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Impact of Vitamin A and Vitamin D3 in sperm morphology

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ABSTRACT
Vitamins A and D3 play essential roles in various physiological processes, including reproductive health. This study investigates the effects of Vitamin A and Vitamin D3 supplementation on sperm morphology in male subjects. The experimental design included a control group and two test groups, one receiving Vitamin A and the other Vitamin D3, over a 12-week period. Sperm samples were collected pre- and post-supplementation and analyzed for morphological changes using standardized criteria. Results indicate that both vitamins significantly improve sperm morphology, though through different mechanisms. Vitamin A supplementation was associated with enhanced acrosome integrity and overall sperm motility, while Vitamin D3 primarily contributed to increased sperm concentration and a reduction in morphological abnormalities. These findings suggest that adequate levels of Vitamins A and D3 are vital for optimal sperm health, potentially offering therapeutic avenues for treating male infertility.

KEYWORDS: Vitamin A, Vitamin D3, Sperm health, male infertility.

I. INTRODUCTION

The role of vitamins and micronutrients in reproductive health has gained increasing attention in recent years, as evidence suggests that nutritional status can significantly impact fertility and overall reproductive function. Among the essential vitamins, Vitamin A (retinol) and Vitamin D3 (cholecalciferol) are particularly influential due to their involvement in various physiological processes, including cellular growth, differentiation, and immune regulation. This introduction delves into the significance of these vitamins in male reproductive health, specifically focusing on their impact on sperm morphology—a critical parameter for male fertility.

Importance of Sperm Morphology in Male Fertility

Sperm morphology is one of the essential parameters used to assess male fertility. It refers to the size, shape, and structural integrity of sperm cells, which are crucial factors influencing a sperm's ability to reach and fertilize an egg. Abnormalities in sperm morphology can significantly reduce fertility potential, as they may impair the sperm's motility, ability to penetrate the egg, or capacity to undergo necessary biochemical reactions during fertilization. Understanding sperm morphology is critical for both diagnosing infertility and developing appropriate treatment strategies.[1,2,3]

Understanding Sperm Morphology

The World Health Organization (WHO) and other professional bodies use strict criteria to evaluate sperm morphology, classifying sperm into categories based on specific features of their structure, including:

1. **Head:** The shape and size of the sperm head are essential for carrying the genetic material to the egg. Normal sperm heads are oval-shaped, which facilitates effective movement and penetration of the egg's outer layer. Abnormalities in the head, such as an irregular shape, vacuoles, or double heads, can reduce the sperm's fertilization capability.
2. **Midpiece:** The midpiece contains mitochondria, which provide the energy required for motility. A normal midpiece is aligned properly with the head and tail, facilitating smooth, progressive movement. Abnormal midpieces may be swollen, thin, or irregularly shaped, affecting the sperm's energy production and motility.
3. **Tail:** The tail is responsible for propelling the sperm towards the egg. Normal sperm tails are long and slender, enabling efficient swimming. Abnormal tails may be coiled, double, or extremely short, which can lead to decreased motility and reduce the likelihood of successful fertilization.[3,4]

