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Coenzyme Q10 (CoQ10) and Male Fertility Overview with Reference Publications

The information offered here represents a brief and selective overview of the published medical literature in regards to coenzyme Q10 (CoQ10) supplementation and male fertility*. This review has been prepared by the Center for Human Reproduction (CHR), a leading fertility center in New York City, and is being distributed by Fertility Nutraceuticals, LLC, with permission from CHR.

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Age-related decline in male fertility and role of oxidative stress

Male age has not been conclusively shown to influence fertility rates[1]. However, one recent study suggested that, independent of their partners' age, men might experience a precipitous decline in fertility between ages 35 and 39[2]. Advancing male age is, indeed, associated with declines in various sperm parameters, including semen volume, motility and morphology[3,4,5]. Older men have also been shown to demonstrate a higher rate of DNA fragmentation and more early markers of apoptosis[6,7,8].

Oxidative damage and sperm functions

Oxidative damage has been suggested as one possible cause of observed declines in sperm parameters[1]. Environmental factors, like chemicals, heat and radiation, as well as lifestyle factors including smoking, alcohol consumption and chronic stress have been implicated[9]. Due to their high concentration of polyunsaturated fatty acids, sperm cells are considered particularly vulnerable to oxidative stress[10,11].

Oxidative stress damages sperm membranes and sperm DNA. Compromised sperm membranes reduce sperm motility and its ability to fuse with the oocyte for fertilization. DNA damage inhibits paternal contribution of DNA to the embryo[1]. Studies have also suggested that such DNA damage may increase germ cell apoptosis, lowering sperm count[12].

Oxidative damage to mitochondrial DNA

Oxidative stress can also cause DNA damage in mitochondria, indirectly hampering spermatogenesis. Damage in mitochondrial DNA (mtDNA) can compromise mitochondrial energy metabolism[13], which then reduces energy availability for sperm cells during meiosis. This suboptimal energy metabolism has been suggested as one of the causes of abnormalities in sperm morphology[13] and for sperm DNA abnormalities[1].

Antioxidants: Natural defense mechanisms within the testes

Healthy testicular environment is equipped with antioxidant enzymes, including coenzyme Q10 (CoQ10). CoQ10 and other antioxidants are thought to protect sperm membrane, sperm DNA and mtDNA from oxidative damage. In such a healthy testicular environment, normally functioning mitochondria with full

membrane potential provide energy to "fuel" spermatogenesis, thereby preventing meiotic arrest and abnormal sperm morphology[13].

Recently, age-related decline in serum antioxidant levels have attracted attention as a possible explanation for the observed decline in male fertility with advancing age[1]. Supplementation with vitamin C, vitamin E, glutathione and other antioxidants has, therefore, been suggested as a potential approach toward addressing male infertility.

Supplementation with CoQ10 for male fertility

One such antioxidant, coenzyme Q10 (CoQ10), is naturally synthesized within mitochondria, but its levels decline with age[14]. After Mancinin et al demonstrated that CoQ10 concentrations in the seminal fluid correlated with sperm count and motility[15], a number of studies investigated whether oral supplementation with CoQ10 would improve sperm parameters, partner pregnancy rates and other fertility-related metrics. Some studies have found CoQ10 supplementation to significantly improve sperm parameters, leading to the suggestion by Mancini et al that CoQ10 may lead to new insights into unexplained infertility[16].

Randomized controlled trials

Safarinejad reported significant improvements in sperm density and motility after supplementation with CoQ10 for 26 weeks[17]. The study, investigating infertile men with idiopathic oligoasthenoteratospermia (low semen count, motility and morphology), found a positive correlation between duration of CoQ10 treatment and sperm count, motility and morphology[17].The study also reported that FSH and LH levels declined with CoQ10 supplementation[17]. The same authors later replicated most of those findings, using a reduced form of CoQ10[18]. In another trial, Balercia et al reported significantly increased levels of CoQ10 in seminal plasma and sperm cells, and also noted improved sperm motility[19]. The lower baseline values were before supplementation, the more likely was there a respond to CoQ10 supplementation[19]. The most recently reported study by Nardiarzadeh et al demonstrated that men who received CoQ10 supplementation for 3 months demonstrated higher CoQ10 concentrations, higher antioxidant enzyme activity markers in the seminal plasma and significantly better sperm morphology than men who received placebo[20].

