Turkiye Klinikleri J Health Sci. 2021;6(1):139-47

DERLEME REVIEW

DOI: 10.5336/healthsci.2020-75062

# Coenzyme Q10 in Male Infertility

## Erkek İnfertilitesinde Koenzim Q10

Ayçıl ÖZTURAN ŞİRİN[a], Yasemin AKDEVELİOĞLU[b]

[a]Department of Nutrition and Dietetics, Adnan Menderes University Faculty of Health Sciences, Aydın, TURKEY
[b]Department of Nutrition and Dietetics, Gazi University Faculty of Health Sciences, Ankara, TURKEY

**ABSTRACT** Currently the male factor is frequently encountered in the infertility problem. Basically, the factors that cause sperm dysfunction and male infertility are environmental, physiological and genetic. Excessive amount of reactive oxygen species and other oxidant radicals have been associated with male infertility. In addition, although semen analysis parameters appear normal in idiopathic male infertility, it is suggested that the possible cause of infertility is oxidative stress. Antioxidants in foods that are protective against oxidative stress increase the success of assisted reproductive techniques by protecting spermatozoa from free oxygen radicals, preventing DNA breaks caused by free oxygen radicals, and supporting the sperm maturation process. Coenzyme Q10 (CoQ10), which is found in every cell and has the ability to dissolve in oil, is a vitamin-like compound that acts as a coenzyme in key enzymatic reactions in energy production in the cell. Endogenous CoQ10, is significantly associated with sperm count and motility and is shown as one of the most important antioxidants in seminal plasma. Exogenous CoQ10 administration can be explained by its positive effects on sperm motility, its effectiveness in mitochondria and its antioxidant effects. In this review, articles investigating the effect of oxidative stress on infertility and the role of CoQ10, a natural antioxidant vitamin in the treatment of infertility, were presented. As a result, the positive effects of using CoQ10 as a supportive treatment in male infertility have been shown in studies. However, more comprehensive, long-term and pregnancy-related studies are needed.

**Keywords:** Infertility; coenzyme Q10; oxidative stress

**ÖZET** Günümüzde infertilite problemi içerisinde erkek faktörü sıklıkla karşımıza çıkmaktadır. Temel olarak sperm fonksiyon bozukluğu ve erkek infertilitesine neden olan faktörler çevresel, fizyolojik ve genetiktir. Aşırı miktarda bulunan reaktif oksijen türü ve diğer oksidan radikaller erkek infertilitesi ile ilişkilendirilmiştir. Ayrıca idiyopatik erkek infertilitesinde semen analizi parametreleri normal görünmesine rağmen olası infertilite nedeninin oksidatif stres olduğu öne sürülmektedir. Besinlerde bulunan ve oksidatif strese karşı koruyucu olan antioksidanlar spermatozoayı serbest oksijen radikallerinden koruyarak, serbest oksijen radikallerinin neden olduğu DNA kırılmalarını önleyerek, sperm olgunlaşma sürecine destek vererek yardımcı üreme tekniklerinin başarısını artırmaktadır. Her hücrede bulunan ve yağda çözünebilme özelliğine sahip olan koenzim Q10 (CoQ10), hücrede enerji üretiminde kilit enzimatik reaksiyonlarda koenzim olarak görev yapan vitamin benzeri bir bileşiktir. Endojen CoQ10 sperm sayısı ve hareketliliği ile önemli ölçüde ilişkili olup, seminal plazmada en önemli antioksidanlardan biri olarak gösterilmektedir. Eksojen CoQ10 uygulamasının sperm hareketliliği üzerine olumlu etkilerinin olması, mitokondrideki etkinliği ve antioksidan etkileri ile açıklanabilmektedir. Bu derlemede, oksidatif stresin infertilite üzerindeki etkisini ve infertilite tedavisinde doğal bir antioksidan vitamin olan CoQ10'in rolünü araştıran makaleler incelenmiştir. Sonuç olarak, yapılan çalışmalarda genel olarak CoQ10'in destekleyici bir tedavi olarak erkek infertilitesinde kullanımının olumlu etkileri gösterilmiştir. Ancak, daha kapsamlı, uzun süreli ve gebelikle ilgili sonuçların değerlendirildiği çalışmaların yapılmasına ihtiyaç duyulmaktadır.

**Anahtar Kelimeler:** İnfertilite; koenzim Q10; oksidatif stress

Infertility is defined as "reproductive system disease, defined by the inability to achieve a clinical pregnancy after a year or more of unprotected sexual intercourse".[1] 10-15% of couples worldwide face infertility problem.[2] It is estimated that about 10-20% of couples in Turkey are infertile, according to the Turkey Demographic and Health Survey 2013 data, rate of married women at the ages of 15-49 years, who don't have children and indicating not to have children increased in 2013 compared to 2008 from 3.9% to 11.2%.[3,4] Although the infertility problem may be due to both sexes, an important part is caused

**Correspondence:** Ayçıl ÖZTURAN ŞİRİN
Department of Nutrition and Dietetics, Adnan Menderes University Faculty of Health Sciences, Aydın, TURKEY/TÜRKİYE
**E-mail:** aycilozturan@gmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Health Sciences.