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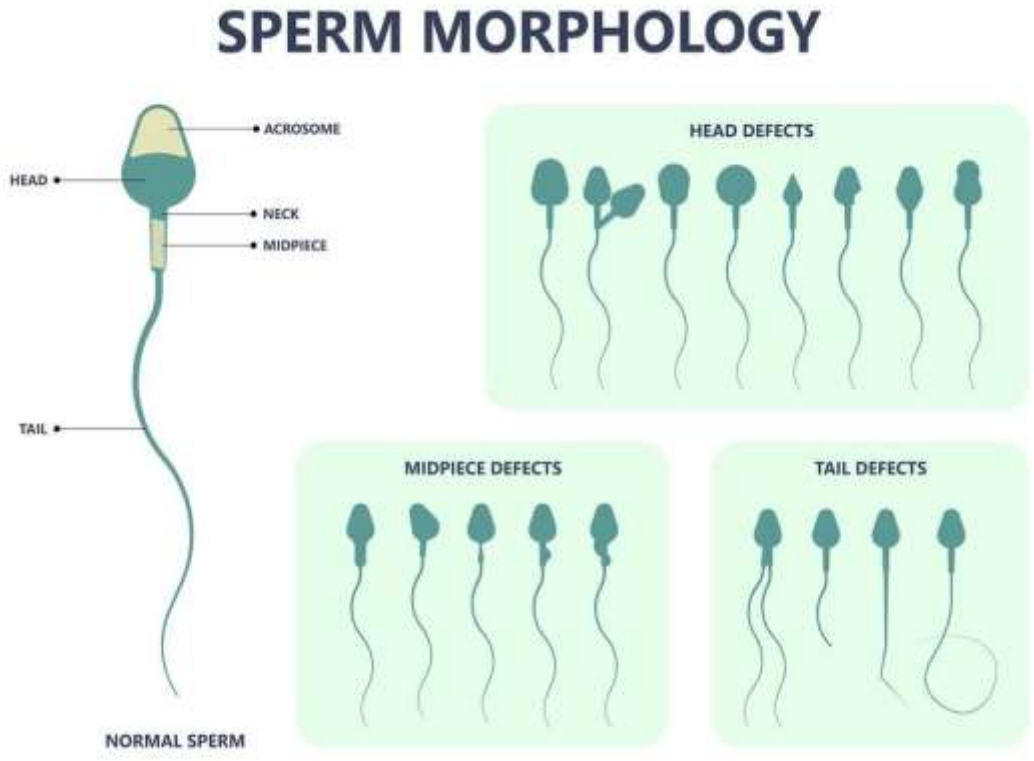

Fig no. 1 Sperm morphology

Sperm morphology is assessed by examining a sample under a microscope and determining the percentage of sperm with a normal structure. According to WHO criteria, typically, a sample with more than 4% normal morphology is considered acceptable, though some labs may use different thresholds based on stricter or modified criteria.

Impact of Abnormal Sperm Morphology on Fertility

Sperm morphology is closely related to other semen parameters, such as sperm concentration, motility, and viability. Even if sperm count and motility are within normal ranges, a high percentage of morphologically abnormal sperm can significantly impair fertility. The following are some of the primary impacts of abnormal sperm morphology on fertility:

1. **Reduced Motility:** Abnormalities in the head or tail can hinder motility, as they interfere with the sperm's ability to swim efficiently. Sperm with poor motility may struggle to reach the egg, reducing the chances of fertilization.
2. **Impaired Fertilization Capability:** Morphological defects, especially in the head, can interfere with the sperm's ability to bind to and penetrate the egg's zona pellucida. Proper head structure is crucial for the acrosome reaction, which is necessary for the release of enzymes that allow the sperm to penetrate the egg.
3. **Increased Risk of DNA Fragmentation:** Some studies suggest a correlation between abnormal morphology and increased DNA fragmentation in sperm. High levels of DNA fragmentation can lead to failed fertilization, miscarriage, or developmental issues in the embryo.
4. **Assisted Reproductive Techniques (ART) Outcomes:** Poor sperm morphology has been associated with lower success rates in assisted reproductive techniques, such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). In ART, selecting sperm with normal morphology can improve fertilization rates and overall success.[5,6,7]

Factors Affecting Sperm Morphology

Numerous factors can contribute to abnormal sperm morphology, including lifestyle habits, environmental exposures, medical conditions, and genetic factors. Some of these factors include:

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- **Oxidative Stress:** Excessive oxidative stress due to factors like smoking, pollution, and poor diet can lead to sperm damage, resulting in abnormal morphology.
- **Hormonal Imbalances:** Hormones such as testosterone play a vital role in spermatogenesis. Imbalances can impair sperm production and lead to structural abnormalities.
- **Nutritional Deficiencies:** Adequate levels of vitamins, minerals, and other nutrients are essential for sperm health. Deficiencies, particularly in antioxidants and vitamins like A, D, E, and C, can lead to morphological abnormalities.
- **Genetic Factors:** Certain genetic mutations and chromosomal abnormalities can affect sperm development and morphology.[8,9]

ROLE OF VITAMIN A IN SPERM MORPHOLOGY

Vitamin A, a fat-soluble vitamin essential for various physiological functions, plays a pivotal role in male reproductive health. Known for its involvement in vision, immune response, and cellular growth, Vitamin A is also crucial for spermatogenesis—the process of sperm production. Its influence extends to sperm morphology, impacting the structure and integrity of sperm cells, which are essential factors in male fertility. This section explores the mechanisms through which Vitamin A affects sperm morphology and how deficiencies or imbalances can lead to abnormalities.

