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Idiopathic Male infertility : Nutraceutical options

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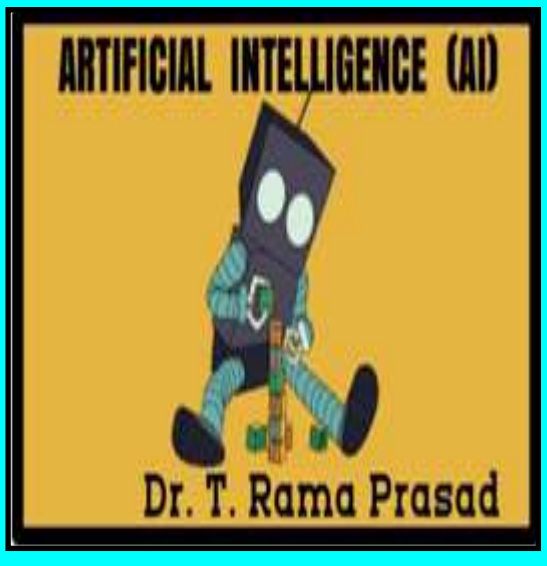

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GENERAL

Idiopathic Male infertility:Nutraceutical options

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INTRODUCTION

Globally, infertility affects about 15% of couples of reproductive age. It is defined as the inability to achieve pregnancy after one year or more of unprotected sexual intercourse[1]. WHO has recognised male infertility as a global public health issue. Male factors only, including decreased semen quality, are responsible for ~25-30% of cases of infertility[2].

Male infertility is a multifactorial condition. The etiological causes of male infertility comprise a wide variety of factors, ranging from infections, anatomical and genetic abnormalities, neurological disease, psychological, environmental and lifestyle factors[3].

Male infertility is generally characterized by morpho-functional anomalies in the sperm analysis, including low sperm count, alteration of the sperm quality parameters (Concentration, motility, morphology), or both. Abnormal spermatozoa parameters (spermatogenic failure) include total absence (azoospermia), low count (oligozoospermia-, < 15 million per millilitre of semen), abnormal morphology (teratozoospermia), and/or abnormal motility (asthenozoospermia- < 40% sperm motility or < 32% with progressive motility). Teratozoospermia represents a heterogeneous group of abnormal sperm phenotypes affecting, solely or simultaneously, the head, neck, midpiece and tail. Oligoasthenoteratozoospermia (OAT) is one of the most common phenotypes of male infertility, characterized by combination of qualitative and quantitative sperm defects[4].

The main causes of male infertility are divided into: (1) extra-testicular (obstructive); (2) testicular (primary); (3) pretesticular (secondary); (4) idiopathic[5]. In idiopathic infertility, the primary cause is not clearly manifest and it accounts for 30–40% of infertile male patients.

Currently, the patho-physiology of suboptimal semen quality is poorly understood, and many environmental and genetic factors, including oxidative stress, have been implicated. Oxidative stress is an imbalance between the production of free radicals, or reactive oxygen species (ROS), and the capacity of the body to counteract their harmful effects through neutralization by antioxidants.

Spermatozoa are particularly vulnerable to free radicals, due to the high content of polyunsaturated fatty acids in their membrane and the lack of cytoplasmic antioxidant repair systems[6]. Approximately 30–80% of men with idiopathic infertility show increased concentrations of free oxygen radicals or Reactive Oxygen Species[7](ROS).

IDIOPATHIC MALE INFERTILITY: NUTRACEUTICAL OPTIONS

Major nutraceuticals that have been studied in the management of male infertility are briefly reviewed here.

ANTI-OXIDANTS:

Overwhelming evidence suggests that oxidative stress (OS) plays a vital role in the etiology of male infertility[8]. OS could lead to abnormal sperm parameters and high levels of sperm deoxyribonucleic acid fragmentation. Several studies have reported the beneficial effects of oral antioxidants on sperm parameters[9].

1.ENZYMATIC ANTI-OXIDANTS-

Glutathione peroxidase and inositol are two enzymatic anti-oxidants known to improve sperm parameters[10].

2.NON-ENZYMATIC ANTI-OXIDANTS-

A total of 23 randomised controlled trials, which included 1,917 adults who received different antioxidants were included in a network meta-analysis. This study reported that L-Carnitine, L-carnitine + L-acetyl carnitine, coenzyme-Q10, omega-3 fatty acid and selenium were more efficacious than placebo in improving sperm quality parameters. L-Carnitine was ranked first in sperm motility and sperm morphology.Omega-3-fatty acid was ranked first in sperm concentration. Coenzyme-Q10 had better effect on sperm motility and concentration[11].

