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Impact of Oxidative Stress on Male Infertility: A Review

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Summary

In recent years, the issue of male infertility has gained significant attention due to psychosocial effects caused on couples. The aim of this review is to identify the impact of oxidative stress on male infertility. The comprehensive literature review focused on the role of reactive oxygen species (ROS) in the testis, its effects on sperm motility, longevity, and fertilizing capacity, as well as the relationship between reactive oxygen species and male infertility. This study highlights the critical role of ROS in sperm function. From the content, it can therefore be concluded that increased ROS along with decreased antioxidant defense result in redox imbalance, reduced sperm motility and sperm DNA damage and in turn male infertility. ROS can induce sperm DNA damage that in turn may cause childhood diseases such as autosomal dominant disorders, neuropsychiatric disorders, and childhood cancers like retinoblastoma. Additionally, the review discussed the physiological and pathological roles of reactive oxygen species in male fertility. Albeit, there is also provisional insights into the prevalence of male infertility worldwide, with a focus on the African region, where male factor infertility was found to account for a significant percentage of infertility cases. Lifestyle changes, including the inclusion of antioxidant vitamins and minerals in treatment regimens to prevent oxidative DNA damage were recommended. Furthermore, healthy lifestyle choices and the avoidance of tobacco smoking, marijuana, and alcohol use may play central role in preserving male fertility.

Keywords: Male Infertility, Oxidative Stress, Reactive Oxygen Species, Antioxidants.

Introduction

Male infertility is defined as the inability of a male to accomplish pregnancy with a fertile female after 12 months of regular unprotected sexual intercourse (Younes *et al.,* 2016). Previously the problem of infertility in couples was ascribed to the female alone and hence bears the majority of the psychosocial effects especially in Africa. This in most cases is due to cultural belief and insufficient knowledge and misunderstanding. Male infertility is well-thought-out when identifiable female causes of infertility are excluded and semen quantity and quality fail to fulfill WHO criteria (Cao *et al.,* 2017).

Researchers had revealed that male factors account for 40-50% of infertility in human. Male infertility is commonly due to deficiencies in the semen and semen quality is used as a surrogate measure of male fertility. It is estimated that 60% of married couples having regular unprotected sexual intercourse, achieve pregnancy after 6 months of co-habitation, 90% achieve pregnancy by 12 months and 95% between 18-24 months (Ahmed *et al.,* 2010). In more than 50% of male infertility cases, the causes remain unknown, and the infertility is thus classified as idiopathic. Idiopathic infertility affects a high percentage of infertile men who cannot be effectively treated by the treatment modalities available (Ahmed *et al.,* 2010).

Male-factor infertility is a notable health issue all over the world including Africa and other developing nations. The prevalent rate differs

between and within countries. For instance, in the United Kingdom and the United States of America, it is estimated to be 6% and 10% respectively. In Denmark, it is estimated to be in the region of 15.7% (Abarikwu, 2018).

The prevalence of infertility in Sub-Sahara Africa ranges from 20% to 40%. Although, in Africa due to its unique socio-cultural setting the focus has been on the female but fertility problems are shared by both male and female genders. Male factor represents 40–50% of all infertility in Nigeria although it varies from one region to another, and the causes also vary from place to place.

A study in the mid-western Nigeria showed that about 50% of the 780 couples evaluated were observed to have varied causes of infertility (Uadia and Emokpae, 2015). In the southwest, male factor was reported to be responsible for 42.4% infertility cases, while in Maiduguri, North-Eastern Nigeria, infertility is the reason for about 40% of all gynecological consultations. In Kano, 40.8% prevalence was reported, 46% in Ile-Ife and 55–93% was observed in Enugu, Eastern Nigeria for male factor infertility (Uadia and Emokpae, 2015).

