

Effect of CoQ10 Supplement on Spermogram Parameters and Sexual Function of Infertile Men Referred to The Infertility Center of Fatemeh Hospital, Hamadan, Iran, 2019: A Randomized Controlled Trial Study

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Abstract

Background: The aim of this study was to investigate the effects of the antioxidant supplement of CoQ10 and placebo in the male infertility treatment.

Materials and Methods: The randomized controlled trial study was designed as a clinical trial. Samples in each group consisted of 30 members. The first group received 1 daily dose of 100 mg coenzyme Q10 capsules and the second group received a placebo treatment. Treatment in both groups lasted 12 weeks. Before and after the intervention of semen analysis, hormonal measurement of testosterone, prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH) and thyroid stimulating hormone (TSH) were done. Sexual function was assessed before and after the intervention by using the International Index of Erectile Dysfunction questionnaire.

Results: The mean age of participants was 34.07 (5.26) years in the CoQ10 group and 34.83 (6.22) in the placebo one. Normal volume of semen ($P=0.10$), viscosity ($P=0.55$), sperm count ($P=0.28$), and sperm motility ($P=0.33$) in the CoQ10 group increased without statistically significant differences. But the normal sperm morphology increased with statistically significant differences in the CoQ10 group ($P=0.01$). There was an increase in normal FSH levels and testosterone levels in the CoQ10 group compared with the placebo patients, but these differences were not statistically significant (respectively $P=0.58$, $P=0.61$). The results also revealed that the scores of erectile function ($P=0.95$), orgasm ($P=0.86$), satisfaction with sexual intercourse ($P=0.61$), overall satisfaction ($P=0.69$) and the score of the International Index of Erectile Function (IIEF, $P=0.82$) were greater after the intervention in the CoQ10 group than in the placebo group although the difference was not statistically significant.

Conclusion: The use of CoQ10 supplement can improve sperm morphology; however, in other sperm parameters and also in some hormones increased after the intervention, this was not statistically significant and therefore the result is not conclusive (registration number: IRCT20120215009014N322).

Keywords: Clinical Trial, CoQ10, Male Infertility, Sexual Dysfunction

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Introduction

According to the WHO, infertility is the inability to conceive after one year of unprotected intercourse. It is one of the most common problems in the world, experienced by about 15% of couples (1). Infertility

and its associated individual and social problems are an important issue for couples, because the cause of male infertility is pathologically that is detectable only in 40% of cases (2). Therefore, infertility treatment

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is more difficult in men than in women, especially in developing countries where treatment is associated with high cost (3). The major causes of male infertility are congenital or acquired anomaly of the genitourinary system, malignancies, urogenital infections, increased scrotal temperature (such as varicocele), endocrine disorders, genetic abnormalities, and immunological problems. However, infertility is idiopathic in 30-40% of infertile men that may have a variety of causes, including environmental pollution, Oxygen free radicals, and genetic and epigenetic abnormalities (4). Male infertility may have other factors, such as seminal tract obstruction, sperm problems (low count, low motility, dysmorphology). A male factor is involved in about half of all infertility cases. The presence of the male factor is often based on abnormal sperm parameters (azoospermia to oligozoospermia) (2). Impaired sperm production, function and damage to the spermatogenesis process are among the most common causes of male infertility. Trauma or anatomical defects in the genital system and the use of certain drugs to treat diseases can lead to impaired sperm production and consequently male infertility (5).

The increased oxidative stress and reactive oxygen species have recently been identified by many studies to be among the physiological causes of male infertility, and antioxidants have been shown to play a major role in its prevention. All the effective factors change the motility, morphology and concentration of sperm in a way that can be detected by experiment (6). A variety of chemical drugs such as clomiphene citrate, tamoxifen, etc. are used for the treatment of infertility with male factor that they may have many side effects. Therefore, infertile men prefer to use supplements, such as CoQ10 instead. Coenzyme Q10 is one of the important components in oxidative phosphorylation in mitochondria and adenosine triphosphate production (6). This coenzyme is produced in the intracellular environment of the body which is one of the important components in the structure of tyrosine (7). It is a vitamin-like compound similar to vitamin K and has three known biological performance. It increases ATP in mitochondria that has an antioxidant function, and increases the stability of cell membranes (8, 9). According to recent studies, this substance can be effective in muscular dystrophy, asthma, AIDS, breast cancer, diabetes, thyroid problems, and male infertility (10). Many studies have investigated the role of CoQ10 and antioxidants in general as a factor influencing infertility. Some of them show that coenzyme Q10 can play an effective role in infertility by increasing sperm volume and concentration (11). Considering the current growing demand for the use of antioxidant supplements in the treatment of male infertility and the undeniable side effects of medical drugs used for this purpose, as well as unpredictable effectiveness of CoQ10 antioxidants, the current researchers have sought to compare the effects of the

