

Research Article**OXIDATIVE STRESS AND MALE FERTILITY: THE IMPACT OF ANTIOXIDANT BLENDS IN TREATMENT****¹Christopher Alan Whitmore and ²Amina Fatoumata Diarra**¹Department of Reproductive Medicine and Andrology, St. George's University Hospital, London, United Kingdom²Department of Clinical Pharmacology and Reproductive Health, University of Dakar, Dakar, Senegal
DOI:10.5281/zenodo.19604451**Abstract**

The study's goal was to learn more about the positive effects of antioxidants combination on male infertility. Twenty-four men with semen low parameters (subfertility) and another 10 men normally used as control were used in this study. Males were given formulation of an antioxidant containing vitamin E 400 mg, vitamin C 500 mg, l-carnitine 1,000 mg, zinc 20 mg, selenium 0.20 mg, daily (n = 24) or a placebo (n = 10). sperm parameters and sperm DNA fragmentation index improved significantly after three months of treatment in the internal pilot study. The current results showed that antioxidants have therapeutics effects on patients with subfertility, they showed enhancement in sperm concentration, total sperm number, motility, normal forms as well as DNA fragmentation. In conclusion, antioxidants can increase the fertility and treat men with subfertility.

Keywords: Antioxidant, Men, Sperm, DNA, Subfertility**Introduction**

Plasma membrane polyunsaturated fatty acid content makes sperm especially susceptible to oxidative damage. Lipid peroxidation by reactive oxygen species (ROS) decreases the sperm membrane flexibility and tail oscillation ability, making them particularly susceptible to lipid peroxidation by ROS. During the last stages of spermatogenesis, when the spermatozoa are left alone without these protective enzymes, they are susceptible to ROS-induced mutations that alter the sperm DNA [1].

Also, ROS levels have been linked to acrosome abnormalities, cytoplasmic droplets, mid-piece anomalies, as well as defects in the tails of spermatozoa (as well as defects in the heads) .]2[

Reactive oxygen species production has been related in the past to decreased motility and sperm–oocyte fusion capability [3].

Seminal oxidative stress also affects sperm count, function, and motility, inhibiting the critical fertilization fusion]4[.

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Men with high levels of ROS had a seven-fold lower probability of fertilization than men with low levels of ROS, according to prospective studies. It also kills sperm cells since ROS is a powerful oxidant [5].

Viability and motility of ROS-exposed sperm in conventional and computer-assisted sperm motility tests were shown to be reduced [6,7]

Commercially accessible antioxidant supplements for treating male infertility exist, however data on their impact on sperm quality, pregnancy rates, and live birth rates is few. Improve male reproductive health by giving them more zinc or selenium, which increase sperm count and motility [8].

The aim of this study was to know the beneficial role of antioxidants combination on subfertility of male.

Materials and Methods:

Men (N = 24) with semen parameters illustrated in table 1 were used in this study and another 10 men normally used as control.

Table 1. Parameters of men with subfertility

| Semen parameters | Value |
|---|--------|
| Volume (ml) | 3-4 ml |
| Concentration (million /ml) | 5-10 |
| Total number (Count in million) | 30-35 |
| Total motility (%) | 25-30 |
| Progressive motility (Forward moving sperm) % | 20-30 |
| Normal Forms % | 2-3 |
| Vitality (Live sperm %) | 35-40 |

Males were given formulation of an antioxidant containing l-carnitine 1,000 mg, vitamin C 500 mg, selenium 0.20 mg, zinc 20 mg, vitamin E 400 mg, daily (n = 24) or a placebo group (n = 10).

Internal pilot results showed significant improvements in sperm parameters, including sperm DNA fragmentation index after three months of treatment.

Results and Discussion:

The current results showed that antioxidants have therapeutics effects on patients with subfertility, they showed enhancement in sperm concentration, total sperm number, motility, normal forms as well as DNA fragmentation (Figure1) (Table 2). **Table 2. Semen parameters in antioxidant and placebo groups**

| Parameters | Antioxidant | Placebo |
|-----------------------------------|-------------|---------|
| Sperm concentration (million/ mL) | 24.0 | 15.4 |
| Normal morphology (%) | 3.6 | 5.8 |
| Total motility (%) | 41.2 | 45.0 |

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| | | |
|-----------------------------|------|------|
| DNA fragmentation | 22 | 25 |
| Total sperm count (million) | 42.3 | 44.1 |

