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Influence of oxidative stress on sperm quality in animal

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Abstract

Oxidative stress has negatively influence on semen quality in human and animals. Reactive oxygen species (ROS) generated by oxidants and antioxidants imbalance lead to DNA including DNA fragmentation, deletions and mutations as well as base degradation, protein and lipids damage in sperm due to poor antioxidant system and high content of polyunsaturated fatty acids (PUFA). In addition, excess ROS can adversely affect plasma membrane fluidity as well as permeation leading to apoptosis. Furthermore, ROS resulted in declined sperm mobility, viability and sperm-oocyte fusion due to a reduction in axonemal protein phosphorylation. In general, oxidative stress can impair the sperm quality affecting reproductive performance.

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Introduction

Fertility in human and animal was affected by some causes in particular oxidative stress. Although reactive oxygen species have been shown to produce by different metabolic and physiological processes, imbalance between the production of reactive oxygen species and the inherent antioxidant capacity leads to oxidative stress (Sikka *et al.,* 1995; Sharma *et al.*, 1996). Heat stress is one of the environmental factors generating free radicals resulting in oxidative stress (Shiraishi *et al.*, 2010). Spermatozoa membrane of bovine (Beconi *et al.*, 1991) and rams (Jones and Mann, 1977) contains polyunsaturated fatty acids resulting in more susceptible to ROS that leads to declined sperm membrane fluidity.

Reactive Oxygen Species

ROS are free radicals derived from the metabolism of oxygen in all aerobic organisms. Since ROS have high reactivity in the body, they are the most important among free radicals in biological systems (Sies, 1997; Therond, 2006) thereby, ROS not only can influence many physiological processes, but also they can affect entire organism (De Lamirande and Gagnon, 1992; Sharma *et al.*, 2001). The damage intensity induced by ROS relays on not only the type and amount of ROS, but also on the duration of ROS exposure (Sikka, 2001). Depends on the nature of free radicals and its molecular target, the mechanisms of free radicals produced by oxidative stress are varied (Therond, 2006). ROS can be able to injury DNA, proteins as well as lipids within cells via the membrane permeation (Henkel, 2005).

ROS sources in sperm

Semen contains various types of sperm cells in different stages of spermatogenic process especially mature and immature spermatozoa, leukocytes as well as epithelial cells. The main sources of ROS in male reproductive system are immature spermatozoa and leukocytes in particular neutrophils and macrophages (Garrido *et al.*, 2004) causing sperm dysfunction (Pasqualotto *et al.*, 2000; Sharma *et al.*, 2001). ROS generation in immature spermatozoa is as a consequence of a defect take places during spermiogenesis causing retention of cytoplasmic droplets (Gomez *et al.*, 1996) that negatively affects semen quality (Gil-Guzman *et al.*, 2001). There are two systems involved in ROS production in sperm. One of them is the NADPH oxidase system in the sperm plasma membrane and another system is NADH-dependent oxido-reductase in mitochondrial level (Gavella and Lipovac, 1992).

Damage to sperm

ROS induces capacitation and acrosome reaction of sperm in bovine (De Lamirande *et al.*, 1998; Goncalves *et al.*, 2010) but excessive ROS is detrimental to sperm motility (Balercia *et al.*, 2004) due to hydroxyl radical formation resulting in oxidation of sperm membrane lipids and thiol proteins (Donnelly *et al.*, 1997). Since the antioxidant defense in sperm cell is minimal, sperm cells are susceptible to oxidative stress (Irvine, 1996). So, damage caused by excessive ROS in spermatozoa did not repair due to the lack of cytoplasmic enzymes required to achieve the repair (Donnelly *et al.*, 1999; Maneesh and Jayalekshmi, 2006). The negative influence of ROS on sperm function has been attributed to rapid loss of intracellular ATP, axoneme damage and morphological defects of mitochondria negatively affecting sperm capacitation and acrosomal reaction (Sikka, 1996). Moreover, excessive ROS have been shown to induce sperm nuclear DNA damage (Moustafa *et al.*, 2004) sperm mitochondrial mutation (Yakes and Van Houten, 1997) as well as loss of plasma membrane fluidity (Alvarez and Storey, 1995) due to high turnover rate and very basic repair. Additionally, ROS production leads to a decline in sperm motility (Baumber *et al.*, 2001; Ball and Vo, 2002; Keskes-Ammar *et al.*, 2003) viability (Baiardi *et al.*, 1997) as well as sperm-oocyte fusion (Blondin *et al.*, 1997 which consequently decrease reproductive outcomes (Agarwal *et al.*, 2006). The relationship between ROS and motility reduction may be because of a cascade of events such as disturbance of energy metabolism resulting in a decline in axonemal protein phosphorylation and sperm immobility that are correlated with a decrease in membrane fluidity required for sperm-oocyte fusion (De Lamirande and

Gagnon, 1995; Storey, 1997). Similarly, Balic *et al.* (2012) showed that heat stress was shown to decrease sperm quality in bull. Impairment in spermatogenesis and a diminished in testosterone (Gwazdauskas, 1984) as a result of high temperature can negatively affect semen quality in goats (Murugaiyah, 1992). Furthermore, high environmental temperature lead to elevated testicular temperature and thereby declined semen quality (Waites, 1970). In addition to high temperature, Frozen bull semen has been employed in artificial insemination. However, during freezing and thawing processes reactive oxygen substrates are generated that impair sperm motility, viability and function (Aitken *et al.*, 1998; White, 1993).

Damage to polyunsaturated fatty acids

H2O2 diffuses across the cell membrane to the cells and inhibits the enzyme activity such as G6DPH used as a source of electrons by spermatozoa to fuel the generation of ROS (Aitken *et al.*, 1997). In addition, a reduction in G6PDH results in a decline in NADPH availability and an accompanying accumulation of oxidized glutathione. These changes lead to a reduction in antioxidant defenses of spermatozoa causing the membrane phospholipids peroxidation (Griveau *et al.*, 1995). The chemical reaction between ROS and PUFA in the cell membrane known as lipid peroxidation (Shekarri *et al.*, 1995) includes three steps such as initiation, propagation and termination. At initiation step, polyunsaturated fatty acids of cell membrane react with free radicals and release lipid free radical. Then, this lipid free radical reacts with molecular oxygen to form peroxyl radical reacting with fatty acid again to produce lipid free radicals during propagation step. Finally, these two radicals react with each other until the end of process (termination) (Halliwell *et al.*, 1985).

Damage to protein

Amino acids containing sulphur and tiol groups are sensitive to oxidative stress. As, activated oxygen separates H atom from cysteine residues leading to form a thiyl radical that cross link to a second thiyl radical to make disulphide bridges (Davies *et al.*, 1987). This leads to cleavage of protein chain.

Damage to DNA

Activated oxygen generates oxygen free radicals stimulating many lesions in DNA such as deletions and mutations and DNA fragmentation (Tominaga *et al.*, 2004). Purines and pyrimydine bases as well as deoxyribose sugar are sensitive to ROS leading to base degradation (Aitken and Krausz, 2001). Also, spermatozoa are not able to repair DNA damage due to lack of functional repair enzymes (Drost and Lee, 1995).

Apoptosis induction

Oxidative stress is one of the main causes of germ cell apoptosis (Shiraishi *et al.*, 2010). High levels of ROS disturb the mitochondrial membrane integrity and induce dysfunctional mitochondria (Evenson *et al.*, 1982) consequently, releasing cytochrome C and caspase enzyme cascade resulting in apoptosis that is negatively associated with semen quality (Moustafa *et al.*, 2004).

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