Oxidative stress (OS) is defined as an imbalance between the production of reactive oxygen species (ROS) and the scavenging capacity of available antioxidants resulting in redox paradox. Sperm cells are vulnerable to ROS because of the abundance of polyunsaturated fatty acids in their plasma membrane and cytoplasm and limited antioxidant capacity and DNA repair system. Significant levels of ROS are required for maturation of spermatozoa, acrosome reaction, capacitation, hyperactivation, and sperm-oocyte fusion. Excessive ROS production, however, overwhelms the neutralizing capability of antioxidants (enzymatic and non-enzymatic) in seminal plasma. ROS are formed as natural byproducts of oxygen during metabolism and have important roles in cell signaling and homeostasis. Sources of ROS can be endogenous or exogenous and body antioxidant defense mechanism aims to neutralize the harmful effects of these pro-oxidants molecules (Huang *et at.,* 2018).

Increased ROS along with decreased antioxidant defense result in redox imbalance, reduced sperm motility and sperm DNA damage. Spermatozoa are extremely prone to the deleterious effects of ROS due to the large amounts of unsaturated fatty acids found in their cell membranes. Reactive oxygen species promote peroxidation of lipids, resulting in intracellular oxidative burden. The sequence of events involves lipid peroxidation, loss of membrane integrity with increased permeability, reduced sperm motility, structural DNA damage, and apoptosis.

Several intrinsic and extrinsic factors have been associated with increased OS in the male reproductive system (Huang *et at.,* 2018).

The aim of this review is to ascertain whether or not OS plays a significant role in male infertility and the objectives are to review the role of OS and ROS in male infertility, functions of ROS, antioxidants in male infertility, relationship between OS, ROS in both spermatozoa and sperm DNA functions. This is a systematic review conducted by first of all using PubMed, Google scholar, Researchgate with the following headings: “male infertility”, “oxidative stress”, spermatogenesis”, and “oxidative DNA damage” to select the articles that are in tandem with the review objectives from over a one hundred down to just about 60. Using meta-analysis to resolve the protocol, research questions and idea validation.

Aim and Scope

The aim of this paper is to investigate the impact of oxidative stress on male infertility. The review aims to explore the role oxidative stress in male fertility by examining its effects in the sperm, its effects on sperm motility and fertilizing capacity, physiological and pathological role of ROS on sperm and the potential relationship between ROS and male infertility. The paper seeks to provide a comprehensive understanding of the functions of ROS in male reproductive health and to explore the potential implications of ROS in contributing to male infertility.

The scope of the paper includes a thorough review of literature on OS and its role in male

infertility, encompassing its impact on sperm function, its association with idiopathic infertility, and the prevalence of male infertility in different regions, particularly in African countries. Additionally, the paper aims to shed light on the potential environmental and physiological factors contributing to male factor infertility and emphasizes the need for further studies to understand the multifactorial implications of ROS in male infertility. Overall, the paper aims to contribute to the existing body of knowledge on male infertility, with a particular focus on the role of OS and to provide insights that may guide future research and potential therapeutic interventions.

This is a systematic review conducted by first of all using PubMed, Google scholar, researchgate with the following headings; "male infertility", "oxidative stress", reactive oxygen species", to select the articles that are in tandem with the review objectives from over a one hundred down to just about 60. Using meta-analysis to resolve the protocol, research questions and idea validation.

Why Are the Results of This Paper Important?

The results of this study are important for several reasons:

1. Understanding Male Infertility: The study sheds light on the complex factors contributing to male infertility, including the role of oxidative stress. By highlighting the impact of ROS on sperm motility, longevity, and fertilizing capacity, the study provides valuable insights into the environmental and physical factors underlying male infertility.
2. Clinical and Research Implications: The findings have implications for clinical practice, as they emphasize the need for comprehensive biochemical evaluations and personalized treatment modalities such as antioxidant vitamins and mineral to address male factor infertility. Furthermore, the study underscores the importance of further research to elucidate the multifactorial implications of ROS in male infertility.
3. Public Health Significance: Male infertility is a significant public health issue globally, and the study's findings contribute to raising awareness about the prevalence of male factor infertility, particularly in African countries. By recognizing the high percentage of idiopathic infertility cases and the varying prevalence rates in different regions, the study underscores the importance of addressing male infertility as a crucial reproductive health concern.
4. Lifestyle and Environmental Counseling: The study also highlights the importance of promoting healthy lifestyle choices and the avoidance of factors such as tobacco smoking, marijuana, and alcohol use, which may contribute to sperm DNA damage and male factor infertility. This emphasizes the need for counseling and education to promote male reproductive health and fertility.