Functions of Vitamin A in Reproductive Health

Vitamin A primarily exists in two forms: retinoids (animal sources) and carotenoids (plant sources). In the body, these are converted into active forms, such as retinol and retinoic acid, which are crucial for reproductive function. Retinoic acid, in particular, plays an essential role in gene regulation, cellular differentiation, and development within the testes. Vitamin A is also involved in the maintenance and function of the seminiferous tubules, where sperm production takes place.

In male reproductive health, Vitamin A serves several vital functions, including:

1. **Regulation of Spermatogenesis**: Vitamin A is necessary for the differentiation of spermatogonia into mature sperm cells. During spermatogenesis, retinoic acid regulates the expression of genes that control the transformation of germ cells into spermatozoa, ensuring proper development and maturation.
2. **Support of Sertoli Cells**: Sertoli cells, which are present within the seminiferous tubules, provide structural support and nourishment to developing sperm cells. Vitamin A enhances Sertoli cell function, promoting an optimal environment for spermatogenesis and helping to maintain the blood-testis barrier, which protects developing sperm from harmful substances.
3. **Regulation of Germ Cell Apoptosis**: Vitamin A influences the process of apoptosis (programmed cell death) within the testes. Proper levels of Vitamin A ensure that defective germ cells are removed, promoting a healthy population of developing sperm cells. Imbalances in apoptosis can lead to an accumulation of abnormal sperm.[10,11,12,13]

Impact of Vitamin A on Sperm Morphology

Vitamin A's role in regulating cell differentiation and growth is directly linked to its impact on sperm morphology. Adequate Vitamin A levels are associated with the proper formation of sperm structures, including the head, midpiece, and tail. Here's how Vitamin A influences specific aspects of sperm morphology:

1. **Formation of the Acrosome and Head Structure**: The acrosome, a cap-like structure covering the sperm head, contains enzymes necessary for penetrating the egg during fertilization. Vitamin A is involved in acrosome formation and its structural integrity. Deficiencies in Vitamin A can lead to malformed acrosomes, which impair the sperm's ability to bind to and fertilize an egg. Furthermore, abnormalities in the head shape, such as round-headed or elongated sperm, are associated with insufficient Vitamin A levels.
2. **Midpiece Integrity and Mitochondrial Function**: The midpiece contains mitochondria that provide energy for sperm motility. Vitamin A's role in cellular differentiation supports the proper development of the midpiece, which is essential for energy production and movement. Abnormal midpieces, such as swollen or irregularly shaped midpieces, can result from inadequate Vitamin A levels, affecting sperm motility and overall fertility.
3. **Tail Formation and Motility**: The tail, or flagellum, propels the sperm toward the egg. Proper tail formation is crucial for effective motility. Vitamin A's involvement in cellular growth supports the development of a normal,

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elongated tail, enabling efficient swimming. Deficiencies can lead to coiled or abnormally short tails, which hinder the sperm's ability to reach the egg.[14,15,16,17]

Vitamin A Deficiency and Sperm Morphological Abnormalities

Vitamin A deficiency is associated with a range of morphological abnormalities in sperm, as well as reduced sperm count and motility. Some of the specific morphological abnormalities linked to Vitamin A deficiency include:

- **Teratozoospermia**: This condition is characterized by a high percentage of abnormally shaped sperm. Vitamin A deficiency is a common contributor to teratozoospermia, leading to defects such as misshapen heads and abnormal tail structures.
- **Abnormal Acrosome Formation**: Without sufficient Vitamin A, the acrosome may develop improperly, leading to reduced fertilization potential. Abnormal acrosome formation affects the sperm's ability to bind to and penetrate the egg.
- **Increased Germ Cell Apoptosis**: Vitamin A deficiency can disrupt the regulation of apoptosis in germ cells, leading to excessive cell death and a decline in the population of healthy sperm. This increase in apoptosis can reduce sperm count and contribute to morphological defects.[18,19,20]

Mechanisms of Action

Vitamin A influences sperm morphology through several mechanisms, primarily involving its metabolite, retinoic acid. Retinoic acid binds to specific nuclear receptors (RARs and RXRs) in Sertoli cells and germ cells, which then modulate the expression of genes critical for cell growth and differentiation. This signaling pathway ensures that spermatogonia develop properly into mature sperm cells, maintaining normal morphology. Additionally, Vitamin A's antioxidant properties help reduce oxidative stress within the testes, preventing damage to sperm cells and preserving their structural integrity.