antioxidant supplement of Q 10 and placebo in the treatment of male infertility.

Materials and Methods

The randomized controlled trial study was recorded with the Iranian Registry of Clinical Trial (IRCT20120215009014N322) and was approved by the Ethics Committee of Hamadan University of Medical Sciences under code (IR.UMSHA.REC.1398.729). All participants signed a research consent form.

Main outcomes

Determining the effect of CoQ10 Supplement on Spermogram Parameters, male hormones, and Sexual Function of Infertile Men.

Study design and subjects

This study was performed as a two-group , double-blind, placebo-controlled randomized clinical trial with parallel design in 1: 1 ration, performed on idiopathic infertile men who had visited the subspecialty clinic of Fatemeh Hospital in Hamadan in 2019 for infertility treatment. The sample size was calculated in Stata 13 software with Sampsi module. The sample size was determined 30 for each group based on the data obtained from Balercia et al.'s study (12) [$M1=10.43$, $M2=15.11$, $Sd1=3.52$, $Sd2=7.34$, $\alpha=0.05$, $power=0.80$ and considering the 25% loss].

The inclusion criteria were a man age of under 40 years of age with primary infertility, abnormality of at least one of the semen parameters (volume, concentration, sperm count, motility, and morphology of sperm), lack of infertility-related disorders such as chromosomal abnormalities, testicular failure, varicocele, cryptorchidism, lack of chronic diseases such as diabetes, kidney disease, infectious diseases, genital infections, thyroid, having a body mass index (BMI) less than 30, non-use of drugs and alcohol, non-use of drugs that disrupt spermatogenesis (methotrexate, nitrofurantoin, colchicine and chemotherapy), pituitary suppressants [testosterone injections, gonadotropin-releasing hormone (GnRh) analogues], anti-androgens (cimetidine, spironolactone), drugs that cause ejaculatory dysfunction (alpha-blockers, antidepressants, phenothiazines), drugs that cause erectile dysfunction (beta-blockers, thiazide diuretics, metoclopramides) and long-term use of drugs such as anabolic steroids, cannabis, heroin and cocaine, no history of testicular and vas deferens surgery, lack of contact with pesticides, heavy metals and solvents, non-use of metals and solvents, and non-use of antioxidant supplements in the last three months (13). Infertile men using drug and alcohol, using the creatinine more than twice, strenuous physical activity, fertility during the study, diet for weight loss, and change of location were not included in the study. A semen sample was initially collected from men referring for infertility

treatment. Samples were collected in case of three-day sexual abstinence. Incubation was performed for 30 to 60 minutes to convert the samples from bulk to liquid. To evaluate sperm parameters in accordance with the WHO standards, 200 microliters of fluid sample was examined (14).

Computer semen analysis was used to assess sperm motility. Also, microscopic tests were performed to evaluate and determine parameters such as sperm concentration per milliliter of semen, sperm viability and sperm morphology. The research goals and methods were explained to those who had the inclusion criteria and then written consent was obtained from all volunteers of the research. The data collection form of the general characteristics of the patients was completed. Furthermore, 10 cc of blood was collected from patients at the beginning of the study to measure their sex hormones [luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and testosterone] and thyroid stimulating hormone (TSH).

The allocation sequence and concealment was determined by using random blocking with 4 blocks before the study by a person not present in the study. Based on the predetermined sequence, the drugs were placed in sealed and opaque envelopes and numbered respectively. Each patient was given an envelope upon admission. Therefore, the patients were placed into two groups of CoQ10 and placebo (Fig.1).

