

The Role of Co-Enzyme Q10 in Male Infertility

*** Dr. Mohammed Hussam Mohammed Saeed, **Dr. Montadher Hameed Nima,*** Dr. Mazin Anwer Yadgar**

***,**Department of urology,College of medicine,Tikrit University,Tikrit Iraq**

****Department of Urology,college of medicine, Baghdad University,Baghdad, Iraq**

Abstract

Background: Male infertility, while being the product of the influence of many factors, can be caused by the dysfunction of sperms as a result of oxidative stress. **Patients and Methods:** This was a randomized controlled placebo study involving 134 infertile male participants between the ages of 20 to 45 years who had idiopathic oligoasthenoteratospermia. 67 participants were randomized to either the treatment and placebo group each. The treatment group was given 200mg of coenzyme Q10 daily for 6 months. After the baseline tests, assessments were performed at week 26 and 52. The participants were evaluated for coenzyme Q10 in the blood and seminal plasma, sperm parameters and testosterone, follicle stimulating hormone, luteinizing hormone and prolactin. **Results:** The size of testis between these two groups was not significantly different (22.3-+2.5 for CoQ10 group and 21.8-+2.5 for placebo). The sperm motility was improved significantly (36.2% for CoQ10 in comparison with 3.2% for the placebo group). There was also a significant improvement in the morphology as shown by 28% for the CoQ10 group in comparison with 5.7% for the placebo group. The sperm count also significantly increased (24% for CoQ10 in comparison with 1.8% for placebo). **Conclusions:** There is sufficient evidence to show that the administration of coenzyme Q10 leads to an improvement of sperm parameters related to normal sperm function as well as the hormones related to spermatogenesis. However, it is known whether the improvement in the sperm parameters and hormones as well as the endogenic environment would translate to an increased rate of pregnancies. **Aims:** The aim of this randomized controlled placebo study was to evaluate the role that the coenzyme Q10 plays in the infertility of human males.

فعالية عقار كو انزيم كيو 10 على عقم الرجال

مازن انور يادكار

منتظر حميد نعمة

مهند حسام محمد

الخلاصة

ان العقم عند الرجال هو نتيجة اسباب مختلفة احداها هي العوامل المؤكسدة

هدف هذه الدراسة هو معرفة تاثير عقار كو انزيم كيو 10 على العقم عند الرجال

هذه الدراسة شملت على عينة عشوائية تشتمل على 134 مريض مصاب بالعقم بين اعمار 20 و 45 سنة للمرضى المصابين بقلة فعالية الحيامن غير معروف الاسباب . تم تقسيم المرضى الى مجموعتين كل مجموعة تحتوي على 67 مريض في الاولى تم اعطاؤهم علاج وهمي وفي الثانية تم اعطائهم كو انزيم كيو 10 (200) ملغم كبسول لمدة 6 اشهر. بعد اجراء تقييم اولي قبل بدء العلاج تم ايضا اجراء تحاليل عند الشهر السادس وعند الشهر الثاني عشر. وقد اشتملت التحاليل على قياس مستوى كو انزيم كيو 10 في الدم وفي المنى تحليل المنى العام وكذلك قياس هورمونات التستستيرون والبرولاكتين وكذلك الهورمون المحفز للبويضات والهورمون اللوتيني. النتائج توضح بان فعالية ونشاط الحيامن قد تحسن بشكل ملحوظ الى 36.2% لمجموعه عقار كو انزيم كيو 10 مقارنة ب 3.2% لمجموعة العلاج الوهمي وكذلك تحسن شكل الحيامن بالنسبة لمجموعة كو انزيم كيو 10 الى 28% مقارنة ب 5.7% لمجموعة العلاج الوهمي واخيرا زاد عدد الحيامن ايضا بشكل ملحوظ الى 28% لمجموعة عقار كو انزيم كيو 10 مقارنة ب 1.8% لمرضى العلاج الوهمي.

