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INVESTIGATE THE IMPACT OF VITAMIN C ON SEX HORMONE LEVELS IN MALE RATS EXPOSED TO COLD STRESS

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Abstract

Stress is a comprehensive physiological reaction to initial external or internal pressures that are perceived as hazardous. This response entails the activation and utilization of various bodily resources to effectively cope with these demands. The oxygen radical stress generated by cold stress may be attributed to the antioxidant qualities exhibited by the cold stress. Cell death may occur as a result of oxidative stress, which is an imbalance between free radical generation and antioxidant supply in the body. Oxygen radical stress is an inherent phenomenon that contributes to the physiological process of aging. A substantial amount of scientific literature indicates that chronic diseases may be influenced by prolonged oxidative stress. Consequently, there has been a growing interest in investigating oxidative stress as a potential cause in male infertility. There is a state of equilibrium that may be observed in the male reproductive organs, wherein there is a fare between the creation of free radical analogs and the activities of antioxidant scavenging. Vit C, a well-documented antioxidant, is found in the testis and serves the specific function of safeguarding this organ against oxidative damage. Furthermore, it might be argued that it plays a role in facilitating spermatogenesis by preserving the activity of antioxidants.

Keywords: *Ameliorative Effects, Preventive Effects, A Physiological Study Introduction.*

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Introduction

Stress is as a state of instability between the generation of free radical analog and the capacity of antioxidant dynamics. Alternatively, Stress may be described as a complex physiological and psychological response of the body to external or internal demands that are first seen as dangerous. This response requires the mobilization of resources in order to properly deal with these demands [1]. It is widely thought that both physical and psychological stress can have detrimental effects on sexual functioning. Numerous scholarly investigations have been conducted to explore the correlation between fatigue and sexual behavior in male rats [2]. According to Vijay et al. (2012). [3], the aforementioned data provide evidence that persistent psychological and physical stress can lead to the mitigate of erectile dysfunction. This condition arises from alterations in neurotransmission within several pathways involved in erectile responses, as well as a decrease in blood circulation to the genital organs. The role of oxidative stress in male factor infertility has been consistently identified as a prominent factor [4]. The cold not only contributes to the development of cardiovascular illnesses but also serves as a common factor in several reproductive system ailments. Numerous research has substantiated the detrimental impact of cold temperatures on the reproductive system [5]. Based on the aforementioned research results, a hypothesis may be formulated that stress posits are a factor that impacts sexual function in both males and females. In addition, there has been an increasing interest in studying oxidative stress as a possible cause of male infertility. A dynamic equilibrium often exists in the male reproductive organs between the generation of reactive oxygen molecules (ROS) and the actions of antioxidant scavenging [3]. Stressful circumstances have the potential to augment the generation of oxygen free radicals. The presence of free radicals initiates a series of reactions that result in the production of lipid peroxidation. Protein oxidation is a significant occurrence triggered by oxidative stress, as highlighted by Yadav et al. (2006) [6]. The testicular membranes contain a significant amount of polyunsaturated fatty acids, which makes them susceptible to damage caused by peroxidation [4]. According to Yadav et al. (2006) [6], experimental cryptorchidism has been found to lead to a reduction in antioxidant enzyme activity, thereby resulting in an elevation of lipid peroxidation. The testis is believed to be susceptible to oxygen radical stress because to the observed elevation in lipid peroxidation. [7]. Spermatogenesis is a highly dynamic and replicative biological process that has the remarkable capacity to produce around 1,000 sperm cells every second. According to John and Roman (2008)[8], the germinal epithelium exhibits elevated levels of mitochondrial oxygen consumption due to the rapid cell division rates associated with this process. Under stressful conditions, sperm cells produce small amounts of reactive oxygen species (ROS), which are essential for the capacitation acrosome response and the fertilisation process. However, an excessive amount of reactive oxygen species (ROS) produced by white blood cells and immature sperm cells might potentially cause injury to healthy sperm cells by triggering protein oxidation and DNA damage [9]. The utilization of swimming in tiny laboratory animals has been extensively employed in the examination of physiological alterations and the organism's ability to cope with stress. Swimming has several benefits when compared to other types of exercise, such as using a treadmill. Nayanatara et al.

