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Response of Overweight Patients with Oligozoospermia to Coenzyme Q10 Treatment

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Abstract:
Background: *Sperm Concentration Could Be Affected By Many Factors And Body Weight May Be One Of These Factors ,So To Increase Sperm Concentration In Overweight Patients With Oligozoospermia; Agents With Effects On Both Body Weight And Sperm Concentration May Produce Good Response.*
Objectives: *To Assess The Effects Of Coenzyme Q10 On The Increased Body Weight And Sperm Concentration In Patients With Oligozoospermia .*
Patients And Methods: *Study Was Carried Out From March 2011 To September 2012 In Which 60patients With Idiopathic Oligozoospermia Were Randomly Assigned 200mg* Coq_{10} *Soft Gel Capsule Once Daily, For Six Months. Standard Seminal Fluid Analysis Was Carried Every Month. Body Mass Index Was (BMI) Evaluated At Baseline And After 6months . Only 52 Patients Completed The Six Months Trial.*
Results: *There Was A Progressive And Significant Improvement In Sperm Concentration (21.42±9.57 Vs 11.12±4.59 At Baseline, P=<0.001). Also There Was A Significant Decrease In BMI After 6 Months As Compared With Baseline Data (From 28.06±6.06 To 25.76±6.06, P < 0.005) And There Was A Significant (P<0.05) Negative Correlation Between BMI And Sperm Concentration For All Patients At Baseline And After 6 Months.*
Conclusion: *There Is A Correlation Between Body Weight And Sperm Concentration And Co Enzyme Q10 Has Effects On Both Body Mass Index And Sperm Concentration.*
Key Words: *Coenzyme Q10,Sperm Concentration, Body Weight.*

I. Introduction

Idiopathic oligoasthenoteratozoospermia (IOAT) is defined as defective spermatogenesis of unknown etiology . "Idiopathic" means that no etiological factor could be found with the common clinical, instrumental or laboratory methods. A combination of genetic predisposing and environmental factors (e.g., environmental pollution and reactive oxygen species) may result in testicular dysfunction and impaired sperm production[1]. These men present with no previous history associated with fertility problems and have normal findings on physical examination and endocrine laboratory testing. Semen analysis reveals a decreased number of spermatozoa (oligozoospermia), decreased motility (asthenozoospermia) and many abnormal forms on morphological examination (teratozoospermia). These abnormalities usually occur together and are described as the oligo-astheno- teratozoospermia (OAT) syndrome. IOAT is classified as: mild OAT (sperm concentration 10-15 X 10^6/mL); moderate OAT (sperm concentration 5-10 X 10^6/mL); or severe OAT (sperm concentration < 5 X 10^6/ mL) (WHO, 2010).

The prevalence of overweight and obesity is commonly assessed by using body mass index (BMI), defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). The BMI values are age-independent and the same for both sexes. In the new graded classification system developed by the World Health Organization, a BMI of 30 kg/m^2 or above denotes obesity. It is highly likely that individuals with a BMI at or above this level have excessive body fat (WHO, 2013).

The negative effect of obesity on an individual's health has been known for a longer time and can be found in the writings of Hippocrates, Galen, and Avicenna [2]. Avicenna was probably among the first who described the relationship between obesity and male infertility in his encyclopedic medical book (Al- Kanoon fil-Tib).

Body mass index (BMI) in male is associated with alterations in sperm parameters in several reports. In a recent study investigating factors associated with semen quality among couples who visited an assisted reproduction clinic, the prevalence of obesity among men with infertility was 3 times greater than among male partners of couples with idiopathic or female factor infertility [3]. A study showed that overweight men who had a body mass index over 25 had a nearly 22% lower sperm concentration and 24% lower total sperm count compared with healthy weight men. And underweight men who had a BMI under 18.5 also suffered from similar reductions in sperm counts. The study also showed that as men's weight increased, blood testosterone levels decreased [4].

In a study of normozoospermic partners in an infertile population, sperm concentration was reduced among men with BMI greater than 30 compared to leaner members of the study group [5].

