DOI: https://doi.org/10.53350/pjmhs2023172114

ORIGINAL ARTICLE

Antioxidants - Reduces Male Infertility

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ABSTRACT

Background: This study takes a microscopic overview of main semen parameters such as sperm motility, morphology, fertility rate, sperm concentration, and DNA damage and their relationship with antioxidants.
Aim: To explain the role of antioxidant minerals including Vitamin E and C, N-Acetyl cysteine, Selenium, Carnitine, CoQ10, and Zinc in improving semen quality across the semen parameters.
Methods: The design of the study is an in-depth review and analysis of minerals that improve semen quality.
Results: The result derived from this study stipulates those aforementioned minerals enhance the overall health and wellbeing of the body, which results in the semen quality improvement. The study determines that it is indeed true that antioxidant supplementation for infertile males produces favorable results.
The practical implications: are immense including early diagnosis and treatment of infertility.
Conclusion: To conclude, supplements such as CoQ10 improve sperm count, the combined dosage of Vitamin C and E diminishes sperm damage, and carnitine enhances sperm morphology and mobility. The study also concludes that with males who have infertility because of Oxidative Stress, the above-mentioned antioxidants produce a positive result.
Keywords: Vitamin C and E, Selenium, Carnitine CoQ10, Zinc, Acetyl Cysteine

INTRODUCTION

Infertility, by definition, is when a couple, male and female, has had frequent unprotected sexual intercourse for at least a year to conceive a baby. Although infertility can be caused by either female or male factor, this paper focuses on male fertility. More specifically, this paper examines the role of antioxidants in male fertility[1]. Founded on research, it is said that close to 12% of couples have some form of infertility during the first year of unprotected sexual intercourse. Of those 12%, it is also stated that 50 percent of all infertility globally is because of male infertility[2,3]. Therefore, it is worth examining the topic given that it is important for many couples to conceive a baby to support and raise future progeny.

There are several established factors behind male infertility. Some of which are caused by unwarranted radiations, testicular infections, smoking, urinary tract infection and diseases, environmental influences, varicocele, nutritional deficiencies, and lack or excess of oxidative minerals, which is also called “Oxidative Stress”[4,5]. In medical terms, the definition of oxidative stress happens when the body’s natural oxidative defenses are lowered or weaker than the production of Reactive Oxygen Specifies, hereby abbreviated as ROS[4,20].

It is stated that an enhanced level of ROS can be caused by socio-environmental factors including high air pollution, increased consumption of alcohol, and deadly presence of insecticides, high temperature, obesity, electromagnetic waves, and poor nutrition[3,5]. The standard values of sperms are determined by pH, semen concentration, semen volume, morphology, and progressive motility[2,7,18]. There are a number of studies that support the hypothesis that ROS contributes to male infertility. According to research, high levels of ROS adversely affect polyunsaturated fatty acids (PUFAs) that improve membrane flexibility[4-6]. A high level of ROS causes lipid peroxidation which in term compromises the functionality of membrane cells and diminishes sperm mobility. Consequently, high ROS reduces male infertility. Lastly, ROS production pathologically affects DNA as the more and more mitochondrial membrane is depleted[7,14,15,17].

Ordinary semen also shows that there are traces of antioxidants in the semen including vitamin C, vitamin E, thioredoxin, superoxide dismutase and glutathione[8,9]. These antioxidants function as a guard to neutralize free radicals in order to protect semen quality from ROS that has been produced in the body. There is clear evidence that lower levels of antioxidants in semen in males afflicted by infertility are as compared to fertile males[7,16]. Additional semen analysis may also reveal several impairments in infertile males such as oligozoospermia (low concentration of sperm), teratozoospermia (sperms with abnormal morphology) and asthenospermia (reduced sperm motility), and the combination of oligoasthenoteratozoospermia[8,9].

The main objective of this study is to evaluate the role and effects of antioxidants in male fertility. More recently, many research papers suggest that there is a positive correlation between oxidative stress and male infertility. Therefore, it is worth exploring as to what oral antioxidant supplements do to improve semen quality for infertile males across important semen parameters, for instance: morphology DNA damage, semen motility, sperm concentration, and fertility rate.