Benefits of Vitamin A Supplementation

Research has demonstrated that Vitamin A supplementation can improve sperm morphology and motility in cases of deficiency. Supplementation may lead to:

- **Improved Acrosome and Head Structure**: Ensuring proper formation of the acrosome and head structure, thereby enhancing fertilization potential.
- **Enhanced Midpiece Development**: Supporting energy production by promoting normal mitochondrial function, which is critical for motility.
- **Reduction of Morphological Abnormalities**: Addressing deficiencies can reduce the prevalence of abnormal shapes and structures, improving overall sperm quality.[21,22,23,24]

ROLE OF VITAMIN D3 IN SPERM MORPHOLOGY

Vitamin D3, or cholecalciferol, is a fat-soluble vitamin synthesized in the skin upon exposure to sunlight and obtained through certain dietary sources. Traditionally associated with bone health and calcium metabolism, Vitamin D3 has emerged as a critical factor in various aspects of male reproductive health. Recent research highlights its influence on sperm morphology, suggesting that adequate levels of Vitamin D3 contribute to normal sperm structure and function. This section explores the mechanisms through which Vitamin D3 impacts sperm morphology and the implications of deficiencies for male fertility.[25,26,27,28]

Functions of Vitamin D3 in Reproductive Health

Vitamin D3 operates as a hormone, primarily regulating calcium and phosphorus levels in the body, which are crucial for maintaining bone health. Beyond its role in mineral metabolism, Vitamin D3 also has significant effects on reproductive tissues, particularly in the testes. It functions by binding to the Vitamin D receptor (VDR), which is expressed in multiple parts of the male reproductive system, including the testis, epididymis, and sperm cells themselves.

The presence of VDR in these areas indicates that Vitamin D3 has a direct role in regulating the production and maturation of sperm cells. Vitamin D3 also influences the expression of enzymes and proteins necessary for sperm motility, morphology, and fertilization capability. Key functions of Vitamin D3 in male reproductive health include:

1. **Modulation of Calcium Influx in Sperm Cells**: Calcium plays a vital role in sperm motility and acrosome reaction, which is essential for fertilization. Vitamin D3 regulates calcium channels in sperm cells, enhancing calcium influx, which promotes proper morphology and motility.

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2. **Regulation of Oxidative Stress**: Vitamin D3 has antioxidant properties that protect sperm cells from oxidative damage. Oxidative stress can lead to sperm abnormalities, and Vitamin D3 helps maintain cellular integrity, thereby supporting normal morphology.
3. **Influence on Testosterone Levels**: Vitamin D3 indirectly affects sperm morphology by modulating testosterone synthesis, which is crucial for spermatogenesis. Adequate testosterone levels are necessary for normal sperm development and structure.[29,30,31,32,33]

Impact of Vitamin D3 on Sperm Morphology

Vitamin D3 contributes to several aspects of sperm morphology, from head structure to tail formation. These effects support the sperm's ability to reach and fertilize the egg, playing a significant role in overall fertility. Here are some specific ways in which Vitamin D3 influences sperm morphology:

1. **Formation of the Head and Acrosome**: The head of the sperm contains genetic material and the acrosome, a vesicle that releases enzymes necessary for penetrating the egg. Vitamin D3 supports the structural integrity of the sperm head, ensuring it is properly shaped and capable of undergoing the acrosome reaction. Deficiencies in Vitamin D3 can lead to misshapen or small heads, reducing the sperm's fertilization capacity.
2. **Midpiece Development and Mitochondrial Function**: The midpiece houses the mitochondria, which supply energy for motility. Vitamin D3 aids in maintaining the proper structure of the midpiece, which is essential for energy production. An adequately formed midpiece ensures that the sperm has sufficient energy to reach the egg, while Vitamin D3's regulation of calcium homeostasis supports mitochondrial function and prevents midpiece abnormalities.
3. **Tail Structure and Motility**: The tail, or flagellum, is responsible for the sperm's motility, allowing it to swim toward the egg. Vitamin D3 supports tail formation by regulating the proteins involved in tail structure and motility. This regulation is vital for efficient swimming, as deficiencies can lead to coiled, broken, or shortened tails, which impair the sperm's ability to reach the egg.[34,35,36,52,53,54]