Coenzyme Q is an antioxidant agent. it is an essential part of the cellular machinery used to produce ATP which provides the energy for muscle contraction and other vital cellular functions. The coenzyme Q is bound to the oriented enzymatic protein complexes. It is oxidized and releases protons to the outside and picks up electrons and protons on the inside of the mitochondrial membrane. [6]. In sperm cells most CoQ10 is concentrated in the mitochondria of the mid piece and energy dependent processes in the sperm cell depend on the availability of CoQ10.[7] CoQ10 in seminal fluid shows a direct correlation with semen parameters.[8] CoQ10 has 2 forms, that is reduced (ubiquinol) and oxidized (ubiquinone) forms. A strong correlation among sperm count, motility and ubiquinol-10 content in seminal fluid has been reported.[9]

II. Patients And Methods

Patient Selection:

Sixty patients (mean age 32 years, range 27–39 years) affected by idiopathic oligozoospermia were enrolled in the study. The patients were selected at the Andrology Unit of AL-Nahrain University, Institute of Embryo Research and Infertility Treatment in Baghdad, Iraq from February 2011 to June 2012. All subjects underwent medical screening, including history and clinical examination, and presented a clinical history of primary infertility >2 years. a complete diagnosis the following investigations were also performed: semen analysis; test for antispermatozoa antibodies; sperm culture for Chlamydia and FSH, LH, T, E2, and PRL assays, with use of commercial RIA kits; and testicular, prostatic, and seminal vesicle ultrasonography and echo–color doppler of venous spermatic plexus, for anatomic abnormalities and varicocele detection. all patients have body mass index of 25 to 30 kg/ m^2.

Study Design And Treatment Assignment:

Double- blind placebo controlled clinical trial was done and consisted of a 4-week screening phase and a 24-week treatment phase.

Preparation Of The Used Drugs:

CoQ_{10} soft gel capsules (Nature's bounty inc.USA) were used after putting each in capsule covers and was labeled with a code number of (1) and 200mg starch in other capsule covers and was labeled with a code number of (2) so the two capsules were look alike.

The capsules were given to the patients by a third person so the prescriber and the patients were blinded to the treatment condition. Capsules administered once daily orally with food for 6 successive months randomization codes were opened only after all patients had completed the whole study protocol.

Assessment Of Study Parameters

Bmi

BMI was measured at the start of the study and at the end of the 6 months treatment by using usual weight measuring device to measure the weight and the usual metric tape measure to measure the height then by applying the equation of

$$BMI = \frac{\text{Weight (kg)}}{\text{Square of height in meters}}$$

Seminal Fluid Analysis: was done monthly

The patients were asked to provide semen samples by masturbation in a private and quite room adjacent to the semen analysis laboratory. Collection is performed using dry, sterilized and warm disposable Petridish, labeled with the name, age, abstinence period of the patient and time of collection, and it always done between 9:00 A.M and 11:00 A.M.

All patients were advised to have an intercourse abstinence period between 2-5 days prior to semen collection. Collected semen is then immediately transferred to the laboratory and placed in an incubator (HERAEUS, Germany) at 37^oC, until semen liquefaction.

This evaluation was performed within 1 hour of ejaculation, and the samples were kept, during this period, in an incubator at 37^oC. A fixed volume of the semen (not more than 10 µl) is delivered onto a warm clean glass slide with a micropipette and covered with 22 mm X 22 mm cover slip. Formation and trapping of bubbles between the cover slip and the slide was carefully avoided. The preparation is examined at a magnification of 400X. The specimens were examined for:

Sperm Concentration:

Sperm concentration per milliliter was calculated from the mean number of spermatozoa in 10 randomly selected microscopical fields and multiplying the mean number by a factor of one million [10].

$$\text{Sperm concentration} = \frac{\text{Number of sperm in 10 random microscopic fields}}{10} \times 10^6$$

Total sperm count was obtained by multiplying sperm concentration by semen volume (WHO, 2010).

III. Statistical Analysis

Collected data were analyzed using SPSS version 12.0 for windows (SPSS, Chicago, Illinosis, USA). Differences of means between groups were examined by paired and unpaired t-test, P. value < 0.05 was considered as statistically significant.

IV. Results

Eight patients dropped out of the study. When the randomization list was opened at the end of the study, it was seen that 27 of the patients included in the CoQ_{10}-treated group and 25 of the patients included in the placebo group completed the study.

The laboratory baseline data of sperm concentration of all patients included in the clinical study are depicted in tables (1). All patients had decrease in sperm count which is below the normal readings of WHO 2010. (i.e. oligozoospermia)

There was no significant difference in sperm concentration, between data of baseline and values obtained after 6months of patients receiving placebo.(table 2).

Patients undergoing Co enzyme Q10 therapy showed significant improvement in these sperm concentration as the data of baseline was compared with the data after 6 months of treatment, from 11.12±4.59to 21.72±25.79 sperm concentration, P= <0.001.(table 3)(figure1).

Table (1): Baseline Data Of Spermconcentration Of All Patients Included In The Clinical Study. Values Are Means ± S.D (N = 25 Placebo Groups; 27 Treatment Groups).