(2005) [10], the level of work performed during swimming exercises surpasses that of treadmill running exercises of the same period. The utilization of drugs that possess numerous mechanisms of protective action, such as antioxidant capabilities, is a potential avenue for mitigating tissue damage in human diseases. Vitamins are important nutrients that can be readily acquired through dietary sources [11]. According to Caritá et al. (2020) [12], vitamins C and E possess inherent non-enzymatic antioxidant properties, enabling them to effectively neutralize free radicals and limit lipid peroxidation.

This article presents a brief summary of the antioxidant characteristics of Vitamin C, specifically in relation to its possible therapeutic benefits on cold-induced stress in male rats. Simultaneously, it confers antioxidant properties to the reproductive function in male rats.

2. Analysis of the literature

2.1. Stress and sperm functions

The testes membranes are rich in fatty acids, rendering them susceptible to damage caused by peroxidation. The presence of cryptorchidism has been shown to cause a reduction in the activity of antioxidant enzymes, resulting in an elevation in lipid peroxidation. The testis's vulnerability to oxygen radical stress is due to its heightened levels of lipid peroxidation. In order to mitigate the potential harm caused by oxidation, the testes have developed an antioxidant system. The composition includes enzymatic antioxidants such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GPX), and ceruloplasmin, as well as non-enzymatic antioxidants such tocopherols, uraate, carotenoids, acrobat, flavonoids, and glutathione [13]. A limited quantity of free radical analog (ROS) is generated by fully developed spermatozoa, serving a crucial role in capacitation, acrosome response, and the process of fertilization. However, it has been observed that during periods of stress, an excessive quantity of free radical analog (ROS) is generated by leukocytes and immature spermatozoa. The induction of protein oxidation and nucleic acid damage has the potential to result in harm to the regular spermatozoa. The involvement of oxygen radical stress in sperm dysfunction is significant, since it leads to the activation of lipid peroxidase in biological membranes [14].

The fluidity of the sperm membrane is reduced [15]. The research conducted by Dorota et al. (2004) [13] examined many factors related to sperm, including total sperm count, quality, concentration, motility, viability, and loss of sperm function. Similarly, Motahareh et al. (2014) [16] investigated the viability and function of sperm.

2.2. Stress and male fertility

Previous studies have established a negative association between male fertility and psychological stress [17]. There are several factors that have an impact on male fertility, as discussed by Manalisha et al. (2011) [18]. One of the crucial factors to consider is oxidative stress. Many types of stress, both physical and mental, are suspected of impairing sexual performance [19]. Extensive research has been conducted on the correlation between stress and sexual behavior in male rats and primates. These findings support James et al. (2012) [20] hypothesis that erectile dysfunction can develop in the midst of chronic psychological and physical stress.

This may be attributed to alterations in neurotransmission within different pathways responsible for erectile response, as well as a decrease in blood circulation within the male genital organs. According to the research conducted by Yoon et al. (2005) [21], there is a suspicion that stress may have an impact on sexual functions in both women and men. The phenomenon of oxygen radical stress, arising from both physical and psychological stressors, has garnered significant attention as a potential etiological factor in infertility of male [19]. The reproductive system of comprises three regulatory components, namely the hypothalamus, the anterior pituitary, and the testes. Unique regulatory tasks are performed only by the hypothalamus and anterior pituitary glands. Hormones secreted by these two organs have a regulatory role in the processes at hand. The third part is made up of the testes. The creation of testosterone, which is accountable for the generation of sperm. The testosterone hormone plays a pivotal role in regulating male sexual traits and actions [22The hypothalamus is responsible for producing and releasing gonadotropin releasing hormone (GnRH), along with other hormones. After being activated by GnRH, the anterior pituitary gland produces and releases two distinct hormones, namely luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These hormones play vital roles in regulating reproductive processes. These hormones are then released into the bloodstream and have varying effects on males and females [23]. The HPA axis is a complex physiological system that involves feedback processes from the gonads (testes and ovaries) to the brain. Luteinizing hormone releasing hormone (LHRH), an essential hormone for reproduction, is released into the portal blood stream. After reaching the pituitary gland, Luteinizing Hormone-Releasing Hormone (LHRH) attaches to certain receptors, triggering an intricate sequence of biochemical reactions that result in the creation and release of two gonadotropin hormones, specifically Luteinizing Hormone and Follicle-Stimulating Hormone [20]. Luteinizing hormone is crucial in the production of androgens in the gonads, particularly testosterone, which is renowned for its masculinizing effects. Follicle-stimulating hormone (FSH) is essential for the optimal growth and maturation of sperm in males and ovarian follicles in females. The gonadal hormones have a feedback mechanism that influences the hypothalamic-pituitary axis, which controls the production of Luteinizing Hormone-Releasing Hormone (LHRH), Luteinizing Hormone (LH), and Follicle-Stimulating Hormone (FSH). This system operates with great precision and coordination [24].