Vitamin D3 Deficiency and Sperm Morphological Abnormalities

Deficiencies in Vitamin D3 are associated with a variety of morphological abnormalities in sperm, as well as issues with sperm count and motility. Research has shown that low levels of Vitamin D3 are linked to:

- **Teratozoospermia**: This condition is characterized by a high proportion of abnormally shaped sperm. Vitamin D3 deficiency is known to contribute to teratozoospermia, resulting in defects such as irregular heads, damaged acrosomes, and malformed tails.
- **Reduced Head Integrity**: Sperm with Vitamin D3 deficiency often show abnormalities in head shape, such as small or asymmetrical heads. These structural irregularities hinder the sperm's ability to bind to and fertilize the egg.
- **Increased Oxidative Stress**: Without adequate Vitamin D3, sperm cells are more susceptible to oxidative damage. This damage can lead to various morphological issues, including midpiece defects and impaired motility. [37,38,39,40,41,42]

Mechanisms of Action

Vitamin D3 influences sperm morphology through several mechanisms, primarily involving calcium regulation, antioxidant defense, and hormonal modulation. These mechanisms are essential for maintaining normal sperm structure and function:

1. **Calcium Regulation**: Vitamin D3 regulates the entry of calcium ions into sperm cells through calcium channels. Calcium is crucial for activating the sperm's motility and the acrosome reaction. By ensuring adequate calcium levels, Vitamin D3 helps maintain the proper formation of sperm structures and promotes efficient motility.
2. **Oxidative Stress Reduction**: Vitamin D3 has antioxidant properties that protect sperm from reactive oxygen species (ROS). High levels of ROS can damage cellular structures, leading to morphological abnormalities. Vitamin D3 helps neutralize ROS, maintaining sperm integrity and supporting normal morphology.
3. **Hormonal Influence on Spermatogenesis**: Vitamin D3 indirectly influences sperm morphology by modulating testosterone levels. Testosterone is necessary for the development and maintenance of normal sperm structures.

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Vitamin D3 interacts with the endocrine system to support testosterone synthesis, thereby promoting healthy spermatogenesis and morphology.[43,44,49,50,51]

Benefits of Vitamin D3 Supplementation

Research has shown that Vitamin D3 supplementation can improve sperm morphology, particularly in individuals with low levels of the vitamin. Potential benefits include:

- **Enhanced Head and Acrosome Structure**: Supplementation can support the development of a normal, symmetrical sperm head, facilitating fertilization.
- **Improved Midpiece Integrity**: By regulating calcium levels and mitochondrial function, Vitamin D3 supplementation helps maintain the structure of the midpiece, ensuring adequate energy for motility.
- **Increased Motility and Reduced Tail Abnormalities**: Vitamin D3 can improve tail formation and motility, enabling sperm to swim more effectively toward the egg.[45,46,47,48]

II. CONCLUSION:

The roles of Vitamin A and Vitamin D3 in male reproductive health, particularly in influencing sperm morphology, are both significant and complementary. Both vitamins contribute to the proper development and structure of sperm cells, which are crucial determinants of male fertility. Adequate levels of Vitamin A are essential for the differentiation and maturation of germ cells, supporting the structural integrity of the sperm head, midpiece, and tail. It plays a vital role in maintaining acrosome formation, ensuring that sperm cells are correctly shaped and function optimally for fertilization. Similarly, Vitamin D3 plays a crucial role in modulating calcium influx and reducing oxidative stress within sperm cells. These actions support the structural integrity and functionality of the sperm midpiece and tail, promoting effective motility and aiding in successful fertilization. The presence of Vitamin D receptors within the male reproductive system further underscores its importance in sperm morphology and overall reproductive health.

Deficiencies in either Vitamin A or Vitamin D3 are associated with increased abnormalities in sperm morphology, including misshapen heads, midpiece defects, and impaired tail formation. Such abnormalities reduce the sperm's ability to reach and fertilize the egg, thereby diminishing fertility potential. However, studies suggest that supplementation of these vitamins can lead to improvements in sperm morphology, offering a potential avenue for therapeutic intervention in cases of male infertility associated with vitamin deficiencies.