In summary, the results of this study are important as they contribute to advancing the understanding of male infertility, highlighting the role of oxidative stress, and emphasizing the need for comprehensive approaches to address male factor infertility and promote reproductive health. The findings have implications for clinical practice, research, and public health interventions aimed at addressing male infertility globally.

Role of Oxidative Stress in Male Infertility

Oxidative Stress

Oxidative stress can be defined as an imbalance between the production of reactive oxygen species (ROS) and the ability of antioxidant to scavenge free radicals resulting in redox paradox. Sperm cells are susceptible to ROS because of the abundance of polyunsaturated fatty acids in their plasma membrane and cytoplasm and limited antioxidant capacity and DNA repair system. Significant levels of ROS are needed for maturation of spermatozoa, acrosome reaction, capacitation, hyper activation, and sperm-oocyte fusion. Excessive ROS production, however, overwhelms the neutralizing ability of antioxidants (enzymatic and non-enzymatic) in the seminal plasma. ROS are byproducts of oxygen during metabolism and play significant roles in cell signaling and homeostasis. ROS can be sourced either endogenous or exogenous and body antioxidant defense mechanism works to neutralize the harmful effects of these pro-oxidants molecules (Huang *et at.,* 2018).

Increased level of ROS along with decreased antioxidant defense result in redox imbalance, reduced sperm motility and sperm DNA damage. Spermatozoa are highly susceptible to the deleterious effects of ROS due to the large amounts of unsaturated fatty acids found in their cell membranes. Reactive oxygen species contribute to lipid peroxidation which result in intracellular oxidative burden. The sequence of events involves lipid peroxidation, loss of membrane integrity with increased permeability, reduced sperm motility, structural DNA damage, and apoptosis. Many intrinsic and extrinsic factors have been associated with increased OS in the male reproductive system (Huang *et at.,* 2018).

Sources of Reactive Oxygen Species

Intrinsic sources

ROS are byproducts of redox reactions in aerobic metabolism. In mitochondria, these reactions require nicotinamide adenine dinucleotide (NADH) as an electron donor and acceptor in the electron transport chain, which allows synthesis of adenosine triphosphate (ATP) Seminal fluid ROS can also originate from cytoplasmic glucose-6-phosphate dehydrogenase. Varicocele, the most common cause of male infertility, has been associated with the increased oxidative burden and ROS-induced sperm DNA damage; as well as with increased scrotal temperature (Huang *et at.,* 2018).

Extrinsic sources

Extrinsic factors such as smoking, alcohol intake, and exposure to radiation and industrial heavy metals have been associated with increased ROS and male infertility. Smoking has been associated with reduced sperm concentration, motility, and altered morphology. Smoking also causes a chronic inflammatory response which recruits leukocytes to the genital tract and causes a significant increase in seminal ROS levels, as well as increased sperm DNA damage. It has been documented that, inhalation of incense Bakhour is associated with increased ROS (Rimi *et at.,* 2022).

Seminal fluid abnormalities have been associated with excessive alcohol intake, including decreased spermatogenesis, abnormal sperm morphology, decreased seminal fluid volume, low levels of testosterone, and increased OS. Indeed, alcohol misuse results in increased production of acetaldehyde which promotes the generation of ROS due to its interactions with proteins and lipids (Huang *et at.,* 2018).

Altered sperm function and increased DNA damage have been related with industrial exposure to heavy metals such as lead, cadmium, iron, and copper, as well as exposure to phthalates, pesticides, and pollution. Malignancies are another important extrinsic source of ROS, along with the accompanying exposure to radiation and chemotherapy. Men treated with chemotherapy medications such as cisplatin, doxorubicin, or cyclophosphamide have been linked to increased OS. Radiotherapy has also been associated with increased OS, while low-level radiation therapy appears to modulate NADH oxidase activity promoting sperm death (Adewoyin *et at.,* 2017).