2.3. Oxygen radical stress and male reproductive function

According to Akpinar et al. (2008) [25], stress has a disruptive effect on testicular physiology and endocrinology. Prolonged bouts of stress in male rats have been reported to lead to a reduced degree of sexual initiation and delayed ejaculation. The activation of catecholamine levels in the brain as a result of acute stress, both mental and physical, has the potential to influence sexual behavior [21]. The process of protein oxidation involves the oxidation of cellular components, resulting in oxygen radical stress (OS) through a radical chain reaction. This sequence of events ultimately results in the degradation of the structural integrity of the membrane. Nevertheless, the higher lipid makeup of testes renders them more sensitive to oxygen radical damage [26].

The presence of polyunsaturated fatty acids (PUFAs) in the sperm plasma membrane leads to protein oxidation as a result of the increased amounts of free radical analogues (ROS). This subsequently results in decreased membrane fluidity and hinders the contact between sperm and egg. The generation of thio-barbituric reactive compounds (TBARS) is maximized in the presence of stress (Rasool and Varalakshmi, 2006). Elevated levels of catecholamines have been observed to induce vascular constriction, suggesting a potential reduction in blood flow and subsequent manifestation of sexual dysfunction during periods of stress. In males, testosterone plays a significant role in regulating various behaviors and responses related to sexual excitement. The testosterone level is observed to drop in conditions of stress [21]. According to Rasool and Varalakshmi (2006) [27], the mitochondrial membranes in the testes contain a significant amount of polyunsaturated lipids. These lipids are particularly vulnerable to oxidative damage, which can lead to impaired function of the gonads.