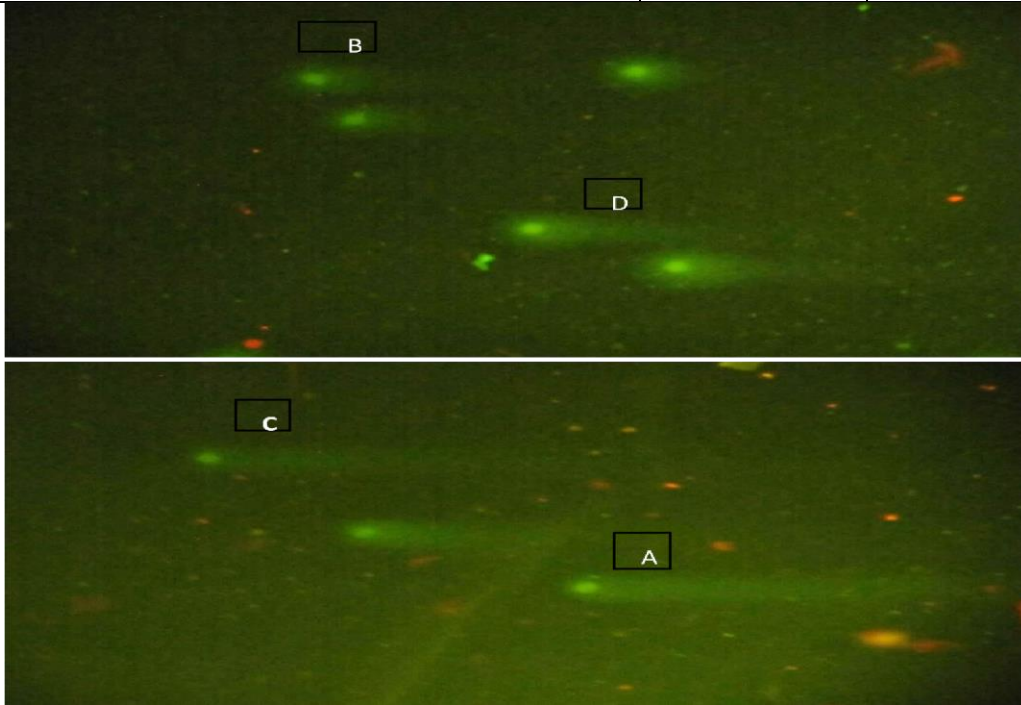


Figure 1. Microscopic Picture of Comet in treated and placebo groups Shows: A. High Comet B-No Comet C. Low Comet D. Moderate (Syber green Stain 10X)

In addition to protecting against ROS, vitamin E's antioxidant action also lowers LPO, which improves sperm functions including concentration and motility. [9]. However, it is unclear whether or not it has any impact on fertility. Despite the fact that vitamin E therapy (300 mg twice daily for three months) increased vitamin E blood serum levels, it had no effect on human seminal plasma, raising concerns about the potential influence on reproductive parameters in this small clinical trial (n = 30). Zona pellucida binding test was not changed in this clinical research, such as the quantity of reactive oxygen species (ROS) [10]. Zinc is a cofactor for DNA transcription and protein synthesis and is found in metalloproteins. Zinc is also required for spermatogenesis, as well as for proper function of the testes, prostate, and epididymis [11], as well as having antioxidant qualities that prevent LPO [12]. Oral zinc sulphate antioxidant treatment (250 mg twice day) for three months enhanced the reproductive success in asthenozoospermic males (hypoosmotic swelling test). Antisperm antibodies were similarly reduced in seminal plasma, although zinc levels remained same. Pregnancies increased by 22.5 percent (11/49) compared to 4.3 percent (2/48) in couples where males got treatment instead of a placebo [13].

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There is a higher concentration of carnitines in seminal plasma than in spermatozoa because carnitines are produced by the organism. In mitochondrial -oxidation, carnitine exists in the form of l-carnitine (LC), which serves as a shuttle for activated long-chain fatty acids to enter the mitochondria [14]. The acyl derivative of LC is L-acetyl-carnitine (LAC). Long-chain fatty acids fuel the maturation and spermatogenic processes of spermatozoa (with good effects on sperm motility) [15].

There were no effects on pregnancy (0 percent) in individuals with high levels of leucocytes who had anaerobic PVE; however, LC consumption of 1g twice daily for three months decreased spermatozoa ROS and improved pregnancy by 11.7% in these patients. These individuals' pregnancies were not improved by LC or LAC. [16].