Sources of Antioxidants and Effect on Male Fertility

Vitamin E &C: Seminal plasma contains a high concentration of Vitamin C. Vitamin C, which is also called Ascorbic Acid, is a water-soluble antioxidant that supports various processes including hydroxylation and amination processes. It is uses in enhancing the synthesis of proteoglycan, collagen and various other components of intercellular chemicals including Vitamin E. Therefore, a higher level of Vitamin C intake enhances and improves the concentration of seminal plasma, which in turn prohibits damage to the DNA[11,12,21].

On the other hand, vitamin E is a fat-soluble antioxidant. It functions as a force that neutralizes free radicals and produces a safeguard that protects the cellular membrane against the free radicals of O_2. Hence, vitamin E constrains the production of ROS in males who are infertile preventing lipid peroxidation[13,19].

In the interventional study on infertile males done by Gerco et al the interventional group was given 1 gram of vitamin C and E each for 2 months to check the semen parameters before and after the intake of an additional dosage of vitamin E and C. It was determined that after two months, the level of damage to the DNA was diminished in the intervention group ($p<0.001$)[26-27]. The study concluded that a two-month treatment of infertile males with 1 gram each of vitamin C and E enhanced ICSI success rate, especially with patients with compromised DNA. In other words, the intervention improved the DNA quality[59]. However, Gerco et al.,

Received on 14-09-2022
Accepted on 17-01-2023

found an insignificant relationship between the major semen parameters, for instance, concentration and motility and intake of vitamin C and E[23,24,26,27].

Another prominent research conducted by Moslemi et. al, determined that 52.6 percent of 690 infertile males with idiopathic asthenoteratospermia received a regular supplement of vitamin E (400 IU) in combination with selenium (200 µg) reported improvement in key semen parameters including semen morphology, sperm motility or both. This depicts that the role of the antioxidants in the fertility of functions is positive[28,54].

Selenium &N-Acetyl-Cysteine: In the formation of testosterone biosynthesis and sperm, selenium plays an important role. There are at least 25 selenoproteins found in animals and humans alike, which help in maintaining normal sperm integrity[28,52,53]. On the other hand, N-acetylcysteine works as a forerunner of glutathione peroxidase. This element originates from the amino acid L-cysteine. The research says that selenium supplements enhanced sperm concentration, morphology, sperm count, and motility in fertile and infertile males[28,53].

In 30 weeks of trial treatment of 468 infertile males with oligoasthenoteratospermia, Safarinejad et al found that with selenium and N-acetyl-cysteine treatment nearly all semen parameters improved substantially. Moreover, the interventionist group responded to better levels of serum testosterone and Inhibin B[51,53,55].

Carnitine: A naturally occurring compound, L-carnitine (LC), is a semi-essential vitamin-like substance that is needed for human metabolism. It is also known as 3-aminobutyric acid[29-30]. While being essential for bio-energetic processes, it has involvement in intermediary metabolism where it plays a significant role in forming long-chain fatty acids of acylcarnitine esters[30,31,36]. The greatest concentrations of LC are present in the epididymis, and it is around 200 times greater than the whole blood concentration. An active secretory process results in a high level of LC in epididymis[14,31,32].

Research proves that there exists a positive relationship between initial sperm movement and high levels of LC in epididymis and L-acetyl in sperm. Several studies have explored L-carnitine supplementation's effect on male fertility. Lenzi et al. undertook an experiment in which a double-blind controlled clinical trial was put in place to evaluate LC's effect on male infertility[33]. For the purpose of the study, 60 infertile men were divided into two groups (intervention and control group). The intervention group got 2 gr/day of LC and 1 gr/day of L-acetyl carnitine (LAC) for 6 months as part of therapy. A direct relation was witnessed where LC and LAC had a positive effect on sperm motility at base-line[33].

Furthermore, Balercia et al. also examined the impact of LC and LAC or combined LC and LAC on the semen motion kinetics as well as total oxygen radical scavenging capacity (TOSC)[34,37,39]. Such a randomized double-blind controlled trial consisted of 60 men with idiopathic asthenoteratospermia. After six months of therapy, it was shown that LC and LAC spiked sperm motility and TOSC in those men. Simultaneously, nine pregnancies were obtained in carnitine-treated patients in the duration of therapy and five of them were achieved after combined LC and LAC administration[34,39].

Coenzyme Q10 (CoQ10): Coenzyme Q10 (CoQ10) is also known as ubiquinone and it is an antioxidant. While being a major component in the electron transport chain, it participates in aerobic cellular respiration that helps to fuel energy. Such an oil-soluble, vitamin-like substance exists in cell membranes and lipoproteins[8,38]. Recently, the role that CoQ10 plays in male infertility has been studied thoroughly. Balercia and some other colleagues explored what its impact was on sperm motility in infertile men[34,39]. Post-therapy, it was discovered that CoQ10 rose in the semen of patients who took CoQ10[60]. Therefore, sperm motility was enhanced in these men, and additionally, twelve spontaneous pregnancies were obtained.