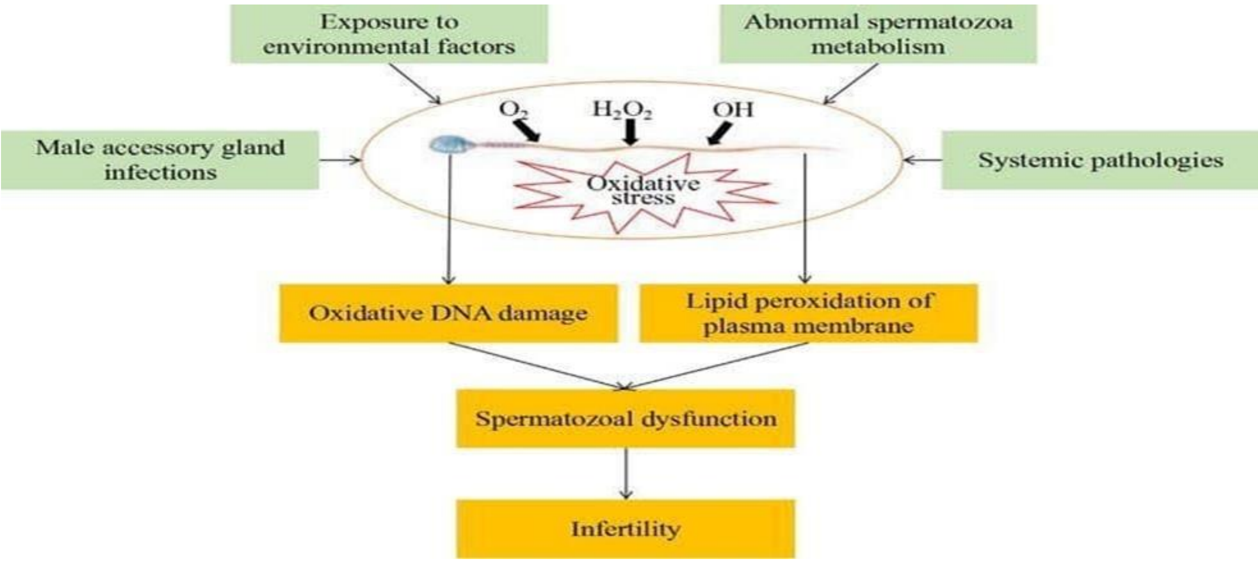

Figure 1: oxygen radical stress and Spermatozoa and male infertility

2.4. Stress and testosterone

The results suggest that stress had a significant effect on decreasing testosterone levels in comparison to group 1. CRH is acknowledged as a suppressor of LH function in Leydig cells. The aforementioned inhibitory activities subsequently result in a decrease in testosterone production by the Leydig cells. Aside from the primary dysfunction of the hypothalamic-pituitary-gonadal (HPG) axis, there are additional possible processes that might lead to a decrease in testosterone production. These include testicular micro trauma or an increase in testicular temperature [4]. Vitamin C treatment increased testosterone levels in healthy rats (Group III), but the improvement was not statistically significant. Vitamin C supplementation significantly increased testosterone levels in comparison to the stress group (group II) after only eight weeks. Vitamin C treatment at high doses significantly increased testosterone levels, in contrast to lower doses. The results showed that a high dose of vitamin supplementation significantly increased testosterone levels compared to the intermediate dose. Vitamin C's ability to boost testosterone levels in the blood not just via the androgen receptor axis is linked to this occurrence [28].

2.5. Antioxidants

Fortunately, the human body produces a variety of crucial antioxidants. Ubiquinol and glutathione are considered to be of almost significance. Enzymes like superoxide dismutase, catalase, and glutathione peroxidase have the ability to counteract free radicals [13].

Antioxidants have a role in several stages of the oxidative process through their ability to scavenge free radicals during initiation, bind metal ions, scavenge peroxyl radicals, and eliminate bio-chemicals that have been damaged by oxidation [29]. Certain antioxidants are essential micronutrients that must be obtained through dietary sources. These nutrients encompass vitamin C, beta-carotene, vitamin E, and trace metals such as selenium. An antioxidant is a substance that, in small amounts compared to an oxidizable substance, effectively slows down or prevents the process of oxidation for that substance [30]. The concept of an oxidizable substrate encompasses a wide range of biomolecules present within living cells, such as proteins, carbohydrates, lipids, and DNA. Antioxidants are chemical substances that possess the ability to donate electrons to free radicals, so stabilizing them without undergoing any changes themselves. This process effectively hinders a chain reaction of interactions that may potentially generate further free radicals [31]. Vitamin C is recognized for its involvement in safeguarding spermatogenesis and its significant contribution to the maintenance of semen integrity and fertility in males, including both human beings and animals. This phenomenon leads to an elevation in testosterone levels and serves as a preventive measure against the agglutination of sperm. The chemical in question functions as a potent antioxidant that plays a vital role in disrupting chains of oxygen radical stress. The contribution of this substance to the antioxidant capacity of seminal plasma, both intracellularly and extracellularly, has been reported to be around 65% [32]. Specific antioxidants are vital micronutrients that must be acquired from dietary sources. These nutrients consist of vitamin C, beta-carotene, vitamin E, and trace metals such as selenium

2.6. Ascorbic acid (Vit C)

Vitamin C have an important role as an antioxidant in various biological processes. Zinc is a micronutrient that exhibits water solubility and is readily absorbed through the gastrointestinal tract. In addition, have a crucial role in numerous biological activities and biochemical process in mammals. The manufacturing of collagen, L-carnitine, and norepinephrine relies on this particular nutrient, making it indispensable. Due to the inability of humans to endogenously synthesis vitamin C, it is imperative for individuals to incorporate a modest quantity of this essential nutrient into their dietary intake. Consequently, the extended absence of vitamin C leads to impairments in the posttranslational alteration of collagen, resulting in the onset of disease and ultimately mortality [32].

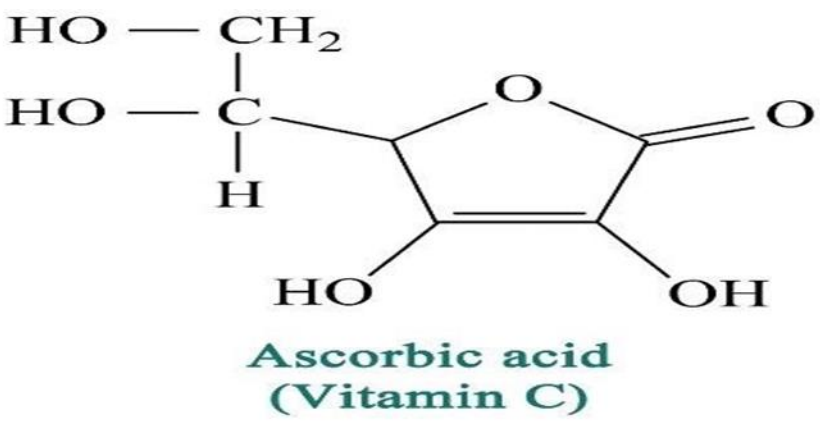

Figure 2: chemical structure of vitamin C [33].