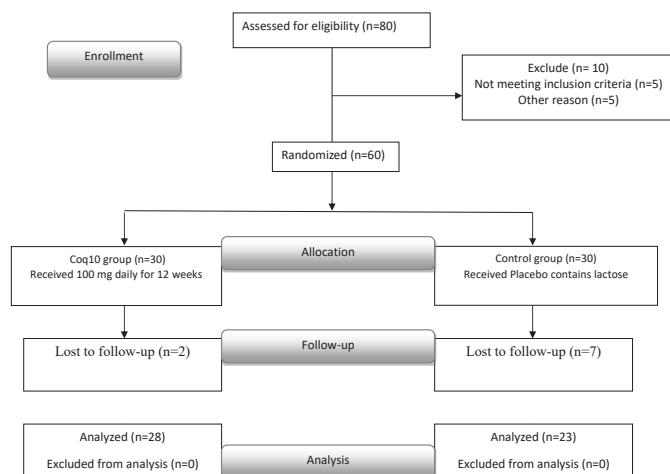


Fig.1: Flowchart of sampling.

Intervention

The researchers and the patients were blind to the study groups. The CoQ10 group received 1 daily dose of 100-mg coenzyme Q10 capsules made by Walmark, USA and the second group received a placebo treatment containing 100 mg of lactose prepared by the School of Pharmacy of Hamadan University of Medical Sciences.

The selection of the prescribed dose in the present study was also based on a pilot study conducted by the researchers. This pilot study was performed on ten

idiopathic infertile by examining the effect of CoQ10 supplements on sperm parameters. Follow-up of patients was conducted by phone once every 15 days in order to control the use of capsules and prevent the loss of samples. Moreover, by counting the remaining capsules, patients who had not used more than 10% of their capsules were excluded finally. Patients were also advised not to change their diet. Finally, after the intervention, the semen samples were evaluated for spermogram and blood samples were examined for sex hormones. LH and FSH were measured using the ELISA method with the CSB E12654r kit made by the Japanese CUSABIO Company. Serum levels of Testosterone, prolactin and TSH were respectively measured using the ELISA hormone measurement kits made by the German DRG Instruments GmbH Company with hormonal sensitivity of 0.083 ng/ml and the RIA prepared by the Iranian Padyab Teb Diagnostic Company with hormonal sensitivity of 0.09.

International index of erectile dysfunction questionnaire

It should be noted that sexual function was examined in the infertile men with the inclusion criteria of two groups in two stages before and after the intervention using the IIEF. This index was completed by researchers via interviews. It contains 15 standard questions which is divided into 5 subscales, namely erectile function, orgasmic function, sexual desire, satisfaction with intercourse and overall satisfaction. It is scored from zero to five and the total score is obtained by adding the scores of the questions of each dimension. Higher score indicates the most optimal sexual function. The scores range from 15 to 75, with scores within the 15-25 range indicating low sexual function, scores within the 25-50 range indicating moderate sexual function, and scores higher than 50 indicating high sexual function. In previous studies, the reliability of the questionnaire was confirmed with the Cronbach's alpha of 0.85% (15).

Statistical analysis

Data were analyzed by using Stata 13 software (StataCorp Company, Canada). Kolmogorov-Smirnov test was used to investigate the distribution of quantitative variables. Demographic and background variables were compared with the independent t test if the distribution was normal and otherwise with the Mann-Whitney test. Chi-square test and Fisher's exact test were used to compare semen and hormone parameters and binomial regression test was used to control the effect of pre-test status. Comparison of different dimensions of sexual function was also performed by Mann-Whitney and Wilcoxon tests. A significance level of 0.05 was considered.

Results

The analysis of demographic and background variables indicated that the mean (standard deviation) age was 34.07

(5.26) years in the CoQ10 group and 34.83 (6.22) years in the placebo group. The mean (SD) BMI was higher in the placebo group than in the CoQ10 one and the majority of members of the two groups had less than high school diploma. The results showed that the two groups are homogeneous in terms of the variables mentioned in the table with no statistically significant difference observed between them.