من خلال ما تقدم يتضح ان استخدام علاج كو انزيم كيو 10 يؤدي الى تحسن ملحوظ في شكل الحيامن ووظائفها

Introduction

Male infertility is a prevalent social problem with which many societies are faced (1). While infertility does not case physical morbidity, impairment of longevity, pain, or mortalities, the impact that it has on the wellbeing of the affected males from social and psychological perspectives is pronounced (2). Men require a sufficiency of

healthy and motile sperms in the seminal fluid in order to be fertile (3). Therefore, of interests are the causes of insufficiency of sperms in the seminal fluid, impediments to the production of healthy sperms and factors that affect their motility.

The production of sperms is controlled by the endocrinal system. Two of the essential hormones that influence the production of sperms by acting on the

testicle include the follicle-stimulating hormone and the luteinizing hormone (3). Hormonal abnormalities, particularly abnormalities affecting the follicle-stimulating hormone and the luteinizing hormone, can lead to infertility.

The membranes of the mammalian spermatozoon contain high quantities of poly-unsaturated fatty acids. The lipid peroxidation of the polyunsaturated fatty acids might result in the formation of free radicals which would alter the endogenic environment (4).

Reactive oxygen species and free radicals are not entirely damaging. They have a prominent role to play during reproduction, particularly, their role during ovulation and the formation of the disulfide bonds in the nuclei of the sperms (5).

When the male body is in its normal physiological state, there are antioxidant enzyme mechanism in the seminal plasma that sacrifice themselves to the reactive oxygen species and in the process attenuate the potential damage that the oxidants might have caused on the spermatozoa (6). The presence of other factors might influence the effectiveness of these antioxidant enzymes in protecting the male gametes to the potential damage of the

reactive oxygen species and the free radicals. For instance, the lipid peroxidation of fatty acids might undermine the effectiveness of the antioxidant mechanisms (7).

These findings have prompted an inquiry into the role that compounds that have an antioxidative effect have on male fertility. Some of these compounds are in the form of nutrients such as micronutrients such as vitamin C, folic acid, vitamin E, selenium and enzymes such as coenzyme Q10 (8). The review of evidence has shown that the antioxidants have a positive impact on male fertility (9). Coenzyme Q10 is an antioxidant. Studies have identified a correlation between the concentration of coenzyme Q10 in the seminal fluid of human males and their sperm count as well as the motility of the sperms (10). Sperm count and their motility are essential factors in male fertility.

The administration of coenzyme Q10 resulted in an increase in the concentration of the antioxidant in their sperm cells as well as their seminal plasma as well as an increase in the motility of their sperms by (10) prompts a further inquiry into the role the oxidant plays in male infertility, therefore, this study aimed to

evaluate the role that the coenzyme Q10 played in male infertility.

Patients and Methods

The study used a randomized placebo-controlled design. A total of 134 infertile males who were between the ages of 20 years and 45 years were selected and included in the study between (February 2016 to October 2017). The patients included in this study were those with more than one year of the regular sexual relationship, normal testicular size and normal female factor.

Male infertility was diagnosed if 1 or more standard semen parameters were below the cutoff levels accepted by WHO based on at least two semen analyses performed 3 months apart to eliminate unexpected and possible adverse effects of various factors on spermatogenesis. There was a two-week period during which preparations were made before the commencement of a treatment period spanning 6 months and a treatment-free period spanning 6 months soon after. During the preparation period, the patients were assessed for testosterone, follicle-stimulating hormone, luteinizing hormone, and prolactin using blood tests. The patients were also evaluated for coenzyme Q10 in their semen and serum. The patients were

also subjected to a face to face assessment using a questionnaire, a Doppler study using Valsalva maneuver and examination for varicoceles.

At the end of the two-week period, 67 patients were randomly assigned into the treatment and another 67 into the placebo group. The patients in the treatment group were given daily doses of 200mg of coenzyme Q10 for a six-month period. The patients in the placebo group were given a sugar pill for the same period. A baseline assessment was done at week zero followed by follow up assessments after 26 weeks, and 52 weeks. During the follow-up assessments, the patients in both treatment and placebo groups gave semen samples that were assessed for coenzyme Q10 in both the semen and plasma as well as the levels of testosterone, follicle-stimulating hormone, luteinizing hormone, and prolactin in their serum.