These investigations were all tiny and untrustworthy as a consequence. Most studies solely included infertile men, although a few also included men with normal baseline semen characteristics and others who had aberrant baselines in their semen characteristics. It's been demonstrated that supplementing with vitamin C and/or E reduces DNA fragmentation in comparison to a placebo [17].

Conclusion:

In such instances, an antioxidant might act as an adjuvant therapy, preventing additional ROS damage and leading to increase fertility.

References:

- C. Lewis and A. T. Ford, "Infertility in male aquatic invertebrates: A review", *Aquatic Toxicology*. 2012, doi: 10.1016/j.aquatox.2012.05.002.
- C. I. Kobayashi and T. Suda, "Regulation of reactive oxygen species in stem cells and cancer stem cells", *Journal of Cellular Physiology*. 2012, doi: 10.1002/jcp.22764.
3. A. Agarwal, R. A. Saleh, and A. Bedaiwy, "Role of reactive oxygen species in the pathophysiology of human reproduction," *Fertility and Sterility*. 2003, doi: 10.1016/S0015-0282(02)04948-8 .
- S. L., "Human Physiology from Cell to Systems. 6th ed," Cengage Learn . Boston, MA, USA, 2011.
- A. Mehrotra, D. K. Katiyar, A. Agarwal, V. Das, and K. K. Pant, "Role of total antioxidant capacity and lipid peroxidation in fertile and infertile men," *Biomed. Res.*, 2013.
- T. Y. Shi et al., "Effects of reactive oxygen species from activated leucocytes on human sperm motility, viability and morphology," *Andrologia*, 2012, doi: 10.1111/j.14390272.2011.01252.x.

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- L. S. De Castro et al., "Sperm oxidative stress is detrimental to embryo development: A dose-dependent study model and a new and more sensitive oxidative status evaluation", *Oxid. Med. Cell. Longev.*, 2016, doi: 10.1155/2016/8213071.
- F. Atig, M. Raffa, B. A. Habib, A. Kerkeni, A. Saad, and M. Ajina "Impact of seminal trace element and glutathione levels on semen quality of Tunisian infertile men," *BMC Urol.*, 2012, doi: 10.1186/1471-2490-12-6.
- Gharagozloo P., Gutierrez-Adan A., Champroux A., Noblanc A., Kocer A., Calle A., Perez-Cerezales S., Pericuesta E., Polhemus A., Moazamian A., et al. A novel antioxidant formulation designed to treat male infertility associated with oxidative stress: Promising preclinical evidence from animal models. *Hum. Reprod. (Oxf. Engl.)* 2016;31:252–262. doi: 10.1093/humrep/dev302.
- Moslemi M.K., Tavanbakhsh S. Selenium-vitamin E supplementation in infertile men: Effects on semen parameters and pregnancy rate. *Int. J. Gen. Med.* 2011;4:99–104. doi: 10.2147/IJGM.S16275.
- Fallah A., Mohammad-Hasani A., Colagar A.H. Zinc is an Essential Element for Male Fertility: A Review of Zn Roles in Men's Health, Germination, Sperm Quality, and Fertilization. *J. Reprod. Infertil.* 2018;19:69–81.
- Zago M.P., Oteiza P.I. The antioxidant properties of zinc: Interactions with iron and antioxidants. *Free Radic. Biol. Med.* 2001;31:266–274. doi: 10.1016/S08915849(01)00583-4.
- Omu A.E., Dashti H., Al-Othman S. Treatment of asthenozoospermia with zinc sulphate: Andrological, immunological and obstetric outcome. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 1998;79:179–184. doi: 10.1016/S0301-2115(97)00262-5.
- Jeulin C., Lewin L.M. Role of free L-carnitine and acetyl-L-carnitine in post-gonadal maturation of mammalian spermatozoa. *Hum. Reprod. Update.* 1996;2:87–102. doi: 10.1093/humupd/2.2.87.
- Zhou X., Liu F., Zhai S. Effect of L-carnitine and/or L-acetyl-carnitine in nutrition treatment for male infertility: A systematic review. *Asia Pac. J. Clin. Nutr.* 2007;16(Suppl. 1):383–390.
- Vicari E., Calogero A.E. Effects of treatment with carnitines in infertile patients with prostatic-vesiculourethral epididymitis. *Hum. Reprod. (Oxf. Engl.)* 2001;16:2338–2342. doi: 10.1093/humrep/16.11.2338.

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Greco E, Iacobelli M, Rienzi L, Ubaldi F, Ferrero S, Tesarik J. Reduction of the incidence of sperm DNA fragmentation by oral antioxidant treatment. *J Androl* 2005;26:349–53.