Comparison of semen fluid parameters in the pre-intervention stage showed that 85.7% of the CoQ10 group and 78.3% of the placebo group members had a normal volume of semen ($P=0.71$). 75% of the CoQ10 group members had normal sperm counts, while this rate was about 74% in the placebo group ($P=0.92$). In terms of progressive motility, the normal motility rate was higher in the placebo group than in the CoQ10 group ($P=0.43$). Sperm shape and WBC count were also normal in the majority of members of the two groups. None of these parameters showed a statistically significant difference between the two groups (Table 1).

The results of multivariate analysis showed that, by controlling the values of semen in the pre-intervention stage, there was an increase in the normal volume of semen by 9% ($P=0.10$), normal viscosity by 10% ($P=0.55$), normal sperm count by 12% ($P=0.28$), and normal sperm motility by 12% ($P=0.33$) in the CoQ10 group compared with the placebo group, but none of these results was statistically significant. The normal sperm morphology increased by 31% in the CoQ10 group compared with the placebo group, which was statistically significant ($P=0.01$, Table 2).

Comparison of the mean scores of erectile function in the pre-intervention stage showed that this score was higher in the placebo group than in the CoQ10 group, but this difference was not statistically

significant ($P=0.16$). In the post-intervention stage, the score of the CoQ10 group was higher than that of the placebo group, but this difference was not statistically significant ($P=0.95$). Comparison of the mean scores of orgasm function in the pre-intervention stage showed that this score was higher in the placebo group than in the CoQ10 group, but this difference was not statistically significant ($P=0.51$). In the post-intervention stage, the score of the CoQ10 group [7.90 (1.89)] was higher than that of the placebo group [7.84 (2.24)], but this difference was not statistically significant ($P=0.86$). Comparison of the mean scores of sexual desire showed that his rate was higher in the CoQ10 group than the placebo group in the pre-intervention stage, and the score of the placebo group was higher than that of the CoQ10 group in the post-intervention stage, but these differences were not statistically significant (respectively $P=0.86$ and $P=0.55$). Comparison of the mean scores of satisfaction with sexual intercourse in both pre- and post-intervention stages showed that this score was higher in the CoQ10 group than in the placebo group, but the difference was not significant (respectively $P=0.94$ and $P=0.61$). Comparison of the mean scores of overall satisfaction in both pre- and post-intervention stages revealed that this score was higher in the placebo group than in the CoQ10 group, but this difference was not statistically significant (respectively $P=0.36$ and $P=0.69$). Comparison of the mean total scores of the International Erectile Performance Index in the post-intervention stage showed that this score was higher in the CoQ10 group than the other ones, but this difference was not statistically significant ($P=0.82$). Also Within-group comparisons did not show a statistically significant difference compared with the pre-intervention stage ($P=0.12$, Table 3).

Table 1: Comparison of semen analysis results before intervention between groups

Variables		Q10 group	Placebo group	Statistical test	P value
Volume (ml)	≥ 1.5	24 (85.7)	18 (78.3)	-	0.71
	< 1.5	4 (14.3)	5 (21.7)		
Viscosity	Normal	19 (67.9)	18 (78.3)	0.68	0.40*
	Abnormal	9 (32.1)	5 (21.7)		
Sperm count per cc (million)	≥ 15	21 (75.0)	17 (73.9)	0.008	0.92*
	< 15	7 (25.0)	6 (26.1)		
Progressive motility	$\geq 32\%$	14 (50.0)	14 (60.9)	0.60	0.43*
	$< 32\%$	14 (50.0)	9 (39.1)		
Sperm morphology	$\geq 4\%$	24 (85.7)	20 (87.0)	-	1.00
	$< 4\%$	4 (14.3)	3 (13.0)		
WBC number	Normal	24 (85.7)	20 (87.0)	-	1.00
	Abnormal	4 (14.3)	3 (13.0)		

Data are presented as n (%). WBC; White blood cell, and *; Chi-square test. The rest: Fisher's exact test.