REFERENCE

[1]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr.YashmiAgwina Xavier, Veerammal, Dr. Suman Sharma, The Impact of Oxidative Stress in Male Infertility; Dr. Borus Andro Lan and Research Center, Chennai, 2024. Volume 9, Issue 5 Sep - Oct 2024, pp: 177-185.

[2]. Dr. Lokesh. K, Dr. Borus Purushothaman,Dr. Harini. V, veerammal, Dr. Suman sharma, Antioxidant Supplementation and Duration of Antioxidant in Male Infertility – A Systemic Review; Dr. Borus Andro Lan and Research Center, Chennai, 2024.

[3]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr. Harini. V, veerammal, Dr. Suman sharma, A Comprehensive Approach and Critical Evaluation of Clinical Practice Guidelines for Sperm DNA Fragmentation; Dr. Borus Andro Lan and Research Center, Chennai, 2024. Volume 9, Issue 3 May-June 2024, pp: 844-848.

[4]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr.YashmiAgwina Xavier, Veerammal, Dr. Suman Sharma, Antioxidants and Idiopathic Male Infertility: Their Impact on Sperm Quality Parameters and Pregnancy Rates; Dr. Borus Andro Lan and Research Center, Chennai, 2024. Volume 9, Issue 5 Sep - Oct 2024, pp: 335-340 www.ijprajournal.com

[5]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr.YashmiAgwina Xavier, Veerammal, Dr. Suman Sharma, Antioxidant therapy in unexplained male infertility; Dr. Borus Andro Lan and Research Center, Chennai; Volume 02, Issue 10, 2024 of International Journal of Pharmaceutical Science.

[6]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr.YashmiAgwina Xavier, Veerammal, Dr. Suman Sharma, Impact of Vitamin B12 and Folic Acid in sperm concentration; Dr. Borus Andro Lan and Research Center, Chennai;
International Journal of All Research Educ

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 840-848 www.ijprajournal.com ISSN: 2456-4494

ation & Scientific Methods; Volume 12, Issue 10, October - 2024.
[7]. Griswold, M.D. (2016). "Vitamin A, retinoic acid, and spermatogenesis." Biology of Reproduction, 94(1), 11-22.
[8]. Amann, R.P., & Schanbacher, B.D. (1983). "Effects of vitamin A deficiency on the male reproductive system." The American Journal of Clinical Nutrition, 36(5), 1210-1216.
[9]. Blomberg Jensen, M. (2014). "Vitamin D and male reproduction." Nature Reviews Endocrinology, 10(3), 175-186.
[10]. Jueraitetixue, D., & Wintour, E.M. (2020). "Vitamin D in male fertility: A narrative review of current evidence." Reproductive Biology and Endocrinology, 18(1), 47.
[11]. Ménézo, Y., et al. (2011). "Antioxidants to reduce sperm DNA fragmentation: an unexpected adverse effect." Reproductive Biomedicine Online, 22(3), 319-324.
[12]. Ramlau-Hansen, C.H., et al. (2011). "Semen quality and reproductive hormones according to serum levels of vitamin D in men." The Journal of Clinical Endocrinology & Metabolism, 96(3), E480-E489.
[13]. Al-Dujaili, E.A.S., &Kumosani, T.A. (2011). "Antioxidant status in semen of men with different fertility potentials." Human Fertility, 14(4), 208-214.
[14]. Rehman, R., et al. (2017). "The role of Vitamin D in male reproductive health: a clinical review." Arab Journal of Urology, 15(2), 157-165.
[15]. Irani, M., & Merhi, Z. (2014). "Role of vitamin D in ovarian physiology and its implication in reproduction: a systematic review." Fertility and Sterility, 102(2), 460-468.
[16]. Mínguez-Alarcón, L., & Gaskins, A.J. (2017). "Chronic diseases and lifestyle factors are associated with poor sperm morphology." Asian Journal of Andrology, 19(6), 652-658.
[17]. Kuchakulla M, Soni Y, Patel P, Parekh N, Ramasamy R. A systematic review and evidence-based analysis of ingredients in popular male fertility supplements. Urology. 2020;136:133–141.
[18]. Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2011;(1):CD007411.
[19]. Showell MG, Mackenzie-Proctor R, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2014;(12):CD007411.
[20]. Majzoub A, Agarwal A. Systematic review of antioxidant types and doses in male infertility: benefits on semen parameters, advanced sperm function, assisted reproduction and live-birth rate. Arab J Urol. 2018;16:113–124.
[21]. Smits RM, Mackenzie-Proctor R, Yazdani A, Stankiewicz MT, Jordan V, Showell MG. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2019;3:CD007411
[22]. Adewoyin M, Ibrahim M, Roszaman R, Isa MLM, Alewi NAM, Rafa AAA, et al. Male infertility: the effect of natural antioxidants and phytocompounds on seminal oxidative stress. Diseases. 2017;5:9.
[23]. Buhling K, Schumacher A, Eulenburg CZ, Laakmann E. Influence of oral vitamin and mineral supplementation on male infertility: a meta-analysis and systematic review. Reprod Biomed Online. 2019;39:269–279.
[24]. McPherson NO, Shehadeh H, Fullston T, Zander-Fox DL, Lane M. Dietary micronutrient supplementation for 12 days in obese male mice restores sperm oxidative stress. Nutrients. 2019;11:2196
[25]. Salas-Huetos A, Bulló M, Salas-Salvadó J. Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies. Hum Reprod Update. 2017;23:371–389.
[26]. Chattopadhyay R, Yasmin S, Chakravarty B. Effect of continuous 6 months oral antioxidant combination with universally recommended dosage in idiopathic male infertility. IJIFM. 2016;7:1–6.
[27]. da Silva TM, Maia MCS, Arruda JT, Approbato FC, Mendonça CR, Approbato MS. Folic acid does not improve semen parametrs in subfertile men: a double-blin, randomized, placebo-controlled study. JBRA Assist Reprod. 2013;17:152–157.
[28]. Keskes-Ammar L, Feki-Chakroun N, Rebai T, Sahnoun Z, Ghozzi H, Hammami S, et al. Sperm oxidative stress and the effect of an oral vitamin E and selenium