The Foundation of the Link Between ROS and Human Sperm

The earliest reports of the presence of ROS in spermatozoa comes from the laboratory of John MacLeod (Izabel *et at.,* 2019). In 1943, MacLeod decided to test the existing knowledge that the metabolism of human spermatozoa was completely dependent on glycolysis and that oxygen consumption was “being Antioxidants" of such small magnitude that it could not properly be interpreted as true respiration” (Izabel *et at.,* 2019). Therefore, to investigate the existence of mitochondrial activity, MacLeod used methylene blue as a redox sensor and observed that human sperm can reduce either glucose or succinate. In the case of succinate, the reduction of methylene blue is likely a consequence of the production of FADH2 in the presence of succinic dehydrogenase (or electron transport chain Complex II), an enzyme of the mitochondrial respiratory complex that oxidizes succinate into fumarate. In addition, the oxidation of p-phenylenediamine by sperm cells was also observed in MacLeod's experiments, indicating the presence of cytochrome b, cytochrome c and cytochrome c oxidase. As such, this was the first evidence that sperm cells have indeed mitochondrial activity, or as better phrased by MacLeod, that they present an

"active cytochrome" system. From these first observations, MacLeod further examined the impact of high oxygen levels on sperm cells (Adewoyin *et at.,* 2017).

For this purpose, he incubated human sperm in a 95% oxygen environment at 38 ◦C. Under these conditions, a drastic reduction in sperm motility occurred over time, which was completely prevented when the experiment was repeated in the presence of catalase, an enzyme that converts hydrogen peroxide (H2O2) into water and oxygen. The notion here is that when forced to use oxidative phosphorylation, a toxic by-product is created in the form of H2O2. In fact, as revealed subsequently by others researchers, up to 0.2% of the oxygen used during mitochondrial respiration undergoes incomplete reduction, forming superoxide anion (O2-), which quickly reacts (dismutation) producing H2O2. The latter can be fully reduced to water or may form oxygen radicals, such as the hydroxyl radical, that will subsequently be detrimental to sperm. Thus, the fundamental concept that ROS can negatively affect spermatozoa function was laid. MacLeod reasoned that spermatozoon were the major source of ROS, but subsequent reports showed that leukocytes within sperm samples, a common feature among human ejaculates, were also involved in ROS production. Leukocytes contain an NADPH-oxidase (NOX) that catalysis the production of O2 - by the oxidation of NAD(P)H. The O2 - is then used to generate a wide range of reactive oxidants, with the main purpose of killing invading microorganisms. However, this enzyme is so active that spermatozoa can be immobilized by as little as 6 × 105 stimulated leukocytes. Motivated by the observations on the NOX activity of leukocytes, Whittington and Ford decided to reinvestigate the impact of high oxygen levels (i.e., 95% O2 and 5% CO2 versus 95% N2 and 5% CO2) using MacLeod's methodology. However, this time, sperm samples were freed of leukocytes following purification by Dynabeads. Of interest, the leukocyte-free sperm populations were less affected by the high oxygen tensions and remained motile for over 6 h, showing only a reduction in curvilinear velocity. This finding clearly raises the question of whether sperm produce enough ROS to cause any significant cell damage (Izabel *et at.,* 2019).

Physiological Role of Reactive Oxygen Species in Male Fertility

The development of male germ cells yields significant amounts of ROS which constitutes a principal source of OS in spermatozoa. Reactive oxygen species modulate sperm chromatin condensation by regulating the number of germ cells and inducing apoptosis or proliferation of spermatozoa. ROS are also involved in the processes of capacitation, acrosome reaction, mitochondrial stability, and sperm motility in mature sperm. ROS can function as messengers, by modulating the NADPH oxidase enzyme complex in the cell membrane, and intervening in the respiratory chain within mitochondria. In spermatozoa, superoxide anion metabolism is regulated by the NADH oxidoreductase enzyme, which works in close conjunction with the mitochondrial respiratory chain and xanthine oxidase found in sperm and seminal plasma. Immature spermatozoa with cytoplasmic residues show increased production of ROS when compared to sperm with normal morphology (Olatunbosun *et at.,* 2018).

