxidants, with SOD being the

most predominant. SOD scavenges both intracellular and extracellular superoxide radical and prevents the lipid peroxidation of plasma membrane [54]. However, it should be conjugated with catalase and GPx to prevent the action of H_2O_2, which promotes the formation of hydroxyl radicals. SOD also prevents hyperactivation and capacitation induced by superoxide radicals. This would suppress the occurrence of these reactions prematurely before ejaculation. SOD can be divided into three different classes according to the catalytic metal present at the active site. SOD1 (CuZn-SOD) is found in the cytosol and contains copper (Cu) and Zn as metal cofactors. SOD2 (Mn-SOD) is present in mitochondria and contains Mn. SOD3 (ECSOD) is present extracellularly. SOD catalyzes the dismutation of superoxide into hydrogen peroxide and oxygen [55].

Glutathione peroxidase (GPX): This enzyme is as an antilipoperoxidative defense in human spermatozoa; it contains selenium at its active center, which is required for its optimal functioning. Four isozymes of GPX present in humans contain selenium in their active center. This explains the importance of selenium in male infertility. The first isozyme GPX1 prevents apoptosis induced by oxidative stress. The second and the third isozymes are found in the gastrointestinal tract and in plasma, respectively. The fourth form acts directly on membrane phospholipids hydroperoxides and detoxifies them. It is present in high levels in the testis [15].

Catalase: Catalase detoxifies both intracellular and extracellular hydrogen peroxide to water and oxygen. In addition catalase activates NO-induced sperm capacitation. Catalase activity has also been detected in human spermatozoa and seminal plasma [15].

Non-enzymatic antioxidants: A variety of non-enzymatic antioxidants are present in the semen, including: vitamin C, vitamin E, glutathione, urate, ubiquinone and bilirubin are present extracellularly in seminal plasma and are considered chain-breaking antioxidants. Other non-enzymatic antioxidants such as vitamin A, transferrin and ceruloplasmin are present in the plasma membrane of the spermatozoa and act as preventive antioxidants [4]. Some oral care, can improve sperm count and sperm motility. Administration of L-carnitine, arginine, zinc, selenium, B_{12} and numerous antioxidants such as coenzyme Q10, glutathione, vitamins E and C affect on sperm [15].

Vitamin E: Vitamin E is a major chain-breaking antioxidant present both in seminal plasma and in the membrane; it reacts directly with free radicals such as the peroxy radical yielding lipid hydroperoxides, which can be removed by phospholipase GSH-Px systems. Vitamin E interrupts the lipid peroxidation process and protect against peroxide radical. It is an important antioxidant in biological membrane which can to neutralize free radicals. It appears that effect of this antioxidant is dose-dependent [56]. It scavenges all three important types of ROS, namely superoxide, H_2O_2, and hydroxyl radicals [41]. Suleiman et al., showed that vitamin E and selenium supplement can lead to decrease in lipid peroxidation and increase sperm motility in asthenozoospermic patients [57].

Vitamin C: Vitamin C is another important chain-breaking antioxidant found intracellular and extracellular. It's contributing up to 65% of the total antioxidant capacity of seminal plasma. It neutralizes hydroxyl, superoxide, and hydrogen peroxide radicals and prevents sperm agglutination [41]. It prevents lipid peroxidation, recycles vitamin E and protects against DNA damage induced by the H_2O_2 radical [15].

Coenzyme Q10: Coenzyme Q is associated with low density lipoproteins (LDL) and it protects lipids against peroxidative damage [58]. It directly reacts with oxygen and reduces superoxide generation. It also reacts with peroxide radicals. It is an energy promoting agent and improves sperm motility [59].

Melatonin: Melatonin can remove and neutralize free radicals, which include: hydroxyl radicals, peroxide and nitrate proxy anions [60]. Melatonin intake in rats protects cells against oxidative damage and reduces oxidative stress from various ways [61]. Moreover, has been shown which it to possess a weak antioxidant activity on human sperm [62]. Melatonin receptors are expressed on various tissues, include: prostate, epithelial cells of epididymal and quantitative level on sperm. Administration of melatonin to human reduces mitochondria of sperm damages by reactive oxygen [63].

L-carnitine: Carnitine (3-hydroxy 4-N-3-methyl amino butyric acid) by Russian scientists at first isolated from bovine muscle. L-carnitine is the biologically active isomer [64]. L-carnitine is derivative of lysine and methionine that is found in meat and dairy. Fritz discover that L-carnitine accelerate lipid metabolism and plays essential role in mitochondrial beta-oxidation of long chain fatty acids for cellular energy production [65]. Carnitine promotes membrane stability. It plays an important role in sperm maturation and development. Like coenzyme Q10, it is an energy promoting agent [66].

Discussion

An imbalance between the production of ROS and the antioxidant defense mechanism is oxidative stress. It plays a vital role in the etiology of many diseases and degenerative processes. Oxidative stress and its role in male infertility have been known. Many free radicals are the result of naturally occurring processes such as oxygen metabolism and inflammation. Environmental stimuli such as ionizing radiation (excessive exposure to solar radiations, cosmic rays, and medical X-rays), environmental toxins, altered atmospheric conditions (e.g. hypoxia and hyperoxia), ozone as well as many infectious conditions greatly enhance ROS production. Lifestyle stressors such as cigarette smoking and excessive alcohol consumption, casting, welding, bakery and driving are also known to affect levels of free radicals and oxidative stress. Oxidative stress affects on male fertility from many ways such as lipid peroxidation, cross-linking and inactivation of proteins, fragmentation of DNA, impair of

sperm motility With professional diagnosis techniques for oxidative stress and antioxidant, we can find appropriate solutions for decreasing of disorders and forecast of increasing in male infertility.

Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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