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 840-848 www.ijprajournal.com ISSN: 2456-4494

supplement on semen quality in infertile men. Arch Androl. 2003;49:83–94.

[29]. Kessopoulou E, Powers HJ, Sharma KK, Pearson MJ, Russell JM, Cooke ID, et al. A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated male infertility. Fertil Steril. 1995;64:825–831.

[30]. Ménézo YJ, Hazout A, Panteix G, Robert F, Rollet J, Cohen-Bacrie P, et al. Antioxidants to reduce sperm DNA fragmentation: an unexpected adverse effect. Reprod Biomed Online. 2007;14:418–421.

[31]. Halliwell B. Free radicals and antioxidants - quo vadis? Trends Pharmacol Sci. 2011;32:125–130.

[32]. Castagné V, Lefèvre K, Natero R, Clarke PG, Bedker DA. An optimal redox status for the survival of axotomized ganglion cells in the developing retina. Neuroscience. 1999;93:313–320.

[33]. Henkel R, Sandhu IS, Agarwal A. The excessive use of antioxidant therapy: a possible cause of male infertility? Andrologia. 2019;51:e13162.

[34]. Panner Selvam MK, Agarwal A, Henkel R, Finelli R, Robert KA, Iovine C, et al. The effect of oxidative and reductive stress on semen parameters and functions of physiologically normal human spermatozoa. Free Radic Biol Med. 2020;152:375–385.

[35]. Bejarano I, Monllor F, Marchena AM, Ortiz A, Lozano G, Jiménez MI, et al. Exogenous melatonin supplementation prevents oxidative stress-evoked DNA damage in human spermatozoa. J Pineal Res. 2014;57:333–339.

[36]. Martínez-Soto JC, Domingo JC, Cordobilla B, Nicolás M, Fernández L, Albero P, et al. Dietary supplementation with docosahexaenoic acid (DHA) improves seminal antioxidant status and decreases sperm DNA fragmentation. SystBiolReprod Med. 2016;62:387–395.

[37]. Hosseini J, Mardi Mamaghani A, Hosseinifar H, Sadighi Gilani MA, Dadkhah F, Sepidarkish M. The influence of ginger (Zingiber officinale) on human sperm quality and DNA fragmentation: a double-blind randomized clinical trial. Int J Reprod Biomed. 2016;14:533–540.

[38]. Stenqvist A, Oleszczuk K, Leijonhufvud I, Giwercman A. Impact of antioxidant treatment on DNA fragmentation index: a double-blind placebo-controlled randomized trial. Andrology. 2018;6:811–816.