Another source of ROS are seminal leukocytes, producing 1000 times more of these molecules than sperm cells under physiological conditions. This is because seminal leukocytes represent the first line of defense against offending infectious agents, using primarily oxidative and inflammatory mechanisms. However, this can become a double-edged sword, as an imbalance between oxidants and antioxidants could result in cellular injury. Indeed, ROS generated to counteract infectious agents can also damage host cells, which can result in the disintegration of the cell membrane or sperm DNA damage (Izabel *et at.,* 2019).

Pathological Effects of Reactive Oxygen Species on Male Fertility

The justification behind the use of antioxidants for the treatment of male infertility relies on excessive levels of ROS and free radicals cause altered sperm function and sperm DNA damage. In a study by Desai *et al.* (2018) found that sperm characteristics were significantly lower in infertile men with high levels of ROS in semen as assessed through chemiluminescence. Reactive oxygen species modify DNA integrity in the

sperm nucleus by inducing breakage of DNA strands, base modifications, and chromatin cross-linking. Moreover, spermatozoa have limited defense mechanisms against ROS-induced DNA damage (Dutta *et at.,* 2019).

Human ejaculate contains sperm cells with various degrees of maturity, along with leukocytes, epithelial cells and round cells from different stages of spermatogenesis. Among these cells, peroxidase-positive leukocytes and immature spermatozoa produce significant number of free radicals. Spermatozoa are particularly vulnerable to oxidative damage due to the presence of abundant polyunsaturated fatty acids in their plasma membrane. These fatty acids are significant as they provide membrane fluidity, a key feature for several membrane fusion events such as acrosome reaction and sperm-egg interactions. However, these unsaturated fatty acids render them susceptible to free radical attacks and ongoing lipid peroxidation (Izabel *et at.,* 2019).

Nonetheless, in around 85% of cases, the sperm genome is protected from free radical damage as it is bound to central nucleoprotamines. Deficient protamination has been observed in infertile men, representing yet another source of ROS-induced DNA damage which is compounded by the limited capacity for sperm DNA repair seen during spermatogenesis. ROS-mediate disruption of mitochondrial membranes leads to caspase activation, resulting in apoptosis. The apoptotic pathways involve cytochrome c release, which augments the levels of ROS, DNA damage, and apoptosis (Izabel *et at.,* 2019).

DNA bases are also susceptible to OS-induced damage with base modifications, strand-breaks, and chromatin cross-linking. Indeed, OS and apoptosis are key events involved in causing DNA damage in the germ line. The major role of ROS in the etiology of sperm DNA damage in infertile men has been corroborated in multiple studies. Spermatozoa carry a complete haploid genome to the ovum to form a new individual. Condensation of the nuclear material in the sperm nucleus is essential for this process to be successful. This condensation is promoted by the unique process of protamination, which involves the replacement of histones by positively charged protamines, which in turn form tight toroidal complexes. This is essential, as chromatin organization is necessary for fertilization and early embryonic development. However, normal sperm appears to possess varying degrees of fragmented DNA; although, infertile men appear to have larger proportions of fragmented DNA. Both extrinsic and intrinsic factors are involved in the pathogenesis of fragmented DNA. The latter include poor chromatin structure and limited repair capacity. Intrinsic factors include abortive apoptosis and defective maturation. Accumulating evidence suggests extrinsic factors are responsible for the increased DNA fragmentation found in the epididymis and ejaculated sperm in comparison to testicular sperm. Recent research posits OS as another extrinsic cause of sperm DNA fragmentation (SDF), as ROS can exceed the limited antioxidant mechanisms of sperm and damage polyunsaturated fatty acids in membranes, resulting in SDF (Dutta *et at.,* 2019).