***Received:*** 25 Mar 2020 ***Received in revised form:*** 24 Jun 2020 ***Accepted:*** 26 Jun 2020 ***Available online***: 21 Jan 2021

by men, not being lower than 50%. In approximately 30-40% of these identified cases, the cause of infertility cannot be explained, environmental factors, lifestyle, diet and professional factors are suggested.[5]

Basically, the factors that cause sperm dysfunction and male infertility are environmental, physiological and genetic. In determining male infertility, semen analysis is performed, and sperm concentration and / or motility and / or morphology are evaluated. Oligozoospermia is a medical situation characterized by low sperm count and quality and is responsible for 90% of male infertility.[6] In a study, excessive amount of reactive oxygen species (ROS) and other oxidants have been related with male infertility.[7] In addition, although semen analysis parameters appear normal in idiopathic male infertility, it is reported that the possible cause of infertility is oxidative stress. The increase in oxidants can occur due to a specific or nonspecific reaction between adjacent cellular components such as unsaturated fatty acids, DNA and proteins.[8] Due to the unsaturated fatty acids contained in the sperm, it is highly susceptible to oxidation and spermatogenic cells with oxidative damaged DNA cause the development of infertility.[5]

It is stated that oxidative stress is associated with male infertility. However, the use of antioxidants in the treatment of infertility is under discussion and is suggested to be a "complementary" treatment instead of a physiopathological treatment.[7] In this review, articles investigating the effect of oxidative stress on infertility and also the effect of coenzyme Q10 (CoQ10), a natural antioxidant vitamin in the treatment of infertility, were presented.

## OXIDATIVE STRESS

Oxidative stress is defined as the disruption of the oxidative balance in the body because of the inadequate antioxidant defense mechanism and increased ROS levels such as superoxide and hydroxyl radical and hydrogen peroxide.[8] ROS are agents carrying a free radical and one or more unpaired electron and that are reactive oxidizing and they play a role in various signaling mechanisms. Although ROS are normally produced during mitochondrial respiration, high levels of ROS can cause serious diseases by interacting with lipids, proteins and DNA, it is even associated with many disease, such as cancer, rheumatic diseases (arthritis, etc.), aging, toxin exposure, physical damage, infection and inflammation.[9,10]

**TABLE 1:** Factors causing the formation of infertility in men.

| Factors that frequently cause infertility in men[12] |
|---|
| • Varicocele |
| • Idiopathic-unexplained infertility |
| • Obstruction |
| • Undescended testicle |
| • Immunological mechanisms |
| • Ejaculation disorder |
| • Testicular failure |
| • Drug-radiation effect |
| • Endocrine disorders |

Excessive amount of free oxygen radicals superoxide anion, hydrogen peroxide, peroxyl radicals and reactive hydroxyl radicals, especially nitric oxide (NO) and peroxynitrite anion, have important effects on reproductive and sperm functions.[10] Sperm production requires low levels of hydrogen peroxide and normal limits of ROS for sperm capacitation during fertilization. However, the emergence or progression of many of the factors that cause infertility formation in men is related to ROS and genetic and environmental factors are also significant (Table 1).[11,12]

Spermatozoa superoxide anion produces various types of ROS, including hydrogen peroxide and NO. Produced in small quantities, ROS plays a functionally important role in directing the tyrosine phosphorylation steps associated with sperm capacitation (cellular changes required for the development of fertilization ability in sperm). ROS is thought to have a positive effect on spermatozoa, thanks to its ability to affect intracellular levels of cAMP on phosphorylation of tyrosine. Also, ROS, especially hydrogen peroxide, may increase tyrosine phosphorylation by selectively suppressing tyrosine phosphatase activity. However, it has been reported that high ROS levels are harmful for gametes and endanger the functions of gametes due to lipid peroxidation, protein damage and DNA strand breakage.[9] In some pathological conditions, levels of ROS occurring in spermatozoa pass over sperm antioxidant defenses, which may lead to oxidative stress and then infertility.[13] It has been suggested that oxidative stress can impair not only the ability of sperm to fertilize, but also the ability to promote the development of a healthy embryo. In addition, DNA damage in human spermatozoa is reported to correlate with increasing low rates and developing morbidity in infants.[9] With the increase in ROS production, the negative effect of oxidative stress on reproductive health increases. Therefore, antioxidant capacity should be at an enough level against the oxidants formed. Mechanisms related to possible beneficial effects of antioxidant use should be investigated and their therapeutic potential should be determined to prevent the negative effects of oxidative stress.[10]