Lycopene is a primary carotenoid found in the testes. It has antiproliferative, immunomodulatory, and anti-inflammatory effects, which promote cell differentiation, improve sperm count, decrease seminal OS, and increase IVF success rates[12].

Lycopene supplementation (25 mg once a day) for 12 weeks was proven to improve sperm count and concentration in a recent Random Clinical Trial[13](RCT). Another RCT reported that oxidative stress in seminal plasma was decreased after 20mg twice daily for 12 weeks of lycopene supplementation[14].

Other antioxidants, such as N-acetyl cysteine (NAC), melatonin, alpha-lipoic acid (ALA), and omega-3 fatty acids (OFA) have also been studied in fertility management. NAC, a precursor of Glutathione Per Oxidase(GPX) , can directly stabilize free radicals by donating an electron from its outer layer. Multiple studies involving NAC have shown that it improves male fertility by increasing seminal fluid, reducing ROS molecules in sperm, and improvingother sperm parameters[15].

Melatonin is an amphiphilic hormone that increases activity of Super Oxide Dismutase (SOD), Catalase(CAT) and GPX to scavenge ROS and it also inhibits apoptosis[16]. Fertile men show higher seminal and serum levels of melatonin than infertile men[17].

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ALA is another potent biological antioxidant that can enter the Krebs cycle and assist in ATP production and also promote the functionality of SOD, CAT, and GPX . Oral supplementation with ALA improved sperm quality parameters, such as total sperm count,concentration, motility, viability, and sperm morphology[18].

OFA intake is known to increase normal sperm morphology, volume, concentration, motility, and total sperm count. A 2019 systematic PRISMA review assessed the evidence regarding OFA supplementation and the effects on semen quality markers in infertile men. They concluded that OFA does seem to have a positive effect on sperm quality parameters[19].

VITAMINS AND MINERALS:

Vitamins play an essential role in the normal functioning of the human body, with vitamins C, E, D and B9 (folic acid) being the most relevant in male fertility.

In sperm cells, vitamin C prevents agglutination and protects DNA against damage caused by ROS[20]. Few studies have shown that vitamin C supplementation improves sperm parameters. A 2016 RCT involving overweight and obese men supplemented with vitamin C reported improved semen concentration and motility[21]. Another prospective cohort study demonstrated a positive relationship between vitamin C intake and fertilization rates in couples undergoing Assisted Reproductive Technology[22](ART).

Vitamin E serves multiple functions in male fertility, including regulation of testosterone biosynthesis, modulation of telomerase activity and prevention of lipid peroxidation[23].

Vitamin D also plays a potentially key role in determining semen quality and androgen status. A cross-sectional study including 300 men showed that men with severe vitamin D deficiency [25(OH) D <10 ng/mL] had a lower proportion of motile spermatozoa (62% vs. 70%; p 0.027), progressive motile spermatozoa (56% vs. 64%; p 0.035) and % of morphologically normal spermatozoa (6% vs. 8%) compared with those with vitamin D sufficiency[24].

In a study, 86 infertile men with idiopathic oligoasthenospermia were randomized to oral cholecalciferol 200 IU/day with calcium 600 mg/day, or a combination of vitamin E 100 mg plus vitamin C 100 mg, t.i.d. After three months, semen quality, especially sperm count per ejaculate and the proportion of progressively motile sperm were increased only in the vitamin D group. In addition, pregnancy rates were higher in the vitamin D group (16.3%) compared with the control group (2.3%) ($p < 0.05$)[25].

Folic acid is essential for DNA metabolism and gene expression to prevent abnormal chromosomal replication and mitochondrial DNA deletions; however, its role in male infertility requires further exploration[26].

Minerals, especially zinc and selenium, influence male fertility. Zinc is a micronutrient that plays an important role in cell signaling, enzyme activity, normal growth and sexual maturation and management of mitochondrial OS. Zinc incorporation into sperm may protect against sperm decondensation and improve sperm motility, membrane stabilization and antioxidant capacity[27].

Low zinc levels are widely reported in the seminal plasma of infertile men[28]. A RCT with asthenzoospermia patients concluded that the zinc supplemented group had a higher conception rate (22.5%) compared to placebo (4.2%)[29].

Selenium promotes DNA repair and is positively associated with sperm count, morphology, motility, and concentration. Higher levels of successful conception and live births are correlated with higher seminal selenium levels[30]..