Table 2: Comparison of semen analysis results after intervention between groups*

Variables		Q10 Group n (%)	Placebo group n (%)	Risk ratio (95% CI)	Statistic	P value
Volume (ml)	≥1.5	25 (89.3)	19 (82.6)	1.09 (0.98, 1.22)	1.64	0.10
	<1.5	3 (10.7)	4 (17.4)			
Viscosity	Normal	22 (78.6)	17 (73.9)	1.10 (0.80, 1.49)	0.59	0.55
	Abnormal	6 (21.4)	6 (26.1)			
Sperm count per cc (million)	≥15	26 (92.9)	18 (78.3)	1.12 (0.91, 1.37)	1.07	0.28
	<15	2 (7.1)	5 (21.7)			
Progressive motility	≥32%	25 (89.3)	16 (69.6)	1.12 (0.88, 1.40)	0.96	0.33
	<32%	3 (10.7)	7 (30.4)			
Sperm morphology	≥4%	28 (100.0)	18 (78.3)	1.31 (1.06, 1.60)	2.58	0.01
	<4%	0	5 (21.7)			
WBC number	Normal	28 (100.0)	23 (100.0)	1 (0.99, 1.00)	0.00	1.00
	Abnormal	0	0			

WBC; White blood cell, CI; Confidence interval, and *; Binomial regression.

Table 3: Comparison within and between groups of the total score of sexual function domains before and after the intervention

Domains	Q10 group		Placebo group		Statistical test before intervention*	Statistical test after intervention*
	Before intervention	After intervention	Before intervention	After intervention		
Erectile function	20.92 ± 5.64	24.09 ± 4.72	22.81 ± 6.63	22.72 ± 7.89	Z = -1.40 P = 0.16	Z = -0.05 P = 0.95
Statistical test**	Z = -1.88 P = 0.07		Z = -0.35 P = 0.73			
Orgasm function	7.48 ± 1.91	7.90 ± 1.89	7.73 ± 2.11	7.84 ± 2.24	Z = -0.65 P = 0.51	Z = -0.16 P = 0.86
Statistical test**	Z = -0.44 P = 0.65		Z = 0.57 P = 0.57			
Sexual desire	7.38 ± 1.62	7.42 ± 1.43	7.34 ± 1.43	7.61 ± 1.09	Z = -0.16 P = 0.86	Z = -0.59 P = 0.55
Statistical test**	Z = 0.40 P = 0.68		Z = -0.79 P = 0.43			
Sexual satisfaction	9.69 ± 2.58	10.04 ± 2.08	9.45 ± 3.52	9.73 ± 3.84	Z = -0.07 P = 0.94	Z = -0.50 P = 0.61
Statistical test**	Z = -0.54 P = 0.59		Z = -0.20 P = 0.84			
Overall satisfaction	7.42 ± 2.31	8.19 ± 2.01	8.04 ± 1.98	8.57 ± 1.53	Z = -0.90 P = 0.36	Z = -0.39 P = 0.69
Statistical test**	Z = -0.95 P = 0.35		Z = -1.10 P = 0.28			
International erection performance index	52.69 ± 11.65	57.66 ± 8.97	54.95 ± 13.09	56.52 ± 14.65	Z = -0.80 P = 0.42	Z = -0.21 P = 0.82
Statistical test**	Z = -1.58 P = 0.12		Z = -0.34 P = 0.73			

Data are presented as mean ± SD. *; Mann-Whitney U test and **; Wilcoxon test.

The results of pre-intervention comparisons of hormone levels showed that normal LH, normal FSH and normal prolactin were more frequent in the CoQ10 group than in the placebo one (respectively P=0.14, P=0.58 and P=0.54), but the normal testosterone and normal TSH levels were more frequent in the placebo group than in the CoQ10 group (respectively P=0.61 and P=0.61). The results of statistical analysis did not show a statistically significant difference between the two groups (Table 4).

The results of multivariate analysis in terms of hormone status showed that by controlling hormone levels in the pre-intervention stage, there was an increase in normal FSH levels by 13% (P=0.20) and in normal testosterone levels by 16% (P=0.30) in the CoQ10 group compared with the placebo patients, but these differences were not statistically significant. For the other hormones mentioned in the table, the normal level of hormones in the CoQ10 group was slightly lower than that in the placebo group, which was not statistically significant (Table 5).