References

1. Amaral S, Amaral A, Ramalho-Santos J. Aging and male reproductive function: A mitochondrial perspective. Front Biosci 2013;S1:181-197.
2. Matorras R, Matorras F, Exposito A, Martinez L, Crisol L. Decline in human fertility rates with male age: a consequence of a decrease in male fecundity with aging? Gynecol Obstet Invest 2011;71:229-235.
3. Kidd S, Eskenazi B, Wyrobek A. Effects of male age on semen quality and fertility: a review of the literature. Fertil Steril 2001;75:237-248.
4. Sartourius G, Nieschlag E. Paternal age and reproduction. Hum Reprod Update 2010;16:65-79.
5. Sloter E, Schmid T, Marchetti F, Eskenazi B, Nath J, Wyrobek A. Quantitative effects of male age on sperm motion. Hum Reprod 2006;21:2868-2875.
6. Singh N, Muller C, Berger R. Effects of age on DNA double-strand breaks and apoptosis in human sperm. Fertil Steril 2003;80:1420-1430.
7. Schmid T, Eskenazi B, Baumgartner A, Marchetti F, Young S, Weldon R, Anderson D, Wyrobek A. The effects of male age on sperm DNA damage in healthy non-smokers. Hum Reprod 2007;22:180-187.

8. Colin A, Barroso G, Gomez-Lopez N, Duran E, Oehninger S. The effect of age on the expression of apoptosis biomarkers in human spermatozoa. Fertil Steril 2010;94:2609-2614.
9. De Celis R, Pedron-Nuevo N, Feria-Velasco A. Toxicology of male reproduction in animals and humans. Arch Androl 1996;37:201-218.
10. Aitken RJ, Gordon E, Harkiss D, Twigg JP, Milne P, Jennings Z, Irvine DS. Relative impact of oxidative stress on the functional competence and genomic integrity of human spermatozoa. Biol Reprod 1998;59(5):1037-46.
11. Sheweita SA, Tilmisany AM, Al-Sawaf H. Mechanisms of male infertility: role of antioxidants. Curr Drug Metab 2005;6(5):495-501.
12. Agarwal A, Saleh R, Bedaiwy M. Role of reactive oxygen species in the pathophysiology of human reproduction. Fertil Steril 2003:79;829-843.
13. Nakada K, Sato A, Yoshida K, Morita T, Tanaka H, Inoue S, Yonekawa H, Hayashi J. Mitochondria-related male infertility. Proc Natl Acad Sci USA 2006;103:15148-15153.
14. Pignatti C, Cocchi M, Weiss H. Coenzyme Q10 levels in rat heart of different age. Biochem Exp Biol 1980;16:39-42.
15. Mancini A, De Marinis L, Oradei A, Hallgass ME, Conte G, Pozza D, Littarru GP. Coenzyme Q10 concentrations in normal and pathological human seminal fluid. J Androl 1994;15(6):591-594.
16. Mancini A, De Marinis L, Littarru GP, Balercia G. An update on coenzyme Q10 implications in male infertility: biochemical and therapeutic aspects. Biofactors 2005;25:165-174.
17. Safarinejad MR. Efficacy of coenzyme Q10 on semen parameters, sperm function and reproductive hormones in infertile men. J Urol 2009;182(1):237-248.
18. Safarinejad MR, Safarinejad S, Shafiei N, Safarinejad S. Effects of the reduced form of coenzyme Q10 (ubiquinol) on semen parameters in men with idiopathic infertility: a double-blind, placebo controlled, randomized study. J Urol 2012;188(2):526-531.
19. Balercia G, Buldreghini E, Vignini A, Tiano L, Paggi F, Amoroso S, Ricciardo-Lamonica G, Boscaro M, Lenzi A, Littarru G. Coenzyme Q10 treatment in infertile men with idiopathic asthenozoospermia: a placebo-controlled, double-blind randomized trial. Fertil Steril 2009;91(5):1785-1792.
20. Nadjarzadeh A, Shidfar F, Amirjannati N, Vafa MR, MOtevalian SA, Gohari MR, Nazeri Kakhki SA, Akhondi MM, Sadeghi MR. Effect of coenzyme Q10 supplementation on antioxidant enzymes activity and oxidative stress of seminal plasma: a double-blind randomized clinical trial. Andrologia 2013 [epub ahead of print].