[39]. Ahmad MK, Mahdi AA, Shukla KK, Islam N, Jaiswar SP, Ahmad S. Effect of Mucuna pruriens on semen profile and biochemical parameters in seminal plasma of infertile men. Fertil Steril. 2008;90:627–635.

[40]. Alizadeh F, Javadi M, Karami AA, Gholaminejad F, Kavianpour M, Haghighian HK. Curcumin nanomicelle improves semen parameters, oxidative stress, inflammatory biomarkers, and reproductive hormones in infertile men: a randomized clinical trial. Phytother Res. 2018;32:514–521.

[41]. Salehi P, Zahra Shahrokhi S, Kamran T, Ajami A, Taghiyar S, Reza Deemeh M. Effect of antioxidant therapy on the sperm DNA integrity improvement; a longitudinal cohort study. Int J Reprod Biomed. 2019;17:99–106.

[42]. Hasoon MA. Using of the L-arginine and co-enzyme Q10 shows improvement of the male subfertility. IJDDT. 2019;9:544–551.

[43]. Nurmawati D, Hinting A, Sudjarwo Astaxanthin improves erythrocyte sedimentation rate (ESR), Malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OH-Dg) levels, and semen quality in human sperm. IJSTR. 2020;9:6896–6903.

[44]. Hadi AM, Abbass YI, Yadgar MA. The impact of L-carnitine supplement on semen variables and the levels of sexual hormones (serum LH, FSH, testosterone, and inhibin) in males with infertility. Medico Leg Update. 2020;20:772–776.

[45]. Schisterman EF, Sjaarda LA, Clemons T, Carrell DT, Perkins NJ, Johnstone E, et al. Effect of folic acid and zinc supplementation in men on semen quality and live birth among couples undergoing infertility treatment: a randomized clinical trial. JAMA. 2020;323:35–48.

[46]. Comhaire FH, Christophe AB, Zalata AA, Dhooge WS, Mahmoud AM, Depuydt CE. The effects of combined conventional treatment, oral antioxidants and essential

fatty acids on sperm biology in subfertile men. Prostaglandins Leukot Essent Fatty Acids. 2000;63:159–165.

[47]. Paradiso Galatioto G, Gravina GL, Angelozzi G, Sacchetti A, Innominato PF, Pace G, et al. May antioxidant therapy improve sperm parameters of men with persistent oligospermia after retrograde embolization for varicocele? World J Urol. 2008;26:97–102.

[48]. Oliva A, Dotta A, Multigner L. Pentoxifylline and antioxidants improve sperm quality in male patients with varicocele. Fertil Steril. 2009;91(4 Suppl):1536–1539.

[49]. Festa R, Giacchi E, Raimondo S, Tiano L, Zuccarelli P, Silvestrini A, et al. Coenzyme Q10 supplementation in infertile men with low-grade varicocele: an open, uncontrolled pilot study. Andrologia. 2014;46:805–807.

[50]. Pourmand G, Movahedin M, Dehghani S, Mehrsai A, Ahmadi A, Pourhosein M, et al. Does L-carnitine therapy add any extra benefit to standard inguinal varicocelectomy in terms of deoxyribonucleic acid damage or sperm quality factor indices: a randomized study. Urology. 2014;84:821–825.

[51]. Nematollahi-Mahani SN, Azizollahi GH, Baneshi MR, Safari Z, Azizollahi S. Effect of folic acid and zinc sulphate on endocrine parameters and seminal antioxidant level after varicocelectomy. Andrologia. 2014;46:240–245.

[52]. Cyrus A, Kabir A, Goodarzi D, Moghimi M. The effect of adjuvant vitamin C after varicocele surgery on sperm quality and quantity in infertile men: a double blind placebo controlled clinical trial. Int Braz J Urol. 2015;41:230–238.

[53]. Gual-Frau J, Abad C, Amengual MJ, Hannaoui N, Checa MA, Ribas-Maynou J, et al. Oral antioxidant treatment partly improves integrity of human sperm DNA in infertile grade I varicocele patients. Hum Fertil (Camb) 2015;18:225–229.

[54]. Barekat F, Tavalaee M, Deemeh MR, Bahreinian M, Azadi L, Abbasi H, et al. A preliminary study: N-acetyl-L-cysteine improves semen quality following varicocelectomy. Int J Fertil Steril. 2016;10:120–126.