Table 4: Comparison of hormones levels before the intervention between groups

Hormone		Q10 Group	Placebo group	Statistical test	P value
LH (IU/L)	Normal	21 (75.0)	12 (52.2)	2.88	0.14*
	Abnormal	7 (25.0)	11 (47.8)		
FSH (IU/L)	Normal	27 (96.4)	21 (91.3)	-	0.58
	Abnormal	1 (3.6)	2 (8.7)		
Prolactin (ng/ml)	Normal	17 (60.7)	12 (52.2)	0.37	0.54*
	Abnormal	11 (39.3)	11 (47.8)		
Testosterone (ng/ml)	Normal	25 (89.3)	22 (95.7)	-	0.61
	Abnormal	3 (10.7)	1 (4.3)		
TSH (mIU/L)	Normal	25 (89.3)	22 (95.7)	-	0.61
	Abnormal	3 (10.7)	1 (4.3)		

Data are presented as n (%). *: Chi-square test and the rest of Fisher's exact test.

Table 5: Comparison of hormones levels after the intervention between groups*

Hormone		Q10 group	Placebo group	Risk ratio (95% CI)	Statistic	P value
LH (IU/L)	Normal	18 (64.3)	12 (52.2)	0.93 (0.60, 1.45)	-0.29	0.76
	Abnormal	10 (35.7)	11 (47.8)			
FSH (IU/L)	Normal	27 (96.4)	18 (78.3)	1.13 (0.93, 1.37)	1.28	0.20
	Abnormal	1 (3.6)	5 (21.7)			
Prolactin (ng/ml)	Normal	19 (67.9)	14 (60.9)	0.93 (0.71, 1.22)	-0.51	0.60
	Abnormal	9 (32.1)	9 (39.1)			
Testosterone (ng/ml)	Normal	24 (85.7)	17 (73.9)	1.16 (0.87, 1.55)	1.03	0.30
	Abnormal	4 (14.3)	6 (26.1)			
TSH (mIU/L)	Normal	23 (82.1)	21 (91.3)	0.89 (0.73, 1.07)	-1.21	0.22
	Abnormal	5 (17.9)	2 (8.7)			

Data are presented as n (%). *: Binomial regression and CI; Confidence interval.

Discussion

Infertility is one of the disorders with an increasing rate of prevalence under the influence of various factors. However, increased oxidative stress is one of the strongest factors that can increase the prevalence of this disorder by influencing various factors. Therefore, antioxidants can improve fertility parameters by increasing the level of antioxidant capacity. One of these antioxidants, used in large quantities in the treatment of male infertility, is CoQ10. The results of our study demonstrated that the normal volume of semen, normal viscosity, normal count, normal motility, and normal shapes of sperm increased as a result of CoQ10 use. Oxidative stress is one of the most common factors involved in infertility (16). Sperm cells are rich in unsaturated fatty acids. Sperm parameters change in infertile individuals and become abnormal. In such individuals, sperms are very vulnerable to oxidative stress due to a lack of antioxidant enzymes in the cytoplasm as well as the presence of unsaturated fatty acids in the plasma membrane. Hence, oxidative stress reduces the quality of semen through damage to DNA

and destruction of plasma membranes (17). Coenzyme Q10 is a compound with antioxidant properties and one of the components of the respiratory chain. It can be effective against heart disease, hypertension, diabetes, infertility, and many other diseases. The function of this coenzyme in energy production in the cell and its acting as an antioxidant depends on its ability to exchange two electrons between ubiquinol and ubiquinone (18). Decreased 8-isoprostane, a measure of lipid peroxidation, has also been shown to be effective in reducing oxidative stress in infertile individuals. Catalase and superoxide dismutase are the first line of defense of the enzyme against oxidative stress. In a study on 47 infertile men, 200 mg/day of CoQ10 supplement increased the activity of catalase and SOD enzymes. The results of this study indicated that, despite the improvement of oxidative stress resulting from the activity of these two enzymes, sperm motility and morphology did not improve.

Another study showed that the increased levels of these two enzymes cause stability of sperm parameters (19). Another study found a relationship between reduced 8-isoprostane and improved sperm motility

and morphology. A study on 194 infertile men showed that daily intake of 300 mg of CoQ10 supplement improved sperm motility and morphology (20). However, another study indicated no relationship between the concentration of CoQ10 in the seminal fluid and the improvement of sperm motility (19). A qualitative analysis of the literature has shown that CoQ10 supplements, alone or with other antioxidant molecules, has an effective effect on semen quality, especially in sperm motility. Indirect symptoms result from improved semen antioxidant capacity and sperm chromatin integrity. Improvement in semen parameters begins after 3-6 months of treatment but disappears when the supplement is discontinued. Further studies are needed to determine the optimal dose of CoQ10 (11). Although most studies have shown an improvement in sperm motility, studies of sperm concentration and density have shown contradictory results. A clinical trial on 22 infertile men receiving 400 mg/day of CoQ10 supplement showed no effect on sperm morphology and concentration. Another study indicated the positive effect of CoQ10 on sperm morphology and concentration without statistically significant differences (12).