Sperm DNA Damage Induced by Reactive Oxygen Species

Although ROS seem to play a physiological role in the acrosome reaction, normal sperm function, activation, motility, and capacitation; their potentially deleterious effects cannot be overlooked. Spermatozoa are especially vulnerable to ROS as they contain large amounts of polyunsaturated fatty acids in their plasma membrane and cytoplasm (Barati *et at.,* 2019).

OS could induce a rapid loss of intracellular ATP, resulting in axonemal damage with decreased sperm viability and mobility and increased mid-piece structural defects, with lethal effects on sperm capacitation and the acrosome reaction. Lipid peroxidation of the sperm membrane is a key mediator of ROS-induced sperm damage, leading to infertility (Darbandi *et at.,* 2018). Hydrogen peroxide is the principal ROS in human spermatozoa, while excessive production of ROS by abnormal spermatozoa or leukocytes appears to be associated with male infertility. Moderately elevated concentrations of hydrogen peroxide cause sperm immobilization, mostly through depletion of intracellular ATP and reduced phosphorylation of axonemal proteins, with no impact on viability. In contrast, higher

concentrations of hydrogen peroxide promote lipid peroxidation and cell death (Takeshima *et at.,* 2021b).

In a study by Pasqualotto *et al.* (2016) the levels of antioxidants in seminal plasma from infertile men were significantly lower than in fertile controls, and the levels of ROS produced by spermatozoa were negatively correlated with sperm quality. In semen of infertile men, pathological levels of ROS are likely to be the result of increased ROS production and impaired antioxidant capacity (Takeshima *et at.,* 2021b). Exogenous or endogenous sources of ROS can induce sperm DNA damage that in turn may cause childhood diseases such as autosomal dominant disorders, neuropsychiatric disorders, and childhood cancers like retinoblastoma. OS tends to target telomeres, which are key genome protectors. Telomeres erode faster when exposed to OS, resulting in telomere dysfunction, chromosome instability, and apoptosis; all of which have been related to aging and carcinogenesis. This form of DNA damage could be particularly important in recurrent spontaneous abortion (RSA). Various paternal factors have been linked to RSA, including ROS-induced sperm DNA damage. In a study on 25 couples with idiopathic RSA and 25 proven fertile controls, ROS levels and DNA damage were significantly higher among the men in the RSA group (Barati *et at.,* 2020).

Mitochondrial dysfunction and OS have been associated with cancer, cellular senescence, apoptosis and aging; as well as with isolated cases of asthenozoospermia. Antioxidants may prevent telomere loss and promote genomic stability in cells with mitochondrial dysfunction, corroborating the association with OS. Furthermore, nuclear transfer protected the genomes from telomere dysfunction and reconstitution of the mitochondria, thereby promoting cell survival (Takeshima *et at.,* 2021b). Lipid peroxidation cascade contributes to the production of free radicals and induces the production of lipid aldehydes such as acrolein, 4-hydorxynonenal (4-HNE), and malondialdehyde (MDA). These have been linked with OS and damage to nuclear and mitochondrial DNA, with shorter telomeres, formation of the base product 8-hydroxy-deoxyguanine (8-OHdG), and fragmentation of mitochondrial DNA. They can also affect sperm plasma membranes, thus affecting their motility and ability to fuse with the oocyte. Production of 8-OHdG facilitates DNA damage by limiting the repairing capacity of spermatozoa. Because fragmented DNA carries a high mutagenic potential, the oocyte may skip the base-excision repair and correction of 8-OHdG-associated changes, resulting in genomic hypermutability and instability, as well as infertility. A high incidence of genetic aberrations in embryos have been attributed to ROS-induced OS in the male germ line; in association with conditions such as childhood cancers, neuropsychiatric disorders such as autism and schizophrenia, and dominant gene mutations such as Apert syndrome and achondroplasia (Takeshima *et at.,* 2021a).