## ANTIOXIDANTS

Antioxidants represent a wide range of products because many chemical structures have antioxidant activity directly or indirectly. Definition of antioxidants related to "dietary antioxidants" is; "a compound that significantly reduces the negative impact of ROS, reactive nitrogen species, or both, on normal physiological mechanism in men".[14] Antioxidant contents and bioavailability of foods may differ according to the type of food, harvest time and methods, climate and storage conditions, preparation method and consumption habits of individuals. Antioxidants are divided into two groups, enzymatic and non-enzymatic. Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px), glutathione reductase (GR) and glucose 6-phosphate dehydrogenase (G6PD) enzymatic; Minerals (Se, Zn), vitamins (A, C, K and E), carotenoids (β-carotene, lycopene, lutein, zeaxanthin), organosulfur compounds (allium, allyl sulfite, indoles), low molecular weight antioxidants (GSH-Px, uric acid), antioxidant co-factors (coenzyme Q10) and polyphenols are grouped non-enzymatically.[15] In addition to being protective against many diseases by preventing oxidative stress of antioxidants in foods, it increases the success of assisted reproductive techniques by protecting spermatozoa from free oxygen radicals, by preventing DNA breaks caused by free oxygen radicals.[7,15] In addition to CAT, SOD, GR and GSH-Px, seminal plasma contains non-enzymatic antioxidants such as ascorbate, albumin, urate, pyruvate, glutathione, vitamin E, vitamin A, ubiquinol and hypothaurine.[16]

Another important source of sperm oxidative stress is sperm use during assisted reproductive techniques and cryopreservation procedures.[17] In an in vitro study, it has been reported that it is imperative to prevent oxidative stress in order to store the sperm by freezing and then use them in assisted reproduction. It has been stated that the use of suitable antioxidants for sperm media has positive effects on the evaluation of abilities of embryos produced in vitro.[13] Although antioxidant use shows that it improves semen quality in subfertile men, there is still no definitive evidence that this treatment leads to an increase in pregnancy rates, but it is still controversial whether it affects the developmental adequacy of the embryo as a result of fertilization.[13,18]

## COENZYME Q10

### WHAT IS CoQ10?

CoQ10 (Ubiquinol-10 and / or ubiquinon-10) is a vitamin-like compound that acts as a coenzyme in key enzymatic reactions in energy production, which is present in every cell and has a fat-soluble property. CoQ10 is present in tissues as ubiquinol-10 (reduced form) and ubiquinon-10 (oxidized form). Ubiquinone and ubiquinol are derived from "ubiquitous quinine", which means "in everywhere" in Latin because it is present in all cells. CoQ10 has a chemical formula that shares the common benzoquinone ring with an isoprenoid side chain. In humans and several other mammal species, this structure is called CoQ10 because the side chain consists of ten isoprene units.[19,20]

CoQ10, a member of the ubiquinon family, is a compound that can be synthesized in humans and all animals. It acts as a coenzyme in the activities of enzyme systems (complex I, II and III) in the reduction-oxidation reactions in the electron transfer system (ETS). Thanks to the quinone group in the CoQ10 structure, it acts as an electron carrier and by adding the electrons and protons it carries to the quinone ring, it turns into hydroxyquinone. It also allows electrons to be carried from complex I and II to complex III, while ATP production takes place. With this mechanism, CoQ10 plays an important role in energy production.[21,22] Another task of CoQ10 is that it interacts with free radicals and acts as an antioxidant, preventing lipid peroxidation and biomolecule damage. It also takes part in the regeneration of other antioxidants. In addition, it is stated that CoQ10 has functions in ensuring membrane stability, cell signal, gene expression, cell growth and apoptosis control.[22]

## CoQ10 SOURCES

CoQ10, which is found in 2 sources as exogenous and endogenous, is synthesized in a common pathway with cholesterol biosynthesis with acetyl-CoA and exogenous tyrosine amino acid. Vitamin $B_6$ is needed for tyrosine to participate in the synthesis of CoQ10. Endogenous CoQ10 is found in human tissues mostly in the heart, liver and kidney, and the least in lung tissues.[19] Exogenous CoQ10 is taken with diet. CoQ10 is available in different amounts in all vegetable and animal foods, such as beef, chicken, trout, broccoli, soybeans. CoQ10 is a substance with low bioavailability due to its large molecular mass and low water solubility. Although there is no specific intake recommended for CoQ10, the amount taken from food is estimated to be around 10 mg.[23]

The amount of CoQ10 in the body decreases due to aging and some diseases. For this reason, the use of CoQ10 as a supplement has become very popular in recent years. It is stated that the use of CoQ10, which is frequently used as an energy enhancer in the body, can be effective as a support in the treatment of muscle strengthening, immune system, blood pressure, diabetes, cardiovascular and neurodegenerative diseases.[23] In recent years, it has been reported that antioxidant supplements may be beneficial in problems related to the reproductive system and it is stated that the use of CoQ10 as a supplement may have beneficial effects in male infertility due to its antioxidant properties.[7,24,25]

## CELL AGING-MITOCHONDRIAL FOODS

Whether the aging duration in reproductive system functions can be changed is an important issue. It is reported that a mechanism that can increase mitochondrial activity and energy production can improve pregnancy outcomes in elderly women. Mitochondrial nutrients have been successfully used to treat conditions associated with reduced energy production in the mitochondria and are suggested to be highly reliable for both mother and embryo. Supplementation of mitochondrial foods such as r-alpha lipoic acid (ALA) and CoQ10 can decrease the risk of chromosomal aneuploidy due to oocyte aging through increased energy for thrombomy and chromosomal separation. Therefore, it is thought that "mitochondrial nutrition" will have an important effect in the diet of elderly women.