Parameter	normal standard values	Baseline data	
		Placebo	Treatment
Sperm Conc.(million／ml)	≥15	10.50±3.36	11.12±4.59
T. S. C (million／Ej.)	≥40	31.02±11.69	33.45±16.65

Table (2): Statistical Analysis Of Changes On Sperm Concentration Of Patients Receiving Placebo After 6 Months As Compared To The Baseline Values. (N= 25 Patients).

Placebo group	Base Line	after 6 months
Sperm Conc. (million／ml)	10.50±3.36	11.92±3.07
T. S. C (million／Ej.)	31.02±11.69	37.60±13.29

Table (3): Statistical analysis of changes on semen parameters of idiopathic OAT patients receiving treatment regimen after 6 months as compared to the baseline values. (n= 27patients).

Treatment group	Base Line	after 6 months
Sperm Conc.(million／ml)	11.12±4.59	21.72±25.79
T. S. C (million／Ej.)	33.45±16.65	47.17±119.06

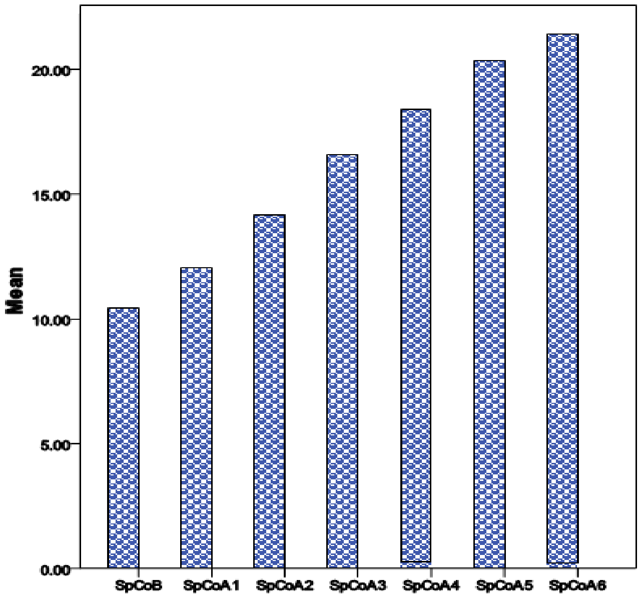

Figure (1): Sperm concentration (SpCo) of patients at baseline(B) and throughout the 6 months course of treatment with CoQ10 (A1 to A6).*= Significant. P<0.005

Body Mass Index (Bmi)

The BMI value in the treated patients at baseline and after 6 months of treatment are depicted in (table 4).

Patients of treatment groups had a significant decrease in BMI after 6 months as compared with baseline data (from 28.06±6.06 to 25.76±6.06, P < 0.005; However the BMI in the placebo groups showed no significant change in patients who completed the trial.

There was significant (p<0.05) negative correlation between BMI and sperm concentration for all patients at baseline (figure 2) and after 6 months (figure 3).

Table (4) Body mass index (BMI) of patients at baseline and after 6 month course of treatment with CoQ_{10} and placebo.

Groups	Baseline BMI	after 6 months BMI
Treatment group	28.06±6.06	25.76±6.06
Placebo group	27.16± 2.9	27.34± 7.43

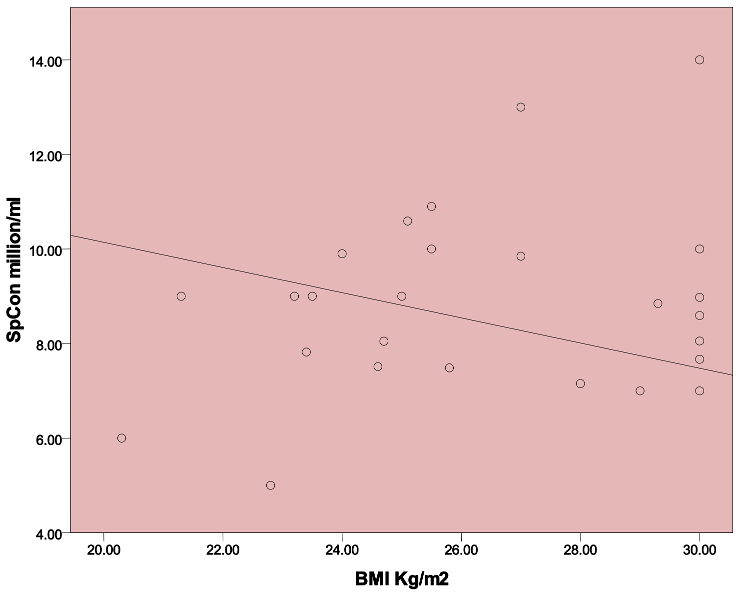

Figure (2): Correlation between (BMI) and sperm concentration for patients at baseline.(r^2 linear=0.650)