A study on 287 infertile men demonstrated that 600 mg/day of CoQ10 improved sperm motility, concentration, and morphology (21). Also, The present study indicated the greater mean scores of the CoQ10 group in the subscales of orgasm function, IIEF, satisfaction with sexual intercourse, and overall scores of the questionnaire in comparison with the placebo group. Safarinejad (22) found a significant difference between the mean score of penile pain and the mean score of post-treatment function in patients with early chronic Peyronie's Disease who had received CoQ10, so that improvement in the function score was observed in the CoQ10 group. Also, there was a significant difference between the average volume of plaque and the penile curvature in the two groups of CoQ10 and placebo. Increased plaque size and worsened penile curvature in the placebo group have shown the potential protective effect of CoQ10. One way to boost sperm is to use CoQ10. It is one of the most important antioxidants needed to protect cell DNA from free radical damage. Thus, CoQ10 affects sperms by maintaining their motility and health. This antioxidant is mostly found in seafood and meat, but it is very difficult to get it through diet. Taking ubiquinol, a coenzyme Q10 supplement, is the best solution to get coenzyme Q10 in order to boost male sperm. The amount of this substance decreases in the body with aging. The use of CoQ10 is useful in improving male sexual function. The results of our study indicated the higher normal levels of FSH and testosterone in the CoQ10 group than in the placebo group. However, studies have shown that increased free radicals and generated oxidative stress reduce the potential of mitochondrial membranes and increase lipid peroxidation in testicular tissue which have a destructive effect on this tissue. Cao et al. (23)

found that an increase in oxidative stress leads to a decrease in the levels of important enzymatic and non-enzymatic oxidants in Leydig cells as well as reduction in testosterone synthesis and secretion.

Ghanbarzadeh et al. (24) found that increased coenzyme Q10 decreased the level of free radicals and increased the level of sex hormones in isoproterenol-treated rats. Safarinejad et al. (21) conducted a study on 228 infertile men, finding a significant decrease in LH and FSH levels as well as a significant increase in serum inhibin B levels after receiving 200 mg of CoQ10 for 26 weeks. However, there was no significant change in the amount of testosterone, although there was a slight increase. After 12 weeks of follow-up, the FSH level still decreased significantly. The positive effect of CoQ10 supplement on spermatogenesis by decreasing FSH levels and increasing inhibin B levels has also been confirmed. Inhibin B is produced by Sertoli cells and its serum level is strongly associated with the testis. Inhibin B controls FSH secretion via a negative feedback (25). Therefore, an increase in inhibin B along with a decrease in FSH level strongly indicates an improvement in testicular performance. In any case, the beneficial effects of CoQ10 on semen parameters diminish after cessation of treatment (11). Studies on male infertility have not shown a significant effect of coenzyme Q10 supplement on testosterone levels yet. They have shown no beneficial effect of coenzyme Q10 supplement on infertile men. Similarly, animal studies have not shown a positive effect of coenzyme Q10 on testosterone. However, coenzyme Q10 supplementation is widely used to counteract testosterone reduction caused by toxins generated in chemical drugs. In order to increase testosterone, other alternative treatment strategies may be needed instead of coenzyme Q10 supplementation. Further research needs to be done in this area (26).

Conclusion

The use of CoQ10 supplement was shown able to improve sperm morphology; however, in other sperm parameters and also in some hormones that increased after the intervention, this was not statistically significant and therefore the result is not conclusive.

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Authors' Contributions

S.Z.M., T.Gh.B.; Proposed the initial idea. Sh.P.;

Designed the study and collected the data. F.K.; Performed the statistical analysis. Sho.M.; Contributed to the intervention design and drafting of the manuscript. Shi.M; Helped with the preparation of medicines. All authors read and approved the final manuscript.

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