The term of "mitochondrial nutrition" shows that it may be possible to increase the mitochondrial activity in several tissues to affect the whole organism by adding the essential cofactors, energy boosters and antioxidants to the diet. Many cofactors and coenzymes that are essential for chemical reactions occurring in mitochondria are included in the diet. Although it is not required directly for chemical reactions, antioxidants are reported to be beneficial because they are responsible for reducing ROS accumulation which are harmful derivatives of oxygen metabolism also, has the potential to damage intracellular proteins and mitochondrial membranes. As a nutritional cofactor, energy enhancer and antioxidant, today, the most focused on CoQ10, C, E and $B_6$ vitamins, selenium, catechins, carnitine, proanthocyanidins, ALA.[26]

The beneficial effects of carnitine and CoQ10 have been demonstrated in many organ systems in animals. When both of carnitine and CoQ10 use were examined in humans, both showed their ability to enhance mitochondrial function and reduce oxidative damage. Antioxidants such as proanthocyanidins, catechins, N-acetylcysteine and vitamin E have been shown to have beneficial effect the mitochondrial function on reproductive cells and various organ systems, including sperm and oocytes.[27]

With aging in the human body, a decrease in CoQ10 concentration occurs in the tissues. In a study, the effects of CoQ10 insufficiency on ROS production, cell viability and mitochondrial activity were examined, and high deficiency (less than 20% of normal) was shown to be a significant bioenergetic problem.[28] Age-related CoQ10 deficiency is generally seen as moderate insufficiency (30-45% of normal) and creates a pronounced bioenergetic problem. However, increased ROS production, cell death and lipid oxidation has been reported. CoQ10 support given to these patients normalized the bioenergetic state and oxidative balance in fibroblasts.[29] Another study concluded that antioxidants such as L-carnitine (LC) and CoQ10 have beneficial effects on sperm parameters.[30]

As a result, the data available to humans are often inadequate, although positive, making it difficult to determine effectiveness and safety.[27] Large sample, randomized and controlled studies are needed to examine the impact of mitochondrial nutrients on reproductive problems.

## MALE INFERTILITY

Endogenous CoQ10, one of the primary antioxidants in seminal plasma, is significantly associated with sperm motility and count. It is stated that sperm motility increases with exogenous CoQ10 application.[7] CoQ10 plays a role in mitochondrial bioenergetics, which is important in sperm maturation as it functions in ETS in mitochondria.[31] Although some studies have shown that CoQ10 has a beneficial effect in increasing sperm motility and concentration, there was no difference in pregnancy rates.[32-34] A more recent study showed that CoQ10 is effective in enhanced semen parameters in men individuals with varicocele.[35] Two large studies have confirmed that CoQ10 and ubiquinol (reduced form of CoQ10) improve sperm parameters in men with idiopathic infertility effectively and safely. Patients supplemented with CoQ10 and ubiquinol had higher levels of CAT and SOD, inhibin B and lower levels of FSH vs. placebo.[36,37] In a study, pregnancy was detected in 34% of spouses of idiopathic oligoasthenozoospermia (OAT) treated with CoQ10. However, since there was no control group in this study, no comparison was made.[38] In a recent meta-analysis study, it was concluded in the literature that there is no clear data that CoQ10 improves live birth or pregnancy rates, but it provides a global enhancement in sperm parameters.[39] It is thought that CoQ10 may have a beneficial effect in the treatment of asthenozoospermia due to its function in the mitochondria as well as its antioxidant features. It is stated that there is a relationship between increased CoQ10 concentration and sperm motility in seminal plasma and sperm cells, also CoQ10 plays a role in protecting sperm DNA against oxidative damage.[7]