CONCLUSION:

Even though few clinical trials have shown promising role of anti-oxidants, vitamins and minerals, more well designed RCTs with larger patient population are needed to establish their role in the management of male infertility. Since lifestyle choices and environmental factors influence male fertility, their integration in comprehensive management of male infertility is also essential.

REFERENCES:

1. Zegers-Hochschild, F.; Adamson, G.D.; de Mouzon, J.et al. Fertil. Steril. 2009, 92, 1520–1524.
2. Mehra, B.L.; Skandhan, K.P.; Prasad, B.S.et al. Urol. J.2018, 85, 22–24.
3. Anifandis, G.; Katsanaki, K.; Lagodonti, G.et al. Int. J. Environ. Res Public Health 2018, 15, 1117.
4. Coutton C, Escoffier J, Martinez G, et al. Hum Reprod Update 2015;21:455-485 .
5. Szkodziak, P.; Wozniak, S.; Czuczwar, P.et al. Ann. Agric. Environ. Med. 2016, 23, 227–230.
6. Majzoub A, Agarwal A. Indian J Urol Soc India.2017;33:207–14.
7. Agarwal, A.; Parekh, N.; Selvam, M.K.P.et al. World J. Men's Health 2019, 37, 296–312.
8. Russo A, Troncoso N, Sanchez F, et al. Life Sci 2006; 78:1401–6. Russo A, Troncoso N, Sanchez F, et al. Life Sci 2006; 78:1401–6.
9. Arafa M, Agarwal A. Antioxid (Basel) 2020 9:219.
10. Governini, L.; Ponchia, R.; Artini, P.G.; et al.. J. Clin. Med. 2020, 9, 1638.
11. Kun-peng Li , Xue-song Yang and Tao Wu. Frontiers in Endocrinology; February 2022 I Volume 13 I Article 810242
12. Nouri, M.; Amani, R.; Nasr—Esfahani, M. et al. Phytother. Res. 2019,33,3203–3211.
13. Nouri, M.; Amani, R.; Nasr-Esfahani, M.et al. Phytother. Res. 2019, 33,3203–3211.
14. Oborna, I.; Malickova, K.; Fingerova, H.et al.Am. J. Reprod. Immunol. 2011,66, 179–184.
15. Torres-Arce, E.; Vizmanos, B.; Babio, N.et al.. Biology 2021, 10, 241.
16. Malmir, M.; Naderi Noreini, S.; Ghafarizadeh, et al.Andrologia 2020, 53, e13944.
17. Hassan, M.; El-Taieb, M.; Fares, N.et al. Exp.Ther. Med. 2020, 20, 235–242.
18. Haghighian, H.K.; Haidari, F.; Mohammadi-asl, J.et al. Men.Fertil. Steril. 2015, 104, 318–324.
19. Falsig, A.-M.L.; Gleerup, C.S.; Knudsen, U.B. Andrology 2019, 7, 794–803.
20. Angulo, C.; Maldonado, R.; Pulgar, E.et al. Biol. Res. 2011, 44, 169–180.
21. Rafiee, B.; Morowvat, M.H.; Rahimi-Ghalati, N.et al. Urol. J. 2016, 13, 2635–2639.
22. Li, M.-C.; Chiu, Y.-H.; Gaskins et al. J. Nutr. 2019, 149, 1977–1984.
23. Miyazawa, T.; Burdeos, G.C.; Itaya, M.; et al IUBMB Life 2019, 71, 430–441.
24. Blomberg Jensen, M.; Bjerrum, P.J.; Jessen, T.E.; et al. Human Reprod. (Oxford, England) 2011, 26, 1307–1317.
25. Deng, X.L.; Li, Y.M.; Yang, X.Y.; et al.. Zhonghua Nan Ke Xue 2014, 20, 1082–1085.
26. Irani, M.; Amirian, M.; Sadeghi, R.; et al. Urol. J. 2017, 14, 4069–4078.
27. Kerns, K.; Zigo, M.; Sutovsky, P. IJMS 2018, 19, 4097.
28. Zhao, J.; Dong, X.; Hu, X.et al.. Sci. Rep. 2016, 6, 22386.
29. Omu, A.E.; Dashti, H.; Al-Othman, S.. Eur. J. Obstet. Gynecol. Reprod. Biol. 1998, 79, 179–184.
30. Alahmar, A.T;Sengupta,P.Biol. Trace Elem. Res. 2021, 199, 1246–1252.