All samples were given to a lab. within 20 minutes, the interpretation was done in accordance with WHO 1999 criteria (11). Semen morphology was done according to Krugar criteria(11). Serum hormones were assessed using radioimmunoassay kits. Blood and semen

CoQ10 were evaluated with liquid chromatography.

Statistical Analysis : . P value and T test has been used for significance of data.

Results

Table(1) showing the characteristics of the patients included in the study including their hormones and semen parameters .

Domain	Mean±SD (Placebo)	Mean±SD (CoQ10)
Age	27± 10	26 ± 10
Serum Hormones:		
Testosterone(nmol/l)	14.2±4.8	14.8±5.0
FSH (IU/L)	15.1±5.0	15.1±5.2
Prolactin (Pmol/l)	355±136	350±130
LH (IU/L)	11.3±3.0	11.2±3.0
Semen Parameters:		
Ejaculate vol (ml)	3.0±1.1	3.0±1.2
% of motility	26.0±2.6	26.2±2.5
Morphology	9.2±3.2	9.1±3.1
Total number	51.2±8.1	50.5±8.2

At the end of the study, the size of testis between these two groups was not

significantly different (22.3±2.5 for CoQ10 group and 21.8±2.5 for placebo).

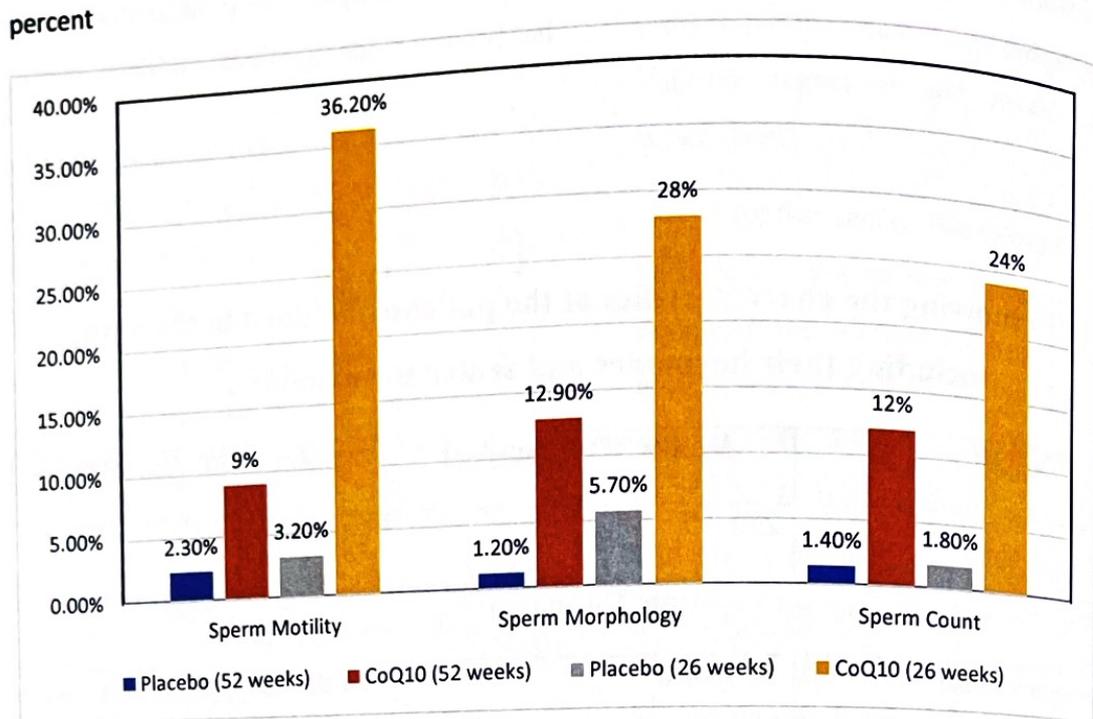


Fig.(1) : Comparison of sperm parameters at 26 weeks and 52 weeks for treatment and placebo group.