One of the mechanisms by which CoQ10 has a positive effect on male infertility is related to the fact that some CoQ10 increase may increase the respiratory rate since the mitochondrial concentration of CoQ10 is close to NADH oxidation. Oxidative phosphorylation recovery, which occurs with an increase in respiratory rate, also positively affects sperm cells. The other is that increased CoQ10 levels require an appropriate and high concentration of lipid carrier.[7] CoQ10 is responsible for protecting cells from damage caused by lipid peroxidation.[40] In a study with male rats with high and oxidized low density lipoprotein (LDL) levels, CoQ10 and LC supplements were found to have protective effects against hypercholesterolemia related fertility problems.[41] In a randomized, placebo-controlled study by Safarinejad, it was found that CoQ10 supplementation in 212 infertile men with idiopathic OAT provided significant improvement in sperm parameters.[34] In different studies, a positive improvement in sperm parameters has been observed in patients receiving CoQ10 (200 mg and 150 mg) orally.[36,42] In the study, it was shown that sperm parameters step by step return to their basic values in the period when CoQ10 was not used, but the observed differences were still important.[36] In another study it was reported that CoQ10 supplementation increased the seminal total antioxidant capacity (TAC) but did not significantly change sperm parameters.[37] Patients supplemented with CoQ10 increased the activity of enzymatic antioxidants, such as CAT and SOD in seminal plasma, for 3 months.[43] In addition, 8-isoprostane levels were shown to be lower in the group of supplemented CoQ10. In that study it was reported that CoQ10 levels correlated significantly with the most important sperm parameters, depending on improvements in TAC. In a meta-analysis it was noted that there was an increase in CoQ10 concentrations in semen and improvements in sperm parameters. However, it has been stated that these results should be interpreted with caution, since this does not provide information on whether this situation increases the likelihood of pregnancy or live birth.[40]

CoQ10 is a vitamin taken into our body with foods consumed daily. Although CoQ10 supplementation effect was investigated in the studies conducted, no relation was found between dietary CoQ10 intake and semen parameters in a study in which the relationship between CoQ10 taken with food and semen parameters was examined. However, according to the data obtained from the study, the average amount of CoQ10 taken with the diet is 10 times less than the amount of CoQ10 given as a supplement in clinical studies. Therefore, as a result of the study, it was reported that the intake of CoQ10 only with nutrients may be insufficient for optimal semen parameters.[44] In a meta-analysis study, it was found that 200-300 mg/day CoQ10 supplementation for 3-6 months improve sperm parameters.[45] It has been stated that taking CoQ10 as a supplement in the treatment of infertility has positive results and improves seminal parameters, and it is reported that men who have been treated with a combination of various antioxidants have a high pregnancy rate in their spouses.[31,46] Some of researches addressed in the study were performed on Table 2.

## CONCLUSION

CoQ10 is an important antioxidant in seminal plasma and significantly associated with sperm parameters. CoQ10 levels correlate with sperm motility in seminal plasma.[7,32] Exogenous CoQ10 application can be explained by its beneficial effects on sperm motility, its effectiveness in mitochondria and its antioxidant effects. The development of semen kinetic properties after CoQ10 treatment and the relationship between CoQ10 levels and sperm motility also supports the positive relationship of CoQ10 with infertility.[24] More detailed studies on these molecular mechanisms will provide more information about unexplained infertility.

The number of studies supporting the use of CoQ10 in infertile men with an increase in live birth and pregnancy rates is insufficient. In studies conducted, live birth or pregnancy rates are considered as secondary results. In addition, the number of patients is insufficient. Studies in animals or in vitro have shown that antioxidant use can have beneficial effects. However, there are controversial data due to some studies.

As a result, studies have shown the positive effects of using CoQ10 as a supportive treatment in male infertility in general. However, the number of studies on live birth and pregnancy is very low. In order to definitely recommend the use of CoQ10 as a therapeutic, more comprehensive, long-term and pregnancy-related studies are needed.


### *Source of Finance*

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### *Conflict of Interest*

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### *Authorship Contributions*

***Idea/Concept:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Design:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Control/Supervision:** Yasemin Akdevelioğlu; **Data Collection and/or Processing:** Ayçıl Özturan Şirin; **Analysis and/or Interpretation:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Literature Review:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Writing the Article:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Critical Review:** Yasemin Akdevelioğlu; **References and Fundings:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin; **Materials:** Yasemin Akdevelioğlu, Ayçıl Özturan Şirin.*

