Role of oxidative stress in Male infertility

Sajjad Zare 1, Yaser Rahmani 1, Tasnim Eghbal Eftekhaari 2, Azita Faramarzi 3, Azin Alavi 4, Soghra Fallahi 2

1. Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
2. Cellular and Molecular Research Center, Hormozgan University of Medical Sciences
3. Student Research Committee, Yazd University of Medical Sciences, Yazd, Iran
4. Hormozgan Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran


Corresponding author: Soghra Fallahi, Hormozgan Fertility and Infertility Research Center, Assisstant professor of Gynecology, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, E-mail: fallahi.leila@gmail.com

Abstract

Oxidative stress is the presence of imbalance between systemic manifestations of reactive oxygen species (ROS) and a biological system’s ability to readily detoxify the reactive intermediates or to repair the resulting damage. It has been suggested that oxidative stress plays a key role in male or female infertility. Reactive oxygen species are oxygen containing molecules that are chemically reactive. Moderate increase in oxidative stress can activate cell growth which results in normal physiologic response. Conversely highly increased oxidative stress causes cell injury (i.e. DNA and protein damage, cell membrane disruption). Nitric Oxide (NO) for instance is a free radical with vasodilating effect, and is one of the important neurotransmitters which are involved in most of the physiologic and pathologic responses. Although vasodilating effect of ROS is therapeutic, but extremely increased ROS can affect structural role of proteins and thus causes varied catabolic enzyme activity, cell signaling and cell structure. Men with increased oxidative stress and DNA destruction have increased risk of infertility which can be definitely diagnosed with sperm motility. ROS and increased oxidative stress causes a decrease in sperm motility and thus increase the probability of infertility.

Keywords: Oxidative Stress, DNA Damage, Infertility, Male.

Introduction:

Oxidative stress can be described as reactive oxygen species (ROS) and biological system’s ability to detoxify the reactive intermediates or to repair the resulting damages (1). Impaired redox state of cells can cause toxic effects by producing peroxides and free radicals resulting in cell damage. Also, to
mention that some ROS act as cellular messengers in cell signaling thus oxidative stress can cause disruptions in normal mechanisms of cellular signaling. Oxidative stress is suggested to be in development In humans, and it is thought to be involved in the development of cancer (2) Parkinson's disease, Alzheimer's disease (3), atherosclerosis, heart failure (4), myocardial infarction (5, 6), fragile X syndrome (7), Sickle Cell Disease (8), lichen planus (9), vitiligo (10), autism (11) and chronic fatigue syndrome (12). It is suggested that oxidative stress plays the main role in male or female fertility (13, 14). Malicious effects of oxidative stress have been well known in number and functionality of sperms (13). On the other hand, these effects on morphology and functionality of ovocytes are still unclear (14). Redox imbalance in women leads to poly cystic ovarian syndrome, endometriosis, and infertility with unknown causes. Spontaneous abortion, recurrent stillbirth and pre-eclampsia may be also associated with oxidative stress (15).

**Reduced oxygen Species**

Production of ROS is the destructive aspect of oxidative stress, which include free radicals and peroxides, and to some less extent superoxide ions which can be converted by redox reactions with transition metals and other redox cycling compounds (including quinones) into more aggressive radical species that can cause extensive cellular damage (16). The major portion of long term effects is inflicted by damage on DNA (17). Short term oxidative stress may protect aging by mitohormesis (18). Depending on the degree of oxidative stress, apoptosis may be triggered, necrosis, even cell death (16). Metabolic processes result in ROS by oxidation of O2 which are free radicals or intermediate products (19). These oxidation-reduction processes involving oxygen and nitrogen occur because of presence of unpaired electrons in outmost layer of the atom and are of significant importance because in pathologic situations or intra-extra cellular interactions cause these (20). Cations such as copper and iron are possibly involved in production of ROS. On the other hand, chelators such as Ethylenediaminetetraacetic acid (EDTA) and transferrin can bond to these cations and prevent further productions of ROS (21). Physiologic processes which use O2 as a base such as oxygenase and electron transferring reactions produce a significant amount of ROS (22). Most often ROS are more produced if electron leaks through inhalation process (19). Other resources of superoxide anions are short endoplasmic electron chains, p450, NADP, NADPH-oxidase and other reducers (19, 20). As mitochondria is the main center of metabolic activity of the cell, dysfunctions of this metabolic center strongly effects the ATP production. Gamete uses the produced ATP for mobility. ROS are produced in mitochondria (23, 24). Increased levels of ROS can affect the mitochondrial function in oocyte which leads to cell division (by oxidative stress). Moderate increase in ROS can accentuate the cell growth and lead to normal physiologic activities and finally severe increase leads to cell injury (i.e. DNA damage, cell membrane damage and protein destruction. super-oxide anion produces H2O2 through superoxide dismutase (SOD), glutathione peroxidase (Gpx) catalyst converts it to H2O. Antioxidants usually control the concentration of ROS, because increased level of SOD and H2O2 may lead to hydroxyl radicals which are more toxic and lead to purine and pyrimidine production. These produced bases break the DNA chain and damage it (25). Apoptosis plays a main role in normal development by homeostasis of tissues and clearing up the
destroyed cells. Apoptosis leads to high level of ROS production, inactivation of electron exchange chain and proteins involved in apoptosis (26). NO is a free radical with vasodilating effect and an important neurotransmitter which is involved in most of physiologic and pathologic processes. Though the vasodilating effect is mostly therapeutic, but increased levels of ROS could modify the protein functionality and change the activity of catabolic enzymes and cell signaling (19, 22). Nitric oxide interacts with superoxide ions and produce ROS (27).

**Oxidative Stress and Male fertility**

Nearly half of infertilities are due to male genital pathologies which may be acquired or congenital. Both types of pathologies can damage spermatogenesis and fertility (28, 29). It has been well known that oxidative stress is one of the most frequent causes of male infertility. Probability of infertility is high in men with high levels of oxidative stress and DNA damage (13) which can be determined by sperm motility which is reduced by ROS, so role of the oxidative stress in male infertility is more pronounced. Low level of ROS is necessary for normal function of spermatozoa, which is mainly produced by immature spermatozoa and leukocytes (30). Furthermore, acrosomal reactions, motility, permeability of spermatozoa are related to ROS (13, 14), which is mainly produced by lipid peroxidation and destroys spermatozoid plasma membrane. Unviable or abnormal spermatozoa can increase the levels of ROS which inhibits maturation of spermatozoa or even apoptosis (14). H2O2 and anion superoxides are well known for main cause of impaired function of spermatozoa (13). High levels of ROS in semen may cause abnormal and dysmorphic spermatozoa, thus, effecting their capability for fertilization (31).

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**References:**


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