The semen parameters were significantly improved at 26 and 52 weeks of treatment and post-treatment visits. The sperm motility was significantly enhanced (36.2% for CoQ10 in comparison with 3.2% for the placebo group). There was also a significant improvement in the morphology as shown by 28% for the CoQ10 group in contrast with 5.7% for the placebo group. The sperm

count also significantly increased (24% for CoQ10 in contrast with 1.8% for placebo). P value for sperm motility is 0.01 for 26 weeks and 0.04 for 52 weeks, P value for sperm morphology is 0.01 for 26 weeks and 0.03 for 52 weeks and at last P value for sperm count is 0.01 at 26 weeks and 0.03 at 52 weeks as shown in table 2 and figure 1.

Table (1): Comparison of domains at 26 weeks and 52 weeks for treatment and placebo groups and their changes from primary readings:

parameters	Treatment 52weeks		P value	Treatment 26weeks		P value
	%Placebo from primary readings	%CoQ10 from primary readings		%Placebo from primary readings	%CoQ10 from primary readings	
Serum Hormones						
Testosterone	0.5%	4%	0.07	1.4%	18%	0.02
LH	0%	"_15%	0.02	1.4%	"_25%	0.01
FSH	0%	"_12%	0.03	1.3%	"_36%	0.01
Prolactin	0.2%	0.4%	0.1	1.2%	"_1.5%	0.1
Plasma CoQ10						
Blood	0%	0%	_	0%	90%	0.001
Seminal	0.6%	0.2%	0.1	0.2%	140%	0.001

" (Those readings with _ markings mean that their values are lower than the primary readings).

Discussion

There was an improvement in the sperm motility, morphology and count in the treatment group during the assessment after

26 weeks when compared to the placebo group. In addition to the improvements noted in the sperm attributes, the serum hormone levels for testosterone was higher in the treatment group to which the coenzyme Q10 was given compared to the placebo group. This was agreed with

Mancini & Balercia (10) they had found that coenzyme Q10 helped increase the concentration of the antioxidant in both the sperm cell as well as the seminal vesicles of infertile men. The researchers also found that the administration of coenzyme Q10 helped increase the motility of the sperms of infertile men. The concentration of the antioxidant in the blood plasma and seminal plasma also increased significantly in the treatment group.

The results of this study have also been corroborated in other studies. For instance, Lafuente et al. (12) found that offering oral supplements of coenzyme Q10 in a member who was infertile improved the seminal concentration of coenzyme Q10. The concentration of sperms, and their motility in a statistically significant manner. Through this study, there was evidence that the use of coenzyme Q10 resulted in an improvement of the sperm parameters that have an influence on male infertility (13). The influence of specific hormones on male infertility is also documented.

Other studies have shown that in addition to significantly improving the sperm parameters, supplementation with coenzyme Q10 also has an influence on the profile of the reproductive hormones in

males diagnosed with infertility. For instance, a study by Sfarinejad (14) found that the levels of the luteinizing hormone and the follicle stimulating hormone in the serum reduced significantly in the group treated with coenzyme Q10 compared to the placebo group. Nonetheless, the same study found a positive correlation between use of coenzyme Q10 and the sperm motility ($r=0.45$, $p=0.04$), sperm count ($r=0.46$, $p=0.03$) and sperm morphology ($r=0.34$, $p=0.04$). These findings show that the noted correlation was statistically significant and that the proportion of the variation in the sperm parameters that was attributable to the use of coenzyme Q10 was relatively high.

The improvement in the attributes of the sperm that have an influence on male infertility is attributed to the role of coenzyme Q10 in attenuating oxidative stress (10). The oral supplementation of the antioxidant in infertile men has been shown to increase its concentration in both the sperm cells and the seminal plasma. This increase is correlated with an increase in the sperm attributes such as motility, concentration and count (15).

The supplementation with coenzyme Q10 has been shown to increase the activity of catalase and superoxide dismutase. The

two are crucial first-line defense antioxidants. Together with glutathione peroxidase, they help defend against the oxidative stress that can result from the free radicals that are produced during the production of energy in the mitochondria (16). The increase in the amount of the coenzyme Q10 in the sperm cells and the seminal vesicles following an oral supplementation as well as increase in the activity of the two first line defense antioxidants shows that the resultant improvement in the sperm parameters is the result of an attenuation of oxidative stress (13) and the dysfunction of the sperms that is caused by the oxidative stress (17, 18, 19, 9).