**TABLE 2:** Studies investigating the effects of CoQ10 on male infertility.

| Source | Type of Work | Applicants | Method | Results |
|---|---|---|---|---|
| Safarinejad MR (2010)[47] | Randomized controlled | 186 people (93 CoQ10-93 placebo) (35-60 years old) | CoQ10 300 mg × 2 / day (48 weeks) | Increase in semen parameters |
| Safarinejad MR (2009)[34] | Randomized controlled | 212 people (21-42 years old) | CoQ10 300 mg × 1 / day (26 weeks) | Increase in semen parameters |
| Safarinejad et al.(2012)[36] | Randomized controlled | 228 people (25-44 years old) | Ubiquinol 200 mg / day (26 weeks) | Increase in sperm parameters |
| Nadjarzadeh et al. (2014)[37] | Placebo- controlled | 47 people (25-40 years old) | 200 mg / day CoQ10 (3 months) | The use of CoQ10 is positive with normal semen parameters shown to be related. |
| Gualtieri et al. (2014)[13] | In vitro | | zinc, D-aspartate, and CoQ10 added medium | It is imperative to prevent oxida tive stress related to the storage of sperm by freezing and use in as sisted reproduction. Sperm media should be supplemented with a suitable antioxidant cocktail. |
| Nadjarzadeh et al. (2011)[42] | Double blind placebo controlled | 47 infertile males | 200 mg CoQ10 (12 weeks) | CoQ10 supplementation does not have a significant effect on sperm parameters. |
| Lewin et al. (1997)[48] | Case - control | 16 males with normal sperm motility, 22 infertile patients (25-39 years old) | 60 mg / day CoQ10 (103 days) | No significant effect in standard sperm parameters. Significant improvement in fertilization rate. |
| Lipovac et al. (2016)[49] | prospective, open-labelled, nonrandomized study | 299 sick males (20-60 years old) | Different amounts / mixtures of LC, l-arginine, zinc, vitamin E, glutathione, selenium, CoQ10, folic acid (once a day) (3 months) | Improvement was seen in all sperm parameters. |
| Lafuente et al. (2013)[39] | Meta-analysis | 296 males (149 CoQ10 - 147 Placebo) | | Improved sperm parameters |
| Balercia et al. (2009)[32] | Placebo-controlled, double-blind randomized trial | 60 sick males(30 CoQ10 - 30 placebo) | CoQ10 100 mg 2x/day (6 months) | Improved sperm parameter |
| Talevi et al. (2013)[50] | In vivo - cell study | 44 patients (23-30 years old) | Zinc, D-aspartate and CoQ10 | Zinc, D-aspartate and CoQ10 show a direct protective effect on human spermatozoa |
| Thakur et al. (2015)[42] | Intervention study | 60 men with age group of 20-40 years in infertile males | 150 mg CoQ10 (6 months) | Increase in semen parameters |
| Eroğlu et al. (2014)[51] | Case - control | 59 males (44 infertile, 15 fertile) | There is no intervention. Selenium, TAC, CoQ10 levels were examined in serum and seminal plasma. | Seminal plasma levels of CoQ-10 are related only to sperm morphology and not to concentration or motility. |
| Gvozdjakova et al. (2015)[52] | Intervention study | 40 infertile males (28-40 years old) | Carni-Q-Nol (440mg LC fumarate + 30mg ubiquinol + 75 IU vitamin E + 12mg vitamin C in each softsule) (2 or 3 capsules per day) (3-6 months) | The effect of additional treatment with Carni-Q-Nol benefited sperm function in mn, which al lowed 45% of women to become pregnant. |