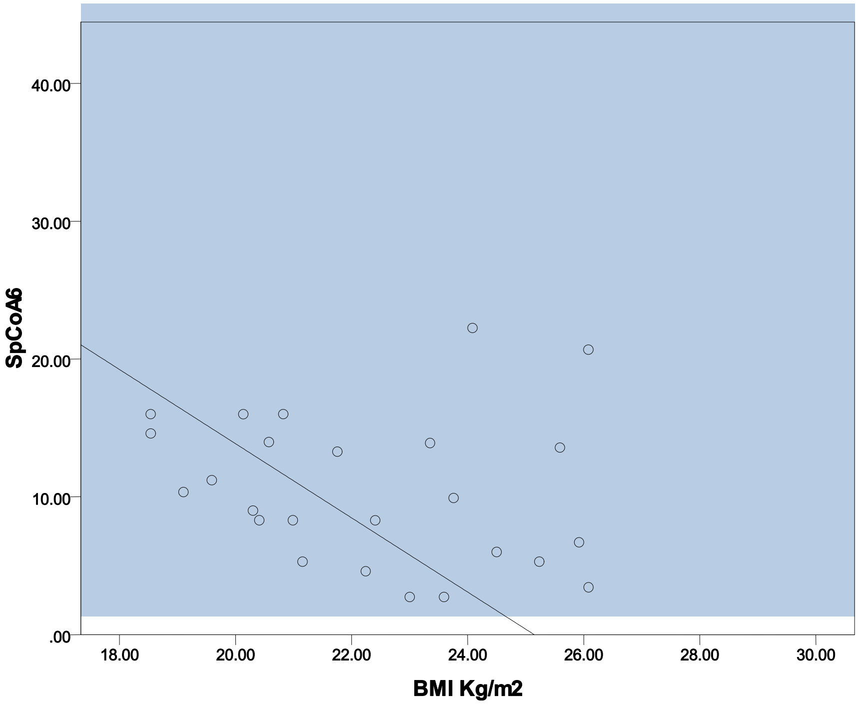

Figure (3): Correlation between (BMI) and sperm concentration for OAT patients <u>after 6 months</u>. (r^2 linear= 0.690)

V. Discussion

CoQ_{10} was able to improve sperm parameters also by modifying the balance between oxygen radicals and antioxidant defense [11].An excess of reactive oxygen species (ROS) and other oxidant radicals has been associated with male infertility [12]. The source of ROS in semen is related to both sperm cells and to infiltrating leukocytes [13]. In fact high free radicals level negatively influenced semen parameters, resulting in decrease of the sperm count, motility and normal morphology.

CoQ_{10} administration for 6 months was associated with a significant decrease in BMI, indicating a significant decrease in body fat mass. This may be due to the effect of CoQ_{10} that decreases the body weight by fat burning process. It has been suggested that CoQ_{10} helps promote weight loss in three ways:

1) By directly increasing fat burning. Co Q_{10} is an essential compound required in the proper transport and breakdown of fat into energy [14-16].

2) By increasing energy levels so patients are more likely to exercise.[17].

3) By decreasing appetite, so patients can find it easier to stick to their eating plans [18].

There is a paucity of data describing the effect of weight loss in obese men on sperm production and fertility. Most reports studied the effect of weight loss on the reproductive hormonal profile. Obese men have lower serum testosterone level compared to normal weight men and they showe increases in testosterone (free and total) after a very-low-energy diet [19-20].

Leptin, a 167-amino acid protein is a product of the obese gene, is secreted mainly by the adipose tissue that has been shown to have direct effects on fertility in both male and female mice [21]. Leptin is a marker of body fat stores [22]. Recently, it has been reported that leptin is expressed in the seminiferous tubules of infertile patients [23]. The expression of leptin on germ cells, mainly spermatocytes, was inversely correlated with sperm concentration, and serum testosterone concentration [24]. Interestingly, CoQ_{10} treatment decreased fat gain and serum leptin levels in rats [25]. In the present study, significant decrease in BMI that's associated with decrease in body weight, in fact by fat burning process due to CoQ_{10} treatment, may result in decrease serum leptin, that's produced from adipose tissue, and inhibit its effect on leptin receptors that are located on Leydig cells which are responsible for inhibition of testosterone production. Consequently, decrease serum leptin level result in decrease their effect on leptin receptors of Leydig cells and then testosterone starts to increase resulting in enhancement of spermatogenesis (i.e. improvement of semen parameters).

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