Vitamin C has been recognized as a safeguarding element for the process of sperm production inside the male reproductive system, exerting a substantial impact on the quality of semen and fertility in both human males and animals. Studies have demonstrated that this intervention effectively increases testosterone levels and prevents sperm from clumping together. The chain-breaking antioxidant in question is essential as it represents up to 65% of the overall antioxidant capacity present in seminal plasma. This antioxidant is present intracellularly and extracellularly [34]. Vitamin C, which is attracted to water, has a restricted ability to counteract fat-loving radicals present in the fatty parts of membranes and lipoproteins since it is located in the watery phase. Vitamin C rapidly interacts with O2-, HO2•, and much more rapidly with OH •, resulting in the formation of semi-hydrous ascorbate. Vitamin C functions as an antioxidant by synergistically interacting with tocopherol, even in the presence of ongoing oxidation. Furthermore, vitamin C is believed to play a critical role in replenishing the body's "vitamin E pool" by interacting with tocopherol radicals. The scientific community has firmly demonstrated the quick ability of vitamin C and vitamin E to counteract the effects of free radicals. The importance of these compounds' antioxidant capabilities to their biological activity is well-established [35]. Vitamin E has more potent antioxidant properties than vitamin C in bio-membranes, particularly in relation to lipid peroxidation, owing to its higher lipophilicity. The ability to target a specific region within the membrane may be crucial in safeguarding against extremely reactive radicals. It is widely known that vitamin E and vitamin C have a synergistic relationship. Vitamin E, being the main antioxidant, produces radicals that interact with vitamin C to convert NADP dehydro-ascorbate back to ascorbate. This discovery aligns with the research reported by Halliwell in (1999) [36]. Vitamin C typically acts as an antioxidant, however under some situations it can actually promote oxidation. In-vitro investigations using the iron ascorbate mixture as a starting system have elucidated its antioxidant properties in great detail.

2.7. Antioxidant activity of vitamin C

Vit C is a dietary element that plays a crucial function in strengthening the body's antioxidant barrier. The reduced form of vitamin C exhibits the ability to undergo reactions with potent oxidizing agents [37]. The property of being an electron donor is responsible for all the known actions of Vitamin C. Vitamin C exhibits strong antioxidant properties in humans due to its ability to donate electrons in an aqueous environment. Numerous in vitro tests have provided evidence for the antioxidant properties of vitamin C [38].

2.8. The Impact of Vitamin C on Reproductivity:

The medicine in issue elevates testosterone levels by influencing the hypothalamic-pituitary-testicular axis. Bedwal et al. (2009) found elevated levels of testosterone [39], are associated with increased fertility. Vitamin C's antioxidant qualities have been shown to shield sperms from the destroying effects of oxygen radicals, allowing for greater sperm concentration and less sperm motility loss, as reported by Ahmed et al. (2010) [26]. It exhibits cytoprotective properties and mitigates testicular damage within the testis. According to Ashamu et al. (2010) [28], it provides an increased number of active and functional seminiferous tubules that exhibit favorable cyto-architecture. A review that has been published by the Cochrane Reviews. The study revealed a statistically significant correlation between the consumption of oral antioxidants and an increase in live birth rates.

The provision of supplementary interventions has been found to significantly enhance the likelihood of achieving pregnant. Vit C has been widely recognized as a critical factor in the development of spermatogonia cells into spermatozoa [40]. As a result of its utilization as an antioxidant in combating free radical analog (ROS). According to Ismail (2012) [41], it is possible that the testicular germ cells experienced destruction as a result of membrane damage or macromolecular degradation caused by free radical analog (ROS). This destruction led to a notable decrease in sperm count, an elevated occurrence of defective sperm, and ultimately a reduction in testicular weight.

3. Conclusion

Sever exercise results in a number of physiological changes that are consistent with it being a valid model for inducing stress in rats. The articles hypothesized that vitamin C intake may alleviate stress-related infertility by raising testosterone levels and enhancing antioxidant capabilities. In order to improve sperm quality, raise the possibility of conception with his partner, and reduce oxygen radical stress, it may be advantageous to offer oral antioxidant supplements to the male partner before trying conception as part of an assisted reproductive program.

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