## REFERENCES


1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al; International Committee for Monitoring Assisted Reproductive Technology; World Health Organization. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. Fertil Steril. 2009;92(5): 1520-4. [Crossref] [PubMed]
2. WHO. World Health Organization, Department of Reproductive Health and Research. WHO laboratory manual for examination and processing of human semen, 5th edn. 2010.
3. Zeren F, Gürsoy E. [The Importance of dyadic adjustment and quality of life in infertile couples]. Koç Üniversitesi Hemşirelikte Eğitim ve Araştırma Dergisi (HEAD). 2019;16(1):68-72.[Link]
4. Hacettepe Üniversitesi Nüfus Etütleri Enstitüsü. 2013 Türkiye Nüfus ve Sağlık Araştırması. Hacettepe Üniversitesi Nüfus Etütleri Enstitüsü, T.C. Kalkınma Bakanlığı ve TÜBİTAK, Ankara; 2014. p.116.[Link]
5. 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(1):9. [Crossref] [PubMed] [PMC]
6. Kumar N, Singh AK. Trends of male factor infertility, an important cause of infertility: A review of literature. J Hum Reprod Sci. 2015;8(4):191-6.[Crossref] [PubMed] [PMC]
7. Balercia G, Mancini A, Tirabassi G, Pontecorvi A. Coenzyme Q10 in Male Infertility. In: Antioxidants in Andrology. Springer; 2017. p. 43-57.[Crossref]
8. Gharagozloo P, Aitken RJ. The role of sperm oxidative stress in male infertility and the significance of oral antioxidant therapy. Hum Reprod. 2011;26(7):1628-40.[Crossref] [PubMed]
9. Aitken RJ, Baker MA, De Iuliis GN, Nixon B. New insights into sperm physiology and pathology. Handb Exp Pharmacol. 2010;(198): 99-115. [Crossref] [PubMed]
10. Tunç L. [Male infertility and nitric oxides] . Gazi Üniversitesi Üroloji AD., Türk Androloji Derneği, Androloji Bülteni. 2006;25(8):128-30. [Link]
11. Karatağ T, Kendirci M. [The place of antioxidant therapy in male infertility]. Androloji Bülteni. 2013;15(55):263-7.[Link]
12. Çayan S, Özdemir UDA, Orhan İ, Altay B, Kadıoğlu A. [The effect of oxidative stress on fertility and the place of anti-oxidant therapy in infertile men]. Androloji Bülteni. 2015;17(61): 118-24. [Link]
13. Gualtieri R, Barbato V, Fiorentino I, Braun S, Rizos D, Longobardi S, et al. Treatment with zinc, d-aspartate, and coenzyme Q10 protects bull sperm against damage and improves their ability to support embryo development. Theriogenology. 2014;82(4):592-8. [Crossref] [PubMed]
14. Cornelli U. Antioxidant use in nutraceuticals. Clin Dermatol. 2009;27(2):175-94.[Crossref] [PubMed]
15. Yılmaz İ. [Some food containing antioxidants and oxidatif stres]. Journal of Inonu University Medical Faculty. 2010;17(2):143-13.[Link]
16. Demirtaş A, Üntan İ. [Antioxidants and oxidative stress in seminal fluid and sperm]. Türk Ürol Sem. 2011;2:24-30.[Link]
17. Balasuriya A, Serhal P, Doshi A, Harper JC. Processes involved in assisted reproduction technologies significantly increase sperm DNA fragmentation and phosphatidylserine translocation. Andrologia. 2014;46(2):86-97.[Crossref] [PubMed]
18. Lombardo F, Sansone A, Romanelli F, Paoli D, Gandini L, Lenzi A, et al. The role of antioxidant therapy in the treatment of male infertility: an overview. Asian J Androl. 2011;13(5):690-7.[Crossref] [PubMed] [PMC]
19. Overvad K, Diamant B, Holm L, Holmer G, Mortensen SA, Stender S, et al. Coenzyme Q10 in health and disease. Eur J Clin Nutr. 1999;53(10):764-70.[Crossref] [PubMed]
20. Parkhideh D. Methods and compositions that enhance bioavailability of coenzyme-Q10. In: Google Patents US20090054530, 2008. [Link]
21. Turunen M, Olsson J, Dallner G. Metabolism and function of coenzyme Q. Biochim Biophys Acta. 2004;1660(1-2):171-99. [Crossref] [PubMed]
22. Crane FL. Biochemical functions of coenzyme Q10. J Am Coll Nutr. 2001;20(6):591-8.[Crossref] [PubMed]
23. Ercan P, Sedef E. [Bioavailability and importance of coenzyme q10 in nutrition and health]. TÜBAV Bilim Dergisi. 2010;3(2):192-200.[Link]
24. Mancini A, Balercia G. Coenzyme Q(10) in male infertility: physiopathology and therapy. Biofactors. 2011;37(5):374-80. [Crossref] [PubMed]
25. Arslan S, Ayaz A. [The role of antioxidants in male infertility]. Journal of Nutrition and Dietetics. 2018;46(2):201-7.[Crossref]
26. Miquel J, Ramírez-Boscá A, Ramírez-Bosca JV, Alperi JD. Menopause: a review on the role of oxygen stress and favorable effects of dietary antioxidants. Arch Gerontol Geriatr. 2006;42(3):289-306.[Crossref] [PubMed]
27. Shaum KM, Polotsky AJ. Nutrition and reproduction: is there evidence to support a "Fertility Diet" to improve mitochondrial function? Maturitas. 2013;74(4):309-12. [Crossref] [PubMed] [PMC]
28. Quinzii CM, Hirano M, DiMauro S. CoQ10 deficiency diseases in adults. Mitochondrion. 2007;7:S122-6.[Crossref] [PubMed] [PMC]
29. López LC, Quinzii CM, Area E, Naini A, Rahman S, Schuelke M, et al. Treatment of CoQ(10) deficient fibroblasts with ubiquinone, CoQ analogs, and vitamin C: time- and compound-dependent effects. PLoS One. 2010; 5(7):e11897. [Crossref] [PubMed] [PMC]
30. Omar MI, Pal RP, Kelly BD, Bruins HM, Yuan Y, Diemer T, et al. Benefits of Empiric Nutritional and Medical Therapy for Semen Parameters and Pregnancy and Live Birth Rates in Couples with Idiopathic Infertility: A Systematic Review and Meta-analysis. Eur Urol. 2019;75(4):615-25.[Crossref] [PubMed]
31. Littarru GP, Tiano L. Clinical aspects of coenzyme Q10: an update. Nutrition. 2010;26(3): 250-4. [Crossref] [PubMed]
32. Balercia G, Mancini A, Paggi F, Tiano L, Pontecorvi A, Boscaro M, et al. Coenzyme Q10 and male infertility. J Endocrinol Invest. 2009; 32(7):626-32.[Crossref] [PubMed]
33. Balercia G, Buldreghini E, Vignini A, Tiano L, Paggi F, Amoroso S, et al. Coenzyme Q10 treatment in infertile men with idiopathic asthenozoospermia: a placebo-controlled, double-blind randomized trial. Fertil Steril. 2009;91(5):1785-92.[Crossref] [PubMed]
34. Safarinejad MR. Efficacy of coenzyme Q10 on semen parameters, sperm function and reproductive hormones in infertile men. J Urol. 2009;182(1):237-48.[Crossref] [PubMed]
35. 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(7):805-7.[Crossref] [PubMed]
36. 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):526-31.[Crossref] [PubMed]
37. Nadjarzadeh A, Shidfar F, Amirjannati N, Vafa MR, Motevalian SA, Gohari MR, et al. Effect of Coenzyme Q10 supplementation on antioxidant enzymes activity and oxidative stress of seminal plasma: a double-blind randomised clinical trial. Andrologia. 2014;46(2):177-83.[Crossref] [PubMed]