Antioxidant Therapy in Male Infertility

The rationale for oral antioxidant therapy is because seminal OS is due to increased ROS production and/or decreased levels of seminal antioxidants. The different oral antioxidants available belong to the exogenous antioxidant category and they include Vitamin C, Vitamin E, coenzyme Q10, N-acetyl cysteine, carnitines, trace elements such as zinc, selenium, pentoxifylline, and a combination of these oral antioxidants. Numerous studies have been conducted to assess the effectiveness of oral antioxidant supplementation for the treatment of male infertility. Most of the studies showed an improvement in one or more of seminal fluid parameters, whereas some studies reported no positive effect (Adeoye *et at.,* 2018).

Glutathione and male infertility

A glutathione deficiency can lead to instability of the sperm's mid piece resulting in defective motility. It protects the plasma membrane from lipid peroxidation, scavenges superoxide and prevents oxygen formation. In a study consisting of infertile men with unilateral varicocele or genital tract inflammation, glutathione led to significant improvement in sperm quality (Lenzi *et at.,* 2004). The glutathione/reductase system forms an excellent protection against the lipid peroxidation of the spermatozoa plasma membrane. It scavenges lipid peroxides, thereby

arresting the progressive chain reaction of lipid peroxidation. It also scavenges hydrogen peroxide (H2O2), which is responsible for lipid peroxidation onset. Glutathione reductase stimulates the reduction of glutathione disulphide, to reduced glutathione, thereby recycling it (Adeoye *et at.,* 2018).

Management strategies

With recent advancement in technology and methods, there are numerous treatment options for male infertility. Depending on the cause of infertility, treatments may include:

Medication: Hormone therapy to increase the number of sperm production.

Lifestyle changes; Maintaining a healthy body weight, quitting smoking, stopping drinking of alcohol and avoiding the use of marijuana are potential lifestyle changes that can be used to manage male infertility (Okonofua and Ivanov, 2015).

Surgery: Vasectomy reversal; This is a common outpatient surgical procedure. The surgeon reconnects the vas deferens which is the tube in the scrotum through which the sperm passes. Viewing the vas deferens through a high-power surgical microscope, the surgeon will carefully sew the ends back together (Olooto, 2012).

Vasoepididymostomy: Blockages in the vas deferens are repaired with a similar technique of vasectomy reversal. The vas deferens is surgically split, the blockage is removed and the ends of the tube are reconnected (Okonofua and Ivanov, 2015).

Sperm retrieval: In some severe cases, a biopsy of the testicle is required

Intracytoplasmic sperm injection: Artificial techniques of reproduction have advanced to the point where a single sperm can be physically injected into an egg. This procedure, called intracytoplasmic sperm injection (ICSI) has dramatically changed the treatment available for even the most severe male factor infertility. Because of this technique, 90% of all infertile males have the potential to conceive their own genetic child (Fainberg and Kashanian, 2019).

Invitro fertilization; Couples dealing with male infertility, invitro fertilization (IVF) is the treatment of choice. During the IVF process, the ovaries are stimulated with injectable fertility medications to cause multiple eggs to mature. When the eggs are ready, they are collected in a minor procedure (Fainberg and Kashanian, 2019). Fertilization is accomplished by exposing the eggs to sperm in a culture dish, or by directly injecting a single sperm into each mature egg, a process called intracytoplasmic sperm injection. After fertilization, embryo development is monitored over the next three to five days, and two to three embryos are then placed into the uterus by way of a small catheter inserted through the cervix (Olooto, 2012).

Conclusion

In conclusion, oxidative stress plays a pivotal role in male infertility by impairing sperm function and viability through various mechanisms. Understanding the underlying pathways and implementing targeted therapeutic approaches are crucial steps toward addressing this multifaceted issue and improving reproductive outcomes for affected individuals.

Recommendations

1. In the diagnosis of male infertility, it is recommended that reactive oxygen species level should be evaluated to assess the oxidative stress.
2. Antioxidant's vitamins and mineral should be included as part of treatment regimen in order to prevent oxidative DNA damage.
3. Healthy lifestyle is recommended. Individuals should avoid tobacco smoking, marijuana and alcohol use as it damages sperm DNA.

Conflict of Interest: The authors have no conflict of interest to declare.

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