Similarly, there was another double-blind controlled intervention conducted by Safarinejad et al. in which 228 men with abnormal sperm concentration, motility, and morphology improved their sperm density, sperm motility, and sperm morphology within 28 weeks of treatment when given ubiquinone[40]. Moving on, Nadjarzadeh et al. examined a double-blind placebo-controlled clinical trial in which 47 infertile men randomly received 200 mg CoQ10 or placebo on a daily basis for 10 weeks in total. It resulted in non-significant changes in semen parameters including density, motility, and morphology, and additionally, total antioxidant capacity soared significantly ($p<0.05$)[41,42]. A positive correlation between CoQ10 concentration and normal sperm morphology was seen.

It was found that the concentration of CoQ10 correlated with key semen parameters such as sperm concentration, motility, and morphology as the total antioxidant capacity improves[40-42]. For this reason, Thakur suggests that a daily administration of 150 mg CoQ10 enhanced semen parameters in infertile men. Through conducting a meta-analysis, it was shown that supplementing infertile men with CoQ10 does not affect or increase live birth or pregnancy rates[34,43]. However, there is an improvement in sperm parameters such as sperm concentrations and motility along with CoQ10 concentration in semen globally.

Zinc: The element of Zinc is said to be the second most abundant metal in the body. Iron is the first one. There are multiple sources of Zinc including fish, red meat, milk, etc. However, the World Health Organization (WHO) stated that approximately one-third of the world's population has zinc deficiency[18]. It has been proven that taking zinc supplements shields the spermatozoa against bacteria as well as helps to minimize damage to chromosomes[44,45]. Therefore, it can be concluded that zinc plays a vital role in testicular development and sperm maturation. The deficiency of zinc is related to hypogonadism along with the incomplete development of sex characteristics in humans. Low levels of zinc in the semen have been associated with a reduced sperm fertilization capacity[46,47].

For this purpose, Ebisch and colleagues discovered that men who were given 5 mg of folic acid and 66 mg of zinc for 26 weeks reported improvement in sperm concentration. At the baseline, a positive correlation was seen between serum zinc and sperm concentration, motility, and inhibin B[49,50]. Furthermore, Hadwan and colleagues studied zinc supplements' effect on quantitative and qualitative characteristics of semen and ligands. The equalnumber of fertile and infertile men (37 in each group) was provided with zinc sulphate capsules every day for 3 months. The results proved that zinc supplements increase the volume of semen, progressive sperm motility percentage as well as total normal sperm count[46-48].

Multi-Antioxidant Supplementation: For the effectiveness of male infertility, multi-antioxidant supplements are considered a potent treatment[22,25]. Multi-antioxidants create a synergetic effect in improving fertility, which has made many researchers more interested in administering this treatment[57,58]. After retrograde embolization, infertile males with oligospermia (5-20 million/ml) for 6 months, Galatioto et al concluded that multi antioxidant therapy was effective in improving the seminal fluids and resulted in natural pregnancies of their spouses. Nearly twenty males with varicocele who received multi-antioxidant treatment including Vitamin E, vitamin A, vitamin C, riboflavin, manganese, zinc, copper, B12, and thiamine showed satisfactory statistically enhancement in the sperms quality of the intervention group. After the treatment, the level of DNA degradation was significantly reduced[25,51,56].

CONCLUSION

To conclude, it is imperative to mention that this study undertook an extensive review of meta-analysis of several well-established studies. This cross-sectional study concludes that there was a significant correlation between anti-oxidant supplementation and one or more aspects of semen parameter. Antioxidants like selenium, vitamin C and E, and L-Carnitine had s substantial impact on the semen morphology, motility, concentration, and DNA integrity. All in all, this study recommends future researchers delve even deeper into the topic and add more compounds to strengthen the conclusion of the study that antioxidants do play a significant role in reducing male infertility.

Acknowledgment: We are very thankful to Dr. Ayesha Jalbani consultant OBGYN, for her guidance and advice on this article.
Conflict of interest: Conflict of interests regarding the publication of this paper is none.
Funding: This research received no specific grant from any funding agency

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