38. Safarinejad MR. The effect of coenzyme Q10 supplementation on partner pregnancy rate in infertile men with idiopathic oligoasthenoteratozoospermia: an open-label prospective study. Int Urol Nephrol. 2012;44(3):689-700. [Crossref] [PubMed]

39. Lafuente R, González-Comadrán M, Solà I, López G, Brassesco M, Carreras R, et al. Coenzyme Q10 and male infertility: a meta-analysis. J Assist Reprod Genet. 2013;30(9): 1147-56.[Crossref] [PubMed] [PMC]

40. Alahmar AT. The effects of oral antioxidants on the semen of men with idiopathic oligoasthenoteratozoospermia. Clin Exp Reprod Med. 2018;45(2):57-66.[Crossref] [PubMed] [PMC]

41. Ghanbarzadeh S, Garjani A, Ziaee M, Khorrami A. CoQ10 and L-carnitine attenuate the effect of high LDL and oxidized LDL on spermatogenesis in male rats. Drug Res (Stuttg). 2014;64(10):510-5.[Crossref] [PubMed]

42. Thakur AS, Littarru GP, Funahashi I, Painkara US, Dange NS, Chauhan P, et al. Effect of Ubiquinol Therapy on Sperm Parameters and Serum Testosterone Levels in Oligoasthenozoospermic Infertile Men. J Clin Diagn Res. 2015;9(9):BC01-3.[PubMed] [PMC]

43. Nadjarzadeh A, Sadeghi MR, Amirjannati N, Vafa MR, Motevalian SA, Gohari MR, et al. Coenzyme Q10 improves seminal oxidative defense but does not affect on semen parameters in idiopathic oligoasthenoteratozoospermia: a randomized double-blind, placebo controlled trial. J Endocrinol Invest. 2011;34(8):e224-8.[PubMed]

44. Tiseo BC, Gaskins AJ, Hauser R, Chavarro JE, Tanrikut C; EARTH Study Team. Coenzyme Q10 Intake From Food and Semen Parameters in a Subfertile Population. Urology. 2017;102:100-5.[Crossref] [PubMed] [PMC]

45. Salas-Huetos A, Rosique-Esteban N, Becerra-Tomás N, Vizmanos B, Bulló M, Salas-Salvadó J, et al. The Effect of Nutrients and Dietary Supplements on Sperm Quality Parameters: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Adv Nutr. 2018;9(6):833-48.[Crossref] [PubMed] [PMC]

46. Ross C, Morriss A, Khairy M, Khalaf Y, Braude P, Coomarasamy A, et al. A systematic review of the effect of oral antioxidants on male infertility. Reprod Biomed Online. 2010;20(6):711-23.[Crossref] [PubMed]

47. Safarinejad MR. Safety and efficacy of coenzyme Q10 supplementation in early chronic Peyronie's disease: a double-blind, placebo-controlled randomized study. Int J Impot Res. 2010;22(5):298-309.[Crossref] [PubMed]

48. Lewin A, Lavon H. The effect of coenzyme Q10 on sperm motility and function. Mol Aspects Med. 1997;18:S213-9. [Crossref] [PubMed]

49. Lipovac M, Bodner F, Imhof M, Chedraui P. Comparison of the effect of a combination of eight micronutrients versus a standard mono preparation on sperm parameters. Reprod Biol Endocrinol. 2016;14(1):84. [Crossref] [PubMed] [PMC]

50. Talevi R, Barbato V, Fiorentino I, Braun S, Longobardi S, Gualtieri R, et al. Protective effects of in vitro treatment with zinc, d-aspartate and coenzyme q10 on human sperm motility, lipid peroxidation and DNA fragmentation. Reprod Biol Endocrinol. 2013;11:81. [Crossref] [PubMed] [PMC]

51. Eroglu M, Sahin S, Durukan B, Ozakpinar OB, Erdinc N, Turkgeldi L, et al. Blood serum and seminal plasma selenium, total antioxidant capacity and coenzyme q10 levels in relation to semen parameters in men with idiopathic infertility. Biol Trace Elem Res. 2014;159(1-3):46-51.[Crossref] [PubMed]

52. Gvozdjáková A, Kucharská J, Dubravicky J, Mojto V, Singh RB. Coenzyme Q10, α-tocopherol, and oxidative stress could be important metabolic biomarkers of male infertility. Dis Markers. 2015;2015:827941.[Crossref] [PubMed] [PMC]