Conclusions

This study showed that the use of the antioxidant lead to an improvement in the sperm parameters as well as the concentration of the hormones. Through the attenuation of oxidative stress, coenzyme Q10 plays a role in improving the quality of gametes in males. Future research should explore whether the improvement in sperm quality translates into higher rates of pregnancies.

References

1. Miyamoto T , Tsujimura A , Miyagawa Y , Koh, E , Namiki M , Sengoku K. Male Infertility and Its Causes in Human. *Advances in Urology*.2012; 2(10):1155.
2. Kumar R. Male infertility – Current concepts. *Indian Journal of Urology*.2011; 27(10): 39-40.
3. Kashanian J, Brannigan R . Male Infertility. *Journal of the American Medical Association*.2015; 313(17): 1770.
4. Adewoyin, M , Ibrahim, M , Roszaman, R , Isa, M., Alewi, N , Rafa, A .et al. The Effect of Natural Antioxidants and Phytocompounds on Seminal Oxidative Stress. *Diseases. Male Infertility*.2017; 5(1): 9.
5. Fujii J , Luchi Y, & Okada F. Fundamental roles of reactive oxygen species and protective mechanisms in the female reproductive system. *Reproductive Biology and Endocrinology*.2005; 3(43) :10-11.
6. Bansal, A , Bilaspuri G. Impacts of Oxidative Stress and Antioxidants on Semen Functions. *Veterinary Medicine International* . 2011; 2:10
7. Marseglia L , Manti S , D'Angelo G , Nicotera A , Parisi E , Di Rosa G .et al.

- Oxidative Stress in Obesity: A Critical Component in Human Diseases. *International Journal of Molecular Sciences*.2015; 15: 378-400.
8. Ahmadi, S , Bashiri, R , Ghadiri-Anari, A & Nadjarzadeh, A . Antioxidant supplements and semen parameters: An evidence-based review. *International Journal of Reproductive Biomedicine*.2016; 14(12): 729-736.
9. Majzoub A, Agarwal A. Systematic review of antioxidant types and doses in male infertility: Benefits on semen parameters, advanced sperm function, assisted reproduction and live-birth rate. *Arab Journal of Urology*.2018; 16(1):113-124.
10. Mancini A, Balercia G. Coenzyme Q (10) in male infertility: physiopathology and therapy. *Biofactors*.2011; 37(5):374-80.
11. Johannes Van Waart, TF Krugar CJ .*Human Reproduction Update*7.2001; 5 :495-500.
12. Lafuente R , Gonzalez M , Sola I , Lopez G , Brassesco M , Carreras R. et al . Coenzyme Q10 and male infertility: a meta-analysis. *Journal of Assisted Reproduction and Genetics*.2013; 30(9): 1147-1156.
13. Nadjarzadeh A , Sadeghi M R , Amirjannati N , Vafa M R , Motevalian S A , Gohari M R .et al. Coenzyme Q10 improves seminal oxidative defense but does not effect on semen parameters in idiopathic oligoasthenoteratozoospermia: a randomized double-blind, placebo-controlled trial. *Journal of Endocrinological Investigation*.2011; 34(8): 224-228.
14. Sfarinejad M R. Efficacy of coenzyme Q10 on semen parameters, sperm function and reproductive hormones in infertile men. *Journal of Urology*.2009; 182(10): 237-248.
15. Nadjarzadeh A, Shidfar F , Amirjannati N , Vafa M R , Motevalian S A , Gohari M R .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):177-183.
16. Ighodaro, O M , Akinloye O A . First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. *Alexandria Journal of Medicine*.2017; 2(10):1016.

17. Sikka S C Oxidative stress and role of antioxidants in normal and abnormal sperm function. *Frontiers in Bioscience*.1996; 1: 78-86.

18. Sikka S C . Relative impact of oxidative stress on male reproductive function. *Current Medicinal Chemistry*.2001; 8(7): 851-862.

19. Benedetti, S , Tagliamonte, M C , Catalani, S , Primiterra, M , Canestrari, F , De Stefani S et al. Differences in blood and semen oxidative status in fertile and infertile men, and their relationship with sperm quality. *Reproductive Biomedicine Online*.2012; 25(3):300-6.